



**TREATMENT OF OSTEOARTHRITIS OF THE
KNEE**

**EVIDENCE-BASED GUIDELINE
2ND EDITION**

**Adopted by the American Academy of Orthopaedic Surgeons
Board of Directors
May 18, 2013**

Disclaimer

This clinical practice guideline was developed by an AAOS work group comprised of volunteer physicians and interdisciplinary clinicians as well as staff researchers with expertise in systematic reviews and statistical methods used to evaluate empirical evidence. It is an educational tool that integrates the current scientific literature and the proficiency and sound judgment that physicians typically acquire in clinical practice. The recommendations that make up this guideline are not intended to be absolute as patients vary in how they experience symptoms and respond to treatment interventions. There may be variability between patients in practice and those who participate in clinical trials. Medical care should always be based on a physician's expertise that is individually tailored to the patient's circumstances, preferences and rights.

Disclosure Requirement

In accordance with AAOS policy, all individuals whose names appear as authors or contributors to this clinical practice guideline provided full disclosure of and were vetted for potential conflicts of interest prior to the introductory meeting.

Funding Source

The American Academy of Orthopaedic Surgeons funded this clinical practice guideline without any financial support from outside commercial sources.

FDA Clearance

Some drugs or medical devices referenced or described in this clinical practice guideline may not have been cleared by the Food and Drug Administration (FDA) or may have been cleared for a specific use only. The FDA has stated that it is the responsibility of the physician to determine the clearance status of each drug or device prescribed in clinical practice.

Copyright

All rights reserved. No part of this clinical practice guideline may be reproduced or stored in a retrieval system or transmitted in any form or by any means (electronic, mechanical, photocopying, recording, or otherwise) without prior written permission from the AAOS.

Published 2013 by the American Academy of Orthopaedic Surgeons
6300 North River Road
Rosemont, IL 60018
Second Edition
Copyright 2013 by the American Academy of Orthopaedic Surgeons

TABLE OF CONTENTS

Table of Contents	iii
List of Tables	ix
List of Figures	xv
Summary of Recommendations	1
Conservative Treatments: Recommendations 1-6	1
Recommendation 1	1
Recommendation 2	1
Recommendation 3a.....	1
Recommendation 3b	2
Recommendation 3c.....	2
Recommendation 4	2
Recommendation 5	2
Recommendation 6	3
Pharmacologic Treatments: Recommendation 7	3
Recommendation 7a.....	3
Recommendation 7b	3
Procedural Treatments: Recommendation 8-11.....	4
Recommendation 8	4
Recommendation 9	4
Recommendation 10	4
Recommendation 11	4
Surgical Treatments: Recommendation 12-15.....	5
Recommendation 12	5
Recommendation 13	5
Recommendation 14	5
Recommendation 15	5
Introduction.....	6
Overview.....	6
Goals and Rationale	6
Intended Users	6
Patient Population	7
Scope.....	7
Etiology.....	7
Incidence and Prevalence.....	7
Burden of Disease	8
Emotional and Physical Impact	8
Potential Benefits, Harm, and Contraindications.....	8
Differences Between the Present and Previous Guidelines	8
Preventing Bias in an AAOS Clinical Practice Guideline	10
Methods.....	13
Formulating Preliminary Recommendations	13
Full Disclosure Information.....	13
Study Selection Criteria	13
Best Evidence Synthesis	14
Outcomes Considered	15

Literature Searches.....	15
Appraising Evidence Quality and Applicability	15
<i>Quality</i>	15
<i>Applicability</i>	17
Minimum Clinically Important Improvement	17
Grade of Recommendation	18
Defining the Strength of the Recommendations	19
Wording of the Final Recommendations	19
Consensus Recommendations.....	21
Voting on the Recommendations.....	21
Statistical Methods.....	22
Network Meta-Analysis	22
Placebo Data Regression Analysis.....	23
Inclusion Criteria	23
Statistical Analysis.....	23
Results.....	24
New To Meta-Analysis In This Guideline: Minimal Important Difference (MID)	
Units.....	24
Peer Review	25
Public Comment.....	26
The AAOS Guideline Approval Process	27
Revision Plans.....	27
Guideline Dissemination Plans	27
AAOS Clinical Guideline on Treating Osteoarthritis of the Knee	30
Guideline Recommendations	30
Recommendation 1	30
Rationale	30
Supporting Evidence.....	31
Quality.....	31
Applicability	33
Final Strength of Evidence.....	34
Results.....	45
Evidence Tables and Figures	60
Quality and Applicability.....	60
Findings.....	97
Recommendation 2	137
Rationale	137
Supporting Evidence.....	137
Quality.....	137
Applicability	138
Final Strength of Evidence.....	138
Results.....	140
Evidence Tables and Figures	145
Quality and Applicability.....	145
Findings.....	151
Recommendation 3a.....	158

Recommendation 3b	158
Recommendation 3c.....	158
Rationale	158
Supporting Evidence.....	160
Quality.....	160
Applicability	161
Final Strength of Evidence.....	161
Results.....	169
Evidence Tables and Figures	176
Quality and Applicability.....	176
Findings.....	200
Recommendation 4	227
Rationale	227
Supporting Evidence.....	227
Quality.....	227
Applicability	227
Final Strength of Evidence.....	228
Results.....	229
Evidence Tables and Figures	233
Quality and Applicability.....	233
Findings.....	240
Recommendation 5	248
Rationale	248
Supporting Evidence.....	248
Quality.....	248
Applicability	248
Final Strength of Evidence.....	249
Results.....	250
Evidence Tables and Figures	252
Quality and Applicability.....	252
Findings.....	255
Recommendation 6	261
Rationale	261
Supporting Evidence.....	262
Quality.....	262
Applicability	262
Final Strength of Evidence.....	262
Results.....	272
Evidence Tables and Figures	278
Quality and Applicability.....	278
Findings.....	305
Recommendation 7a.....	341
Recommendation 7b	341
Rationale	341
Supporting Evidence.....	342
Quality.....	342

Applicability	342
Final Strength of Evidence.....	343
Results.....	428
Evidence Tables and Figures	440
Quality and Applicability.....	440
Findings.....	624
Recommendation 8	747
Rationale	747
Supporting Evidence	747
Quality.....	747
Applicability	748
Final Strength of Evidence.....	748
Results.....	752
Evidence Tables and Figures	754
Quality and Applicability.....	754
Findings.....	762
Recommendation 9	770
Rationale	770
Supporting Evidence	771
Quality.....	771
Applicability	771
Final Strength of Evidence.....	772
Results.....	783
Evidence Tables and Figures	789
Quality and Applicability.....	789
Findings.....	813
Recommendation 10	854
Rationale	854
Supporting Evidence	854
Quality.....	854
Applicability	854
Final Strength of Evidence.....	855
Results.....	855
Evidence Tables and Figures	857
Quality and Applicability.....	857
Findings.....	860
Recommendation 11	863
Rationale	863
Supporting Evidence	863
Quality.....	863
Applicability	864
Final Strength of Evidence.....	864
Results.....	865
Evidence Tables and Figures	867
Quality and Applicability.....	867
Findings.....	871

Recommendation 12	876
Rationale	876
Supporting Evidence	877
Quality.....	877
Applicability	877
Final Strength of Evidence.....	877
Results.....	887
Evidence Tables and Figures	889
Quality and Applicability.....	889
Findings.....	913
Recommendation 13	932
Rationale	932
Supporting Evidence	932
Quality.....	932
Applicability	932
Final Strength of Evidence.....	932
Results.....	934
Evidence Tables and Figures	935
Quality and Applicability.....	935
Findings.....	937
Recommendation 14	939
Rationale	939
Supporting Evidence	939
Quality.....	939
Applicability	939
Final Strength of Evidence.....	940
Results.....	945
Evidence Tables and Figures	946
Quality and Applicability.....	946
Findings.....	956
Recommendation 15	969
Rationale	969
Supporting Evidence	969
Quality.....	969
Applicability	969
Final Strength of Evidence.....	970
Results.....	970
Evidence Tables and Figures	971
Quality and Applicability.....	971
Findings.....	972
Future Research	974
Appendix I	976
Work Group	976
Revision Work Group.....	976
Original Work Group.....	937
Appendix II	939

Decision-Makers Who Approve This Clinical Practice Guideline	939
Appendix III.....	940
Determining Critical Outcomes	940
Work Group Participation.....	940
Critical Outcomes Form.....	940
Determining Outcomes	940
Appendix IV.....	944
Study Attrition Flowchart	944
Appendix V.....	945
Literature Search Strategies	945
PubMed/MEDLINE	945
Embase.....	947
Cochrane Library (Wiley Interface).....	949
Appendix VI.....	951
Quality and Applicability Questions.....	951
Studies of Interventions	951
Quality.....	951
Applicability	953
Appendix VII	954
Form For Assigning Strength of Recommendation	954
Appendix VIII.....	955
Opinion Based Recommendations.....	955
Rules for Making Opinion Based Recommendations.....	955
Checklist For Voting on Opinion Based Recommendations	956
Voting by the Nominal Group Technique	956
Appendix IX.....	957
Structured Peer Review Form.....	957
Appendix X.....	961
Participating Peer Review Organizations	961
Appendix XI.....	962
Interpreting the Forest Plots.....	962
Abbreviations Used In This Report	962
Appendix XII	964
Conflict of Interest	964
Appendix XIII.....	965
Network Meta Analysis Checks for Consistency	965
Appendix XIV.....	975
Confidence Intervals of Treatment Effects that Range in Statistical and Clinical Significance.....	975
Appendix XV	976
Bibliography	976
Additional References.....	994
Excluded Studies.....	1005

LIST OF TABLES

Table 1. Relationship between Quality and Domain Scores for Interventions.....	16
Table 2. Relationship between Applicability and Domain Scores for Interventions.....	17
Table 3. Brief Description of the PRECIS Questions and Domains.....	17
Table 4. Descriptive Terms for Results with MCII	18
Table 5. AAOS Guideline Language	19
Table 6. Recommendation Strengths, Descriptions, and Clinical Implications	20
Table 7. Quality and Applicability Summary: Strength Training Versus Control	34
Table 8. Quality and Applicability Summary: Isokinetic Versus Isotonic Versus Isometric Strength Training	35
Table 9. Quality and Applicability Summary: High Versus Low Resistance Strength Training.....	35
Table 10. Quality and Applicability Summary: Isokinetic Versus Isotonic Versus Isometric Strength Training	35
Table 11. Quality and Applicability Summary: Proprioception Versus Control.....	36
Table 12. Quality and Applicability Summary: Physical Therapy Versus Control.....	36
Table 13. Quality and Applicability Summary: Kinesthesia Plus Strengthening Versus Strengthening Only	38
Table 14. Quality and Applicability Summary: Agility Plus Perturbation Versus Standard Exercise Therapy	38
Table 15. Quality and Applicability Summary: Self-Management Plus Exercise Versus Exercise Alone	39
Table 16. Quality and Applicability Summary: Aerobic Exercise Versus Education.....	39
Table 17. Quality and Applicability Summary: Home-Based Exercise, Self-Management, and Coping Strategies Versus Usual Care	40
Table 18. Quality and Applicability Summary: Water Versus Land-Based Exercises	43
Table 19. Quality and Applicability Summary: Supervised Walking Versus Usual Care	43
Table 20. Quality and Applicability Summary: Yoga Plus Physiotherapy Versus Physiotherapy Only.....	44
Table 21. Quality and Applicability Summary: Standardized Consultation Versus Usual Care	44
Table 22. Quality and Applicability: Strength Training Versus Control.....	60
Table 23. Quality and Applicability: High Versus Low Resistance Training	65
Table 24. Quality and Applicability: Isokinetic Versus Isotonic Versus Isometric Strength Training.....	66
Table 25. Quality and Applicability: Strength Training Versus Education.....	67
Table 26. Quality and Applicability: Proprioceptive Versus Control.....	68
Table 27. Quality and Applicability: Physical Therapy Versus Control	69
Table 28. Quality and Applicability: Kinesthesia Plus Strengthening Versus Strengthening Alone	73
Table 29. Quality and Applicability: Agility Plus Perturbation Versus Standard Exercise Therapy	74
Table 30. Quality and Applicability: Self-Management Versus Control	77
Table 31. Quality and Applicability: Supervised Walking Versus Control.....	83
Table 32. Quality and Applicability: Water Versus Land-Based Exercise	84
Table 33. Quality and Applicability: Aerobic Exercise Versus Education	85

Table 34. Quality and Applicability: Weight Bearing and Non-Weight Bearing Exercise Programs	87
Table 35. Quality and Applicability: Home and Class-Based Exercise Programs	89
Table 36. Quality and Applicability: Standardized Structured Physician Consultation Program (Education) Versus Control.....	92
Table 37. Quality and Applicability: Integrated Exercise, Self-Management, and Coping Strategies Versus Usual Care.....	93
Table 38. Quality and Applicability: Yoga Plus Physiotherapy Versus Physiotherapy Only.....	95
Table 39. Strength Training Compared to Control: Pain Outcomes.....	97
Table 40. Isokinetic Versus Isotonic Versus Isometric Exercise: Pain	98
Table 41. Strength Training Versus Control: Functional Measure	99
Table 42. Strengthening Versus Control: WOMAC Total	102
Table 43. High Versus Low Resistance Training: Function.....	103
Table 44. Resistance Strength Training Versus Health Education	103
Table 45. Physical Therapy Versus Control: Pain Measures.....	104
Table 46. Physical Therapy Versus Control: Functional Measures.....	105
Table 47. Exercise Plus Manual Physical Therapy Versus Non-Therapeutic Intensity Ultrasound.....	107
Table 48. Proprioceptive Training Versus Control: Pain Measures	108
Table 49. Proprioceptive Training Versus No Exercise: Function	108
Table 50. Agility and Perturbation Training Plus Usual Exercise Versus Exercise Only (Fitzgerald 2011).....	108
Table 51. Agility and Perturbation Training Plus Usual Exercise Versus Exercise Only: Odds of Improvement From Baseline for WOMAC Functional Tasks (Teixeira 2011)	109
Table 52. Kinesthesia Plus Strength Training Versus Strength Training: Function.....	111
Table 53. Weight Bearing and Non-Weight Bearing Exercise.....	112
Table 54. Water Versus Land-Based Exercise: Pain	114
Table 55. Water Versus Land-Based Exercise: Lequesne Index.....	115
Table 56. Home-Based and Hospital-Based Exercise Programs	116
Table 57. Aerobic Exercise Versus Control: Function	119
Table 58. Aerobic Exercise Versus Control: Functional Task	120
Table 59. Supervised Walking Versus Usual Care: Pain.....	120
Table 60. Supervised Walking Versus Usual Care: Function.....	121
Table 61. Supervised Walking Versus Control: Arthritis Impact Measurement Scale (Medications Use).....	121
Table 62. Self-Management Versus Waitlist Control.....	122
Table 63. Self-Management Plus Exercise Versus Usual Care: Pain.....	128
Table 64. Self-Management Plus Exercise Versus Usual Care: Function.....	128
Table 65. Structured Consultation Versus Control: Function.....	129
Table 66. Integrated Exercise, Self-Management, and Coping Strategies Versus Usual Care (Hurley 2007)	131
Table 67. Yoga Plus Physiotherapy Versus Physiotherapy Only (Ebenezer 2011)	134
Table 68. Quality and Applicability Summary: Weight Loss Versus Education	138
Table 69. Quality and Applicability Summary: Low Energy Diet Versus Conventional Diet.....	139

Table 70. Quality and Applicability Summary: Diet Versus Exercise	140
Table 71. Quality and Applicability: Exercise-Based Weight Loss Program Versus Health Education	145
Table 72. Quality and Applicability: Weight Loss Versus Education Programs	146
Table 73. Quality and Applicability: Low Energy Diet Versus Control Diet	148
Table 74. Quality and Applicability: Diet Versus Exercise.....	150
Table 75. Weight Loss-Exercise Only Versus Control: Function	151
Table 76. Weight Loss-Exercise Only Versus Control: Functional Task.....	151
Table 77. Dietary Weight Loss (With and Without Exercise) Versus Education Control	152
Table 78. Low Energy Diet Versus Control Diet	154
Table 79. Diet Versus Exercise.....	156
Table 80. Quality and Applicability Summary: Acupuncture Versus Control	161
Table 81. Quality and Applicability Summary: Periosteal Stimulation Therapy	165
Table 82. Quality and Applicability Summary: Pulsed Electrical Stimulation	165
Table 83. Quality and Applicability Summary: Pulsed Electromagnetic Therapy.....	167
Table 84. Quality and Applicability Summary: Swedish Massage Therapy	167
Table 85. Quality and Applicability Summary: Ultrasound	168
Table 86. Quality and Applicability: Acupuncture Versus Control	176
Table 87. Quality and Applicability: Periosteal Stimulation Therapy.....	187
Table 88. Quality and Applicability: Pulsed Electrical and Electromagnetic Therapy ..	188
Table 89. Quality and Applicability: TENS, Interferential Current, and Short Wave Diathermy	191
Table 90. Swedish Massage Therapy Versus Usual Care.....	196
Table 91. Ultrasonic Wave Plus Exercise Versus Exercise Alone	198
Table 92. Acupuncture Versus Control: Pain	200
Table 93. Acupuncture Versus Control: Function	201
Table 94. Acupuncture Versus Usual Care: Hospital Anxiety and Depression Score ...	206
Table 95. Acupuncture Versus Control: Lequesne Index	207
Table 96. Acupuncture Versus Control: Consumption of Concomitant Medication.....	208
Table 97. Periosteal Stimulation Therapy Versus Regular Acupuncture (Weiner 2007)	208
Table 98. TENS, Interferential Current, and Short Wave Diathermy Versus Sham (Atamaz et al., 2012).....	210
Table 99. Swedish Massage Therapy Versus Usual Care (Perlman 2006).....	215
Table 100. Ultrasound Versus Control	217
Table 101. Pulsed Electrical and Electromagnetic Therapy	219
Table 102. Quality and Applicability Summary: Brace Versus Usual Care.....	228
Table 103. Quality and Applicability Summary: Brace Versus Sleeve.....	229
Table 104. Quality and Applicability Summary: Brace Versus Insoles	229
Table 105. Quality and Applicability: Brace Versus Usual Care	233
Table 106. Quality and Applicability: Unloader Brace Versus Neoprene Sleeve	237
Table 107. Quality and Applicability: Braces Versus Insoles	239
Table 108. Brace Plus Usual Care Versus Usual Care: Pain	240
Table 109. Brace Plus Usual Care Versus Usual Care: Functional Tasks.....	242
Table 110. Brace Plus Usual Care Versus Usual Care: Function	243
Table 111. Brace plus Usual Care Versus Usual Care: Other Outcomes	244

Table 112. Brace Versus Neoprene Sleeve	245
Table 113. Braces Versus Insoles	247
Table 114. Quality and Applicability Summary: Lateral Wedge Insole	249
Table 115. Quality and Applicability Summary: Rubber Versus Urethane Insole.....	250
Table 116. Quality and Applicability: Lateral Wedge Insole	252
Table 117 Quality and Applicability: Rubber versus Urethane Insoles	254
Table 118. Lateral Wedge versus Neutral Insoles: Critical Outcomes	255
Table 119. Lateral Wedge versus Neutral Insoles: other outcomes.....	255
Table 120. Urethane Versus Rubber Insole (Both With Subtalar Strapping)	257
Table 121. Quality and Applicability Summary: Dietary Supplements	263
Table 122. Quality And Applicability: Glucosamine Versus Control	278
Table 123. Quality and Applicability: Chondroitin	288
Table 124. Glucosamine Versus Placebo: Pain	305
Table 125. Glucosamine Versus Placebo: Function	306
Table 126. Glucosamine Versus Placebo: WOMAC Stiffness.....	307
Table 127. Glucosamine Versus Placebo: WOMAC Total	308
Table 128. Glucosamine Versus Placebo: Other Outcomes	309
Table 129 Glucosamine HCL Plus Sodium Chondroitin Plus Manganese Ascorbate Versus Placebo: Patient Global Assessment.....	311
Table 130. Glucosamine Versus Placebo: NSAID Consumption.....	311
Table 131. Glucosamine Versus Placebo: Adverse Events	312
Table 132. Glucosamine Versus Reparagen: Pain.....	313
Table 133. Glucosamine Versus Enzymatic Hydrolyzed Collagen.....	314
Table 134. Chondroitin Sulfate Versus Placebo: Pain.....	315
Table 135. Chondroitin Sulfate Versus Placebo: Function.....	317
Table 136. Chondroitin Sulfate Versus Placebo: WOMAC Stiffness	318
Table 137. Chondroitin Sulfate Versus Placebo: WOMAC Total.....	318
Table 138. Chondroitin Sulfate Versus Placebo: Lequesne Index	319
Table 139. Chondroitin Versus Placebo: Additional Analgesic Use.....	321
Table 140. Chondroitin Sulfate Versus Placebo: Other Outcomes.....	321
Table 141. Chondroitin Sulfate Plus Glucosamine Versus Placebo	323
Table 142. Chondroitin Sulfate Plus Glucosamine: Stratified By Severity (Clegg 2006)	324
Table 143. Piascledine Versus Chondroitin Sulfate	325
Table 144. Quality and Applicability Summary: Analgesics	343
Table 145. Network Meta-Analysis: Statistically Significant Treatment Comparisons.	437
Table 146. Results Summary: Drug Treatments Versus Placebo (Patient and Physician Assessments).....	438
Table 147. Statistically Significant Active Treatment Comparisons: Global Assessments	439
Table 148. Quality and Applicability: Cox-2	440
Table 149. Quality and Applicability: NSAIDs Versus Control	513
Table 150. Quality and Applicability: Cox-2s Versus NSAIDs	570
Table 151. Quality and Applicability: Acetaminophen Versus Control.....	603
Table 152. Quality and Applicability: Interleukin Versus Control.....	617
Table 153. Quality and Applicability: Tramadol Versus Control.....	632

Table 154. Quality and Applicability: Orgotein Versus Control	638
Table 155. Cox-2s Versus Placebo	624
Table 156. Cox-2s Versus Cox-2s	640
Table 157. NSAIDs Versus Placebo	657
Table 158. NSAIDs Versus NSAIDs	661
Table 159. Cox-2s Versus NSAIDs	675
Table 160. Topical NSAIDs Versus Control	680
Table 161. Interleukin Versus Control	685
Table 162. Acetaminophen Versus Control	692
Table 163. Tramadol Versus Control	694
Table 164. Active Treatments Versus Placebo: Patient and Physician Global Assessments	697
Table 165. Active Treatment Comparison: Patient and Physician Global Assessments	702
Table 166. Quality and Applicability Summary: IA Corticosteroids Versus Placebo ...	748
Table 167. Quality and Applicability Summary: IA Corticosteroids Versus Hyaluronic Acid	750
Table 168. Quality and Applicability Summary: IA Corticosteroids Versus Needle Lavage	751
Table 169. Quality and Applicability: IA Corticosteroids Versus Placebo	754
Table 170. Quality and Applicability: IA Corticosteroids Versus Hyaluronic Acid	758
Table 171. Quality and Applicability: Needle Lavage Versus IA Corticosteroids	761
Table 172. IA Corticosteroids Versus Placebo	762
Table 173. IA Corticosteroids Versus Hyaluronic Acid (Caborn et al., 2004)	766
Table 174. Needle Lavage Versus Corticosteroids	768
Table 175. Quality and Applicability Summary: Hyaluronic Acid Versus Control	772
Table 176. Quality and Applicability Summary: High Versus Low Molecular Weight Hyaluronic Acid	780
Table 177. Quality and Applicability: Hyaluronic Acid Versus Control	789
Table 178. Quality and Applicability: High Versus Low Molecular Weight Hyaluronic Acid	807
Table 179. Hyaluronic Acid Versus Control: Pain	813
Table 180. High Versus Low Molecular Weight: Pain	821
Table 181. Hyaluronic Acid Versus Control: Function	829
Table 182. High Versus Low Molecular Weight: WOMAC Function	833
Table 183. Hyaluronic Acid Versus Control: WOMAC Stiffness	834
Table 184. High Versus Low Molecular Weight: WOMAC Stiffness	836
Table 185. Hyaluronic Acid Versus Conventional Treatment: WOMAC Total (Kahan et al., 2003)	837
Table 186. High Versus Low Molecular Weight: WOMAC Total (Juni et al., 2007) ...	838
Table 187. Hyaluronic Acid Versus Control: Lequesne Index	839
Table 188. High Versus Low Molecular Weight: Other Outcomes	841
Table 189. High Versus Low Molecular Weight Hyaluronic Acid: Adverse Events	845
Table 190. Quality and Applicability Summary: Growth Factor and Platelet Rich Plasma	855
Table 191. Quality and Applicability: Platelet Rich Plasma and Growth Factor Injections	857

Table 192. Growth Factor Injections Versus Hyaluronic Acid (Sanchez et al., 2008 and Sanchez et al., 2012)	860
Table 193. Platelet Rich Plasma (PRP) Versus Hyaluronic Acid (Spakova et al., 2012)	862
Table 194. Quality and Applicability Summary: Needle Lavage.....	864
Table 195. Quality and Applicability Summary: Needle Lavage Versus Corticosteroids	865
Table 196. Results Summary: Needle Lavage Versus Sham.....	866
Table 197. Quality and Applicability: Needle Lavage Versus Control	867
Table 198. Quality and Applicability: Needle Lavage Versus IA Corticosteroid	870
Table 199. Needle Lavage Versus Control: WOMAC Pain	871
Table 200. Needle Lavage Versus Sham: Function.....	872
Table 201. Needle Lavage Versus Sham: Quality of Well-Being Score.....	873
Table 202. Needle Lavage Versus Sham: Acetaminophen Consumption	874
Table 203. Needle Lavage Versus Corticosteroids.....	875
Table 204. Quality and Applicability Summary: Arthroscopy with Lavage and/or Debridement.....	878
Table 205. Quality and Applicability: Arthroscopy with Lavage and/or Debridement ..	889
Table 206. Debridement Versus Placebo: Pain.....	913
Table 207. Debridement Versus Placebo: Function	914
Table 208. Debridement Versus Lavage: Pain	916
Table 209. Debridement Versus Lavage: Function	918
Table 210. Arthroscopic Lavage Versus Placebo: Pain.....	921
Table 211. Arthroscopic Lavage Versus Placebo: Function.....	922
Table 212. Arthroscopic Surgery with Lavage and Debridement Versus Usual Care: Pain	924
Table 213. Arthroscopic Surgery with Lavage and Debridement Versus Usual Care: Function	926
Table 214. Arthroscopic Surgery with Lavage and Debridement Versus Usual Care: Arthritis Self-Efficacy Score (Other Arthritis Related Symptoms).....	930
Table 215. Full Versus Minimal Irrigation at One Year.....	931
Table 216. Quality and Applicability Summary: Arthroscopic Partial Meniscectomy ..	933
Table 217. Quality and Applicability: Partial Meniscectomy with Exercise Versus Exercise Only.....	935
Table 218. Exercise and Meniscectomy Versus Exercise Only (Herrlin et al., 2007) ...	937
Table 219. Quality and Applicability Summary: Osteotomy	940
Table 220. Quality and Applicability Summary: Lateral Closing Wedge Versus Medial Open Wedge with Puddu Plate	944
Table 221. Quality and Applicability: Osteotomy.....	946
Table 222. Quality and Applicability: Closing Wedge Versus Open Wedge Osteotomy	953
Table 223. High Tibial Osteotomy: Other Outcomes	959
Table 224. Osteotomy: Adverse Events.....	959
Table 225. Open Versus Closed Wedge Osteotomy.....	965
Table 226. iBalance HTO Versus Control HTO (Getgood et al., 2011)	967
Table 227. Quality and Applicability Summary: Free-floating Interpositional Device ..	970

Table 228. Quality and Applicability: Free-Floating Interpositional Device	971
Table 229. Network Meta-Analysis Consistency Check: WOMAC Pain	965
Table 230. Network Meta-Analysis Consistency Check: WOMAC Function	967
Table 231. Network Meta-Analysis Consistency Check: WOMAC Stiffness	969
Table 232. Network Meta-Analysis Consistency Check: WOMAC Total.....	971
Table 233. Network Meta-Analysis Consistency Check: Adverse Events.....	972

LIST OF FIGURES

Figure 1. AAOS Clinical Practice Guidelines Development Process.....	29
Figure 2. Results Summary: Strength Training Versus Control	49
Figure 3. Results Summary: Physical Therapy	50
Figure 4. Results Summary: Proprioception Versus Control.....	51
Figure 5. Results Summary: Agility and Perturbation Training Plus Usual Exercise Versus Exercise Only.....	52
Figure 6. Results Summary: Kinesthesia Versus Control.....	53
Figure 7. Results Summary: Exercise Versus Control.....	54
Figure 8. Self-Management and Structured Consultation Versus Control	55
Figure 9. Results Summary: Integrated Exercise, Self-Management, and Coping Strategies Versus Usual Care.....	57
Figure 10. Results Summary: Water Versus Land-Based Exercise.....	58
Figure 11. Results Summary: Yoga Versus Control.....	59
Figure 12. Strength Training Versus Control: Pain	136
Figure 13. Summary of Results: Diet, Exercise, and Weight Loss.....	142
Figure 14. Results Summary: Low Energy Diet Versus Conventional Diet	143
Figure 15. Results Summary: Diet Versus Exercise	144
Figure 16. Results Summary: Acupuncture Versus Control.....	171
Figure 17. Results Summary: Electro-acupuncture Versus Control	172
Figure 18. Results Summary: Swedish Massage Therapy and Ultrasound Versus Control	173
Figure 19. Results Summary: Pulsed Electrical Stimulation	174
Figure 20. Results Summary: Electromagnetic Fields.....	175
Figure 21. Acupuncture: WOMAC pain in MID Units	223
Figure 22. Acupuncture: WOMAC Function in MID Units.....	224
Figure 23. Acupuncture Versus Placebo: WOMAC Pain (1999).....	225
Figure 24. Acupuncture Versus Control: WOMAC Function	226
Figure 25. Results Summary: Brace Versus Usual Care	230
Figure 26. Results Summary: Brace vs. Sleeve and Insoles	232
Figure 27. Results Summary: Foot Orthotics	251
Figure 28. Lateral Wedge Insole Versus Neutral Insoles: Critical Outcomes.....	258
Figure 29. Lateral Wedge Insoles Versus Neutral Insoles: Other Outcomes	259
Figure 30. Urethane Versus Rubber Insoles	260
Figure 31. Results Summary: Glucosamine Versus Placebo.....	274
Figure 32. Results Summary: Chondroitin Sulfate Versus Placebo	276
Figure 33. Chondroitin Sulfate Versus Placebo: VAS Pain	332
Figure 34. Glucosamine Versus Placebo: WOMAC Pain in MID Units.....	333

Figure 35. Glucosamine Versus Placebo: WOMAC Function in MID Units.....	334
Figure 36. Glucosamine Versus Placebo: WOMAC Stiffness in MID Units.....	335
Figure 37. Glucosamine Versus Placebo: WOMAC Total in MID Units	336
Figure 38. Glucosamine Versus Placebo: WOMAC Pain	337
Figure 39. Glucosamine Versus Placebo: WOMAC Function	338
Figure 40. Glucosamine Versus Placebo: WOMAC Stiffness	339
Figure 41. Glucosamine Versus Placebo: WOMAC Total	340
Figure 42. Network Meta-Analysis Model: Pain.....	432
Figure 43. Network Meta-Analysis Model: WOMAC Function.....	433
Figure 44. Network Meta-Analysis Model: WOMAC Stiffness	434
Figure 45. Network Meta-Analysis Model: WOMAC Total.....	435
Events Figure 46. Network Meta-Analysis Model: Adverse Events.....	436
Figure 47. Network Meta-Analysis: Analgesics Versus Placebo (Pain)	713
Figure 48. Network Meta-Analysis: Cox-2 Versus NSAIDS (Pain)	714
Figure 49. Network Meta-Analysis: Cox-2 Versus Cox-2 (Pain).....	715
Figure 50. Network Meta-Analysis: NSAID Versus NSAID (Pain)	716
Figure 51. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (Pain)	717
Figure 52. Network Meta-Analysis: Topical NSAIDS Versus Oral Analgesics (Pain) .	718
Figure 53. Network Meta-Analysis: Analgesics Versus Placebo (WOMAC Function)	719
Figure 54. Network Meta-Analysis: Cox-2 Versus NSAIDS (WOMAC Function)	720
Figure 55. Network Meta-Analysis: NSAID Versus NSAID (WOMAC Function)	721
Figure 56. Network Meta-Analysis: Cox-2 Versus Cox-2 (WOMAC Function).....	722
Figure 57. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (WOMAC Function).....	723
Figure 58. Network Meta-Analysis: Topical NSAIDS Versus Other Analgesics (WOMAC Function).....	724
Figure 59. Network Meta-Analysis: Analgesics Versus Placebo (WOMAC Stiffness).	725
Figure 60. Network Meta-Analysis: Cox-2 Versus NSAIDS (WOMAC Stiffness)	726
Figure 61. Network Meta-Analysis: NSAIDS Versus NSAIDS (WOMAC Stiffness) ..	727
Figure 62. Network Meta-Analysis: Cox-2 Versus Cox-2 (WOMAC Stiffness).....	728
Figure 63. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (WOMAC Stiffness)	729
Figure 64. Network Meta-Analysis: Analgesics Versus Placebo (WOMAC Total)	730
Figure 65. Network Meta-Analysis: NSAIDS Versus Cox-2 (WOMAC Total)	731
Figure 66. Network Meta-Analysis: NSAIDS Versus NSAIDS (WOMAC Total).....	732
Figure 67. Network Meta-Analysis: Cox-2 Versus Cox-2 (WOMAC Total)	733
Figure 68. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (WOMAC Total).....	734
Figure 69. Network Meta-Analysis: Analgesics Versus Placebo (Adverse Events)	735
Figure 70. Network Meta-Analysis: Cox-2 Versus Cox-2 (Adverse Events)	736
Figure 71. Network Meta-Analysis: NSAID Versus NSAID (Adverse Events).....	737
Figure 72. Network Meta-Analysis: Cox-2 Versus NSAID (Adverse Events)	738
Figure 73. Network Meta-Analysis: Acetaminophen Versus Cox-2 and NSAIDS (Adverse Events).....	739

Figure 74. Network Meta-Analysis: Diacerein (Interleukin) Versus Cox-2 Inhibitors and NSAIDS (Adverse Events)	740
Figure 75. Network Meta-Analysis: Gastrointestinal Cox-2 Versus NSAIDS (Adverse Events)	741
Figure 76. Network Meta-Analysis: Cox-2 Versus NSAID Non-Gastrointestinal (Adverse Events)	742
Figure 77. Network Meta-Analysis: Acetaminophen Versus Celecoxib (Adverse Events)	743
Figure 78. Network Meta-Analysis: Acetaminophen Versus Rofecoxib 12.5 mg (Adverse Events)	744
Figure 79. Network Meta-Analysis: Acetaminophen Versus Rofecoxib 25mg (Adverse Events)	745
Figure 80. Network Meta-Analysis: Acetaminophen Versus Ibuprofen-Adverse Events (Bradley 1991)	746
Figure 81. Results Summary: IA Corticosteroids	753
Figure 82. Network Meta-Analysis: IA Corticosteroids Versus Placebo (Pain)	769
Figure 83. Results Summary: Intraarticular Hyaluronic Acid Versus Control.....	785
Figure 84. Results Summary: High Versus Low Molecular Weight Hyaluronic Acid ..	787
Figure 85. Hyaluronic Acid Versus Placebo: Pain in MID Units	847
Figure 86. Hyaluronic Acid Versus Placebo: WOMAC Function in MID Units	848
Figure 87. Hyaluronic Acid Versus Placebo: WOMAC Stiffness in MID Units	849
Figure 88. Hyaluronic Acid Versus Placebo: WOMAC Pain.....	850
Figure 89. Hyaluronic Acid Versus Placebo: VAS Weight Bearing Pain	851
Figure 90. Hyaluronic Acid Versus Placebo: Function	852
Figure 91. Hyaluronic Acid Versus Placebo: WOMAC Stiffness.....	853
Figure 92. Results Summary: Arthroscopic Surgery, Lavage, and Debridement Versus Control	888
Figure 93. Open-Wedge High Tibial Osteotomy: VAS Pain Change from Baseline (Pongsoipetch et al., 2009).....	956
Figure 94. Open Wedge High Tibial Osteotomy with TomoFix Plate: VAS Pain at 3 Year Follow-Up (El-Azab et al., 2011)	956
Figure 95. Hospital for Special Surgery: Pain and Function (Rudan and Simurda, 1990)	957
Figure 96. International Knee Documentation Committee Score: Open-Wedge HTO with Internal Fixator Plate (Niemeyer et al., 2010)	957
Figure 97. Open-Wedge High Tibial Osteotomy: Knee Society Score (Pongsoipetch et al., 2009)	958
Figure 98. High Tibial Osteotomy: International Knee Society Score (Flamme et al., 2003)	958
Figure 99. Closed Versus Open Osteotomy: VAS Pain (Brouwer et al., 2006)	962
Figure 100. Open Versus Closed Wedge Osteotomy: Mild to Severe Knee Pain on Stair Climb (Song et al., 2012).....	963
Figure 101. Open Versus Closed Wedge Osteotomy (Brouwer et al., 2006)	964
Figure 102. Adverse Events: Open Versus Closed Wedge Osteotomy (Brouwer et al., 2006)	966

Figure 103. iBalance HTO Versus Control HTO: Adverse Events (Getgood et al., 2011)	968
Figure 104. Knee Society Scores (Sisto and Mitchell 2005)	972
Figure 105. VAS Pain (Sisto and Mitchell, 2005)	973
Figure 106. Percent Revised to Total Knee Arthroplasty (Sisto and Mitchell, 2005)	973

SUMMARY OF RECOMMENDATIONS

This summary of the AAOS clinical practice guideline, “Treatment of Osteoarthritis of the Knee” contains a list of the evidence based treatment recommendations and includes only less invasive alternatives to knee replacement. Discussion of how and why each recommendation was developed and the evidence report are contained in the full guideline at www.aaos.org/guidelines. Readers are urged to consult the full guideline for the comprehensive evaluation of the available scientific studies. The recommendations were established using methods of evidence-based medicine that rigorously control for bias, enhance transparency, and promote reproducibility.

The summary of recommendations is not intended to stand alone. Medical care should always be based on a physician’s expert judgment and the patient’s circumstances, values, preferences and rights. For treatment procedures to provide benefit, mutual collaboration with shared decision-making between patient and physician/allied healthcare provider is essential.

Conservative Treatments: Recommendations 1-6

RECOMMENDATION 1

We recommend that patients with symptomatic osteoarthritis of the knee participate in self-management programs, strengthening, low-impact aerobic exercises, and neuromuscular education; and engage in physical activity consistent with national guidelines.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm and/or that the quality of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 2

We suggest weight loss for patients with symptomatic osteoarthritis of the knee and a BMI ≥ 25 .

Strength of Recommendation: Moderate

Description: A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

RECOMMENDATION 3A

We cannot recommend using acupuncture in patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 3B

We are unable to recommend for or against the use of physical agents (including electrotherapeutic modalities) in patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 3C

We are unable to recommend for or against manual therapy in patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 4

We are unable to recommend for or against the use of a valgus directing force brace (medial compartment unloader) for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 5

We cannot suggest that lateral wedge insoles be used for patients with symptomatic medial compartment osteoarthritis of the knee.

Strength of Recommendation: Moderate

Description: A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

RECOMMENDATION 6

We cannot recommend using glucosamine and chondroitin for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

Pharmacologic Treatments: Recommendation 7

RECOMMENDATION 7A

We recommend nonsteroidal anti-inflammatory drugs (NSAIDs; oral or topical) or Tramadol for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm and/or that the quality of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 7B

We are unable to recommend for or against the use of acetaminophen, opioids, or pain patches for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Procedural Treatments: Recommendation 8-11

RECOMMENDATION 8

We are unable to recommend for or against the use of intraarticular (IA) corticosteroids for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 9

We cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 10

We are unable to recommend for or against growth factor injections and/or platelet rich plasma for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 11

We cannot *suggest* that the practitioner use needle lavage for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Moderate

Description: A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

Surgical Treatments: Recommendation 12-15

RECOMMENDATION 12

We cannot recommend performing arthroscopy with lavage and/or debridement in patients with a primary diagnosis of symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 13

We are unable to recommend for or against arthroscopic partial meniscectomy in patients with osteoarthritis of the knee with a torn meniscus.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 14

The practitioner might perform a valgus producing proximal tibial osteotomy in patients with symptomatic medial compartment osteoarthritis of the knee.

Strength of Recommendation: Limited

Description: A **Limited** recommendation means that the quality of the supporting evidence is unconvincing, or that well-conducted studies show little clear advantage to one approach over another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might counter the current findings. Patient preference should have a substantial influencing role.

RECOMMENDATION 15

In the absence of reliable evidence, it is the opinion of the work group not to use the free-floating (un-fixed) interpositional device in patients with symptomatic medial compartment osteoarthritis of the knee.

Strength of Recommendation: Consensus

Description: A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus**, although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

INTRODUCTION

OVERVIEW

This clinical practice guideline is based on a systematic review of published studies examining the nonarthroplasty treatment of knee osteoarthritis in adults. It provides recommendations that will help practitioners to integrate the current evidence and clinical practice, and it highlights gaps in the literature in need of future research.

This guideline is intended to be used by appropriately trained physicians and clinicians who manage the treatment of osteoarthritis of the knee. It also serves as an information resource for developers and applied users of clinical practice guidelines.

GOALS AND RATIONALE

The purpose of this clinical practice guideline is to evaluate the current best evidence associated with treatment. Evidence-based medicine (EBM) standards advocate for use of empirical evidence by physicians in their clinical decision making. To assist with access to the large resources of information, a systematic review of the literature in publication between April 2010 and May 2012 has been conducted. It highlights where there is good evidence, where evidence is lacking, and what topics future research will need to target in order to help facilitate evidence-based decision making in the treatment of patients with osteoarthritis of the knee. AAOS staff methodologists assisted the physician/clinician work group in evaluating the existing literature so that they could formulate the following recommendations based on a rigorous systematic process.

Musculoskeletal care is provided in many different settings and by a variety of providers. We created this guideline as an educational tool to guide qualified physicians and clinicians in making treatment decisions that improve the quality and efficacy of care. This guideline should not be construed as including all possible methods of care or excluding acceptable interventions similarly directed at obtaining favorable outcomes. The final decision to use a specific procedure must be made after assessing all concerns presented by the patient and consideration of locality-specific resources.

INTENDED USERS

This guideline is intended to be used by orthopaedic surgeons and other healthcare providers managing patients with osteoarthritis of the knee. It serves as an information resource for medical practitioners. In general, individual practicing physicians and clinicians do not have the resources required to complete a project of comparable scope and duration involving the evaluation of an extensive literature base. The AAOS intends for this guideline to assist treatment providers not only in making clinical decisions with their patients, but also in describing to patients and their loved ones why a selected intervention represents the best available course of treatment.

This guideline is not intended for use as a benefits determination document. It does not cover allocation of resources, business and ethical considerations, and other factors needed to determine the material value of orthopaedic care.

Users of this guideline may also want to consider appropriate use criteria (AUC) related to the treatment of osteoarthritis of the knee. The focus of AUC that the AAOS began developing in 2012 is to determine the appropriateness of clinical practice guidelines for the heterogeneous patient population routinely seen in practice. The best available scientific evidence is synthesized with collective expert opinion on topics where gold standard randomized clinical trials are not available or are inadequately detailed for identifying distinct patient types. When there is evidence corroborated by consensus that expected benefits substantially outweigh potential risks exclusive of cost, a procedure is determined to be appropriate.

Similar to other areas of medicine, evidence for the effectiveness of orthopaedic services is not always identifiable. An important distinction to make is that if available data is lacking or evidence is absent, a recommendation is not assumed to be ineffective. When the AAOS cannot recommend for or against an intervention, available data do not provide empirically-based direction on what course of action is best. If data are absent, medical necessity should prevail especially where the disease, disorder, or condition in question can result in loss of life or limb (which is one reason some recommendations incorporate expert opinion).

The AAOS believes evidence-based medicine is an integral component of treatment decisions and that the best results are predicated on reciprocal communication between the patient and physician and an individualized regimen where risks are minimized and benefits are maximized. Medical expertise that is informed by research and takes into account all possible options increases the likelihood that patients will recover effectively.

PATIENT POPULATION

This guideline is intended for use with adults (ages 19 years and older) who have been diagnosed by a physician with osteoarthritis of the knee and are undergoing treatment.

SCOPE

The scope of this guideline includes nonpharmacologic and pharmacologic interventions for symptomatic osteoarthritis of the knee as well as operative procedures less invasive than knee replacement (arthroplasty). It does not provide recommendations for patients diagnosed with rheumatoid arthritis, osteoarthritis of other joints, or other inflammatory arthropathies.

ETIOLOGY

Osteoarthritis results from an imbalance between breakdown and repair of the tissues in the synovial joint organ and occurs as a result of multiple risk factors including trauma, overuse, and genetic predisposition.

INCIDENCE AND PREVALENCE

The incidence of knee osteoarthritis in the United States is estimated at 240 persons per 100,000 per year.

BURDEN OF DISEASE

Osteoarthritis (of any joint) was the primary diagnosis that led to 11.3 million ambulatory care visits in 2009. It was estimated that 9.9 million adults had symptomatic osteoarthritis of the knee in 2010.

Risk factors of the condition increase with age, especially in women. Anywhere from 6%-13% in men and 7%-19% in women over 45 years of age have osteoarthritis of the knee, suggesting that the risk in women is 45% higher than in men. Genetics, large body mass, certain occupations, repetitive knee bending or heavy lifting, and hereditary vulnerability are other factors that increase one's risk of developing the disease.

EMOTIONAL AND PHYSICAL IMPACT

Older adults with self-reported osteoarthritis visit their physicians more frequently and experience greater functional limitations than others in the same age group. The aging of the baby boomers, rise in rates of obesity, and greater emphasis on staying active among the elderly population suggest that the emotional and physical impact of knee osteoarthritis will continue to be widespread.

POTENTIAL BENEFITS, HARM, AND CONTRAINDICATIONS

Individuals with osteoarthritis of the knee often complain of joint pain, stiffness, and difficulty with purposeful movement. The aim of treatment is to provide pain relief and improve the patient's functioning. Most interventions are associated with some potential for adverse outcomes, especially if invasive or operative. Contraindications vary widely by procedure. Reducing risks improves treatment efficacy and is accomplished through collaboration between patient and physician.

DIFFERENCES BETWEEN THE PRESENT AND PREVIOUS GUIDELINES

This updated clinical practice guideline replaces the first edition that was completed in 2008, "Treatment of Osteoarthritis of the Knee (Non-Arthroplasty)."

There have been changes in the methods used to develop the current guideline including new processes for preventing bias that are outlined in the section, "Preventing Bias in an AAOS Clinical Practice Guideline." We incorporated network meta-analysis to compare pharmaceuticals of interest not evaluated in the published sources, and we have implemented more rigorous methods for evaluating quality and applicability (i.e. generalizability) of included studies.

This update considered the literature that we previously examined as well as the empirical evidence published since the 2008 guideline. Changes in article selection criteria necessitated exclusion of some studies that were included in the first edition. The key differences are explained below.

First, the inclusion of only original research and elimination of secondary analyses explained the major differences in recommendation strengths between the previous and present guidelines. Systematic reviews of the Osteoarthritis Research Society

International^{1,2} and Agency for Healthcare Research and Quality (AHRQ)³ were not included in this revised guideline since they comprised secondary analyses. Similarly, the Annual Reports of the Australian Orthopaedic Association Joint Replacement Registry (2004-2007) were excluded after they no longer met inclusion criteria.

Eliminating systematic reviews as described above resulted in the need to develop a consensus recommendation in place of an evidence-graded recommendation because the previous supporting evidence no longer met inclusion criteria for this guideline.

A requisite four week follow up period and minimum study sample of 30 patients (increased from ten) were the other essential modifications to the selection criteria that changed the database. The complete listing of inclusion criteria for this guideline is detailed in the section, “Study Selection Criteria,” (beginning on page 13).

PREVENTING BIAS IN AN AAOS CLINICAL PRACTICE GUIDELINE

Clinical practice guidelines (CPGs) are sometimes met with skepticism because of perceived lack of objectivity. Shaneyfelt and Centor assert that most current guidelines have strayed from those originally intended by the Institute of Medicine (IOM)⁴ and that the IOM has been critical of CPG development processes because of questionable adherence to quality standards.⁵ The AAOS understands that only high-quality guidelines are credible, and we go to great lengths to ensure the integrity of our evidence analyses. The purpose of this section is to describe the Academy's process. Additional details of how we eliminate bias also appear in the methods section.

The AAOS addresses bias beginning with the selection of work group members. Applicants with financial conflicts of interest (COI) related to the guideline topic cannot participate if the conflict occurred within one year of the start date of the guideline's development or if an immediate family member has, or has had, a relevant financial conflict.

Financial COIs are not the only source of bias that can hamper the systematic development of a guideline. The IOM has noted that long time service on government committees or with private insurers, authorship of articles on guideline-related subjects, and one's personal experiences likewise can cause diminished objectivity.⁶

The AAOS establishes a guideline development team free of COIs. The individuals who conduct the literature searches, evaluate the strength of the included studies, and synthesize the data are vetted prior to formalizing their participation (see Appendix I for a list of the work group members and methodologists involved in the assembly of this guideline). Hirsh and Guyatt⁷ assert that involving conflict-free participants is crucial.

Our use of methodologists changes the traditional role of the clinicians involved in guideline development. The members of an AAOS work group serve as the content experts. One of their primary tasks is to frame the scope and provide structure for the systematic review by developing preliminary recommendations (see below for further information). Another task is to develop the selection criteria of studies. The AAOS medical librarian conducts a comprehensive literature search based on the key phrases. Suggestions to include specific articles are not accepted at this time to reduce the subjectivity of ad hoc recommendations.

Research analysts identify the full articles to be recalled and determine whether the inclusion criteria are met for each study. The clinician work group receives a detailed listing of the recalled articles with the reasons for inclusion or exclusion noted, and they make criteria-based modifications that they view as necessary. The purpose of this step is to promote the integrity of the guideline's data set. Differences in perspectives at this stage are reconciled according to what is most clinically and methodologically appropriate. Articles that become included as a result of this step in the literature review are integrated into the data base as part of the empirical evidence.

The methodologists then appraise the quality and applicability¹ of each included study. This step entails coding answers to a series of research-design based questions from which final ratings are aggregated. Determination of the quality and generalizability criteria preceding guideline and recommendation topics selection and the use of an automated coding scheme to quantify scientific merit of each study removes virtually all subjectivity from these ratings. Greater rigor is employed over other evidence grading systems. The definitions of each study grade are operationalized to eliminate the possibility of bias that would likely arise with appraisals that are otherwise not replicable. (See Appendix VI for a complete description.) There are more than 50 grading systems⁸ and few among them report the use of adequate safeguards to prevent bias even when rating the highest level of evidence.⁶

The AAOS system is somewhat stringent compared to the GRADE system⁹ when it comes to the final determination about the scientific strength of a study. Good interrater reliability is maintained by involving a second reviewer who independently appraises a sampling of 10% of the evidence base. The GRADE system allows the investigator to identify “other sources of bias.” Although eliminating bias is essential to appropriately evaluating evidence strength, determinations that occur retrospectively allow for possible *post hoc* criticisms of a study and would potentially diminish the a priori orientation and objectivity of the development of the guideline. The AAOS believes that an emphasis on eliminating bias is prudent and needs to be managed systematically.

The AAOS system, unlike GRADE, also specifically addresses the issue of statistical power (i.e. number of patients enrolled). Low statistical power is a common problem in the medical literature¹⁰ that increases the likelihood of making false negative conclusions. We regard low power studies as very low quality, and do not consider them when formulating a final recommendation.²

Similar to the GRADE system, the AAOS will include observational studies after performing evidence syntheses to determine if they constitute the best that is available. We rely on using the best available evidence for substantive value over lower strength findings since higher strength results are less likely to be contradicted in future studies.

When including non-randomized controlled studies, prospective case series that meet a number of other quality-related criteria constitute evidence as is the case in the GRADE system. However, retrospective case series are not incorporated in our systematic reviews under any circumstances. The latter do not establish empirically testable comparisons or relationships a priori, are not based on systematic assignment of patients to treatment groups, and do not appropriately control for measurement bias. Including only prospective case series studies is consistent with our a priori orientation in the evidence grading system used by the AAOS.

¹ Here we use “quality” as synonymous with “risk of bias” since the same methods are used to evaluate them. Similarly, we use the terms “applicability” and “generalizability” as synonyms.

² We include low power studies in meta-analyses since one purpose is to overcome the low power of individual studies.

Also unlike the GRADE system, the AAOS will base recommendations on expert opinion when they concern necessary routine services for which the empirical evidence is lacking or when they are directed at preventing loss of limb or life. A consensus-based recommendation is issued only when the service in question has virtually no associated harm and is of low cost (e.g. a history and physical) or when the absence of direction could have catastrophic consequences. To prevent potential bias in recommendations based on expert opinion, we have established specific rules governing their use.

METHODS

The work group met for the introductory meeting on April 25, 2010 to establish preliminary recommendations and search terms for the guideline's systematic review. A two-day final meeting convened on August 25-26, 2012 where members voted on final recommendations following a review of the evidence, wrote the rationales, and approved the methodological contents of the guideline.

FORMULATING PRELIMINARY RECOMMENDATIONS

Based on their expert views of what works best, with whom, and under what circumstances, the work group's preliminary recommendations establishes the focus of the systematic review and determines the contents for the final conclusions. All preliminary recommendations are worded in the affirmative direction.

Modifications to the preliminary recommendations are not permitted between the introductory and final work group meetings. Only editing in accordance with the best available evidence and AAOS rules for wording recommendations based on evidence strengths are adopted. (See below for a discussion on language construction.) Modifications that require new literature searches or are not evidence-based are also not permitted.

FULL DISCLOSURE INFORMATION

The work group's preliminary recommendations are represented in this guideline and the empirical studies that the analysts examined are cited. The AAOS has always striven for total transparency in the guideline development process.

STUDY SELECTION CRITERIA

We develop *a priori* article inclusion criteria that are our "rules of evidence" for the systematic review and meta-analyses. Articles that did not have the selection characteristics were not eligible to be included as evidence for purposes of this guideline.

To be included an article had to meet the following selection criteria:

- Study was of osteoarthritis of the knee
- Study reported on 80% of the patient population of interest
- Article provided full report of a clinical study
- Retrospective non-comparative case series, medical records review, meeting abstracts, historical articles, editorials, letters, and commentaries were **excluded**
- Case series studies that gave patients the treatment of interest AND another treatment were **excluded**
- Case series studies that had non-consecutive enrollment of patients were **excluded**
- Controlled trials in which patients were not stochastically assigned to groups AND in which there was heterogeneity in patient characteristics or outcomes at baseline AND where the authors did not statistically adjust for these differences when analyzing the results were **excluded**
- All studies of "Very Limited" evidence strength were **excluded**

- Composite measures or outcomes were **excluded** even if they were patient-oriented
- Case series studies were **excluded** if no baseline values were reported
- Study was published in a peer-reviewed journal
- Study had a sample of 30 or more patients per treatment group
- Study was of humans
- Study was published in English
- Study was published during or after 1966
- Study results were presented quantitatively
- Study treatment follow up period was at least 4 weeks
- At least 80% of the enrolled study population were 19 years of age or older
- For any included study that used “paper-and-pencil” outcome measures (e.g. SF-36), only those that were validated were included [unless the outcome was identified *a priori* by the work group in the critical outcomes Delphi round]
- “Paper and pencil” outcomes reported by a single group of investigators (i.e. a single study) were excluded
- Study was in vitro
- Study was not performed on cadavers

When a study’s time period was not the same as those examined by the work group (i.e. 0-2 weeks, 2-6 weeks, etc.), assignment was made based on mean duration. If a range rather than the mean was provided, the upper end dictated the duration category. For example, time periods of 0-4 weeks was categorized into “2-6 weeks” (when applicable) as established by the work group.

We did not incorporate systematic reviews, meta-analyses, or other guidelines not specified by the AAOS work group to avoid including studies that did not meet our own criteria for selection. Rather, we recalled individual studies if the abstracts suggested that they might constitute evidence for one of our recommendations and also searched the bibliographies of published systematic reviews for any additional studies that potentially supplemented our evaluation.

BEST EVIDENCE SYNTHESIS

When determining the best available evidence, we first include the highest-strength studies available for the outcomes examined. If there are two or more high-strength studies, the recommendation grade is strong. In this case, moderate- and low- strength evidence do not influence the grade of the recommendation. If there is one high- or at least two moderate- strength studies, the recommendation grade is moderate. If there is one moderate- or at least two low- strength studies, the recommendation grade is limited. Inconclusive recommendation grades are assigned when there is one low-strength study, no evidence, or contradictory findings. In this case, the rules for using expert opinion are not applicable so consensus recommendations are not appropriate. Consensus based recommendations are established only when the strength of the evidence would otherwise be inconclusive and the rules for consensus recommendations apply. See the section on Consensus Recommendations in the guideline (page 21).

OUTCOMES CONSIDERED

The work group identifies the critical outcomes that the recommendations are to be based on prior to the literature search. Measures necessary to determine whether or not medical treatment is effective are deemed critical and are listed in the evidence summary tables immediately following each recommendation. As an example, for Recommendation 12 the critical outcomes were:

- Pain
- Functional status
- Disability
- Other arthritis-related symptoms

Please see “Appendix III: Determining Critical Outcomes” for a detailed description of the AAOS process. Other important, although noncritical, outcomes reported by authors are evaluated as well. We analyzed 149 unique outcomes of which six were critical.

LITERATURE SEARCHES

We begin the systematic review with a comprehensive search of the literature. Articles we consider were published prior to May 2012 in four electronic databases; PubMed, EMBASE, CINAHL, and The Cochrane Central Register of Controlled Trials. The medical librarian conducts the search using key terms determined from the work group’s preliminary recommendations.

We supplement the electronic search with a manual search of the bibliographies of all retrieved publications, recent systematic reviews, and other review articles for potentially relevant citations. Recalled articles are evaluated for possible inclusion based on the study selection criteria and are summarized for the work group who assist with reconciling possible errors and omissions.

The study attrition diagram in Appendix IV provides a detailed description of the numbers of identified abstracts and recalled and selected studies that were evaluated in the systematic review of this guideline. The search strategies used to identify the abstracts are contained in Appendix V.

APPRAISING EVIDENCE QUALITY AND APPLICABILITY QUALITY

As noted earlier, we judge quality based on *a priori* research questions and use an automated numerical scoring process to arrive at final ratings. Extensive measures are taken to determine quality ratings so that they are free of bias.

We evaluate the quality of evidence separately for each outcome reported in every study using research design domains suggested by GRADE work group members and others.^{9,11} The GRADE evidence appraisal system is used in the Cochrane Collaboration¹² and has been developed for studies evaluating matched control groups. We incorporate a coding scheme adaptable to all research designs that involves incremental increases for:

- Prospective design (evaluation of a priori hypotheses)
- Adequate statistical power
- Stochastic random assignment of patients to comparison groups
- Sufficient blinding to mitigate against a placebo effect
- Comparability of the patient groups at the beginning of the study
- Delivery of treatment in a manner where observed differences between the comparison groups could reasonably be attributed to the treatment
- Validated outcome measures
- Absence of investigator bias

Each of the above quality domains is rated for possible flaws based on up to four indicator questions that define them. See Appendix VI for a discussion of the AAOS appraisal system. Domains are considered “flawed” if one indicator is coded “No” or at least two defining questions are “Unclear.” The Statistical Power domain is considered flawed if sample size is too small to detect at least a small effect size of 0.2.

If there are flawed domains then the evidence quality is downgraded according to the reductions shown in Table 1. As an example, the evidence reported in a randomized controlled trial (RCT) for any given outcome is rated as “High” quality if zero or one domain is flawed. If two or three domains are flawed, the rating is reduced to “Moderate.” If four or five domains are flawed, the quality of evidence is downgraded to “Low.” The quality of evidence is reduced to “Very Low” if six or more domains are flawed. As indicated above, very low quality evidence is not included in this AAOS guideline.

Table 1. Relationship between Quality and Domain Scores for Interventions

Number of Domains With No More Than One “Unclear” Answer	Strength of Evidence
0	High
1-2	Moderate
3-4	Low
>5	Very Low

The following flaws are so detrimental that we appraise the evidence as “Very Low” quality regardless of the computed domain scores.

- Non-consecutive enrollment of patients in a case series
- Case series involving the administration of multiple treatments
- Heterogeneity in outcome measurement
- Low statistical power

Quality is one of two dimensions that determines the strength of the final recommendations.

APPLICABILITY

We rate the applicability (also referred to as “generalizability” or “external validity”) of each outcome reported in the studies. As with quality, applicability ratings are based on pre-established indicators that are coded and scored algorithmically. Applicability is rated as “High,” “Moderate,” or “Low,” based on the number of domains that are flawed. A study is rated “High” if none of the domains are flawed, “Low” if all of the domains are flawed, and “Moderate” in all other cases.

Table 2. Relationship between Applicability and Domain Scores for Interventions

Number of Flawed Domains	Applicability
0	High
1, 2, 3	Moderate
4	Low

Our applicability appraisal system is derived from the PRECIS instrument²¹ originally intended for randomized controlled trials but also appropriate for other types of research design. It is comprised of 10 questions that are divided into four domains. The defining characteristics and domains are presented in Table 3.

Table 3. Brief Description of the PRECIS Questions and Domains

Question	Domain
All Types of Patients Enrolled	Participants
Flexible Instructions to Practitioners	Interventions and Expertise
Full Range of Experimental Practitioners	Interventions and Expertise
Usual Practice Control	Interventions and Expertise
Full Range of Control Practitioners	Interventions and Expertise
No Formal Follow-up	Interventions and Expertise
Usual and Meaningful Outcome	Interventions and Expertise
Compliance Not Measured	Compliance and Adherence
No Measure of Practitioner Adherence	Compliance and Adherence
All Patients in Analysis	Analysis

MINIMUM CLINICALLY IMPORTANT IMPROVEMENT

Without consideration of clinical significance to patients, analysis of statistical significance is limited. The latter provides information about sample size and does not quantify the size of the effect that differentiates the treatment groups. Whenever the data is available, we identified minimum clinically important improvement (MCII) treatment effects in addition to statistical significance. The MCII reflects the smallest clinical change that is important to patients and recognizes that there are some treatment-related statistically significant improvements that are too small to be relevant. We incorporated terminology based on Armitage et al.¹³ that is outlined in Table 4. See Appendix XIV for a visual presentation of the descriptive terms.

Table 4. Descriptive Terms for Results with MCII

Descriptive Term	Condition for Use
Clinically Significant	Statistically significant and lower confidence limit > MCII
Possibly Clinically Significant	Statistically significant and confidence intervals contain the MCII
Not Clinically Significant	Statistically significant and upper confidence limit < MCII
True Negative Finding	Not statistically significant and upper confidence limit < MCII
Inconclusive Finding	Not statistically significant but confidence intervals contain the MCII

When MCII calculations from the specific guideline patient population are not available, we use thresholds from the most closely related population for which published data exists. Although possible variability between diseases and subjectivity in what patients view as improvement can cause discrepancies, calculations of the MCII based on closely related populations function as a reasonable proxy for evaluating meaningful effects.

The values we used for MCII are derived from the published literature. We used the effect sizes reported by Angst et al. to compute the MCII of pain (0.39) and function (0.37) for the WOMAC instrument¹⁴ and calculated effect sizes reported in their data to compute the MCII of stiffness (0.39) and total score (0.40).

We also used data from the same study to calculate the effect sizes for the MCII of the Short Form-36 (SF-36) bodily pain (0.47), physical function (0.17), and role physical (0.26) composite scores.¹⁵ We used data reported by Tubach et al. to calculate the effect sizes for the MCII of the Visual Analog Scale (VAS) pain (1.23) and global assessment (1.0) subscale scores.¹⁶ For all calculated MCII, we standardized the effect sizes of the applicable instruments by dividing the minimum clinically important difference from baseline to follow-up by the standard deviation of the mean baseline score.

GRADE OF RECOMMENDATION

The recommendation grades are based on the strengths of evidence and express the confidence one can have in the final recommendations. Grades reflect how likely it is current findings will be replicated in future studies. They are assigned as “Strong,” “Moderate,” or “Limited.”

We base evidence grades on the quality and applicability ratings, whether or not the studies report critical outcomes, and potential harm to patients. More specifically, we begin by setting the strength as equal to the quality of available evidence. High quality evidence is preliminarily rated as “Strong,” moderate quality as “Moderate,” and low quality as “Limited.” The ratings are downgraded if the evidence is: 1) of “Low” applicability; 2) inconsistent (comprised of studies with discrepant findings or a high

degree of heterogeneity in the meta- or network meta- analyses); 3) based on only one study; or, 4) lacking “critical” outcomes. Preliminary recommendation grades are adjusted upward if the evidence is of “High” applicability or if the intervention is associated with decreased likelihood of catastrophic harm (i.e. possible loss of life or limb). In the present guideline, reducing potential harm is the reason that the evidence strength of one recommendation was raised.

DEFINING THE STRENGTH OF THE RECOMMENDATIONS

Judging the strength of evidence is only one step in the process of arriving at the final grade of a guideline recommendation. The overall strength is also based on clinical appropriateness, volume of the evidence, benefit versus potential harm to the patient’s well-being, magnitude of treatment effects, and available data on critical outcomes.

It is highly unlikely that future evidence will overturn a recommendation supported by numerous high strength randomized controlled trials that show a large treatment effect. There is a greater likelihood for future evidence to contradict recommendations that are based on a small number of case series. Since RCTs tend to have higher scientific merit, they are usually associated with higher evidence strengths than case series studies.

When determining strength, AAOS staff first assigns a preliminary grade for each recommendation that reflects the quality and applicability ratings as well as volume of the evidence. Work group members then modify the preliminary recommendation strengths using the ‘Form for Assigning Strength of Recommendation (Interventions)’ shown in Appendix VI. Table 6 on the following page describes the possible grades, definitions, and implications that can be assigned to recommendations.

WORDING OF THE FINAL RECOMMENDATIONS

To prevent bias in the way recommendations are worded, the AAOS uses specific predetermined language stems that are governed by the evidence strengths. The format of guideline language is shown in Table 5.

Table 5. AAOS Guideline Language

Guideline Language Stem	Grade
We <i>recommend</i>	Strong
We <i>suggest</i>	Moderate
The practitioner <i>might</i>	Limited
We are <i>unable to recommend for or against</i>	Inconclusive
In the absence of reliable evidence, the <i>opinion</i> of this work group is*	Consensus*

*Consensus recommendations are made only if specific criteria are met (see below).

Table 6. Recommendation Strengths, Descriptions, and Clinical Implications

Evidence Rating	Description of Evidence Strength	Implication for Practice
Strong	Evidence is based on two or more “High” strength studies with consistent findings in support of recommending for or against the intervention. A Strong (positive) recommendation means that the benefits of the recommended approach clearly exceed the potential harm, and/or that the strength of the supporting evidence is high. A Strong (negative) recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.	Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate	Evidence from two or more “Moderate” strength studies with consistent results, or evidence from a single “High” strength study recommending for or against the intervention. A Moderate recommendation means that the benefits exceed the potential harm (or that the potential harm exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.	Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.
Limited	Evidence from two or more “Low” strength studies with consistent results, or evidence from a single Moderate strength study recommending for or against the intervention. A Limited recommendation means that the strength of the supporting evidence is unconvincing, or that well-conducted studies show little clear advantage to one approach over another.	Practitioners should exercise clinical judgment when following a recommendation classified as Limited , and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.
Inconclusive	Evidence from a single low strength study or otherwise conflicting evidence that does not allow a recommendation to be made for or against the intervention. An Inconclusive recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.	Practitioners should feel little constraint in following a recommendation labeled as Inconclusive , exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.
Consensus	The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A Consensus recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria in the systematic review.	Practitioners should be flexible in deciding whether to follow a recommendation classified as Consensus , although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

CONSENSUS RECOMMENDATIONS

Consensus recommendations are based on expert opinion. While they are prudent in certain instances, their liberal use can cause a source of bias. When the AAOS uses consensus-based recommendations, we follow the procedures described by the U.S. Preventative Services Task Force (USPSTF).¹⁷ In our view, there are only two circumstances that warrant their use. The first is in the case of procedures that have virtually no associated harm, are of relatively low cost, and reflect routine clinical care. The second pertains to medical interventions that potentially prevent loss of life or limb.

In making consensus-based recommendations, work group members consider:

- Preventable burden of disease
- Applications in current practice
- Potential harm that could result from providing a medical service
- Relative difference in costs of a recommended service over alternatives

The AAOS employs additional rules to manage the potential bias that may influence consensus recommendations. First, the rationale cannot contain references to studies that are not a part of the systematic review. Excluded articles are not viewed as evidence. Second, the final recommendation must use the language shown in Table 5 that eliminates stating “we recommend,” “we suggest,” or “the practitioner might” to avoid confusion with the evidence-based recommendations. Third, the rationale must address any apparent discrepancies in logic with other recommendations. For example, if a guideline does not endorse an intervention in some instances but the work group has nevertheless issued a consensus-based recommendation, the rationale must explain the reason for the discrepancy in decisions.

When a recommendation is equivocal (i.e., when the recommendation reads “we are unable to recommend for or against”), the explanation why cannot contain an implied recommendation. For example, in the case of a new device, drug, or procedure, the work group may not incorporate such statements as, “Although treatment X *appears to be promising*, there is currently insufficient evidence to recommend for or against its use.” The italicized phrase implies effectiveness in treatment X when “not being able to recommend for or against” implies that effectiveness remains undetermined.

VOTING ON THE RECOMMENDATIONS

The recommendations and their strengths are voted on using the nominal group technique. We present the details in Appendix VIII. Voting is conducted by secret ballot; work group members are blinded to the responses of the other members. If there is significant disagreement, negotiation takes place and is followed by up to an additional three rounds of voting. If the disagreements cannot be resolved, the applicable recommendation is not adopted. Lack of agreement is a reason some grades might be labeled “Inconclusive.”

Formal vote by work group members was used to approve all of the recommendations. Only the work group chair is required to approve the rationales with the editing support of staff unless the evidence grade is consensus. However, the rationales for this guideline

were approved by the entire work group. All components of consensus recommendations require formal vote.

STATISTICAL METHODS

NETWORK META-ANALYSIS

During evidence appraisal of this guideline Bayesian network meta-analyses (also known as mixed treatment comparisons analysis) of randomized controlled trials were performed to ascertain the comparative effectiveness of analgesic treatments not directly compared in the literature, as explained below. For all interventions connected in one network by pairwise relationships, if there is no direct evidence about two analgesics but they are each compared to the same reference treatment then their relative effectiveness can be estimated based on their computable effects with the common comparator. Both direct and indirect comparisons contribute to the totality of evidence for selecting the best choices of treatment. The mixed treatment comparisons analysis follows methodology described by Lu and Ades¹⁸ using Winbugs version 1.4.

Network meta-analysis assumes that randomization within the individual trials is maintained. Additionally, it is appropriate when interactions and covariates that affect trial AB have similar effects on trial AC, and the same indirect effect BC could be obtained as if it had been evaluated as a true direct effect (i.e. third arm of the RCT). Breaking randomization and permitting effect modifying heterogeneity leads to biased estimates of the indirect comparisons. Consistency, the second important assumption, helps to produce interpretable results along with the similarity requisite. Similarity is required of the treatment effects among studies; consistency addresses the potential for significant variability between the direct and indirect comparisons.

Network meta-analysis requires statistical consistency between the direct and indirect pairwise effects. We use the “back calculation” method as described by Dias et al.¹⁹ summarized as follows. Indirect effect BC is calculated as the difference between direct effects AB and AC and evaluated against the direct effect estimation for BC. The z-statistic for the difference between the direct and indirect effects of BC is compared to a standard normal distribution to test the null hypothesis evaluating consistency. If statistical significance is found, then the model is interpreted as having questionable reliability and is excluded from the data analysis. The results of the tests of statistical consistency between the direct and indirect comparisons of the pairs of analgesics examined in this guideline indicated that the consistency assumption was met; the output summary can be found in Appendix XIII.

Network meta-analysis is based on multiple pairwise comparisons across at least three RCTs that connect at least three interventions where there is at least one closed loop (i.e. common comparator; direct comparison). It is an extension of traditional meta-analysis that incorporates a process where the outcome of a given comparison can affect the next outcome requiring the convergence of Markov chains that is based on this type of sampling. A total of k-1 parameters are estimated that allow for multiple pairwise comparisons across a range of k distributions. The results are assessed by examination of trace plots that graphically display the values a parameter took during the runtime of the

chain. In general, for each network model we performed 100,000 iterations of which the first 50,000 were discarded as “burn in” pre-convergence iterations. Occasionally models required 100,000 burn-in pre-convergence iterations, which resulted in a total of 150,000 iterations.

PLACEBO DATA REGRESSION ANALYSIS

INCLUSION CRITERIA

As part of the studies included in the full guideline, articles that met inclusion criteria for a supplementary osteoarthritis of the knee placebo project were also recalled. Selection criteria included:

- Studies written in English
- Placebo-controlled randomized controlled trial study design evaluating treatment for knee osteoarthritis
- $\geq 80\%$ of participants have osteoarthritis of the knee (or the results for those with knee osteoarthritis reported separately)
- Study reported patient-oriented outcomes (i.e. pain, function, global assessment)
- Study reported sufficient data from the placebo group to perform statistical analysis: baseline and follow-up measures or change from baseline measures, including measures of dispersion (95% confidence interval, standard deviation, or standard error)
- Withdrawal rate of placebo group $<20\%$ (measured at each treatment follow up duration)

Because of differences in inclusion criteria between the placebo data project and the full guideline, some articles were included only in the placebo study while others were a part of both. As an example, sample size ≥ 30 was not a selection criterion for the regression analysis but it was for the full guideline.

We searched placebo controlled trials relevant to all the recommendations for the following outcomes: WOMAC pain, stiffness, function, and total subscales, VAS pain, SF-36 role- physical and mental subscales, and the Lequesne Index. The only data available examined the treatment efficacy of osteotomy using the VAS; so only placebo controlled trials that measured change in VAS pain following osteotomy were incorporated.

STATISTICAL ANALYSIS

Data from 48 articles were extracted to predict differences between baseline and treatment scores in the experimental and placebo groups of two case series designed studies. Prais-Winsten regression analysis was conducted using STATA's XTP CSE command used specifically with panel data affected by heteroskedasticity and autocorrelation. Since each observation represented study-level averages of VAS pain scores, the regression was weighted by size of the study samples.

The initial regression model predicted change in VAS pain using pretreatment score, age, percent female, follow up duration in weeks, multicenter study (0 = yes, 1 = no), and allowance for concomitant treatment (0 = no, 1 = yes) as independent variables. Blinding was not used as a predictor variable because patients were masked to the treatment assignments in all but one of the studies.

RESULTS

Baseline VAS pain score, age, and duration of treatment follow up were the only statistically significant covariates retained in the final model. For every one point increase in baseline VAS pain score, follow up VAS pain decreased by .32 millimeters ($p < .001$). A study population with baseline VAS pain score = 70 showed more improvement than one with baseline score = 60.

There were negative coefficients that reflected regression to the mean effects. Regression to the mean refers to the tendency for outlying values to become less extreme as large positive values decrease and extreme negative ones increase.

Placebo treatments had a larger effect on study populations of older adults. For every one year increase in age, post treatment VAS pain score decreased by .30 millimeters ($p < .001$). Similarly, VAS pain scores were significantly associated with duration of treatment follow up time. For every one additional week of treatment, VAS pain scores decreased by .123 millimeters ($p < .001$).

The final regression model was:

$$\Delta \text{VAS pain} = 25.83 - .32(\text{baseline VAS score}) - .30(\text{mean age}) - .123(\text{duration})$$

NEW TO META-ANALYSIS IN THIS GUIDELINE: MINIMAL IMPORTANT DIFFERENCE (MID) UNITS

In following the Cochrane Collaboration method of systematic reviews we compute standardized mean differences otherwise referred to as effect sizes, that are reported essentially in standard deviation units. The calculation describes the average change between the treatment and control groups taking into account the degree of dispersion within each of the two groups. Wider variation indicates that patients in both groups report improvements as well as no improvements. Treatment effects are adjusted mathematically to reflect this lower relative responsiveness.

The calculations of MCII that we used were validated based on patients with knee osteoarthritis whose final outcome of treatment was, “good, satisfactory effect with occasional episodes of pain or stiffness.” Final response to treatment anchored by baseline value was calculated for each patient. Our determinations of clinical significance required patients in the studies included in this guideline to achieve a change score comparable to that achieved by 75% of patients reporting good outcomes in the population (which amounted to about half of one likert rating on a five-point likert scale). Knowing the threshold that identifies successfully treated patients, it was possible for us to discern clinically effective from suboptimal treatment effects.

One lesson learned in clinical practice guideline development is that while meta-analysis effectively pools the individual effect sizes by assigning greater weight to studies with less variability and lesser weight to effects where dispersion is higher, there is still heterogeneity in the treatment effects that diminishes their data analytic interpretation and the output does not easily resonate with clinicians to whom they are meant to be relevant.

Since it is the AAOS' intent to develop guidelines for the benefit of patients and healthcare providers, we have incorporated the use of MID units. When reported statistically, effect sizes are interpreted as:

<u>Effect Size</u>	<u>Interpretation</u>
.20	Small
.50	Moderate
.80	Large

Since these values of are limited usefulness to clinicians, we have also conducted meta-analysis in MID units instead of standard deviation units. Instead of dividing the mean difference between groups of each study by its standard deviation, we divided each mean difference by the MID. The MID is the smallest difference in outcome score that informed patients or proxies perceive as important when considering benefit and potential harm and that would lead the patient or clinician to consider a change in the course of treatment ([Guyatt et al.](#)). An MID of one-half of a likert rating on a five-point scale (i.e. equal to our MCII) is comparable to many empirical derivations of the MID [presented by Dr. Guyatt at the *FDA: Minimum Clinically Important Difference (MCID): Defining Outcome Metrics for Orthopaedic Devices* meeting held on November 27 – 28, 2012].

By interpreting effect sizes in MID units, it is possible to assess whether or not an appreciable number of patients achieve clinically important benefits in the outcomes. Degrees of possible efficacy follow a normal distribution so increasingly smaller effects below one MID unit reflect decreasingly lower likelihoods. In this guideline, when the overall treatment effect in meta-analysis was below .5 MID units, we concluded that there was a low likelihood an appreciable number of patients achieved clinically important benefits in the outcomes.

PEER REVIEW

Following the final meeting, the guideline draft undergoes peer review for additional input from external content experts. Written comments are provided on the structured review form (see Appendix IX). All peer reviewers are required to disclose their conflicts of interest.

To guide who participates, the work group identifies specialty societies at the introductory meeting. *Organizations*, not *individuals*, are specified.

The specialty societies are solicited for nominations of individual peer reviewers approximately six weeks before the final meeting. The peer review period is announced

as it approaches and others interested are able to volunteer to review the draft. The chair of the AAOS committee on Evidence Based Quality and Value reviews the draft of the guideline prior to dissemination.

Some specialty societies (both orthopaedic and non-orthopaedic) ask their evidence-based practice (EBP) committee to provide review of the guideline. The organization is responsible for coordinating the distribution of our materials and consolidating their comments onto one form. The chair of the external EBP committees provides disclosure of their conflicts of interest (COI) and manages the potential conflicts of their members.

Again, the AAOS asks for comments to be assembled into a single response form by the specialty society and for the individual submitting the review to provide disclosure of potentially conflicting interests. The peer review stage gives external stakeholders an opportunity to provide evidence-based direction for modifications that they believe have been overlooked. **Since the draft is subject to revisions until its approval by the AAOS Board of Directors as the final step in the guideline development process, confidentiality of all working drafts is essential.**

The clinical practice guidelines manager drafts the initial responses to comments that address methodology. These responses are then reviewed by the work group chair and vice-chair, who respond to questions concerning clinical practice and techniques. The director of the Department of Research and Scientific Affairs provides input as well. All comments received and the initial drafts of the responses are also reviewed by all members of the work group. All changes to a recommendation as a result of peer review are based on the evidence and undergoes majority vote by the work group members via teleconference. Final revisions are summarized in a detailed report that is made part of the guideline document throughout the remainder of the review and approval processes.

The AAOS believes in the importance of demonstrating responsiveness to input received during the peer review process and welcomes the critiques of external specialty societies. Following final approval of the guideline, all individual responses are posted on our website <http://www.aaos.org/research/guidelines/guide.asp> with a point-by-point reply to each non-editorial comment. Reviewers who wish to remain anonymous notify the AAOS to have their names de-identified; their comments, our responses, and their COI disclosures are still posted.

Review of the *Treatment of Osteoarthritis of the Knee* guideline was requested of 19 organizations and 18 external content experts were nominated to represent them. Sixteen individuals returned comments on the structured review form (see Appendix X).

PUBLIC COMMENT

After modifying the draft in response to peer reviewers' input, the guideline is circulated for a 30-day public comment period. Public commentators consist of members of the AAOS Board of Directors (BOD), Council on Research and Quality (CORQ), Board of Councilors (BOC), and Board of Specialty Societies (BOS). The guideline draft is customarily sent to the AAOS BOD and CORQ for requested commentary whereas members of the BOC and BOS are solicited in advance for their interest and receive

materials upon request. Additionally, a copy of this guideline is placed online (in a dropbox) and notices are sent to all members of the BOC and BOS instructing them on access during the Public Comment period.

If warranted and based on evidence, the guideline draft is modified in response to the public comments by the AAOS clinical practice guidelines unit and work group members. Changes that are made are summarized, and those who provide comment are informed of the revisions that result from their review. As indicated above and similar to peer review modifications, changes following the public comment period must be based on the evidence. They are detailed in a summary sheet that accompanies the document throughout the final approval process.

During the public comment period, 42 stakeholders returned the structured review form commenting on the clinical practice guideline (see Appendix X).

THE AAOS GUIDELINE APPROVAL PROCESS

The work group submits the final guideline for approval by the Committee on Evidence Based Quality and Value, Council on Research and Quality, and Board of Directors. These decision-making bodies are described in Appendix II and are not designated to modify the contents. Their charge is to approve or reject its publication by majority vote.

REVISION PLANS

This guideline represents a cross-sectional view of the current literature and may become outdated as additional information becomes available. Future editions will be developed in accordance with new evidence, changing practice, rapidly emerging treatment options, and advances in technology. The *Treatment of Osteoarthritis of the Knee 2nd Edition* guideline will be updated or withdrawn in five years in accordance with the standards of the National Guideline Clearinghouse.

GUIDELINE DISSEMINATION PLANS

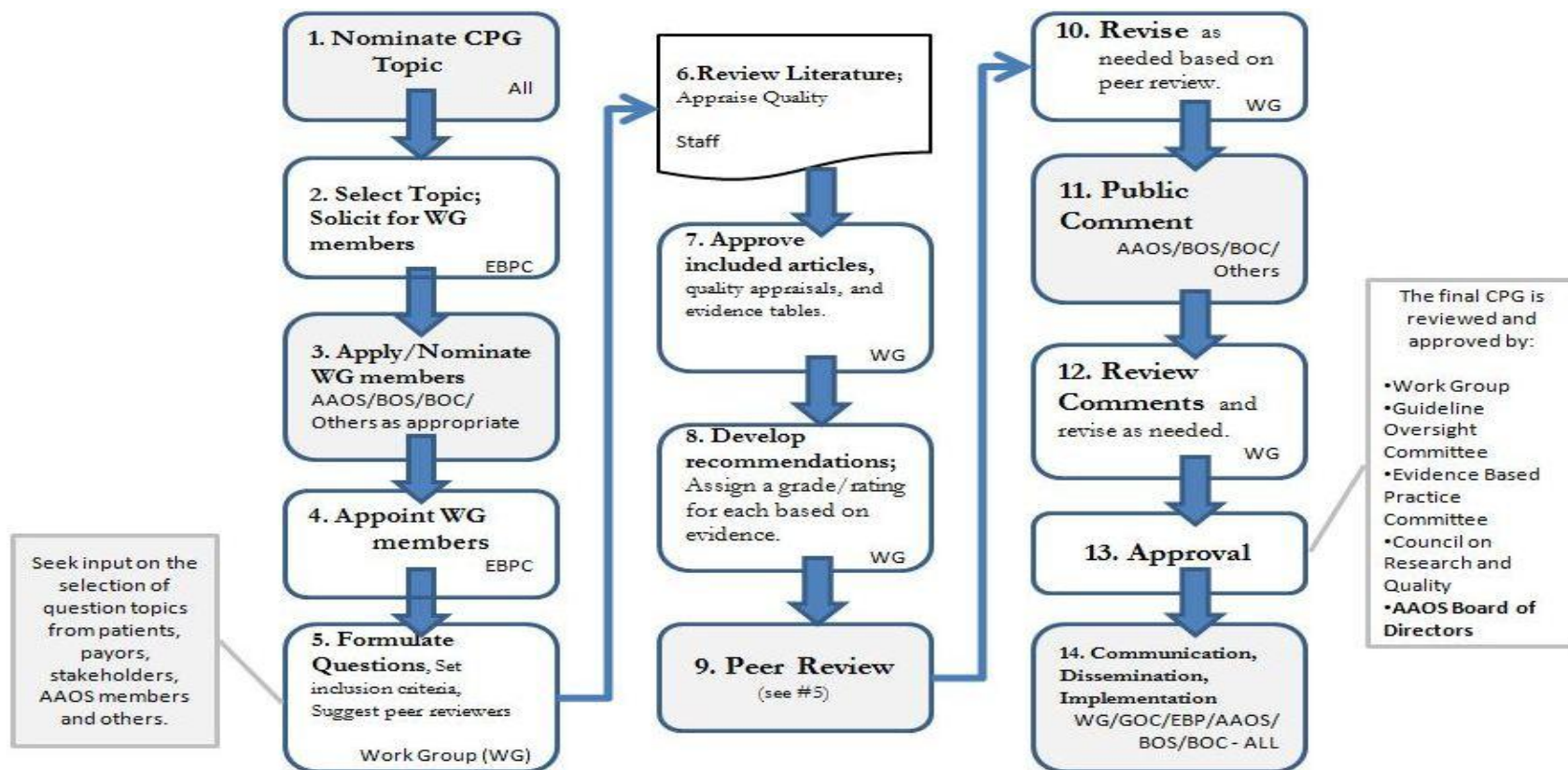
The primary purpose of this guideline is to provide interested readers with comprehensive documentation about our recommendations and the process followed to develop them. All guidelines are available at <http://www.aaos.org/research/guidelines/guide.asp>.

Shorter versions of the guideline are available in other venues. Publication of a guideline is typically announced during an Academy press release, and published in articles authored by the work group in the Journal of the American Academy of Orthopaedic Surgeons and AAOS Now. Most guidelines are also showcased at the AAOS Annual Meeting on Academy Row and as part of the Committee Scientific Exhibits.

Selected guidelines are disseminated by webinar, website, radio, briefings and continuing education. Examples include an online module for the Orthopaedic Knowledge Online website, radio media tours, media briefings, and AAOS' continuing medical education (CME) curriculum and Resource Center.

Other dissemination efforts outside of the AAOS include submission to the National Guideline Clearinghouse and to the Guidelines International Network database, as well as distribution at the annual meetings of other medical specialty societies.

Figure 1. AAOS Clinical Practice Guidelines Development Process



AAOS CLINICAL GUIDELINE ON TREATING OSTEOARTHRITIS OF THE KNEE GUIDELINE RECOMMENDATIONS

RECOMMENDATION 1

We recommend that patients with symptomatic osteoarthritis of the knee participate in self-management programs, strengthening, low-impact aerobic exercises, and neuromuscular education; and engage in physical activity consistent with national guidelines.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm and/or that the quality of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RATIONALE

This recommendation is rated strong because of seven high-strength studies of which five showed beneficial outcomes. The exercise interventions were predominantly conducted under supervision, most often by a physical therapist. The self-management interventions were led by various healthcare providers including rheumatologists, nurses, physical and occupational therapists, and health educators. The evidence supports the use of self-management programs in primary care patients with knee osteoarthritis. One of the studies used an existing evidence-based program, the Arthritis Self-Management Program (ASMP), which was modified to include an exercise component.²⁰ In a high-strength study by Coleman et al.,²¹ patients in a 6-week self-management program demonstrated statistically significant and possibly minimum clinically important improvements in WOMAC Pain, Stiffness, Function, and Total scores at eight weeks as compared to wait-listed controls. The program in that study was based on the same theoretical framework as the ASMP, but included content that was specifically tailored to patients with knee osteoarthritis.

Studies in this review reported improvements in 29 of 37 outcomes favoring strength training over a control (usual care, education, or no treatment). Statistically significant and clinically important improvements were reported for VAS Pain, WOMAC Pain, and WOMAC Function scores.

In addition, 7 of 23 outcomes indicated statistically significant improvements with strengthening exercises, when performed as part of a physical therapy treatment program, versus control.²²⁻²⁴ Three of the seven outcomes were clinically significant and one was possibly clinically significant. One study reported statistically significant and possibly clinically significant improvement in WOMAC Total score following a combination of knee exercise and manual physical therapy as compared to subtherapeutic ultrasound (control).²⁵

Studies also addressed the type and setting for strength training. Long-term outcomes did not vary among isometric, isotonic, or isokinetic exercises.²⁶ Both weight-bearing and nonweight-bearing exercises were superior to control in improving physical function, however, the results were conflicting when the exercises were compared to each other.²⁷ High-resistance strength training led to significantly faster walk times on spongy surfaces as compared to low-resistance training²⁸. Ebnezar et al.²⁹⁻³¹ compared a combination of yoga and physical therapy to physical therapy alone. All eight outcomes were statistically and clinically significant favoring the combined treatment group measured by WOMAC Function and the SF-36 Physical Function and Bodily Pain subscales. Aquatic therapy was also deemed a suitable alternative to land-based strengthening exercises.³² Of the three studies that investigated exercise in the home setting, the highest strength study favored home exercise versus no exercise in reducing patients' global pain rating; however, this finding did not meet the minimum clinically important improvement threshold.³³

Three studies the effects of aerobic walking versus health education and one compared it to usual care in adults with osteoarthritis of the knee. There were statistically significant improvements with aerobic exercise in all but one of the performance-based functional tasks as compared to the education group. In the study by Kovar et al.,³⁴ favorable outcomes were reported by the supervised walking group rather than usual care with statistically significant improvements in 6-minute walking distance and the Arthritis Impact Measurement Scale (AIMS) Physical Activity and Pain subscales.

For neuromuscular education, three of four outcomes were statistically significant favoring combined kinesthesia, balance, and strength training exercises versus strength training alone. A high-strength study by Fitzgerald et al.³⁵ applied an effective treatment for anterior cruciate ligament injury to patients with osteoarthritis of the knee; they found that standard exercise combined with agility and perturbation therapy was not more effective than standard exercise therapy alone. Five of five outcomes were statistically significant for proprioception training. Lin et al.³⁶ randomized 108 patients to nonweight-bearing proprioception training, nonweight-bearing strength training, and non treatment groups. Both proprioception and strength training were significantly more effective in improving WOMAC Pain and Function scores than no treatment.

A number of fitness-related organizations have disseminated guidelines for physical activity. They generally emphasize the importance of aerobic conditioning and muscle- and bone- strengthening, regular activity, and balance exercises for older adults. In 2008, the federal government for the first time published national guidelines. Here is the link to the US Department of Health and Human Service's physical activity guidelines: <http://www.health.gov/paguidelines/guidelines/default.aspx>.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 7](#) [Table 22](#)-[Table 38](#)

There were nine studies that compared strength training to a control group. Seven of the studies were moderate quality and the remaining two were of low and high quality.

Studies by Topp et al.³⁷, Huang et al.²⁶, Jan et al.²⁸, and Bennell et al.³⁸ were flawed in the blinding and investigator bias domains. The Shakoor et al.³⁹ study had investigator bias, but was sufficiently blinded. Topp et al.,³⁷ Maurer et al.,⁴⁰ Azad et al.⁴¹ and Shakoor et al.³⁹ were flawed in group assignment and group comparability. The Jan et al.²⁸ study was flawed in the group comparability domain. The Lin et al.³⁶ study was of high quality and was only flawed by lack of patient blinding. Huang et al.²⁶ compared isokinetic, isotonic, and isometric strength training. All of the outcomes were of moderate quality. The study was flawed in the blinding and investigator bias domains.

Ettinger et al.⁴² compared aerobic exercise and strength training to education programs. Their moderate quality study had uncertain group comparability, as well as flaws in the group assignment and blinding domains.

Lin et al.³⁶ compared proprioceptive training and strength training to no exercise measuring five outcomes. Their high quality study was only flawed by lack of patient blinding.

Three studies of low, moderate and high quality compared physical therapy to control on six outcomes. Fransen et al.²² (moderate quality) and Borjesson et al.²¹ (low quality) were flawed in group assignment, blinding, and investigator bias. The study by Borjesson et al. was also flawed in group comparability. The high quality Bennell et al.²³ study was not flawed in any domain.

Deyle et al.²⁵ compared combined exercise and physical therapy to placebo (non therapeutic intensity ultrasound) and was flawed in the group assignment, treatment integrity, and investigator bias domains

Diracoglu et al.⁴³ compared kinesthesia plus strength training to a control group that received only strength training. All five outcomes that they evaluated were of moderate quality. There were flaws in the group assignment and investigator bias domains.

Teixeira et al.⁴⁴ and Fitzgerald et al.³⁵ compared combined agility and perturbation exercise to standard exercise therapy. Teixeira et al.⁴⁴ conducted a low quality retrospective study that was flawed in the hypothesis, group assignment and blinding domains. The Fitzgerald et al. study was of high quality; its only flaw was investigator bias.

Yip et al.⁴⁵ studied the efficacy of self-management programs combined with an exercise component. Their moderate quality study was flawed in the group comparability, group assignment, and investigator bias domains. Kovar et al.³⁴ compared a supervised walking program to usual care; their study was flawed in the same three domains.

Three studies compared aerobic exercise to education. Two studies were assigned low quality ratings. The study by Ettinger et al.⁴² was of moderate quality and has been described in a previous paragraph. Focht et al.⁴⁶ did not establish a prospective hypothesis and was flawed in the group assignment, blinding, and investigator bias domains. The study by Rejeski et al.⁴⁷ (also of low quality) was determined to have the same flaws.

Home-based exercise programs were evaluated in two high^{33;48} and one moderate⁴⁹ quality studies. One high quality study³³ compared a home-based exercise program to a group that received no intervention. Its only flaw was that evaluators were not blinded to treatment allocation. The other high⁴⁸ and the one moderate⁴⁹ quality studies compared hospital-based to home-based exercise programs. Group assignment and group comparability were flawed in the moderate quality study. Potential investigator bias was the only flaw in the high quality study.

A study by Jan et al.²⁷ of moderate quality compared weight bearing to nonweight-bearing exercise. Although it was sufficiently blinded, was free of investigator bias, used valid measurements, and had treatment integrity, the group assignment and group comparability domains were flawed.

Six outcomes were included from a study by Silva et al.³² that compared water and land-based exercise treatments. The study was flawed in the group assignment and investigator bias domains, producing a moderate quality rating.

The study by Coleman et al.²¹ compared a self-management education program to waitlist control. There were no flaws in the quality domains. Allen et al.⁵⁰ compared telephone based self-management to attention control and usual care. In the comparison to attention control, there was uncertain group comparability at baseline and lack of allocation concealment. In the comparison to usual care, the same limitations occurred and the blinding domain was also flawed.

Hurley et al.⁵¹ studied the effect of an integrated exercise, self-management and coping strategies education program in comparison to usual care. This moderate quality study was flawed in the group assignment, group comparability and treatment integrity domains.

Three studies compared yoga plus physiotherapy to a control group that received physiotherapy only. One study by Ebnezar et al.²⁹ was of high quality, and the other two by Ebnezar et al.^{30,31} were low quality studies. The only flaw in the high quality study was possible investigator bias. The two low quality studies were retrospective and were flawed in the blinding, group assignment and group comparability domains.

Ravaud et al.⁵² compared a standardized structured physician consultation program to usual care. Their moderate quality study was flawed in the treatment integrity and investigator bias domains.

APPLICABILITY

Relevant Tables: [Table 7](#) [Table 22](#)-[Table 38](#)

In all the included studies except the one by Bennell et al.³⁸ there was uncertainty if the treatment administration and those who delivered them represented typical clinical practice. In 27 out of 34 studies, participants may not have been representative of the general patient population. In all but six studies, patient compliance and adherence to the

treatment regimens were representative. Thirty out of 34 studies included a sufficient percentage of enrolled patients in the final analysis.

FINAL STRENGTH OF EVIDENCE

Every included study was of moderate applicability. The strength of evidence ratings remained unchanged from the quality ratings for all outcomes.

Table 7. Quality and Applicability Summary: Strength Training Versus Control

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Bennell (2010)	WOMAC Function	12 weeks	Moderate	Moderate	Moderate
Bennell (2010)	WOMAC Pain	12 weeks	Moderate	Moderate	Moderate
Bennell (2010)	Stair climb	12 weeks	Moderate	Moderate	Moderate
Bennell (2010)	Number of steps	12 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	1 year	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	1 year	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	1 year	Moderate	Moderate	Moderate
Huang (2003)	Walk speed m/minute	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	Walk speed m/minute	1 year	Moderate	Moderate	Moderate
Huang (2003)	Lequesne index	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	Lequesne index	1 year	Moderate	Moderate	Moderate
Jan (2008)	Level ground walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Spongy surface walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Spongy surface walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Stair climb	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Stair climb	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Figure 8 walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Figure 8 walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Level ground walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	WOMAC Pain	8 weeks	Moderate	Moderate	Moderate
Lin (2009)	Level ground walk time	8 weeks	High	Moderate	High
Lin (2009)	Stair walk time	8 weeks	High	Moderate	High

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Lin (2009)	Spongy surface walk time	8 weeks	High	Moderate	High
Lin (2009)	WOMAC Pain	8 weeks	High	Moderate	High
Maurer (1999)	WOMAC Pain	8 weeks	Moderate	Moderate	Moderate
Maurer(1999)	WOMAC Total	8 weeks	Moderate	Moderate	Moderate
Topp (2002)*	WOMAC Pain	16 weeks	Low	Moderate	Low
Azad (2011)	WOMAC Total	4 weeks	Moderate	Moderate	Moderate
Azad (2011)	WOMAC Total	5 weeks	Moderate	Moderate	Moderate
Azad (2011)	WOMAC Total	6 weeks	Moderate	Moderate	Moderate
Shakoor (2010)	WOMAC Total	139 weeks	Moderate	Moderate	Moderate
Shakoor (2010)	WOMAC Total	139 weeks	Moderate	Moderate	Moderate
Shakoor (2010)	WOMAC Total	139 weeks	Moderate	Moderate	Moderate

Table 8 Quality and Applicability Summary: Isokinetic Versus Isotonic Versus Isometric Strength Training

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Ettinger (1997)	Time to get in and out of car	18 weeks	Moderate	Moderate	Moderate
Ettinger (1997)	Lift and carry task	18 weeks	Moderate	Moderate	Moderate
Ettinger (1997)	6-minute walk distance	18 weeks	Moderate	Moderate	Moderate

Table 9. Quality and Applicability Summary: High Versus Low Resistance Strength Training

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Jan (2008)	Stair climb	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Figure 8 walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Level ground walk time	8 weeks	Moderate	Moderate	Moderate
Jan (2008)	Spongy surface walk time	8 weeks	Moderate	Moderate	Moderate

Table 10. Quality and Applicability Summary: Isokinetic Versus Isotonic Versus Isometric Strength Training

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Huang (2003)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	1 year	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	1 year	Moderate	Moderate	Moderate
Huang (2003)	VAS Pain	1 year	Moderate	Moderate	Moderate

Table 11. Quality and Applicability Summary: Proprioception Versus Control

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Lin (2009)	Level ground walk time	8 weeks	High	Moderate	High
Lin (2009)	Stair walk time	8 weeks	High	Moderate	High
Lin (2009)	Spongy surface walk time	8 weeks	High	Moderate	High
Lin (2009)	WOMAC Pain	8 weeks	High	Moderate	High
Lin (2009)	WOMAC Function	8 weeks	High	Moderate	High

Table 12. Quality and Applicability Summary: Physical Therapy Versus Control

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Fransen (2007)	WOMAC Pain	8 weeks	Moderate	Moderate	Moderate
Fransen (2007)	SF-Mental Function	8 weeks	Moderate	Moderate	Moderate
Fransen (2007)	SF-36 Physical	8 weeks	Moderate	Moderate	Moderate
Fransen (2007)	WOMAC Function	8 weeks	Moderate	Moderate	Moderate
Borjesson (1996)	Steps/seconds	5 weeks	Low	Moderate	Low
Borjesson (1996)	Stride length	5 weeks	Low	Moderate	Low
Bennell (2005)	VAS Pain On Movement	12	High	Moderate	High

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Bennell (2005)	VAS Pain On Movement	24	High	Moderate	High
Bennell (2005)	WOMAC Pain	12	High	Moderate	High
Bennell (2005)	WOMAC Pain	24	High	Moderate	High
Bennell (2005)	WOMAC Function	12	High	Moderate	High
Bennell (2005)	WOMAC Function	24	High	Moderate	High
Bennell (2005)	Knee Pain Scale Severity	12	High	Moderate	High
Bennell (2005)	Knee Pain Scale Severity	24	High	Moderate	High
Bennell (2005)	Knee Pain Scale Frequency	12	High	Moderate	High
Bennell (2005)	Knee Pain Scale Frequency	24	High	Moderate	High
Bennell (2005)	SF-36 Physical Role	12	High	Moderate	High
Bennell (2005)	SF-36 Physical Role	24	High	Moderate	High
Bennell (2005)	Assessment of Quality of Life index	12	High	Moderate	High
Bennell (2005)	Assessment of Quality of Life index	24	High	Moderate	High
Bennell (2005)	Number of Steps	12	High	Moderate	High
Bennell (2005)	Number of Steps	24	High	Moderate	High
Bennell (2005)	VAS Pain On Movement	12	High	Moderate	High
Bennell (2005)	VAS Pain On Movement	24	High	Moderate	High
Borjesson (1996)	Meters walked per minute	5 weeks	Low	Moderate	Low
Deyle (2000)	WOMAC Total	8 weeks	Moderate	Moderate	Moderate
Deyle (2000)	6-minute walk distance	4 weeks	Moderate	Moderate	Moderate
Deyle (2000)	6-minute walk distance	8 weeks	Moderate	Moderate	Moderate

Table 13. Quality and Applicability Summary: Kinesthesia Plus Strengthening Versus Strengthening Only

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Diracoglu (2005)	SF-36 Physical Function	8 weeks	Moderate	Moderate	Moderate
Diracoglu (2005)	SF-36 Role Physical	8 weeks	Moderate	Moderate	Moderate
Diracoglu (2005)	SF-36 Vitality	8 weeks	Moderate	Moderate	Moderate
Diracoglu (2005)	WOMAC Function	8 weeks	Moderate	Moderate	Moderate
Diracoglu (2005)	10m walk	8 weeks	Moderate	Moderate	Moderate

Table 14. Quality and Applicability Summary: Agility Plus Perturbation Versus Standard Exercise Therapy

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Fitzgerald (2011)	WOMAC Total	52	High	Moderate	High
Fitzgerald (2011)	WOMAC Function	52	High	Moderate	High
Fitzgerald (2011)	Knee pain (numerical rating scale)	52	High	Moderate	High
Fitzgerald (2011)	Global rating of change	52	High	Moderate	High
Fitzgerald (2011)	Get up and go test	52	High	Moderate	High
Texeira (2011)	When going down stairs?	8	Low	Moderate	Low
Texeira (2011)	When going up stairs?	8	Low	Moderate	Low
Texeira (2011)	Getting up from sitting position	8	Low	Moderate	Low
Texeira (2011)	While standing?	8	Low	Moderate	Low
Texeira (2011)	While bending to the floor?	8	Low	Moderate	Low
Texeira (2011)	When walking on a flat surface?	8	Low	Moderate	Low
Texeira (2011)	While getting in/out of car?	8	Low	Moderate	Low
Texeira (2011)	While going shopping?	8	Low	Moderate	Low

Texeira (2011)	When putting on socks/stockings?	8	Low	Moderate	Low
Texeira (2011)	While getting out of bed?	8	Low	Moderate	Low
Texeira (2011)	When taking off socks/stockings	8	Low	Moderate	Low
Texeira (2011)	While lying in bed?	8	Low	Moderate	Low
Texeira (2011)	When getting in/out of bath?	8	Low	Moderate	Low
Texeira (2011)	While sitting?	8	Low	Moderate	Low

Table 15. Quality and Applicability Summary: Self-Management Plus Exercise Versus Exercise Alone

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Yip (2007)	Arthritis Self-Efficacy Pain	16 weeks	Moderate	Moderate	Moderate
Yip (2007)	VAS Pain	16 weeks	Moderate	Moderate	Moderate
Yip (2007)	Hours of light exercise Health	16 weeks	Moderate	Moderate	Moderate
Yip (2007)	Assessment Questionnaire	16 weeks	Moderate	Moderate	Moderate

Table 16. Quality and Applicability Summary: Aerobic Exercise Versus Education

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Rejeski (2002)	SF-36 Mental Health	18 months	Low	Moderate	Low
Ettinger (1997)	Lift and carry task time(s)	18 weeks	Moderate	Moderate	Moderate
Ettinger (1997)	Stair climb	18 weeks	Moderate	Moderate	Moderate
Ettinger (1997)	Time to get in/out of car	18 weeks	Moderate	Moderate	Moderate
Ettinger (1997)	Walk distance	18 weeks	Moderate	Moderate	Moderate
Focht (2005)	Stair climb time	18 months	Low	Moderate	Low

Table 17. Quality and Applicability Summary: Home-Based Exercise, Self-Management, and Coping Strategies Versus Usual Care

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Hurley (2007)	WOMAC Function	26	Moderate	Moderate	Moderate
Hurley (2007)	WOMAC Pain	26	Moderate	Moderate	Moderate
Hurley (2007)	WOMAC Total	26	Moderate	Moderate	Moderate
Hurley (2007)	Functional Performance time(s) Exercise	26	Moderate	Moderate	Moderate
Hurley (2007)	Health Beliefs Self-Efficacy Subscale	26	Moderate	Moderate	Moderate
Hurley (2007)	Exercise Health Beliefs Total	26	Moderate	Moderate	Moderate
Hurley (2007)	Hospital Anxiety and Depression Scale	26	Moderate	Moderate	Moderate
Hurley (2007)	Depression Subscale				
Hurley (2007)	Hospital Anxiety and Depression Scale Anxiety Subscale	26	Moderate	Moderate	Moderate
Hurley (2007)	MACTAR	26	Moderate	Moderate	Moderate
Hurley (2007)	EQ-5D	26	Moderate	Moderate	Moderate
Coleman (2012)	WOMAC Pain	8	High	Moderate	High
Coleman (2012)	WOMAC Pain	26	High	Moderate	High
Coleman (2012)	WOMAC Stiffness	8	High	Moderate	High
Coleman (2012)	WOMAC Stiffness	26	High	Moderate	High
Coleman (2012)	WOMAC Function	8	High	Moderate	High
Coleman (2012)	WOMAC Function	26	High	Moderate	High
Coleman (2012)	WOMAC Total	8	High	Moderate	High

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Coleman (2012)	WOMAC Total	26	High	Moderate	High
Coleman (2012)	SF-36 Physical Function	26	High	Moderate	High
Coleman (2012)	SF-36 Role Physical	26	High	Moderate	High
Coleman (2012)	SF-36 Body Pain	26	High	Moderate	High
Coleman (2012)	SF-36 General Health	26	High	Moderate	High
Coleman (2012)	SF-36 Vitality	26	High	Moderate	High
Coleman (2012)	SF-36 Social Function	26	High	Moderate	High
Coleman (2012)	SF-36 Role Emotional	26	High	Moderate	High
Coleman (2012)	SF-36 Mental Health	26	High	Moderate	High
Coleman (2012)	SF-36 Physical Function	8	High	Moderate	High
Coleman (2012)	SF-36 Role Physical	8	High	Moderate	High
Coleman (2012)	SF-36 Body Pain	8	High	Moderate	High
Coleman (2012)	SF-36 General Health	8	High	Moderate	High
Coleman (2012)	SF-36 Vitality	8	High	Moderate	High
Coleman (2012)	SF-36 Social Function	8	High	Moderate	High
Coleman (2012)	SF-36 Role Emotional	8	High	Moderate	High
Coleman (2012)	SF-36 Mental Health	8	High	Moderate	High
Allen (2010)	AIMS2 Pain	52	Moderate	Moderate	Moderate
Allen (2010)	AIMS2 Function	52	Moderate	Moderate	Moderate
Allen (2010)	AIMS2 Walking and Bending	52	Moderate	Moderate	Moderate
Allen (2010)	AIMS2 Mobility	52	Moderate	Moderate	Moderate
Allen (2010)	AIMS2 Affect	52	Moderate	Moderate	Moderate

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Allen (2010)	Arthritis Self-Efficacy Scale	52	Moderate	Moderate	Moderate
Allen (2010)	VAS Pain	52	Moderate	Moderate	Moderate
O'Reilly (1999)	Global pain score	26	High	Moderate	High
O'Reilly (1999)	VAS walking	26	High	Moderate	High
O'Reilly (1999)	VAS stairs	26	High	Moderate	High
O'Reilly (1999)	SF-36 Physical Function	26	High	Moderate	High
O'Reilly (1999)	SF-36 Mental Health	26	High	Moderate	High
O'Reilly (1999)	Energy	26	High	Moderate	High
O'Reilly (1999)	Health perception	26	High	Moderate	High
O'Reilly (1999)	Role limitation physical	26	High	Moderate	High
O'Reilly (1999)	Role limitation emotional	26	High	Moderate	High
McCarthy (2004)	WOMAC Pain	52	High	Moderate	High
McCarthy (2004)	WOMAC Stiffness	26	High	Moderate	High
McCarthy (2004)	WOMAC Stiffness	52	High	Moderate	High
McCarthy (2004)	VAS Pain	26	High	Moderate	High
McCarthy (2004)	VAS Pain	52	High	Moderate	High
McCarthy (2004)	WOMAC Pain	26	High	Moderate	High
Tunay (2010)	Left knee VAS Rest	6	Moderate	Moderate	Moderate
Tunay (2010)	Left knee VAS Activity	6	Moderate	Moderate	Moderate
Tunay (2010)	Left knee VAS Night	6	Moderate	Moderate	Moderate
Tunay (2010)	Right knee VAS Rest	6	Moderate	Moderate	Moderate
Tunay (2010)	Right knee VAS Activity	6	Moderate	Moderate	Moderate

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Tunay (2010)	Right knee VAS Night	6	Moderate	Moderate	Moderate
Tunay (2010)	Proprioception	6	Moderate	Moderate	Moderate
Tunay (2010)	WOMAC Total	6	Moderate	Moderate	Moderate
Tunay (2010)	TUG (sec)	6	Moderate	Moderate	Moderate

Table 18. Quality and Applicability Summary: Water Versus Land-Based Exercises

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Silva (2008)	VAS Pain	8 weeks	Moderate	Moderate	Moderate
Silva (2008)	VAS Pain after 50 foot walk	8 weeks	Moderate	Moderate	Moderate
Silva (2008)	VAS Pain after 50 foot walk	8 weeks	Moderate	Moderate	Moderate
Silva (2008)	VAS Pain before 50 foot walk	8 weeks	Moderate	Moderate	Moderate
Silva (2008)	VAS Pain before 50 foot walk	8 weeks	Moderate	Moderate	Moderate
Silva (2008)	Lequesne index	8 weeks	Moderate	Moderate	Moderate

Table 19. Quality and Applicability Summary: Supervised Walking Versus Usual Care

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Kovar (1992)	AIMS Arthritis Pain	8 weeks	Moderate	Moderate	Moderate
Kovar (1992)	6 minute walk distance	8 weeks	Moderate	Moderate	Moderate
Kovar (1992)	AIMS Arthritis Impact	8 weeks	Moderate	Moderate	Moderate
Kovar (1992)	AIMS Medications Use	8 weeks	Moderate	Moderate	Moderate
Kovar (1992)	AIMS Physical Activity	8 weeks	Moderate	Moderate	Moderate
Kovar (1992)	AIMS Arthritis Pain	8 weeks	Moderate	Moderate	Moderate

Table 20. Quality and Applicability Summary: Yoga Plus Physiotherapy Versus Physiotherapy Only

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Ebnezar (2012)	SF-36 Physical Functioning	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 Role Limitations	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 Emotional Problems	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 Energy/Fatigue	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 Emotional Well-Being	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 Social Function	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 Pain	13	Low	Moderate	Low
Ebnezar (2012)	SF-36 General Health	13	Low	Moderate	Low
Ebnezar (2012)	Resting pain	13	Low	Moderate	Low
Ebnezar (2012)	Early morning stiffness	13	Low	Moderate	Low
Ebnezar (2011)	Walking pain	13	High	Moderate	High
Ebnezar (2011)	WOMAC Function	13	High	Moderate	High
Ebnezar (2011)	Walking time	13	High	Moderate	High

Table 21. Quality and Applicability Summary: Standardized Consultation Versus Usual Care

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Ravaud (2009)	SF-12 Mental Function improvement	16 weeks	Moderate	Moderate	Moderate
Ravaud (2009)	SF-12 Physical Function improvement	16 weeks	Moderate	Moderate	Moderate
Ravaud (2009)	WOMAC Function improvement	16 weeks	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Figure 2-Figure 11](#), [Table 39-Table 67](#), [Figure 12](#)

The results of statistical testing for the comparison of strength training to control (usual care, education, or no treatment) can be found below ([Figure 2](#)). Twenty-nine out of 37 outcomes were statistically significant in favor of strength training.

There were three critical outcomes: VAS Pain, WOMAC Pain and WOMAC Function. A total of ten measurements comprised these outcomes and eight showed statistically significant benefits from strength training. Four of the statistically significant critical outcomes were clinically significant, and three were possibly clinically significant.

For VAS Pain, two out of four outcomes were clinically significant showing benefit in strength training. The other two outcomes were possibly clinically significant. Three out of five WOMAC Pain outcomes were statistically significant in favor of strength training. One was clinically significant and another was possibly clinically significant. Clinical importance was unknown for the significant WOMAC Pain outcome in the Topp et al. study because the article did not provide sufficient data to determine it. Also, one WOMAC Function outcome was clinically significant.

A meta-analysis of four studies was computed comparing strength training to control groups in pain outcome. Three of the studies used the visual analogue versions of the WOMAC Pain subscale, and the fourth used the VAS pain scale. The treatment group reported significantly less pain than the control group (see [Figure 12](#)). Clinical significance could not be determined since nonidentical pain measures were used in the meta-analysis.

One strength training study investigated treatment effect on WOMAC Function at eight weeks. This study found a clinically significant improvement reported by the strength training group.

VAS pain was evaluated in a study that compared isokinetic, isotonic and isometric strength training. At eight weeks there was a possibly clinically significant treatment effect suggesting isometric strength training was superior to isotonic training. However, at 52 weeks, patients in the isotonic group had lower VAS pain scores than isometric patients although the effect was not clinically significant. VAS pain was significantly lower in the isotonic group than the isokinetic group at week eight, but this difference was not statistically significant at the 52nd week. Isokinetic was significantly more effective at 8 and 52 weeks than isometric strength training although the effect was not clinically significant.

Jan et al.²⁸ examined the effect of high versus low resistance strength training and found that the high resistance strength training group had a significantly faster spongy surface walk time. The treatment effect was not statistically significant for the timed stair climb or level ground and figure-8 walk times.

Seven out of 23 outcomes showed statistically significant improvement from physical therapy over the control group. Seven of 18 critical outcomes significantly favored physical therapy. Of the seven significant outcomes, three were clinically significant and one was possibly clinically significant. Functional performance tasks, such as number of steps walked per second, stride length, and meters walked per minute were not statistically significant. Additionally, all three outcomes in the study by Deyle et al.²⁵ were statistically significant endorsing combined manual physical therapy and exercise over the placebo treatment. Finally, only the timed walk outcome out of seven measures was statistically significant in comparisons of home and center based physiotherapy.

Coleman et al.²¹ compared a class-based self-management program to waitlist control. Fourteen of 24 outcomes were statistically significant in favor of the treatment group. Pain and function were the critical outcomes. Ten out of 18 functional outcomes and one out of two pain outcomes were significantly improved in the self-management group compared to the control group.

Allen et al.⁵⁰ compared a telephone-based self-management program to an attention control group and usual care. The treatment group received written and audio osteoarthritis self-management materials as well as monthly phone calls from a health educator. The health educator discussed self-management strategies and helped the patient develop goal-oriented action plans. The attention control group received general health education materials and phone calls that were not specifically related to osteoarthritis. Compared to the attention control group, osteoarthritis self-management patients reported significantly better VAS pain, AIMS-2 pain, AIMS-2 walking and bending and Arthritis Self-Efficacy scale scores. AIMS-2 function, mobility, and affect scores did not differ statistically. VAS pain scores were lower for patients in the osteoarthritis telephone self-management group than for those who received usual care. However, the AIMS-2 subscales and Arthritis Self-Efficacy scores were not statistically improved over usual care.

One study²⁷ compared weight bearing and non-weight bearing exercise to a control group using self reported function and functional performance outcomes. Both exercise treatment groups were associated with significantly better scores than the control group. The results comparing weight bearing and non-weight bearing exercise were inconsistent. Patients in the non-weight bearing group were able to climb stairs significantly faster than those in the weight bearing group. However, the weight bearing group produced significantly faster walk times on a spongy surface. All other outcomes did not show statistically significant differences between the two groups.

Three out of four outcomes were statistically significant for combined kinesthesia, balance, and strength training compared to strength training alone in the control group. Two out of three self reported functional outcomes were higher for the treatment group. Ten meter walk times were significantly faster in the kinesthesia plus balance group.

Exercise combined with agility and perturbation therapy was not found to be significantly more effective than exercise therapy alone. Out of 22 outcomes in the Fitzgerald et al. and Teixeira et al. studies, only one was statistically significant for the treatment group.

There was one self reported functional outcome examining the effect of aerobic exercise. Rejeski et al. reported that the exercise group did not have significantly better SF-36 Mental Health scores. However, the aerobic exercise group performed better on all functional tasks except timed stair climb.

Kovar et al.³⁴ compared a supervised walking program and education to routine care. AIMS Pain and physical activity were significantly better in the walking group than in the control group. AIMS-arthritis impact was not statistically significant, but six minute walking distances were significantly longer for patients in the treatment group.

O'Reilly et al.³³ compared the effect of a home-based exercise program to no intervention. VAS overall pain, VAS pain on walking, VAS pain climbing stairs, and WOMAC function were all statistically significant in favor of the treatment. The improvement in WOMAC function was possibly clinically important. However, the lower confidence limit of each VAS measure was lower than the MCII, meaning home-based exercise did not result in a clinically significant improvement in self reported pain relative to the control group. The study also measured the treatment effects using each subscale of the SF-36 (we excluded SF-36 physical function and bodily pain because they were not sufficiently powered). Each subscale was not significantly different between the treatment and control groups.

McCarthy et al.⁴⁸ and Tunay et al.⁴⁹ compared home-based and classroom format exercise programs. The former found that supplementing home-based programs with in-class ones resulted in significant improvements in pain and stiffness for patients compared to those who participated in home-based exercise only. The Tunay et al. study, however, did not find hospital-based proprioception and strengthening programs to be more effective than those conducted at home; except when they measured VAS activity score of the left knee.

One study compared the efficacy of water-based exercise programs to land-based programs. The treatment effect for VAS pain before and after walking was not statistically significant at nine weeks, but was significant at 18 weeks. However, the effect was not clinically important. Overall VAS pain and Lequesne index scores were not significantly different for water- and land- based exercise programs.

Yip et al.⁴⁵ compared self-management plus exercise to usual care. Both pain outcomes were significantly lower in the treatment group. However, the difference in VAS pain was not clinically important. There was not a statistically significant difference in Health Assessment Questionnaire scores, but the treatment group reported significantly higher Arthritis Self-Efficacy Other Symptoms Scores, and spent a greater number of hours exercising per week.

[Figure 8](#) contains the summary of results for the effect of a standardized structured physician consultation program that focused on educating the patient in osteoarthritis treatment, exercises, and weight loss. Three critical outcomes are presented: SF-12 Mental function, SF-12 Physical Function and WOMAC Function. While the effect of education on mental function was clinically significant, the other two critical outcomes were not statistically significant.

Hurley et al.⁵¹ studied found that a program integrating exercise with self-management and coping strategies education resulted in statistically significant improvements over the control group in seven out of ten outcomes. The treatment effects for WOMAC Pain function and total scores were possibly clinically important.

Ebnezar et al.²⁹⁻³¹ compared a group undergoing yoga and physiotherapy to a control group that only received physiotherapy. All eight outcomes were significantly higher in the treatment group. The treatment effects for WOMAC function, SF-36 physical function and pain were clinically significant.

Figure 2. Results Summary: Strength Training Versus Control

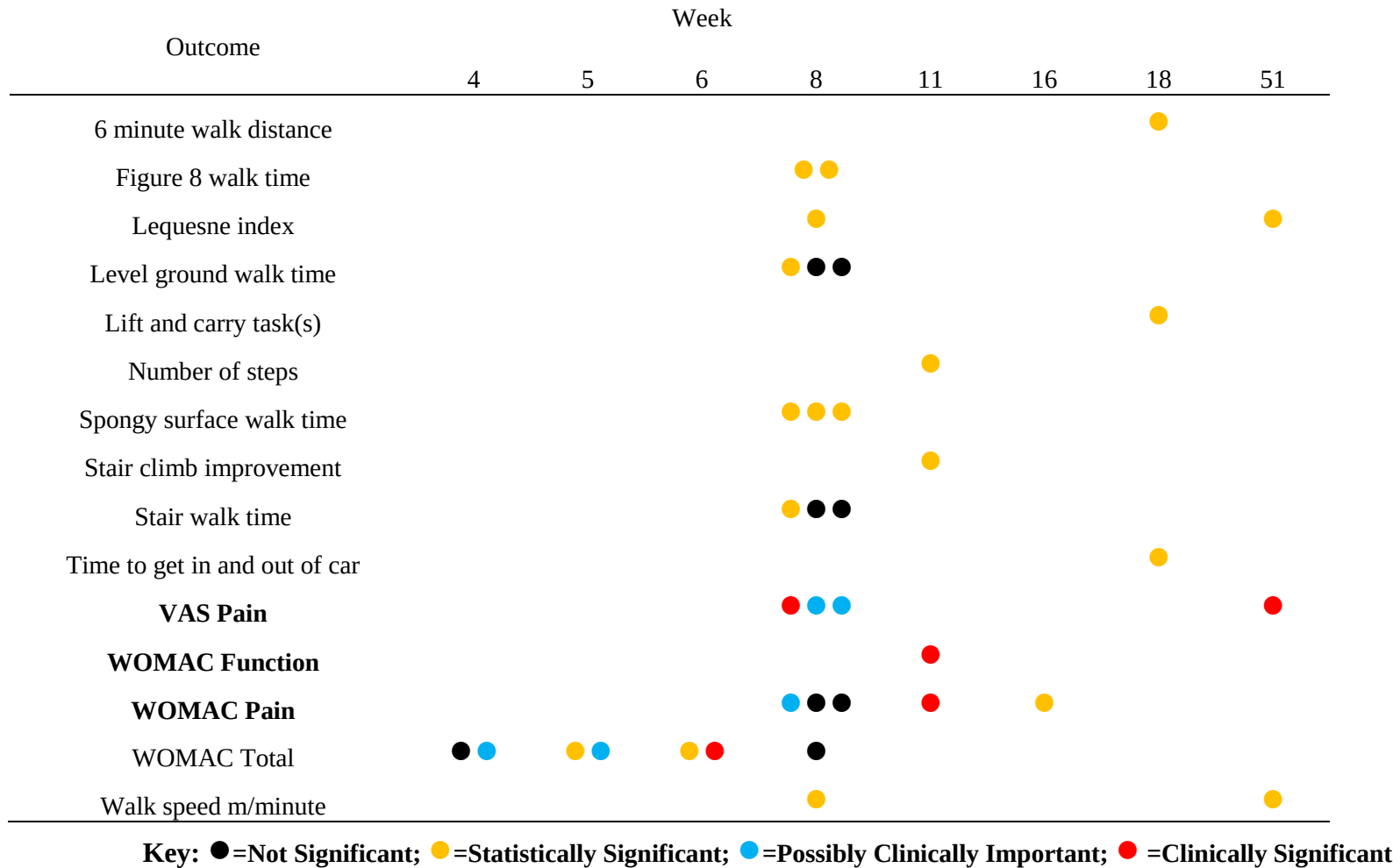


Figure 3. Results Summary: Physical Therapy

Outcome	4	Week 5	8	12	24
6 minute walk distance (m)	●		●		
Meters walked per minute		●			
SF-36 Physical Function			●		
SF-36 Mental Function			●		
SF-36 Physical Role				●	●
Assessment of quality of life				●	●
Knee Pain Scale-Severity				●	●
Knee Pain Scale-Frequency				●	●
Step test		●		●	●
Stride length		●			
WOMAC Function			●	●	●
WOMAC Pain			●	●	●
WOMAC Total			●		
VAS Pain				●	●

Key: ●=Not Significant; ●=Statistically Significant; ●=Possibly Clinically Important; ●=Clinically Significant

Symbols with bold lettering indicate a critical outcome.

Figure 4. Results Summary: Proprioception Versus Control

	Outcome	Week 8
Proprioceptive Training	WOMAC Pain	●
	Walk time- level ground	●
	WOMAC Function	●
	Spongy surface walk time	●
	Stair climb walk time	●

Key: ● =Statistically significant; ● =Clinically significant

Figure 5. Results Summary: Agility and Perturbation Training Plus Usual Exercise Versus Exercise Only

Outcome	Week 8	52
WOMAC Total		●
WOMAC Function		●
Knee pain (numerical rating scale)		●
Global rating of change		●
Get up and go test		●
WOMAC Function Subscale: Get up and go test	●	
WOMAC Function Subscale: When walking down the stairs?	●	
WOMAC Function Subscale: When going up stairs?	●	
WOMAC Function Subscale: Getting up from sitting position	●	
WOMAC Function Subscale: While standing?	●	
WOMAC Function Subscale: While bending to the floor?	●	
WOMAC Function Subscale: When walking on a flat surface?	●	
WOMAC Function Subscale: While getting In/out of car?	●	
WOMAC Function Subscale: While going shopping?	●	
WOMAC Function Subscale: When putting on socks/stockings?	●	
WOMAC Function Subscale: While getting out of bed?	●	
WOMAC Function Subscale: When taking off socks/stockings?	●	
WOMAC Function Subscale: While lying in bed?	●	
WOMAC Function Subscale: When getting in/out of bath?	●	
WOMAC Function Subscale: While sitting?	●	
WOMAC Function Subscale: When getting on/off toilet?	●	
WOMAC Function Subscale: Doing heavy household chores?	●	
WOMAC Function Subscale: Doing light household chores?	●	

Key: ●=Not Significant; ●=Statistically Significant

Figure 6. Results Summary: Kinesthesia Versus Control

Outcome	Week
	8
SF-36 Physical	
SF-36 Role Limitations	
SF-36 Vitality	
10m walk	

Key: ●=Not Significant; ●=Statistically Significant; ●=Clinically Significant

Figure 7. Results Summary: Exercise Versus Control

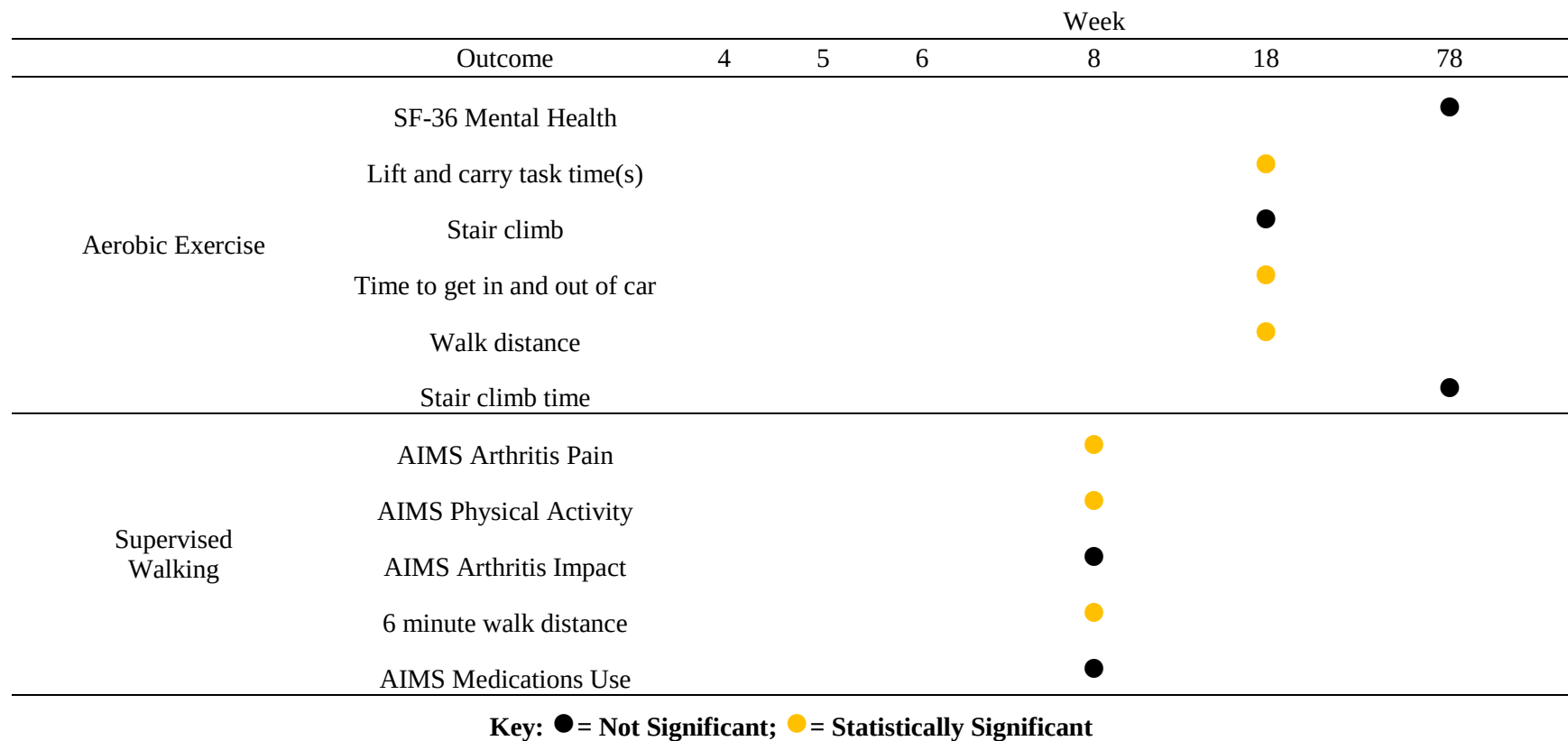


Figure 8. Self-Management and Structured Consultation Versus Control

		Week			
Outcome		8	16	26	52
Class Based Self-Management Versus Waitlist Control	WOMAC Pain	●		●	
	WOMAC Stiffness	●		●	
	WOMAC Function	●		●	
	WOMAC Total	●		●	
	SF-36 Physical function	●		●	
	SF-36 physical role	●		●	
	SF-36 bodily pain	●		●	
	SF-36 general health	●		●	
	SF-36 vitality	●		●	
	SF-36 social function	●		●	
	SF-36 role emotional	●		●	
	SF-36 Mental Health			●	
Telephone-Based Self-Management Versus Attention Control	AIMS2 Pain				●
	AIMS2 Function				●
	AIMS2 walking and bending				●
	AIMS2 Mobility				●
	AIMS2 Affect				●
	Arthritis Self-Efficacy Scale				●

	VAS Pain	●
Telephone-Based Self-Management Versus Usual Care	AIMS2 Pain	●
	AIMS2 Function	●
	AIMS2 walking and bending	●
	AIMS2 Mobility	●
	AIMS2 Affect	●
	Arthritis Self-Efficacy Scale	●
	VAS Pain	●
Self-Management Plus Exercise Versus Usual Care	Health Assessment Questionnaire improvement	●
	Arthritis Self-Efficacy: Other Symptoms improvement	●
	Hours of light exercise improvement	●
	Arthritis Self-Efficacy: Pain Score improvement	●
	VAS Pain improvement	●
Structured Consultation Versus Control: Function	SF-12 Mental Function improvement	●
	SF-12 Physical Function improvement	●
	WOMAC Function improvement	●

Key: ●=Not Significant; ●= Possibly Clinically Important; ●= Statistically Significant;

●= Statistically Significant But Not Clinically Important

Figure 9. Results Summary: Integrated Exercise, Self-Management, and Coping Strategies Versus Usual Care

Outcome	Week 26
WOMAC Function	●
WOMAC Pain	●
WOMAC Total	●
Aggregate Functional Performance time(s)	●
Exercise Health Beliefs Self-Efficacy Subscale	●
Exercise Health Beliefs Total Score	●
Hospital Anxiety and Depression Scale Depression Subscale	●
Hospital Anxiety and Depression Scale Anxiety Subscale	●
MACTAR	●
EQ-5D	●

Key: ● =Not Significant; ● =Statistically Significant; ● =Statistically Significant But Not Clinically Important

Figure 10. Results Summary: Water Versus Land-Based Exercise

Outcome	Week	
	9	18
VAS Pain		●
VAS Pain after 50 foot walk	●	●
VAS Pain before 50 foot walk	●	●
Lequesne index		●

Key: ●=Not Significant; ● = Statistically Significant But Not Clinically Important

Figure 11. Results Summary: Yoga Versus Control

Outcome	Week 13
Physical functioning	●
Role limitations	●
Emotional problems	●
Energy/fatigue	●
Emotional well-being	●
Social function	●
Pain	●
General health	●
WOMAC Function	●
Walking pain	●
Resting pain	●
Timed walk	●
Early morning stiffness	●

Key: ● = Statistically Significant ● = Clinically Important

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 22. Quality and Applicability: Strength Training Versus Control

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Azad (2011)	WOMAC Total	4	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Azad (2011)	WOMAC Total	5	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Azad (2011)	WOMAC Total	6	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Bennell (2010)	Number of steps	12	●	●	●	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Bennell (2010)	WOMAC Function improvement	12	●	●	●	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Bennell (2010)	WOMAC Pain improvement	12	●	●	●	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Bennell (2010)	Stair climb improvement	12	●	●	●	○	●	●	●	○	Moderate	●	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Huang (2003)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	Walk speed m/minute	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	Walk speed m/minute	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	Lequesne index	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Huang (2003)	Lequesne index	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Stair climb	8	●	◐	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Stair climb	8	●	◐	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	WOMAC Pain	8	●	○	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Figure 8 walk time	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Figure 8 walk time	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Level ground walk time	8	●	◐	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Level ground walk time	8	●	◐	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Spongy surface walk time	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Jan (2008)	Spongy surface walk time	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Lin (2009)	WOMAC Pain	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	Level ground walk time	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	Stair walk time	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	Spongy surface walk time	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Topp (2002)	WOMAC Pain	16	●	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Topp (2002)	WOMAC Pain	16	●	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Maurer (1999)	WOMAC Pain	8	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Maurer (1999)	WOMAC Total	8	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Shakoor (2010)	WOMAC Total	139	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Shakoor (2010)	WOMAC Total	139	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Shakoor (2010)	WOMAC Total	139	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate

Table 23. Quality and Applicability: High Versus Low Resistance Training

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Jan (2008)	WOMAC Pain	8	●	○	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Stair climb	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Figure 8 walk time	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Level ground walk time	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Jan (2008)	Spongy surface walk time	8	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

Table 24. Quality and Applicability: Isokinetic Versus Isotonic Versus Isometric Strength Training

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Huang (2003)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2003)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate

Table 25. Quality and Applicability: Strength Training Versus Education

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Ettinger (1997)	Time to get in and out of car	18	●	●	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate
Ettinger (1997)	Lift and Carry Task	18	●	●	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate
Ettinger (1997)	6 minute walk distance	18	●	●	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate

Table 26. Quality and Applicability: Proprioceptive Versus Control

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Lin (2009)	WOMAC Pain	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	Walk time-level ground	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	WOMAC Function	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	Spongy surface walk time	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate
Lin (2009)	Stair climb walk time	8	●	●	●	○	●	●	●	●	High	●	○	●	●	Moderate

Table 27. Quality and Applicability: Physical Therapy Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Fransen (2007)	WOMAC Pain improvement	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Fransen (2007)	SF-Mental Function	8	●	◐	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Fransen (2007)	SF-36 Physical	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Fransen (2007)	WOMAC Function improvement	8	●	●	○	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Borjesson (1996)	Stride length	5	●	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Borjesson (1996)	Number of steps walked/second	5	●	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Borjesson (1996)	Meters walked per minute	5	●	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Deyle (2000)	WOMAC Total	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Deyle (2000)	WOMAC Total	4	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Bennell (2005)	VAS Pain On Movement	12	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	VAS Pain On Movement	24	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Bennell (2005)	WOMAC Pain	12	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	WOMAC Pain	24	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	WOMAC Function	12	●	●	●	●	●	●	●	●	High	●	○	○	●	Moderate
Bennell (2005)	WOMAC Function	24	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Bennell (2005)	Knee Pain Scale Severity	12	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate
Bennell (2005)	Knee Pain Scale Severity	24	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bennell (2005)	Knee Pain Scale Frequency	12	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	Knee Pain Scale Frequency	24	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Bennell (2005)	SF-36 Physical Role	12	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	SF-36 Physical Role	24	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	Assessment of Quality of Life index	12	●	◐	●	●	●	●	●	●	High	●	○	○	●	Moderate
Bennell (2005)	Assessment of Quality of Life index	24	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Bennell (2005)	Step test (number of steps) improvement	12	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate
Bennell (2005)	Step test (number of steps) improvement	24	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bennell (2005)	VAS Pain On Movement	12	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bennell (2005)	VAS Pain On Movement	24	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Deyle (2000)	WOMAC Total	8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

Table 28. Quality and Applicability: Kinesthesia Plus Strengthening Versus Strengthening Alone

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Diracoglu (2005)	SF-36 Physical	8	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Diracoglu (2005)	SF-36 Role Limitations	8	●	◐	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Diracoglu (2005)	SF-36 Vitality	8	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Diracoglu (2005)	10m walk	8	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate

Table 29. Quality and Applicability: Agility Plus Perturbation Versus Standard Exercise Therapy

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Fitzgerald (2011)	WOMAC Total	52	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald (2011)	WOMAC Function	52	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald (2011)	Knee pain (numerical rating scale)	52	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald (2011)	Global Rating of Change	52	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald (2011)	Get Up and Go Test	52	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Texeira (2011)	When down the stairs?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	When going up stairs?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	Getting up from sitting position?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Texeira (2011)	While standing?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While bending to the floor?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	When walking on a flat surface?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While getting in/out of car?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While going shopping?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	When putting on socks/stockings?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While getting out of bed?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	When taking off socks/stockings?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While lying in bed?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Texeira (2011)	When getting in/out of bath?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While sitting?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	When getting on/off toilet?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While doing heavy household chores?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Texeira (2011)	While doing light household chores?	8	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate

Table 30. Quality and Applicability: Self-Management Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Yip (2007)	Arthritis Self-Efficacy Pain Score improvement	16	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Yip (2007)	VAS Pain improvement	16	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Yip (2007)	Hours of light exercise improvement	16	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Yip (2007)	Health Assessment Questionnaire improvement	16	●	◐	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Coleman (2012)	WOMAC Pain	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	WOMAC Pain	26	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	WOMAC Stiffness	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Coleman (2012)	WOMAC Stiffness	26	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	WOMAC Function	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	WOMAC Function	26	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	WOMAC Total	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	WOMAC Total	26	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Physical Function	26	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Role Physical	26	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Body Pain	26	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Coleman (2012)	SF-36 General Health	26	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Vitality	26	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Social Function	26	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Role Emotional	26	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Mental Health	26	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Physical Function	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Role Physical	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Body Pain	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Coleman (2012)	SF-36 General Health	8	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Vitality	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Social Function	8	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Role Emotional	8	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Coleman (2012)	SF-36 Mental Health	8	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Allen (2010)	AIMS2 Pain	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Function	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Walking and Bending	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Allen (2010)	AIMS2 Mobility	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Affect	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	Arthritis Self-Efficacy Scale	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	VAS Pain	52	●	●	○	●	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Pain	52	●	●	○	○	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Function	52	●	●	○	○	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Walking and Bending	52	●	●	○	○	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	AIMS2 Mobility	52	●	●	○	○	○	●	●	●	Moderate	○	●	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Allen (2010)	AIMS2 Affect	52	●	●	○	○	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	Arthritis Self-Efficacy Scale	52	●	◐	●	○	○	●	●	●	Moderate	○	●	●	●	Moderate
Allen (2010)	VAS Pain	52	●	●	●	○	○	●	●	●	Moderate	○	●	●	●	Moderate

Table 31. Quality and Applicability: Supervised Walking Versus Control

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Kovar (1992)	AIMS Arthritis Pain	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Kovar (1992)	6 minute walk distance	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Kovar (1992)	AIMS Arthritis Impact	8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Kovar (1992)	AIMS Medications Use	8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Kovar (1992)	AIMS Physical Activity	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

Table 32. Quality and Applicability: Water Versus Land-Based Exercise

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Silva (2008)	VAS Pain	18	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Silva (2008)	VAS Pain after 50 foot walk	9	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Silva (2008)	VAS Pain after 50 foot walk	18	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Silva (2008)	VAS Pain before 50 foot walk	9	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Silva (2008)	VAS Pain before 50 foot walk	18	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Silva (2008)	Lequesne index	18	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

Table 33. Quality and Applicability: Aerobic Exercise Versus Education

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Rejeski (2002)	SF-36 Mental Health	78	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Rejeski (2002)	SF-36 Physical Component Score	78	○	○	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Ettinger (1997)	Lift and carry task time(s)	18	●	●	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate
Ettinger (1997)	Stair climb	18	●	◐	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate
Ettinger (1997)	Time to get in and out of car	18	●	●	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate
Ettinger (1997)	Walk distance	18	●	●	○	○	○	●	●	●	Moderate	○	○	○	●	Moderate
Focht (2005)	Stair climb time	78	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Yip (2007)	Arthritis Self-Efficacy Pain Score improvement	16	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Yip (2007)	VAS Pain improvement	16	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Yip (2007)	Hours of light exercise improvement	16	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Yip (2007)	Health Assessment Questionnaire improvement	16	●	◐	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate

Table 34. Quality and Applicability: Weight Bearing and Non-Weight Bearing Exercise Programs

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Jan (2009)	WOMAC Function	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Level ground walking time(s)	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Stair climb time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Figure 8 walking time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Sponge walk time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	WOMAC Function	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Level ground walking time(s)	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Stair climb time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Jan (2009)	Figure 8 walking time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Sponge walk time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Level ground walking time(s)	8 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Stair climb time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Figure 8 walking time	8 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jan (2009)	Sponge walk time	8 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

Table 35. Quality and Applicability: Home and Class-Based Exercise Programs

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
O'Reilly (1999)	Global pain score	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	VAS walking	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	VAS stairs	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	Physical function	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	Mental health	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	Energy	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	Health perception	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	Role limitation physical	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	<i>Quality</i>	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
O'Reilly (1999)	Role limitation emotional	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
O'Reilly (1999)	Social functioning	6 months	●		●	○	●	●	●	●	High	○	○	○	●	Moderate
McCarthy (2004)	WOMAC Pain	12-month	●		●	●	●	●	●	○	High	●	○	○	●	Moderate
McCarthy (2004)	WOMAC Stiffness	6 months	●		●	●	●	●	●	○	High	●	○	○	●	Moderate
McCarthy (2004)	WOMAC Stiffness	12-month LVCF	●		●	●	●	●	●	○	High	●	○	○	●	Moderate
McCarthy (2004)	VAS Pain	6 months	●		●	●	●	●	●	○	High	●	○	○	●	Moderate
McCarthy (2004)	VAS Pain	12 months	●		●	●	●	●	●	○	High	●	○	○	●	Moderate
McCarthy (2004)	WOMAC Pain	6 months	●		●	●	●	●	●	○	High	●	○	○	●	Moderate
Tunay (2010)	Left knee VAS Rest	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	<i>Quality</i>	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Tunay (2010)	Left knee VAS Activity	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	Left knee VAS Night	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	Right knee VAS Rest	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	Right knee VAS Activity	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	Right knee VAS Night	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	Proprioception	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	WOMAC Total	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Tunay (2010)	TUG (sec)	6 weeks	●		○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

Table 36. Quality and Applicability: Standardized Structured Physician Consultation Program (Education) Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Ravaud (2009)	SF-12 Mental Function improvement	16	●	◐	●	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ravaud (2009)	SF-12 Physical Function improvement	16	●	◐	●	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ravaud (2009)	WOMAC Function improvement	16	●	●	●	●	●	○	●	○	Moderate	○	○	●	●	Moderate

Table 37. Quality and Applicability: Integrated Exercise, Self-Management, and Coping Strategies Versus Usual Care

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Hurley (2007)	WOMAC Function	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	WOMAC Pain	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	WOMAC Total	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	Aggregate Functional Performance time(s)	26	●	○	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	Exercise Health Beliefs Self-Efficacy Subscale	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	Exercise Health Beliefs Total Score	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	Hospital Anxiety and Depression Scale Depression Subscale	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Hurley (2007)	Hospital Anxiety and Depression Scale Anxiety subscale	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	MACTAR	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Hurley (2007)	EQ-5D	26	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate

Table 38. Quality and Applicability: Yoga Plus Physiotherapy Versus Physiotherapy Only

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Ebnezar (2011)	Physical functioning	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	Role limitations	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	Emotional problems	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	Energy/fatigue	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	Emotional well-being	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	Social function	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	Pain	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2011)	General health	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Ebnezar (2012)	Resting pain	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2012)	Early morning stiffness	13	○	●	○	○	○	●	●	○	Low	○	○	○	●	Moderate
Ebnezar (2010)	Walking pain	13	●	●	●	●	●	●	●	○	High	○	○	○	●	Moderate
Ebnezar (2010)	WOMAC Function	13	●	●	●	●	●	●	●	○	High	○	○	○	●	Moderate
Ebnezar (2010)	Walking time	13	●	●	●	●	●	●	●	○	High	○	○	○	●	Moderate

FINDINGS

Table 39. Strength Training Compared to Control: Pain Outcomes

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bennell (2010)	WOMAC Pain	89	Yes	12	Hip strengthening	No exercise	.86(.392, 1.33)	Favors hip strengthening	Clinically important	Moderate
Topp (2002)	WOMAC Pain	67	Yes	16	Dynamic strength training	No exercise	Mean difference=1.71	Favors strength training (ST) group	Unclear	Low
Topp (2002)	WOMAC Pain	67	Yes	16	Isometric strength training	No exercise	Mean difference=1.39	Favors ST	Unclear	Low
Jan (2008)	WOMAC Pain	64	No	8	High resistance training	No exercise	-.41(-.91,.08)	No	Inconclusive	Moderate
Lin (2009)	WOMAC Pain	72	Yes	8	Strength training	No exercise	-.96(-.71, -.06)	Favors ST	Possibly clinically significant	High
Huang (2003)	VAS Pain	128	Yes	8	Isotonic strength training	Control	-3.16(-3.69, -2.64)	Favors ST	Clinically important	Moderate
Huang (2003)	VAS Pain	128	Yes	8	Isometric strength training	Control	-1.57(-1.97, -1.17)	Favors ST	Possibly clinically important	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Huang (2003)	VAS Pain	124	Yes	8	Isokinetic strength training	Control	-1.48(-1.88, -1.08)	Favors ST	Possibly clinically important	Moderate
Huang (2003)	VAS Pain	112	Yes	52	Isotonic strength training	Control	-3.01(-3.56, -2.46)	Favors ST	Clinically important	Moderate
Huang (2003)	VAS Pain	124	Yes	52	Isometric strength training	Control	-1.97(-2.42, -1.52)	Favors ST	Clinically important	Moderate
Huang (2003)	VAS Pain	110	Yes	52	Isokinetic strength training	Control	-2.27(-2.75, -1.79)	Favors ST	Clinically important	Moderate
Maurer (1999)	WOMAC Pain	98	Unclear	8	Isokinetic quadriceps exercise	Education	Mean difference=15.09 (p>.05)	NS	Unclear	Moderate

Table 40. Isokinetic Versus Isotonic Versus Isometric Exercise: Pain

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Huang (2003)	VAS Pain	120	Yes	8	Isokinetic	Isometric	-.53(-.89,-.16)	Favors isokinetic	Not clinically important	Moderate

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Huang (2003)	VAS Pain	120	Yes	8	Isokinetic	Isotonic	.51(15, .87)	Favors isotonic	Not clinically important	Moderate
Huang (2003)	VAS Pain	124	Yes	8	Isometric	Isotonic	1.52(1.12, 1.93)	Favors isometric	Possibly clinically important	Moderate
Huang (2003)	VAS Pain	116	Yes	52	Isometric	Isokinetic	.41(.04, .78)	Favors isokinetic	Not clinically important	Moderate
Huang (2003)	VAS Pain	118	Yes	52	Isometric	Isotonic	.79(.42, 1.17)	Favors isotonic	Not clinically important	Moderate
Huang (2003)	VAS Pain	114	Yes	52	Isokinetic	Isotonic	.31(-.06, .68)	No	Inconclusive	Moderate

Table 41. Strength Training Versus Control: Functional Measure

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bennell (2010)	Stair climb improvement	76	Yes	12	Hip strengthening	No exercise	.61(.15, 1.07)	Favors hip strengthening	Unclear	Moderate
Bennell (2010)	Number of steps	76	Yes	12	Hip strengthening	No exercise	.48(.03, .94)	Favors HS	Unclear	Moderate
Jan (2008)	Stair climb	64	Unclear	8	Low resistance exercise	No exercise	-.03(-.52, .46)	No	Unclear	Moderate
Jan (2008)	Stair climb	64	Unclear	8	High resistance exercise	No exercise	-.09(-.59, .40)	No	Unclear	Moderate

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Huang (2003)	Walk speed m/minute	64	Yes	8	Isotonic strength training	Control	4.21 (3.31, 5.11)	Favors isotonic strength training	Unclear	Moderate
Huang (2003)	Walk speed m/minute	64	Yes	52	Isometric	Control	1.93 (1.33, 2.53)	Favors isometric strength training	Unclear	Moderate
Huang (2003)	Lequesne index	64	Yes	8	Isotonic	Control	-1.32 (-1.86, -0.77)	Favors isotonic strength training	Unclear	Moderate
Huang (2003)	Lequesne index	64	Yes	52	Isometric	Control	-1.38 (-1.93, -0.83)	Favors isometric strength training	Unclear	Moderate
Jan (2008)	Figure 8 walk time	64	Yes	8	Low resistance training	No Exercise	-0.63 (-1.13, -0.12)	Favors LRT	Unclear	Moderate
Jan (2008)	Figure 8 walk time	64	Yes	8	High resistance training	No exercise	-0.71 (-1.21, -0.20)	Favors HRT	Unclear	Moderate
Jan (2008)	Level ground walk time	64	Unclear	8	Low resistance training	No exercise	-0.15 (-0.65, 0.34)	No	Unclear	Moderate
Jan (2008)	Level ground walk time	64	Unclear	8	High resistance training	No exercise	-0.09 (-0.59, 0.40)	No	Unclear	Moderate
Jan (2008)	Spongy surface walk time	64	Yes	8	Low resistance training	No exercise	-0.60 (-1.10, -0.09)	Favors LRT	Unclear	Moderate

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Jan (2008)	Spongy surface walk time	64	Yes	8	High resistance training	No exercise	-0.70 (-1.21, - 0.19)	Favors HRT	Unclear	Moderate
Lin (2009)	Level ground walk time	72	Yes	8	Strength training	No exercise	-0.54 (-1.01, - 0.07)	Favors ST	Unclear	High
Lin (2009)	Stair walk time	72	Yes	8	Strength training	No exercise	-1.30 (-1.81, - 0.78)	Favors ST	Unclear	High
Lin (2009)	Spongy surface walk time	72	Yes	8	Strength training	No exercise	-0.93 (-1.42, - 0.44)	Favors ST	Unclear	High
Bennell (2010)	WOMAC Function	76	Yes	12	Hip strengthening	No exercise	0.86 (0.39, 1.33)	Favors HS	Clinically important	Moderate

Table 42. Strengthening Versus Control: WOMAC Total

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Azad (2011)	WOMAC Total	68	Yes	4	Quadriceps muscle strengthening plus NSAIDS	NSAIDS only	-0.37 (-0.76, 0.01)	No	Unclear	Moderate
Azad (2011)	WOMAC Total	68	Yes	5	Quadriceps muscle strengthening plus NSAIDS	NSAIDS only	-0.59 (-0.98, -0.20)	Favors quadriceps muscle strengthening plus NSAIDS	Unclear	Moderate
Azad (2011)	WOMAC Total	68	Yes	6	Quadriceps muscle strengthening plus NSAIDS	NSAIDS only	-0.77 (-1.17, -0.38)	Favors quadriceps muscle strengthening plus NSAIDS	Unclear	Moderate
Maurer (1999)	WOMAC Total	98	Unclear	8	Isokinetic quadriceps exercise	Education	Mean Difference=3(p>.05)	NS	Unclear	Moderate
Shakoor (2010)	WOMAC Total	139	Yes	4 weeks	Isometric strengthening plus NSAIDS	NSAIDS only	-0.44 (-0.78, -0.11)	Favors exercise plus NSAIDS	Possibly clinically important	Moderate
Shakoor (2010)	WOMAC Total	139	Yes	5 weeks	Isometric strengthening plus NSAIDS	NSAIDS only	-0.59 (-0.93, -0.25)	Favors exercise plus NSAIDS	Possibly clinically important	Moderate
Shakoor (2010)	WOMAC Total	139	Yes	6 weeks	Isometric strengthening plus NSAIDS	NSAIDS only	-0.74 (-1.09, -0.4)	Favors exercise plus NSAIDS	Clinically significant	Moderate

Table 43. High Versus Low Resistance Training: Function

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Jan (2008)	Stair climb	68	Unclear	8	High resistance exercise	Low resistance exercise	-.16(-.64, .31)	No	Unclear	Moderate
Jan (2008)	Figure 8 walk time	68	Unclear	8	High resistance training	Low resistance training	-0.40 (-0.88, 0.08)	No	Unclear	Moderate
Jan (2008)	Level ground walk time	68	Unclear	8	High resistance training	Low resistance training	0.30 (-0.17, 0.78)	No	Unclear	Moderate
Jan (2008)	Spongy surface walk time	68	Yes	8	High resistance training	Low resistance training	-0.49 (-0.97, -0.01)	Favors HRT	Unclear	Moderate

Table 44. Resistance Strength Training Versus Health Education

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Ettinger (1997)	Time to get in and out of car	259	Yes	18	Resistance exercise	Health education	-.55(-.80, -.31)	Favors resistance exercise	Unclear	Moderate
Ettinger (1997)	Lift and carry task	259	Yes	18	Resistance exercise	Health education	-.51(-.75, -.26)	Favors resistance exercise	Unclear	Moderate

Study	Outcome	N	Powered for MCH	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Ettinger (1997)	6 minute walk distance	259	Yes	18	Resistance exercise	Health Education	.87(.61, 1.12)	Favors resistance exercise	Unclear	Moderate

Table 45. Physical Therapy Versus Control: Pain Measures

Study	Outcome	N	Powered for MCH	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Fransen (2007)	WOMAC Pain improvement	126	Yes	8	Physical therapy	Waitlist control	3.04 (2.51, 3.57)	Favors physical therapy	Clinically important	Moderate
Bennell (2005)	VAS Pain on movement	140	Yes	12 weeks	Physiotherapy	No treatment	-0.1 (-0.43, 0.23)	NS	Inconclusive	High
Bennell (2005)	VAS Pain on movement	140	Yes	24 weeks	Physiotherapy	No treatment	-0.21 (-0.54, 0.12)	NS	Inconclusive	High
Bennell (2005)	WOMAC Pain	140	Yes	12 weeks	Physiotherapy	No treatment	0.03 (-0.3, 0.37)	NS	True negative	High
Bennell (2005)	WOMAC Pain	140	Yes	24 weeks	Physiotherapy	No treatment	-0.12 (-0.45, 0.21)	NS	Inconclusive	High
Bennell (2005)	Knee pain scale severity	140	Unclear	12 weeks	Physiotherapy	No treatment	-0.08 (-0.41, 0.25)	NS	Unclear	High
Bennell (2005)	Knee pain scale severity	140	Unclear	24 weeks	Physiotherapy	No treatment	-0.24 (-0.57, 0.09)	NS	Unclear	High

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bennell (2005)	Knee pain scale frequency	140	Yes	12 weeks	Physiotherapy	Placebo	-1.42 (-1.79, -1.05)	Favors physiotherapy	Unclear	High
Bennell (2005)	Knee pain scale frequency	140	Yes	24 weeks	Physiotherapy	Placebo	-0.79 (-1.13, -0.44)	Favors physiotherapy	Unclear	High

Table 46. Physical Therapy Versus Control: Functional Measures

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Fransen (2007)	SF-36 Mental Function	126	Unclear	8	Physical therapy	Waitlist control	1.13 (0.74, 1.53)	Favors physical therapy	Unclear	Moderate
Bennell (2005)	SF-36 Physical Role	140	Unclear	12 weeks	Physiotherapy	No treatment	-0.03 (-0.36, 0.3)	NS	Unclear	High
Bennell (2005)	SF-36 Physical Role	140	Unclear	24 weeks	Physiotherapy	No treatment	0.04 (-0.29, 0.37)	NS	Unclear	High

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bennell (2005)	Assessment of Quality of Life index	140	Unclear	12 weeks	Physiotherapy	No treatment	0.09 (-0.24, 0.42)	NS	Unclear	High
Bennell (2005)	Assessment of Quality of Life index	140	Yes	24 weeks	Physiotherapy	Placebo	0.45 (0.12, 0.79)	Favors physiotherapy	Unclear	High
Bennell (2005)	Step test (number of steps) improvement	140	Unclear	12 weeks	Physiotherapy	No treatment	0.04 (-0.29, 0.37)	NS	Unclear	High
Bennell (2005)	Step test (number of steps) improvement	140	Unclear	24 weeks	Physiotherapy	No treatment	0.1 (-0.23, 0.44)	NS	Unclear	High
Bennell (2005)	WOMAC Function	140	Yes	12 weeks	Physiotherapy	No treatment	0.06 (-0.27, 0.39)	NS	True negative	High
Bennell (2005)	WOMAC Function	140	Yes	24 weeks	Physiotherapy	No treatment	-0.07 (-0.4, 0.26)	NS	Inconclusive	High
Fransen (2007)	SF-36 Physical	126	Yes	8	Physical therapy	Waitlist control	0.80 (0.42, 1.19)	Favors physical therapy	Clinically important	Moderate
Fransen (2007)	WOMAC Function improvement	126	Yes	8	Physical therapy	Waitlist control	1.01 (0.62, 1.40)	Favors physical therapy	Clinically important	Moderate
Borjesson (1996)	Steps/second	68	Unclear	5	Physiotherapy	No treatment	-0.08 (-0.55, 0.40)	No	Unclear	Low

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Borjesson (1996)	Stride length	68	Unclear	5	Physiotherapy	No treatment	0.06 (-0.41, 0.54)	No	Unclear	Low
Borjesson (1996)	Meters walked per minute	68	Unclear	5	Physiotherapy	No treatment	-0.11 (-0.59, 0.36)	No	Unclear	Low

Table 47. Exercise Plus Manual Physical Therapy Versus Non-Therapeutic Intensity Ultrasound

Study	Outcome	N	Powered for MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Deyle (2000)	WOMAC Total	69	Yes	8	Exercise plus manual physical therapy	Placebo (non-therapeutic intensity ultrasound)	-0.83 (-1.33, -0.34)	Favors exercise plus PT	Possibly clinically significant	Moderate
Deyle (2000)	6 minute walk distance (m)	70	Yes	4	Exercise plus manual physical therapy	Placebo (non-therapeutic intensity ultrasound)	0.65 (0.16, 1.13)	Favors exercise plus PT	Unclear	Moderate
Deyle (2000)	6 minute walk distance (m)	71	Yes	8	Exercise manual physical therapy	Placebo (non-therapeutic intensity ultrasound)	0.61 (0.13, 1.09)	Favors exercise plus PT	Unclear	Moderate

Table 48. Proprioceptive Training Versus Control: Pain Measures

Study	Outcome	N	Powered for MCH	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Lin (2009)	WOMAC Pain	72	Yes	8	Proprioceptive training	No exercise	-1.02 (-1.52, -0.53)	Favors proprioceptive training	Clinically important	High

Table 49. Proprioceptive Training Versus No Exercise: Function

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Lin (2009)	Walk time-level ground	72	Yes	8	Proprioceptive training	No exercise	-0.55 (-1.02, -0.08)	Favors PrT	Unclear	High
Lin (2009)	WOMAC Function	72	Yes	8	Proprioceptive training	No exercise	-0.95 (-1.44, -0.46)	Favors PrT	Clinically important	High
Lin (2009)	Spongy surface walk time	72	Yes	8	Proprioceptive training(PrT)	No exercise	-1.57 (-2.11, -1.04)	Favors PrT	Unclear	High
Lin (2009)	Stair climb walk time	72	Yes	8	Proprioceptive training(PrT)	No exercise	-1.29 (-1.80, -0.78)	Favors PrT	Unclear	High

Table 50. Agility and Perturbation Training Plus Usual Exercise Versus Exercise Only (Fitzgerald 2011)

Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	Sig	Clinical Importance	Strength of Evidence
WOMAC Total	183	Yes	52	Agility plus perturbation	Exercise only	-0.02 (-	No	True	High

						0.31, 0.27)		negative	
WOMAC Function	183	Yes	52	Agility plus perturbation	Exercise only	-0.26 (-0.55, 0.03)	No	True negative	High
Knee pain (numerical rating scale)	183	Unclear	52	Agility plus perturbation	Exercise only	0.11 (-0.18, 0.40)	No	True negative	High
Global rating of change	183	Unclear	52	Agility plus perturbation	Exercise only	0.00 (-0.29, 0.29)	No	True negative	High
Get up and go test	183	Unclear	52	Agility plus perturbation	Exercise only	0.26 (-0.03, 0.55)	No	True negative	High

Table 51. Agility and Perturbation Training Plus Usual Exercise Versus Exercise Only: Odds of Improvement From Baseline for WOMAC Functional Tasks (Teixeira 2011)

Outcome	N	Sufficient Power	Week	Group 1	Group 2	Odds Ratio	Sig	Clinical Importance	Strength of Evidence
When down the stairs?	91	Unclear	8	Agility plus perturbation	Exercise only	1.25 (0.55 ,2.87)	No	Unclear	Low
When going up stairs?	91	Unclear	8	Agility plus perturbation	Exercise only	1.25 (0.55 ,2.87)	No	Unclear	Low
Getting up from sitting position	91	Unclear	8	Agility plus perturbation	Exercise only	0.98 (0.44 ,2.16)	No	Unclear	Low
While standing?	91	Unclear	8	Agility plus perturbation	Exercise only	1.7 (0.70 ,4.09)	No	Unclear	Low
While bending to the floor?	91	Unclear	8	Agility plus perturbation	Exercise only	2.57 (1.2 ,5.52)	Favors agility plus perturbation	Unclear	Low
When walking on a flat surface?	91	Unclear	8	Agility plus perturbation	Exercise only	1.57 (0.71 ,3.50)	No	Unclear	Low

Outcome	N	Sufficient Power	Week	Group 1	Group 2	Odds Ratio	Sig	Clinical Importance	Strength of Evidence
While getting in/out of car?	91	Unclear	8	Agility plus perturbation	Exercise only	0.89 (0.41 ,1.96)	No	Unclear	Low
While going shopping?	91	Unclear	8	Agility plus perturbation	Exercise only	1.56 (0.73 ,3.35)	No	Unclear	Low
When putting on socks/stockings?	91	Unclear	8	Agility plus perturbation	Exercise only	1.02 (0.42 ,2.46)	No	Unclear	Low
While getting out of bed?	91	Unclear	8	Agility plus perturbation	Exercise only	1.25 (0.58 ,2.68)	No	Unclear	Low
When taking off socks/stockings?	91	Unclear	8	Agility plus perturbation	Exercise only	0.81 (0.36 ,1.84)	No	Unclear	Low
While lying in bed?	91	Unclear	8	Agility plus perturbation	Exercise only	1.14 (0.48 ,2.72)	No	Unclear	Low
When getting in/out of bath?	91	Unclear	8	Agility plus perturbation	Exercise only	0.79 (0.36 ,1.70)	No	Unclear	Low
While sitting?	91	Unclear	8	Agility plus perturbation	Exercise only	1.33 (0.64 ,2.77)	No	Unclear	Low
When getting on/off toilet?	91	Unclear	8	Agility plus perturbation	Exercise only	1.37 (0.60 ,3.1)	No	Unclear	Low
While doing heavy household chores	91	Unclear	8	Agility plus perturbation	Exercise only	1.52 (0.64 ,3.6)	No	Unclear	Low
While doing light household chores?	91	Unclear	8	Agility plus perturbation	Exercise only	1.23 (0.54 ,2.82)	No	Unclear	Low

Table 52. Kinesthesia Plus Strength Training Versus Strength Training: Function

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Diracoglu (2005)	SF-36 Physical	126	Yes	8	Kinesthesia (K) plus balance (B) plus strengthening (S)	Strengthening exercises	0.75 (0.22, 1.27)	Favors K plus B plus S	Clinically important	Moderate
Diracoglu (2005)	SF-36 Role Limitations	126	Unclear	8	Kinesthesia plus balance plus strengthening	Strengthening exercises	0.50 (-0.02, 1.01)	No	Unclear	Moderate
Diracoglu (2005)	SF-36 Vitality	126	Yes	8	Kinesthesia plus balance plus strengthening	Strengthening exercises	0.55 (0.03, 1.06)	Favors K plus B plus S	Unclear	Moderate
Diracoglu (2005)	10m walk	126	Yes	8	Kinesthesia plus balance plus strengthening	Strengthening exercises	-0.56 (-1.07, -0.04)	Favors K plus B plus S	Unclear	Moderate

Table 53. Weight Bearing and Non-Weight Bearing Exercise

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Jan (2009)	WOMAC Function	71	Yes	8 weeks	Weight bearing exercise	Control	-1.16 (-1.66, -0.65)	Favors weight bearing exercise	Clinically significant	Moderate
Jan (2009)	Level ground walking time(s)	71	Yes	8 weeks	Weight bearing exercise	Control	-0.59 (-1.07, -0.11)	Favors weight bearing exercise	Unclear	Moderate
Jan (2009)	Stair climb time	71	Yes	8 weeks	Weight bearing exercise	Control	-1.01 (-1.5, -0.51)	Favors weight bearing exercise	Unclear	Moderate
Jan (2009)	Figure 8 walking time	71	Yes	8 weeks	Weight bearing exercise	Control	-0.97 (-1.46, -0.47)	Favors weight bearing exercise	Unclear	Moderate
Jan (2009)	Sponge walk time	71	Yes	8 weeks	Weight bearing exercise	Control	-1.76 (-2.31, -1.21)	Favors weight bearing exercise	Unclear	Moderate
Jan (2009)	WOMAC Function	70	Yes	8 weeks	Non-weight bearing exercise	Control	-1.33 (-1.85, -0.81)	Favors non-weight bearing exercise	Clinically significant	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Jan (2009)	Level ground walking time(s)	70	Yes	8 weeks	Non-weight bearing exercise	Control	-0.85 (-1.34, -0.36)	Favors non-weight bearing exercise	Unclear	Moderate
Jan (2009)	Stair climb time	70	Yes	8 weeks	Non-weight bearing exercise	Control	-1.49 (-2.03, -0.96)	Favors non-weight bearing exercise	Unclear	Moderate
Jan (2009)	Figure-8 walking time	70	Yes	8 weeks	Non-weight bearing exercise	Control	-0.48 (-0.96, -0.01)	Favors non-weight bearing exercise	Unclear	Moderate
Jan (2009)	Sponge walk time	70	Yes	8 weeks	Non-weight bearing exercise	Control	-0.61 (-1.09, -0.13)	Favors non-weight bearing exercise	Unclear	Moderate
Jan (2009)	Level ground walking time(s)	71	Unclear	8 weeks	Weight bearing exercise	Non-weight bearing exercise	0.24 (-0.23, 0.7)	NS	Unclear	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Jan (2009)	Stair climb time	71	Yes	8 weeks	Weight bearing exercise	Non-weight bearing exercise	0.58 (0.11, 1.06)	Favors non-weight bearing exercise	Unclear	Moderate
Jan (2009)	Figure 8 walking time	71	Unclear	8 weeks	Weight bearing exercise	Non-weight bearing exercise	-0.44 (-0.91, 0.04)	NS	Unclear	Moderate
Jan (2009)	Sponge walk time	71	Yes	8 weeks	Weight bearing exercise	Non-weight bearing exercise	-1.06 (-1.55, -0.56)	Favors weight bearing exercise	Unclear	Moderate

Table 54. Water Versus Land-Based Exercise: Pain

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Silva (2008)	VAS Pain	64	Yes	18	Water exercise	Land exercise	-0.41 (-0.91, 0.08)	No	Negative	Moderate
Silva (2008)	VAS Pain after 50 foot walk	64	Yes	9	Water exercise	Land exercise	-0.19 (-0.68, 0.30)	No	Negative	Moderate

Study	Outcome	N	Power to Detect MCH	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Silva (2008)	VAS Pain after 50 foot walk	64	Yes	18	Water exercise	Land exercise	-0.68 (-1.19, -0.18)	Favors water exercise	Not clinically important	Moderate
Silva (2008)	VAS Pain before 50 foot walk	64	Yes	9	Water exercise	Land exercise	-0.19 (-0.68, 0.30)	No	Negative	Moderate
Silva (2008)	VAS Pain before 50 foot walk	64	Yes	18	Water exercise	Land exercise	-0.53 (-1.03, -0.03)	Favors water exercise	Not clinically important	Moderate

Table 55. Water Versus Land-Based Exercise: Lequesne Index

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Silva (2008)	Lequesne index	64	Unclear	18	Water exercise	Land exercise	-0.39 (-0.89, 0.10)	No	Unclear	Moderate

Table 56. Home-Based and Hospital-Based Exercise Programs

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
O'Reilly (1999)	Global Pain Score	180	Yes	26	Home exercise	No intervention	-0.54 (-0.84, -0.24)	Favors home exercise	Not clinically important	High
O'Reilly (1999)	VAS Walking	180	Yes	26	Home exercise	No intervention	-0.33 (-0.63, 0.03)	Favors home exercise	Not clinically important	High
O'Reilly (1999)	VAS Stairs	180	Yes	26	Home exercise	No intervention	-0.35 (-0.63, 0.05)	Favors home exercise	Not clinically important	High
O'Reilly (1999)	WOMAC Physical function	180	Yes	26	Home exercise	No intervention	-0.4 (-0.7, -.10)	Favors home exercise	Possibly clinically important	High
O'Reilly (1999)	Mental health	180	Unclear	26	Home exercise	No intervention	0.18 (-0.11, 0.48)	NS	Unclear	High
O'Reilly (1999)	Energy	180	Unclear	26	Home exercise	No intervention	0.11 (-0.19, 0.41)	NS	Unclear	High
O'Reilly (1999)	Health perception	180	Unclear	26	Home exercise	No intervention	0.19 (-0.11, 0.48)	NS	Unclear	High
O'Reilly (1999)	Role limitation physical	180	Unclear	26	Home exercise	No intervention	0.28 (-0.02, 0.58)	NS	Unclear	High
O'Reilly (1999)	Role limitation emotional	180	Unclear	26	Home exercise	No intervention	0.03 (-0.27, 0.32)	NS	Unclear	High

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
O'Reilly (1999)	Social functioning	180	Unclear	26	Home exercise	No intervention	0 (-0.3, 0.3)	NS	Unclear	High
McCarthy (2004)	WOMAC Pain	151	Yes	52	Home-based exercise alone	Home-based plus class based exercise	0.42 (0.09, 0.74)	Favors home-based and class based programs	Possibly clinically important	High
McCarthy (2004)	WOMAC Stiffness	151	Yes	26	Home-based exercise alone	Home-based plus class based exercise	0.40 (0.08, 0.73)	Favors home-based and class based programs	Possibly clinically important	High
McCarthy (2004)	WOMAC Stiffness	151	Yes	52	Home-based exercise alone	Home-based plus class based exercise	0.39 (0.07, 0.71)	Favors home-based and class based programs	Possibly clinically important	High
McCarthy (2004)	VAS Pain	151	Yes	26	Home-based exercise alone	Home-based plus class based exercise	0.58 (0.25, 0.91)	Favors home-based and class based programs	Not clinically important	High
McCarthy (2004)	VAS Pain	151	Yes	52	Home based exercise alone	Home-based plus class based exercise	0.78 (0.45, 1.11)	Favors home-based and class based programs	Not clinically important	High
McCarthy (2004)	WOMAC Pain	151	Yes	26	Home-based exercise alone	Home-based plus class based exercise	0.29 (-0.03, 0.61)	NS	True negative	High

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Tunay (2010)	Left knee VAS Rest	60	Yes	6	Hospital-based proprioceptive and strength exercise	Home-based proprioceptive and strength exercise	0.07 (-0.44, 0.57)	NS	True negative	Moderate
Tunay (2010)	Left knee VAS Activity	60	Yes	6	Hospital-based proprioceptive and strength exercise	Home-based proprioceptive and strength exercise	-0.65 (-1.17, -0.13)	Favors hospital-based proprioceptive and strength exercise	Not clinically important	Moderate
Tunay (2010)	Left knee VAS Night	60	Yes	6	Hospital-based proprioceptive and strength exercise	Home-based proprioceptive and strength exercise	-0.3 (-0.81, 0.21)	NS	True negative	Moderate
Tunay (2010)	Right knee VAS Rest	60	Yes	6	Hospital-based proprioceptive and strength exercise	Home-based proprioceptive and strength exercise	-0.24 (-0.75, 0.27)	NS	True negative	Moderate
Tunay (2010)	Right knee VAS Activity	60	Yes	6	Hospital-based proprioceptive and strength exercise	Home-based proprioceptive and strength exercise	-0.46 (-0.98, 0.05)	NS	True negative	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Tunay (2010)	Right knee VAS Night	60	Yes	6	Hospital-based proprioceptive and strength exercise	Home-based proprioceptive and strength exercise	0.19 (-0.32, 0.69)	NS	True negative	Moderate

Table 57. Aerobic Exercise Versus Control: Function

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Rejeski (2003)	SF-36 Mental Health	69	Unclear	78	Aerobic exercise	Healthy life style education control	0.08 (-0.26, 0.41)	No	Unclear	Low

Table 58. Aerobic Exercise Versus Control: Functional Task

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Ettinger (1997)	Lift and carry task time(s)	265	Yes	18	Aerobic exercise	Education	-0.38 (-0.63, -0.14)	Favors aerobic exercise	Unclear	Moderate
Ettinger (1997)	Stair climb	265	Unclear	18	Aerobic exercise	Education	-0.15 (-0.39, 0.09)	No	Unclear	Moderate
Ettinger (1997)	Time to get in and out of car	265	Yes	18	Aerobic exercise	Education	-0.46 (-0.71, -0.22)	Favors aerobic exercise	Unclear	Moderate
Ettinger (1997)	Walk distance	265	Yes	18	Aerobic exercise	Education	0.30 (0.06, 0.54)	Favors aerobic exercise	Unclear	Moderate
Focht (2005)	Stair climb time	80	Unclear	78	Aerobic exercise	Health education	-0.14 (-0.45, 0.17)	No	Unclear	Low

Table 59. Supervised Walking Versus Usual Care: Pain

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kovar (1992)	AIMS Arthritis Pain	92	Yes	8	Supervised walking plus	Usual care	-0.51 (-0.93, -0.10)	Favors walking	Unclear	Moderate

					education					

Table 60. Supervised Walking Versus Usual Care: Function

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kovar (1992)	AIMS Physical Activity	92	Yes	8	Supervised walking plus education	Usual care	-0.88 (-1.30, -0.45)	Favors walking	Unclear	Moderate
Kovar (1992)	AIMS Arthritis Impact	92	Unclear	8	Supervised walking plus education	Usual care	-0.10 (-0.51, 0.30)	No	Unclear	Moderate
Kovar (1992)	6 minute Walk Distance	92	Yes	8	Supervised walking plus education	Usual care	0.91 (0.48, 1.34)	Favors supervised walking	Unclear	Moderate

Table 61. Supervised Walking Versus Control: Arthritis Impact Measurement Scale (Medications Use)

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kovar (1992)	AIMS Medications Use	92	Unclear	8	Supervised walking plus education	Usual care	0.37 (-0.04, 0.79)	No	Unclear	Low

Table 62. Self-Management Versus Waitlist Control

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD/Mean difference	Sig	Clinical Importance	Strength of Evidence
Coleman (2012)	WOMAC Pain	139	Yes	8	Class-based self-management program	Weight list control	-1.46 (-2.18, -.73)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	WOMAC Pain	136	Yes	26	Class-based self-management program	Weight list control	-.49(-1.26, .28)	No	True negative	High
Coleman (2012)	WOMAC Stiffness	139	Yes	8	Class-based self-management program	Weight list control	-.5(-.91, -.08)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	WOMAC Stiffness	136	Yes	26	Class-based self-management program	Weight list control	-.29(-.73, .15)	No	Inconclusive	High
Coleman (2012)	WOMAC Function	139	Yes	8	Class-based self-management program	Weight list control	-5.55(-7.38, -3.31)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	WOMAC Function	136	Yes	26	Class-based self-management program	Weight list control	-4.35(-6.2, -.91)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	WOMAC Total	139	Yes	8	Class-based self-management program	Weight list control	-7.73(-9.98, -4.49)	Favors self-management	Possibly clinically significant	High

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD/Mean difference	Sig	Clinical Importance	Strength of Evidence
Coleman (2012)	WOMAC Total	136	Yes	26	Class-based self-management program	Weight list control	-4.08(-7.47, -.68)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	SF-36 Physical Function	136	Yes	26	Class-based self-management program	Weight list control	5.67 (0.40, 10.93)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	SF-36 Role Physical	136	Unclear	26	Class-based self-management program	Weight list control	7.37 (-5.93, 20.67)	No	Unclear	High
Coleman (2012)	SF-36 Body Pain	136	Yes	26	Class-based self-management program	Weight list control	6.06 (0.04, 12.07)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	SF-36 General Health	136	Unclear	26	Class-based self-management program	Weight list control	3.59 (-1.19, 8.37)	No	Unclear	High
Coleman (2012)	SF-36 Vitality	136	Unclear	26	Class-based self-management program	Weight list control	4.72 (-0.11, 9.55)	No	Unclear	High
Coleman (2012)	SF-36 Social Function	136	Unclear	26	Class-based self-management program	Weight list control	4.07(-2.08, 12.22)	No	Unclear	High

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD/Mean difference	Sig	Clinical Importance	Strength of Evidence
Coleman (2012)	SF-36 Role Emotional	136	Unclear	26	Class-based self-management program	Weight list control	1.35 (-11.06, 13.76)	No	Unclear	High
Coleman (2012)	SF-36 Mental Health	136	Unclear	26	Class-based self-management program	Weight list control	3.85 (-0.21, 7.91)	No	Unclear	High
Coleman (2012)	SF-36 Physical Function	139	Yes	8	Class-based self-management program	Weight list control	5.61 (1.84, 9.37)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	SF-36 Role Physical	139	Yes	8	Class-based self-management program	Weight list control	17.06 (5.90, 28.21)	Favors self-management	Unclear	High
Coleman (2012)	SF-36 Body Pain	139	Yes	8	Class-based self-management program	Weight list control	7.19 (1.93, 12.44)	Favors self-management	Possibly clinically significant	High
Coleman (2012)	SF-36 General Health	139	Unclear	8	Class-based self-management program	Weight list control	2.11 (-1.45, 5.67)	No	Unclear	High
Coleman (2012)	SF-36 Vitality	139	Yes	8	Class-based self-management program	Weight list control	6.02 (1.87, 10.16)	Favors self-management	Unclear	High

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD/Mean difference	Sig	Clinical Importance	Strength of Evidence
Coleman (2012)	SF-36 Social Function	139	Yes	8	Class-based self-management program	Weight list control	10.72 (4.81, 16.62)	Favors self-management	Unclear	High
Coleman (2012)	SF-36 Role Emotional	139	Unclear	8	Class-based self-management program	Weight list control	5.18 (-5.64, 16.00)	No	Unclear	High
Allen (2010)	AIMS2 Pain	344	Yes	52	Telephone-based self-management program	Attention control	-.6 p=.007	Favors telephone-based self-management	Unclear	Modereate
Allen (2010)	AIMS2 Function	344	Unclear	52	Telephone-based self-management program	Attention control	-.2 p=.093	No	Unclear	Modereate
Allen (2010)	AIMS2 walking and bending	344	Yes	52	Telephone-based self-management program	Attention control	-.5 p=.035	Favors telephone-based self-management	Unclear	Modereate
Allen (2010)	AIMS2 Mobility	344	Unclear	52	Telephone-based self-management program	Attention control	-.2 p=.21	No	Unclear	Modereate
Allen (2010)	AIMS2 Affect	344	Unclear	52	Telephone-based self-management program	Attention control	.1 p=.78	No	Unclear	Modereate

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD/Mean difference	Sig	Clinical Importance	Strength of Evidence
Allen (2010)	Arthritis Self-Efficacy Scale	344	Yes	52	Telephone-based self-management program	Attention control	.4 p=.043	Favors telephone-based self-management	Unclear	Modereate
Allen (2010)	VAS Pain	344	Yes	52	Telephone-based self-management program	Attention control	-10 p<.001	Favors telephone-based self-management	Unclear	Modereate
Allen (2010)	AIMS2 Pain	343	Unclear	52	Telephone-based self-management program	Usual care	-.4 p=.105	No	Unclear	Modereate
Allen (2010)	AIMS2 Function	343	Unclear	52	Telephone-based self-management program	Usual care	-.1 p=.43	No	Unclear	Modereate
Allen (2010)	AIMS2 walking and bending	343	Unclear	52	Telephone-based self-management program	Usual care	-.2 p=.41	No	Unclear	Modereate
Allen (2010)	AIMS2 Mobility	343	Unclear	52	Telephone-based self-management program	Usual care	-.0 p=.93	No	Unclear	Modereate
Allen (2010)	AIMS2 Affect	343	Unclear	52	Telephone-based self-management program	Usual care	.00 p=.79	No	Unclear	Modereate

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD/Mean difference	Sig	Clinical Importance	Strength of Evidence
Allen (2010)	Arthritis Self-Efficacy Scale	343	Unclear	52	Telephone-based self-management program	Usual care	.4 p=.066	No	Unclear	Modereate
Allen (2010)	VAS Pain	343	Yes	52	Telephone-based self-management program	Usual care	-11 p<.001	Favors telephone-based self-management	Unclear	Modereate

Table 63. Self-Management Plus Exercise Versus Usual Care: Pain

Study	Outcome	N	Powered to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Yip (2007)	Arthritis Self-Efficacy Pain Score improvement	176	Yes	16	Self-management plus exercise plus usual care	Usual care	0.54 (0.24, 0.84)	Favors self-management plus exercise plus usual care	Unclear	Moderate
Yip (2007)	VAS Pain improvement	176	Yes	16	Self-management plus exercise plus usual care	Usual care	0.62 (0.31, 0.92)	Favors self-management plus exercise plus usual care	Not clinically important	Moderate

Table 64. Self-Management Plus Exercise Versus Usual Care: Function

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Yip (2007)	Health Assessment Questionnaire improvement	176	Unclear	16	Self-management plus Exercise plus usual care	Usual care	0.12 (-0.17, 0.42)	No	Unclear	Moderate

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Yip (2007)	Arthritis Self-Efficacy other symptoms improvement	176	Yes	16	Self-management plus exercise plus usual care	Usual care	0.51 (0.21, 0.81)	Favors Self-management plus exercise plus usual care	Unclear	Moderate
Yip (2007)	Hours of light exercise improvement	176	Yes	16	Self-management plus exercise plus usual care	Usual care	0.57 (0.27, 0.87)	Favors Self-management plus exercise plus usual care	Unclear	Moderate

Table 65. Structured Consultation Versus Control: Function

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Ravaud (2009)	SF-12 Mental Function improvement	327	Unclear	16	Standardized structured physician consultation program (education)	Usual care	0.30 (0.08, 0.51)	Favors education	Unclear	Moderate

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Ravaud (2009)	SF-12 Physical Function improvement	327	Yes	16	Standardized structured physician consultation program (education)	Usual care	0.16 (-0.06, 0.38)	No	Inconclusive	Moderate
Ravaud (2009)	WOMAC Function improvement	327	Yes	16	Standardized structured physician consultation program (education)	Usual care	0.15 (-0.06, 0.37)	No	Inconclusive	Moderate

Table 66. Integrated Exercise, Self-Management, and Coping Strategies Versus Usual Care (Hurley 2007)

Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
WOMAC Function	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	-.29(-.52, -.07)	Favors Group 1	Possibly clinically important	Moderate
WOMAC Pain	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	-0.27 (-0.5, -0.05)	Favors Group 1	Possibly clinically important	Moderate
WOMAC Total	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	-0.28 (-0.5, -0.05)	Favors Group 1	Possibly clinically important	Moderate

Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Aggregate Functional Performance time(s)	342	Unclear	26	Integrated exercise, self-management and coping strategies	Usual care	-0.17 (-0.41,0.06)	No	Unclear	Moderate
Exercise Health Beliefs Self-Efficacy Subscale	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	0.41 (0.17,0.63)	Favors Group 1	Unclear	Moderate
Exercise Health Beliefs Total Score	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	0.51 (0.28,0.75)	Favors Group 1	Unclear	Moderate
Hospital Anxiety and Depression Scale Depression Subscale	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	-0.23 (-0.46,-0.01)	Favors Group 1	Unclear	Moderate

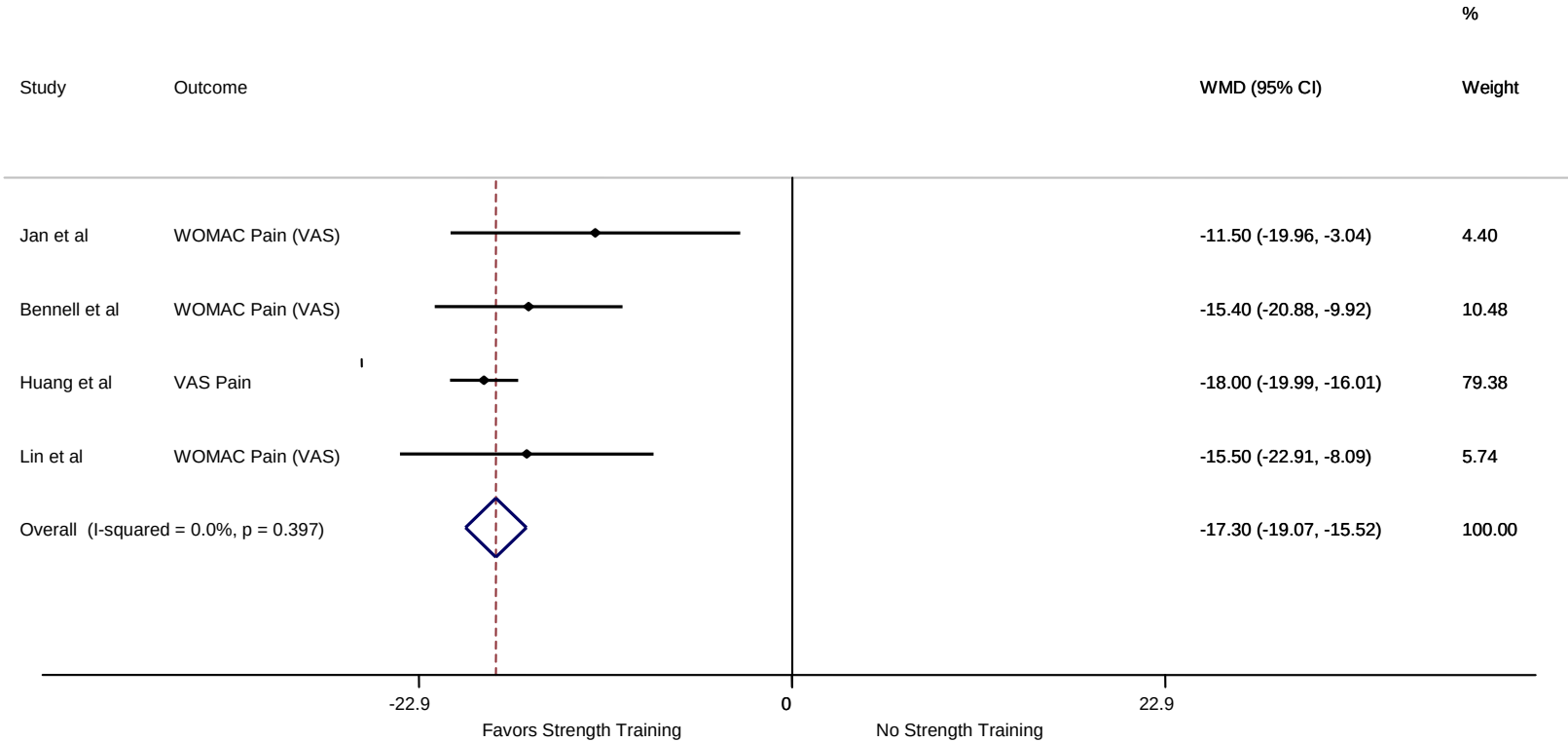
Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Hospital Anxiety and Depression Scale Anxiety Subscale	342	Unclear	26	Integrated exercise, self-management and coping strategies	Usual care	-0.16 (-0.38,0.07)	No	Unclear	Moderate
MACTAR	342	Yes	26	Integrated exercise, self-management and coping strategies	Usual care	0.27 (0.04,0.5)	Favors Group 1	Unclear	Moderate
EQ-5D	342	Unclear	26	Integrated exercise, self-management and coping strategies	Usual care	-0.09 (-0.39,0.21)	No	Unclear	Moderate

Table 67. Yoga Plus Physiotherapy Versus Physiotherapy Only (Ebenezer 2011)

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Ebnezar (2011)	Physical functioning	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	1.35 (1.06, 1.63)	Favors yoga plus physiotherapy	Clinically significant	Low
Ebnezar (2011)	Role limitations	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	0.84 (0.57, 1.1)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2011)	Emotional problems	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	0.91 (0.64, 1.18)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2011)	Energy/fatigue	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-2.59 (-2.94, -2.24)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2011)	Emotional well-being	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-3.14 (-3.53, -2.76)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2011)	Social function	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	0.71 (0.44, 0.97)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2011)	Pain	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	2.24 (1.91, 2.56)	Favors yoga plus physiotherapy	Clinically significant	Low

Ebnezar (2011)	General health	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	1 (0.73, 1.27)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2012)	Resting pain	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-1.678 (-1.976, -1.38)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2012)	Early morning stiffness	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-1.285 (-1.567, -1.004)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2010)	Walking pain	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-1.577 (-1.871, -1.284)	Favors yoga plus physiotherapy	Unclear	Low
Ebnezar (2010)	WOMAC Function	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-1.746 (-2.047, -1.444)	Favors yoga plus physiotherapy	Clinically significant	High
Ebnezar (2010)	Walking time	235	Yes	13	Yoga plus physiotherapy	Physiotherapy only	-1.553 (-1.846, -1.261)	Favors yoga plus physiotherapy	Unclear	High

Figure 12. Strength Training Versus Control: Pain



RECOMMENDATION 2

We suggest weight loss for patients with symptomatic osteoarthritis of the knee and a BMI ≥ 25 .

Strength of Recommendation: Moderate

Description: A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

RATIONALE

There was one moderate- and two low- strength studies included in this recommendation. Physical Function on the SF-36 showed minimum clinically important improvement in outcomes for this patient population. WOMAC function also showed statistical improvement which was possibly clinically significant. Diet and exercise combined revealed improved results. The workgroup considers that the public and patient health benefits of weight loss warranted an upgrade of the recommendation strength to moderate.⁵³⁻⁵⁵

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 68-Table 70](#), [Table 71-Table 74](#)

Two low quality studies^{46;47} compared exercise-based weight loss to health education. Neither had treatment integrity, group comparability or measurement flaws. However, they were flawed in their hypotheses were retrospective. Additionally, they were flawed in the group assignment, blinding, and investigator bias domains. Focht et al.⁴⁶ was the only aerobic exercise study that was sufficiently blinded.

There were three included studies that compared weight loss programs (diet and/or exercise) to health education controls. Two studies were of low quality^{46;47}, and the other was of moderate quality⁵⁶. The treatment integrity, group comparability and measurement domains were not flawed. The group assignment and investigator bias domains were. Rejeski et al.⁴⁷ and Focht et al.⁴⁶ were retrospective and therefore flawed in the hypothesis domain. Miller et al.⁵⁶ was the only study that was sufficiently blinded.

Three studies compared very low energy diets to conventional low energy diets. Bliddal et al.⁵⁷ and Riecke et al.⁵⁸ were low quality, and Christiansen et al.⁵⁹ was of moderate quality. The studies were not flawed in terms of treatment integrity and measurement, but flawed in the group assignment, group comparability and investigator bias domains. Additionally, Reicke et al. and Bliddal et al. did not contain prospective hypotheses and were flawed in the blinding domain.

Two included studies compared diet to exercise. Jenkinson et al.⁶⁰ was a high quality study that was appropriate in every quality domain except for investigator bias. The other

study⁴⁶ was not flawed in the treatment integrity and measurement domains. However, it was flawed in the hypothesis, group assignment, blinding, group comparability, and investigator bias domains and was given a low quality rating.

APPLICABILITY

Relevant Tables: [Table 68-Table 70](#), [Table 71-Table 74](#)

The participants and the administration of the interventions may not have been representative of clinical practice in the included exercise-based weight loss studies^{46;47}. Compliance and adherence were similar in both studies. Intent to treat analysis was used in both studies.

The three studies that compared weight loss to education likewise contained uncertainty as to whether the participants and the treatment interventions reflected typical clinical practice^{46;47;56}. Compliance and adherence were not representative in the Miller et al. study. The studies included all enrolled patients in their final analysis.

Compliance and adherence were representative of clinical practice in the studies that compared low energy diets to conventional diets. However, it was unclear if the treatment intervention was representative. Christiansen et al.⁵⁹ enrolled participants that might not have been representative of clinical practice, and did not include all enrolled patients in the final analysis.

The diet versus exercise studies had a non-representative application of the treatment intervention, and Focht et al.⁴⁶ included patients that might not have been similar to those seen in clinical practice. Compliance and adherence were representative of clinical practice in one of the studies, and both included all enrolled patients in their final analyses.

FINAL STRENGTH OF EVIDENCE

All studies in this recommendation were rated as having moderate applicability. Therefore, low quality studies were rated as low strength of evidence, and moderate quality studies were rated as moderate strength.

Table 68. Quality and Applicability Summary: Weight Loss Versus Education

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Miller et al. (2006)	WOMAC Function improvement	26	Moderate	Moderate	Moderate
Focht (2005)	6 minute walk distance(ft)	78	Low	Moderate	Low
Focht (2005)	6 minute walk distance(ft)	78	Low	Moderate	Low
Focht (2005)	Stair climb time(s)	78	Low	Moderate	Low

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Focht (2005)	Stair climb time(s)	78	Low	Moderate	Low
Miller et al. (2006)	WOMAC Pain improvement	26	Moderate	Moderate	Moderate
Miller et al. (2006)	WOMAC Total improvement	26	Moderate	Moderate	Moderate
Rejeski et al. (2002)	SF-36 Mental Function	26 and 78 week average	Low	Moderate	Low
Rejeski et al. (2002)	SF-36 Mental Function	26 and 78 week average	Low	Moderate	Low
Rejeski et al. (2002)	SF-36-Physical Function	26 and 78 week average	Low	Moderate	Low
Rejeski et al. (2002)	SF-36-Physical Function	26 and 78 week average	Low	Moderate	Low

Table 69. Quality and Applicability Summary: Low Energy Diet Versus Conventional Diet

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Christiansen (2005)	WOMAC Function improvement	8	Moderate	Moderate	Moderate
Bliddal (2011)	Health Assessment Questionnaire KOOS	52	Low	Moderate	Low
Riecke (2010)	Function in Daily Life improvement	16	Low	Moderate	Low
Riecke (2010)	KOOS Sports and Recreation improvement	16	Low	Moderate	Low
Riecke (2010)	SF-36 MCS improvement	16	Low	Moderate	Low
Riecke (2010)	SF-36 PCS improvement	16	Low	Moderate	Low
Riecke (2010)	VAS Disability improvement	16	Low	Moderate	Low
Riecke (2010)	VAS Global improvement	16	Low	Moderate	Low
Riecke (2010)	KOOS Pain improvement	16	Low	Moderate	Low
Riecke (2010)	VAS Pain improvement	16	Low	Moderate	Low
Riecke (2010)	KOOS Quality of Life improvement	16	Low	Moderate	Low

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Christiansen (2005)	WOMAC Total improvement	8	Moderate	Moderate	Moderate
Christiansen (2005)	Lequesne index improvement KOOS	8	Moderate	Moderate	Moderate
Riecke (2010)	Symptoms improvement	16	Low	Moderate	Low
Riecke (2010)	OARSI Responders	16	Low	Moderate	Low

Table 70. Quality and Applicability Summary: Diet Versus Exercise

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Focht (2005)	6 minute walk distance(ft)	78	Low	Moderate	Low
Focht (2005)	6 minute walk distance(ft)	78	Low	Moderate	Low
Focht (2005)	6 minute walk distance(ft)	78	Low	Moderate	Low
Focht (2005)	Stair climb time(s)	78	Low	Moderate	Low
Focht (2005)	Stair climb time(s)	78	Low	Moderate	Low
Focht (2005)	Stair climb time(s)	78	Low	Moderate	Low
Jenkinson et al. (2009)	WOMAC Pain 30% reduction	104	High	Moderate	High

RESULTS

Relevant Tables: [Figure 13-Figure 15](#), [Table 75-Table 79](#)

Focht et al.⁴⁶ and Rejeski et al.⁴⁷ used data from the arthritis, diet, and activity promotion trial (ADAPT) to evaluate exercise-based weight loss programs. When SF-36 Mental Health and timed stair climb scores were compared to a healthy lifestyle education control group, there were no statistically significant differences.

[Figure 13](#) contains a summary of results for studies comparing weight loss programs to health education controls. The weight loss programs consisted of dietary interventions alone, or a combination of exercise and diet. Six out of 11 outcomes were statistically significant in favor of the weight loss intervention. Pain and function were the critical outcomes for this recommendation. Three of five self-reported functional outcomes were statistically significant in favor of weight loss; two of which were clinically important, and one possibly clinically significant. The pain outcome was clinically significant in favor of the weight loss intervention.

Three out of 15 outcomes were statistically significant in favor of low energy versus conventional diets. WOMAC total was significantly improved in the low energy diet group, and two out of seven functional outcomes were higher. There were no significant differences in the pain or quality of life outcomes ([Figure 14](#)).

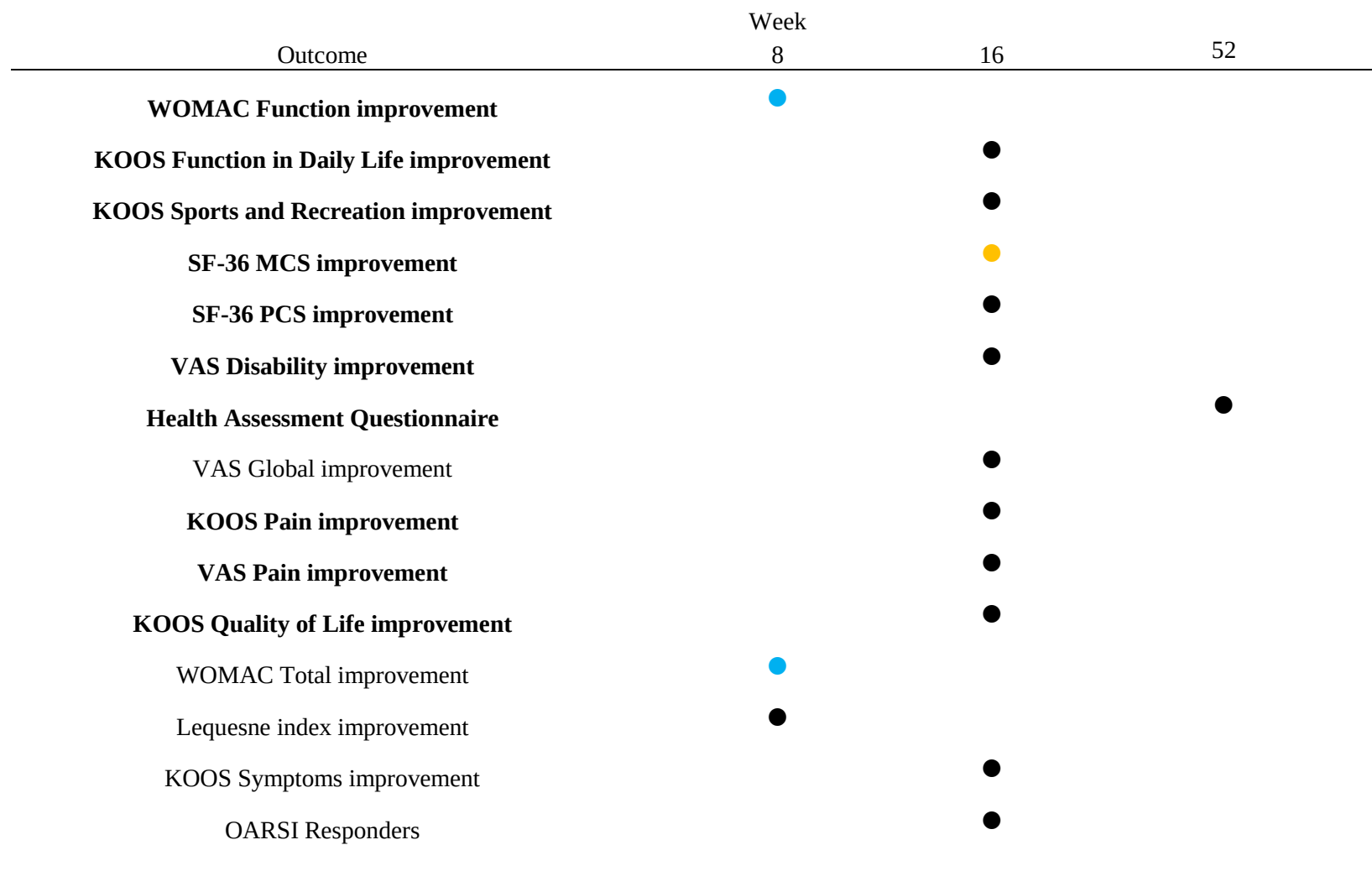
There were two studies that compared diet to exercise. Focht et al.⁴⁶ found that 6-minute walk distances were significantly longer in the exercise group than in the diet group. Furthermore, participants who received exercise and diet walked significantly lengthier distances than those treated with a diet intervention alone, but there was no significant difference compared to patients in the exercise-only group. Jenkinson et al.⁶⁰ found that the proportion of patients who achieved a 30% reduction in WOMAC pain did not differ significantly in the exercise group compared to the group receiving diet treatments.

Figure 13. Summary of Results: Diet, Exercise, and Weight Loss

		Week		
Outcome		26	Average of 26 and 78	78
Targeted Weight Loss Versus Education	WOMAC Total improvement	●		
	WOMAC Function improvement	●		
	WOMAC Pain improvement	●		
Diet Versus Health Education	SF-36 Mental Function		●	
	SF-36-Physical Function		●	
	6 minute walk distance(ft)			●
	Stair climb time(s)			●
Diet Plus Exercise Versus Health Education	SF-36 Mental Function		●	
	SF-36-Physical Function		●	
	6 minute walk distance(ft)			●
	Stair climb time(s)			●

Key: ●=Not Significant; ●=Statistically Significant; ●=Possibly Clinically Important; ● =Clinically Significant

Figure 14. Results Summary: Low Energy Diet Versus Conventional Diet



Key: ●=Not Significant; ●=Statistically Significant; ●=Possibly Clinically Important

Figure 15. Results Summary: Diet Versus Exercise

		Week	
		78	104
Exercise Versus Diet	6 minute walk distance(ft)	●	
	Stair climb time(s)	●	
Diet Plus Exercise Versus Diet Only	6 minute walk distance(ft)	●	
	Stair climb time(s)	●	
Diet Plus Exercise Versus Exercise Only	6 minute walk distance(ft)	●	
	Stair climb time(s)	●	
	30% WOMAC Pain improvement		●

Key: ●=Not Significant; ●= Statistically Significant in Favor of Exercise; ●= Statistically Significant in Favor of Diet Plus Exercise

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 71. Quality and Applicability: Exercise-Based Weight Loss Program Versus Health Education

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Rejeski (2002)	SF-36 Mental Health	78	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	Stair climb time	78	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate

Table 72. Quality and Applicability: Weight Loss Versus Education Programs

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Miller et al. (2006)	WOMAC Function improvement	26	●	●	○	●	●	●	●	○	Moderate	○	○	○	●	Moderate
Focht (2005)	6 minute walk distance(ft)	78	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	6 minute walk distance(ft)	78	○	●	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	Stair climb time(s)	72	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	Stair climb time(s)	72	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Miller et al. (2006)	WOMAC Pain improvement	26	●	●	○	●	●	●	●	○	Moderate	○	○	○	●	Moderate
Miller et al. (2006)	WOMAC Total improvement	26	●	●	○	●	●	●	●	○	Moderate	○	○	○	●	Moderate
Rejeski et al. (2002)	SF-36 Mental function	26 and 78 week average	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Rejeski et al. (2002)	SF-36 Mental Function	26 and 78 week average	○	◐	○	○	●	●	●	○	Low	○	○	●	●	Moderate
Rejeski et al. (2002)	SF-36 Physical Function	26 and 78 week average	○	●	○	○	●	●	●	○	Low	○	○	●	●	Moderate

Table 73. Quality and Applicability: Low Energy Diet Versus Control Diet

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Christiansen (2005)	WOMAC Function improvement	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Riecke (2010)	KOOS Function in Daily Life improvement	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	KOOS Sports and Recreation improvement	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	SF-36 MCS improvement	16	○	●	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	SF-36 PCS improvement	16	○	●	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	VAS Disability improvement	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	VAS Global improvement	16	○	●	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	KOOS Pain improvement	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Riecke (2010)	VAS Pain improvement	16	○	●	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	KOOS Quality of Life improvement	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Christiansen (2005)	WOMAC Total improvement	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Christiansen (2005)	Lequesne index improvement	8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Bliddal(2011)	Health Assessment Questionnaire		○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Riecke (2010)	KOOS Symptoms improvement	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate
Riecke (2010)	OARSI Responders	16	○	◐	○	○	○	●	●	○	Low	●	○	●	●	Moderate

Table 74. Quality and Applicability: Diet Versus Exercise

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Focht (2005)	6 minute walk distance(ft)	78	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	6 minute walk distance(ft)	78	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	6 minute walk distance(ft)	78	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	Stair climb time(s)	78	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	Stair climb time(s)	78	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Focht (2005)	Stair climb time(s)	78	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Jenkinson et al. (2009)	WOMAC Pain 30% reduction	104	●	◐	●	●	●	●	●	○	High	●	○	○	●	Moderate
Focht (2005)	6 minute walk distance(ft)	78	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

FINDINGS

Table 75. Weight Loss-Exercise Only Versus Control: Function

Study	Outcome	N	Sufficient Power	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Rejeski et al. (2003)	SF-36 Mental Health	69	Unclear	72	28+	Aerobic exercise	Healthy life style education control	0.08 (-0.26, 0.41)	No	N/A	Low

Table 76. Weight Loss-Exercise Only Versus Control: Functional Task

Study	Outcome	N	Sufficient Power	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Focht (2005)	Stair climb time	80	Unclear	72	28+	Aerobic exercise	Health education	-0.14 (-0.45, 0.17)	No	N/A	Low

Table 77. Dietary Weight Loss (With and Without Exercise) Versus Education Control

Outcome Type	Study	Outcome	N	Powered	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Function	Miller et al. (2006)	WOMAC Function	74	Yes	26	30+	Weight loss program	Weight stable education	-0.65 (-1.11, -0.18)	Favors diet plus weight loss	Possibly clinically significant	Moderate
	Rejeski et al. (2002)	SF-36 Mental Function	141	Unclear	26 and 78 averaged	28+	Diet	Monthly health education session	0.07 (-0.26, 0.40)	No	N/A	Low
	Rejeski et al. (2002)	SF-36 Mental Function	136	Unclear	26 and 78 averaged	28+	Diet plus exercise	Monthly health education session	0.11 (-0.23, 0.45)	No	N/A	Low
	Rejeski et al. (2002)	SF-36-Physical Function	141	Yes	26 and 78 averaged	28+	Diet	Monthly health education session	0.51 (0.18, 0.85)	Favors diet	Clinically significant	Low
	Rejeski et al. (2002)	SF-36 Physical Function	136	Yes	26 and 78 averaged	28+	Diet plus exercise	Monthly health education session	0.62 (0.27, 0.96)	Favors diet plus exercise	Clinically significant	Low
Functional Tasks	Focht (2005)	6 minute walk distance(ft)	160	Unclear	78	28+	Diet	Health education control	0.08 (-0.23, 0.39)	No	N/A	Low

	Focht (2005)	6 minute walk distance(ft)	240	Yes	78	28+	Diet plus exercise	Health education control	0.38 (0.10, 0.65)	Favors diet plus exercise	N/A	Low
	Focht (2005)	Stair climb time(s)	160	Unclear	72	28+	Diet	Health education control	0.00 (-0.31, 0.31)	No	N/A	Low
	Focht (2005)	Stair climb time(s)	240	Unclear	72	28+	Diet plus exercise	Health education control	-0.19 (-0.46, 0.08)	No	N/a	Low
Pain	Miller et al. (2006)	WOMAC Pain	74	Yes	26	30+	Weight loss program	Weight stable education	-0.78 (-1.25, -0.31)	Favors diet plus weight loss	Possibly clinically significant	Moderate
WOMAC Total	Miller et al. (2006)	WOMAC Total	74	Yes	26	30+	Weight loss program	Weight stable education	-0.67 (-1.14, -0.20)	Favors diet plus weight loss	Possibly clinically significant	Moderate

Table 78. Low Energy Diet Versus Control Diet

Outcome Type	Study	Outcome	N	Powered	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Function	Christiansen (2005)	WOMAC Function	80	Yes	8	28+	Low energy diet (3.4mj/day)	Control diet (5mj/day)	-0.51 (-0.96, -0.07)	Favors low energy diet	Possibly clinically significant	Moderate
	Riecke (2010)	KOOS Function in Daily Life	192	Unclear	16	30+	Very low energy diet	Low energy diet control	-0.01 (-0.29, 0.27)	No	N/A	Low
	Riecke (2010)	KOOS Sports and Recreation	192	Unclear	16	30+	Very low energy diet	Low energy diet control	0.02 (-0.27, 0.30)	No	N/A	Low
	Riecke (2010)	SF-36 Mental	192	Yes	16	30+	Very low energy diet	Low energy diet control	0.37 (0.08, 0.65)	Favors very low energy diet	N/A	Low
	Riecke (2010)	SF-36 Physical	192	Yes	16	30+	Very low energy diet	Low energy diet control	-0.06 (-0.34, 0.22)	No	True negative	Low
	Riecke (2010)	VAS Disability	192	Unclear	16	30+	Very low energy diet	Low energy diet control	-0.08 (-0.36, 0.20)	No	N/A	Low

Outcome Type	Study	Outcome	N	Powered	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Bliddal	HAQ	89	Yes	52	28+	Low energy diet	Conventional diet	-0.28 (-0.70, 0.14)	No	N/A	Low
Global Assessment	Riecke (2010)	VAS Global	192	Yes	16 weeks	30+	Very low energy diet	Low energy diet control	0.09 (-0.19, 0.37)	No	True negative	Low
Pain	Riecke (2010)	KOOS Pain	192	Unclear	16	30+	Very low energy diet (415 kcal/day)	Low energy diet control (810 kcal/day)	-0.12 (-0.40, 0.16)	No	N/A	Low
	Riecke (2010)	VAS Pain	192	Yes	16	30+	Very low energy diet (415 kcal/day)	Low energy diet control (810 kcal/day)	-0.06 (-0.34, 0.22)	No	True negative	Low
Quality of Life	Riecke (2010)	KOOS Quality of Life	192	Unclear	16	30+	Very low energy diet (415 kcal/day)	Low energy diet control (810 kcal/day)	-0.03 (-0.32, 0.25)	No	N/A	Low
WOMAC Total	Christiansen (2005)	WOMAC Total	80	Yes	8	28+	Low energy diet (3.4mj/day)	Control diet (5mj/day) diet	-0.49 (-0.93, -0.04)	Favors low energy diet	Possibly clinically significant	Moderate
Lequesne index	Christiansen (2005)	Lequesne index	80	Unclear	8	28+	Low energy diet (3.4mj/day)	Control diet (5mj/day) diet	-0.08 (-0.52, 0.36)	No	N/A	Moderate

Outcome Type	Study	Outcome	N	Powered	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Symptoms	Riecke (2010)	KOOS Symptoms	192	Unclear	16	30+	Very low energy diet (415 kcal/day)	Low energy diet control (810 kcal/day)	0.03 (-0.25, 0.32)	No	N/A	Low
OARSI Responders	Riecke (2010)	OARSI Responders	192	Unclear	16	30+	Very low energy diet (415 kcal/day)	Low energy diet control (810 kcal/day)	0.84 (0.46, 1.50)	No	N/A	Low

Table 79. Diet Versus Exercise

Study	Outcome	N	Sufficient Power	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Focht (2005)	6 minute walk distance(ft)	242	Unclear	78	28+	Exercise plus diet	Exercise	-0.09 (-0.35, 0.18)	No	N/A	Low
Focht (2005)	6 minute walk distance(ft)	162	Yes	78	28+	Diet	Exercise	-0.42 (-0.73, -0.11)	Favors exercise	N/A	Low
Focht (2005)	6 minute walk distance(ft)	244	Yes	78	28+	Diet	Exercise plus diet	-0.30 (-0.57, -0.04)	Favors exercise plus diet	N/A	Low

Study	Outcome	N	Sufficient Power	Week	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Focht (2005)	Stair climb time(s)	162	Unclear	78	28+	Diet	Exercise	0.10 (-0.21, 0.41)	No	N/A	Low
Focht (2005)	Stair climb time(s)	244	Unclear	78	28+	Diet	Exercise plus diet	0.15 (-0.12, 0.42)	No	N/A	Low
Focht (2005)	Stair climb time(s)	242	Unclear	78	28+	Exercise plus diet	Exercise	-0.06 (-0.33, 0.21)	No	N/A	Low
Jenkinson et al. (2009)	WOMAC Pain 30% reduction	0	Yes	104	28+	Diet or diet plus exercise	Exercise or leaflet	OR=0.98 (0.65, 1.48)	No	N/A	High

RECOMMENDATION 3A

We cannot recommend using acupuncture in patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 3B

We are unable to recommend for or against the use of physical agents (including electrotherapeutic modalities) in patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RECOMMENDATION 3C

We are unable to recommend for or against manual therapy in patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

Variable strengths of evidence were reported in studies of patients with osteoarthritis of the knee.

3A

There were five high- and five moderate- strength studies that compared acupuncture to comparison groups receiving non-intervention sham, usual care, or education. The five moderate-strength studies were included because they reported outcomes that were different than the high-strength evidence. High-strength studies included: Berman et al,⁶¹ Suarez-Almazor et al.,⁶² Weiner et al.,⁶³ Williamson et al.⁶⁴ and Taechaarpornkul et al.⁶⁵ Moderate-strength studies included: Sandgee et al.,⁶⁶ Vas et al.,⁶⁷ Witt et al.⁶⁸ and Berman et al.⁶⁹ The majority of studies were not statistically significant and an even larger

proportion of the evidence was not clinically significant. Some outcomes were associated with clinical- but not statistical- significance. The strength of this recommendation was based on lack of efficacy, not on potential harm.

3B

The evidence was mixed regarding the efficacy of physical agents and electrotherapeutic modalities because of contradiction in findings, design flaws, or a low count of like studies. A single low-strength⁷⁰ and a single-moderate strength study⁷¹ comparing pulsed electrical stimulation to placebo produced contradictory results. See the results of the Fary et al.⁷⁰ and Zizic et al.⁷¹ articles in table 96. Trock et al.⁷² conducted a moderate-strength study evaluating pulsed electromagnetic stimulation and found that it did not generate a statistically significant effect on pain during passive motion, but that tenderness and physician's overall assessment scores were superior in the experimental group. Atamaz et al.⁷³ conducted a moderate-strength study that compared transcutaneous electrical nerve stimulation (TENS), shortwave diathermy, and interferential current to a sham procedure. None of the treatments were associated with statistically significant effects on pain, physical mobility, or ambulation time at four, 12, or 26 weeks. Battisti et al.,⁷⁴ also in a moderate-strength study, found that therapeutic application of modulated electromagnetic field therapy (TAMMEF) did not produce statistically significant improvements in pain or Lequesne Index scores, compared to extremely low-frequency electromagnetic field therapy.

However, there was evidence that ultrasound was effective in patients with knee osteoarthritis. Huang et al.⁷⁵ and Yang et al.⁷⁶ conducted moderate-strength studies that compared ultrasound to a control group. Huang et al. found that patients who received isotonic exercise with ultrasound had significantly superior ambulation speed, Lequesne Index scores, and VAS pain scores. Yang et al. found VAS pain and Lequesne Index scores were significantly superior at 4 weeks in patients who received ultrasound over those who received a sham treatment.

Due to the overall inconsistent findings for various physical agents and electrotherapeutic modalities, we were unable to make a recommendation for or against their use in patients with symptomatic osteoarthritis of the knee.

3C

We were unable to recommend for or against manual therapy due to the lack of studies examining most manual therapy techniques. No studies evaluating joint mobilization, joint manipulation, chiropractic therapy, patellar mobilization, or myofascial release were found that met our inclusion criteria. Perlman et al.⁷⁷ examined Swedish massage therapy using a low-strength study design. The findings showed statistically significant results at 8 weeks, but not at 16 weeks. A conclusive recommendation regarding Swedish massage therapy could not be made based on this single low strength of evidence study.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 80-Table 85](#), [Table 86-Table 91](#)

There were five high quality studies, and four moderate quality studies that compared acupuncture to a control group (sham, usual care, or education). None of the studies were flawed in the hypothesis, treatment integrity, and measurement domains. Five of nine studies were flawed in the group assignment domain. Seven and six of nine articles were appropriate in the blinding and group comparability domains. Vas et al.,⁶⁷ Witt et al.,⁶⁸ and Taechaarpornkul et al.⁶⁵ had investigator bias.

One high quality study, Wiener et al.,⁶³ compared periosteal stimulation therapy to regular acupuncture and was unflawed in every quality domain except for group assignment.

Pulsed electrical stimulation was compared to placebo by Fary et al.⁷⁰ This study was of low quality with flaws in the hypothesis, blinding, group assignment and group comparability domains.

Pulsed electromagnetic therapy was compared to placebo in studies by Trock et al.⁷² and Zizic et al.⁷¹ The former was of moderate quality with flaws in the group assignment, comparability and investigator bias domains. Quality of the latter was affected by uncertain group comparability as well as investigator bias.

Battisti et al.⁷⁴ compared Therapeutic Application of Modulated Electro Magnetic Field (TAMMEF) treatments to extremely low frequency electromagnetic field therapy. Since there was uncertainty concerning group assignment and group comparability, this study was given a rating of moderate quality.

Atamaz et al.⁷³ compared transcutaneous electrical nerve stimulation (TENS), interferential currents, and short wave diathermy to a sham control group. Since group comparability at baseline was uncertain and the treatment integrity domain was flawed, the study was of moderate quality.

One study⁷⁷ compared Swedish massage therapy to usual care. This low quality study was flawed in the group assignment, blinding, group comparability and treatment integrity domains. Where it was not flawed was in the hypothesis, measurement and investigator bias domains.

Huang et al.,⁷⁵ a moderate quality study, compared ultrasonic wave therapy in combination with exercise to an exercise intervention alone. The study was flawed in the binding and investigator bias domains and not flawed in the hypothesis, group assignment, group comparability, treatment integrity and measurement domains.

Yang et al.⁷⁶ compared ultrasound therapy to placebo. This moderate quality study was only flawed in the group assignment and group comparability domains.

APPLICABILITY

Relevant Tables: [Table 80-Table 85](#), [Table 86-Table 91](#)

In all nine included acupuncture studies, the treatments might not have been administered in a manner representative of clinical practice. Similarly, it was not clear if the study participants were similar to the typical patient population in all but one of the studies. Compliance was similar in all included acupuncture studies. Nine out of 10 studies based their final analyses on all enrolled patients. The studies were of moderate applicability.

Participants, treatment administration, and compliance in the Swedish massage therapy study might not have been similar to that typically found in clinical practice. However, the study included all enrolled patients in the final analysis. It was rated as having moderate applicability.

It was not certain if participants and the treatment administration were representative of typical clinical practice for the ultrasound,^{75;76} pulsed electrical stimulation and pulsed electromagnetic therapy studies.⁷⁰⁻⁷² The study by Battisti et al.⁷⁴ of TAMMEF was flawed in the representativeness of treatment administration. Compliance followed a similar pattern to clinical practice for these studies. Also, with the exception of the Zizic et al.⁷¹ study, all enrolled patients were included in the final analyses. The applicability ratings were determined to be moderate.

The Atamaz et al.⁷³ study examining treatment efficacy of TENS, interferential currents, and short wave diathermy included a sufficient percentage of enrolled patients in the final analysis. However, the treatment administration, patients who received the interventions, and the monitoring of compliance and adherence in the study were not representative of regular clinical practice.

FINAL STRENGTH OF EVIDENCE

All strength of evidence ratings were the same as the quality ratings since all studies were rated as having moderate applicability.

Table 80. Quality and Applicability Summary: Acupuncture Versus Control

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence
Berman (1999)	WOMAC Pain	4	Moderate	Moderate	Moderate
Berman (1999)	WOMAC Pain	4	Moderate	Moderate	Moderate
Berman (1999)	Lequesne index	4	Moderate	Moderate	Moderate
Berman (1999)	Lequesne index	8	Moderate	Moderate	Moderate
Berman (1999)	Lequesne index	12	Moderate	Moderate	Moderate
Berman (1999)	WOMAC Pain	8	Moderate	Moderate	Moderate

Berman (1999)	WOMAC Pain	12	Moderate	Moderate	Moderate
Berman (1999)	WOMAC Function	4	Moderate	Moderate	Moderate
Berman (1999)	WOMAC Function	8	Moderate	Moderate	Moderate
Berman (1999)	WOMAC Function	12	Moderate	Moderate	Moderate
Berman (2004)	6 minute walk distance	8	High	Moderate	High
Berman (2004)	6 minute walk distance	26	High	Moderate	High
Berman (2004)	6 minute walk distance	8	High	Moderate	High
Berman (2004)	6 minute walk distance	26	High	Moderate	High
Berman (2004)	WOMAC Pain	8	High	Moderate	High
Berman (2004)	WOMAC Pain	14	High	Moderate	High
Berman (2004)	WOMAC Pain	26	High	Moderate	High
Berman (2004)	WOMAC Function	4	High	Moderate	High
Berman (2004)	WOMAC Function	8	High	Moderate	High
Berman (2004)	WOMAC Function	14	High	Moderate	High
Berman (2004)	WOMAC Function	26	High	Moderate	High
Sandgee (2002)	50 foot walk time	4	Moderate	Moderate	Moderate
Sandgee (2002)	Lequesne index	4	Moderate	Moderate	Moderate
Suarez-Almazor (2010)	SF-12 Physical Health	4	High	Moderate	High
Suarez-Almazor (2010)	SF-12 Physical Health	6	High	Moderate	High

Suarez-Almazor (2010)	SF-12 Physical Health	13	High	Moderate	High
Suarez-Almazor (2010)	SF-12 Mental Health	4	High	Moderate	High
Suarez-Almazor (2010)	SF-12 Mental Health	6	High	Moderate	High
Suarez-Almazor (2010)	SF-12 Mental Health	13	High	Moderate	High
Suarez-Almazor (2010)	WOMAC Pain	4	High	Moderate	High
Suarez-Almazor (2010)	WOMAC Pain	6	High	Moderate	High
Suarez-Almazor (2010)	WOMAC Pain	13	High	Moderate	High
Suarez-Almazor (2010)	WOMAC Function	4	High	Moderate	High
Suarez-Almazor (2010)	WOMAC Function	6	High	Moderate	High
Suarez-Almazor (2010)	WOMAC Function	13	High	Moderate	High
Taechaarpornkul (2009)	WOMAC Pain	13	High	Moderate	High
Taechaarpornkul (2009)	Cox-2 consumption	5	High	Moderate	High
Taechaarpornkul (2009)	Cox-2 consumption	13	High	Moderate	High
Taechaarpornkul (2009)	WOMAC Pain	5	High	Moderate	High
Taechaarpornkul (2009)	WOMAC Function	5	High	Moderate	High
Taechaarpornkul (2009)	WOMAC Function	13	High	Moderate	High
VAS (2004)	PLQC-Negative Mood	13	Moderate	Moderate	Moderate

VAS (2004)	PLQC-Physical Capability	13	Moderate	Moderate	Moderate
VAS (2004)	PLQC-Psychological Functioning	13	Moderate	Moderate	Moderate
VAS (2004)	PLQC- Social Functioning	13	Moderate	Moderate	Moderate
VAS (2004)	PLQC-Social Well-Being	13	Moderate	Moderate	Moderate
VAS (2004)	NSAID Consumption	13	Moderate	Moderate	Moderate
VAS (2004)	VAS Pain	13	Moderate	Moderate	Moderate
Weiner (2004)	WOMAC Pain	6	High	Moderate	High
Witt (2005)	SF-36-Physical Health	8	Moderate	Moderate	Moderate
Williamson (2007)	OKS	7	High	Moderate	High
Williamson (2007)	OKS	12	High	Moderate	High
Williamson (2007)	OKS	12 post-op	High	Moderate	High
Williamson (2007)	50m walk	7	High	Moderate	High
Williamson (2007)	50m walk	12	High	Moderate	High
Williamson (2007)	50m walk	12 post-op	High	Moderate	High
Williamson (2007)	Post-op stay (days)	12 post-op	High	Moderate	High
Williamson (2007)	VAS (cm)	7	High	Moderate	High
Williamson (2007)	VAS (cm)	12	High	Moderate	High

Williamson (2007)	VAS (cm)	12 post-op	High	Moderate	High
Williamson (2007)	HAD Anxiety	7	High	Moderate	High
Williamson (2007)	HAD Anxiety	12	High	Moderate	High
Williamson (2007)	HAD Anxiety	12 post-op	High	Moderate	High
Williamson (2007)	HAD Score Depression	7	High	Moderate	High
Williamson (2007)	HAD Score Depression	12	High	Moderate	High
Williamson (2007)	HAD Score Depression	12 post-op	High	Moderate	High

Table 81. Quality and Applicability Summary: Periosteal Stimulation Therapy

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence
Weiner (2004)	WOMAC Pain	6	High	Moderate	High
Weiner (2004)	Geriatric Depression Scale	6	High	Moderate	High
Weiner (2004)	Geriatric Depression Scale	12	High	Moderate	High
Weiner (2004)	Pittsburgh Sleep Quality index	6	High	Moderate	High
Weiner (2004)	Pittsburgh Sleep Quality index	12	High	Moderate	High
Weiner (2004)	Stair climb time	6	High	Moderate	High
Weiner (2004)	Stair climb time	12	High	Moderate	High

Table 82. Quality and Applicability Summary: Pulsed Electrical Stimulation

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence

Fary (2011)	Patient Global Assessment of Disease Activity	26	Low	Moderate	Low
Fary (2011)	SF-36 Mental	26	Low	Moderate	Low
Fary (2011)	Human activity profile maximum activity	26	Low	Moderate	Low
Fary (2011)	Human activity profile adjusted activity	26	Low	Moderate	Low
Fary (2011)	Daily accelerometer count	26	Low	Moderate	Low
Fary (2011)	Daily resting time, minutes	26	Low	Moderate	Low
Zizic (1995)	VAS Pain % change	8	Moderate	Moderate	Moderate
Zizic (1995)	VAS Function % change	8	Moderate	Moderate	Moderate
Zizic (1995)	Percent change adjusted mean physician evaluation (VAS)	8	Moderate	Moderate	Moderate
Zizic (1995)	At least 15 minute improvement in morning stiffness	8	Moderate	Moderate	Moderate
Battisti (2004)	Complete reduction of pain	6.4	Moderate	Moderate	Moderate
Battisti (2004)	Lequesne index: Total recovery of articular function	6.4	Moderate	Moderate	Moderate
Fary (2011)	Daily light	26	Low	Moderate	Low

	activity, minutes				
Fary (2011)	Daily moderate activity, minutes	26	Low	Moderate	Low
Fary (2011)	Daily hard activity, minutes	26	Low	Moderate	Low

Table 83. Quality and Applicability Summary: Pulsed Electromagnetic Therapy

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence
Trock (1994)	Pain on passive motion	4	Moderate	Moderate	Moderate
Trock (1994)	Tenderness	4	Moderate	Moderate	Moderate
Trock (1994)	Physician Overall Assessment	4	Moderate	Moderate	Moderate

Table 84. Quality and Applicability Summary: Swedish Massage Therapy

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence
Perlman (2006)	50 foot walk time	8	Low	Moderate	Low
Perlman (2006)	50 foot walk time	16	Low	Moderate	Low
Perlman (2006)	VAS Pain	8	Low	Moderate	Low
Perlman (2006)	VAS Pain	16	Low	Moderate	Low
Perlman (2006)	WOMAC Function	8	Low	Moderate	Low
Perlman (2006)	WOMAC Function	16	Low	Moderate	Low
Perlman (2006)	WOMAC Total	8	Low	Moderate	Low

Perlman (2006)	WOMAC Total	16	Low	Moderate	Low
Perlman (2006)	WOMAC Pain	8	Low	Moderate	Low
Perlman (2006)	WOMAC Pain	16	Low	Moderate	Low
Perlman (2006)	WOMAC Stiffness	8	Low	Moderate	Low
Perlman (2006)	WOMAC Stiffness	16	Low	Moderate	Low

Table 85. Quality and Applicability Summary: Ultrasound

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence
Huang (2005)	Walk speed (m/min)	8	Moderate	Moderate	Moderate
Huang (2005)	Lequesne index	8	Moderate	Moderate	Moderate
Huang (2005)	VAS Pain	8	Moderate	Moderate	Moderate
Huang (2005)	Walk speed (m/min)	52	Moderate	Moderate	Moderate
Huang (2005)	Lequesne index	52	Moderate	Moderate	Moderate
Huang (2005)	VAS Pain	52	Moderate	Moderate	Moderate
Huang (2005)	Walk speed (m/min)	8	Moderate	Moderate	Moderate
Huang (2005)	Walk speed (m/min)	8	Moderate	Moderate	Moderate
Huang (2005)	Lequesne index	8	Moderate	Moderate	Moderate
Yang (2011)	VAS curative effect of	4	Moderate	Moderate	Moderate

	treatment				
Yang (2011)	Lequesne index curative effect of treatment	4	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Figure 16-Figure 20](#), [Figure 21-Figure24](#), [Table 92-Table 101](#)

There were 57 total outcomes comparing acupuncture to a control group. Twelve were statistically significant in favor of acupuncture (see [Figure 16](#) for a summary of the results). The critical outcomes reported by the acupuncture studies were pain, function and quality of life. Meta-analyses were run for WOMAC pain and function at four to five weeks, six to eight weeks, and 12 to 14 weeks and are described in Figures19 and 20. For each outcome, subgroups of studies were combined when their follow-up durations were similar.

There were 13 included pain outcomes, three of which were statistically significant over placebo. The meta-analysis results showed that acupuncture had a statistically non-significant (and not clinically important) effect on pain at four to five weeks and at six to eight weeks ([Figure 16](#)). The acupuncture effect was not statistically significant at 12 to 14 weeks, but the confidence interval did include the MCII (making the 12 to 14 week effect inconclusive).

Three out of 31 functional outcomes were statistically significant in favor of acupuncture over sham/placebo. The meta-analysis results ([Figure 24](#)) indicated that the WOMAC Function scores were significantly superior to sham at six to eight weeks and at 12 to 14 weeks. However, none of the statistically significant outcomes were clinically important.

Vas et al.⁶⁷ addressed the effect of acupuncture on quality of life with the five subsections of the Profile of Quality of Life in the Chronically Ill (PQLC). These subsections included negative mood, physical capability, psychological function, social function and social well being. No outcome achieved statistical significance.

One study compared periosteal stimulation therapy (PST) to regular acupuncture.⁵⁹ There were a total of seven outcomes studied. Only WOMAC pain at six weeks (the only critical outcome) was statistically significant in favor of PST ([Table 97](#)).

Fary et al.,⁷⁰ Trock et al.⁷² and Zizic et al.⁷¹ compared the effectiveness of pulsed electrical stimulation to placebo. Five out of 16 outcomes were statistically significant in favor of the treatment ([Figure 19](#)). The critical outcomes addressed were activities of daily life (ADL), self-reported function, and pain. All of the ADL outcomes were not statistically significant when compared to placebo. One out of two functional outcomes, and one out of two pain outcomes were statistically significant in favor of pulsed electrical stimulation over placebo.

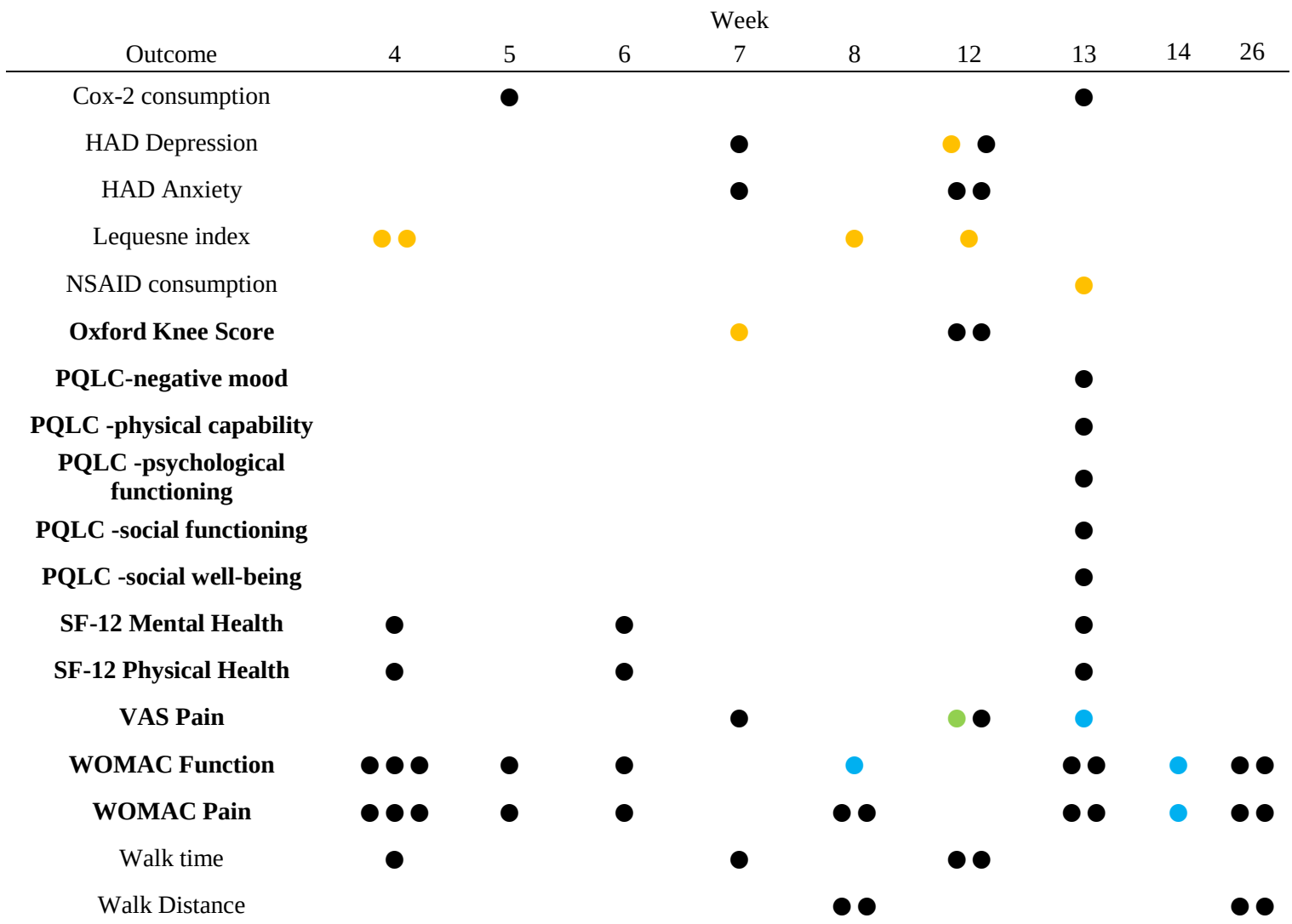
Trock et al.⁷² compared the effect of pulsed electromagnetic fields to placebo. Pain on passive motion was not statistically different between groups. However, tenderness and Physician's Global Assessment were significantly improved in the treatment group. One additional study compared therapeutic application of modulated electro-magnetic field (TAMMEF) therapy to extremely low frequency electromagnetic field therapy.⁷⁴ There were no significant differences in pain and Lequesne index scores between the two treatments.

Pearlman et al.⁷⁷ compared Swedish massage therapy to a waitlist control at eight and 16 weeks based on twelve outcomes ([table 99](#)). The treatment group had significantly better scores on all outcomes at eight weeks. At 16 weeks, every outcome was not significantly different when comparing the treatment arms. However, five outcomes were not sufficiently powered. VAS pain, WOMAC pain and WOMAC function were the critical outcomes included in this study. Massage therapy had a possibly clinically important effect on VAS pain and WOMAC function scores at eight weeks. Swedish Massage Therapy had a clinically significant effect on WOMAC pain scores at eight weeks.

Huang et al.⁷⁵ and Yang et al.⁷⁶ compared ultrasound therapy to a control group. One study compared ultrasound to placebo, and the other compared isotonic exercise plus ultrasound to a control group who only received exercise therapy. Seven out of eight outcomes were statistically significant in favor of ultrasound (see [Figure 18](#)). VAS pain was the only critical outcome included in these studies. Two of three pain outcomes were statistically significant in favor of the ultrasound group ([Figure 18](#)).

Atamaz et al.⁷³ compared TENS, interferential current therapy (IFC), and short wave diathermy (SWD) to sham treatments (sham TENS, sham IFC, sham SWD). There were no statistically significant differences between any active treatments and their sham counterparts.

Figure 16. Results Summary: Acupuncture Versus Control



Key: ●=Not Significant; ●= Statistically Significant; ●=Possibly Clinically Important; ●=Significant But Not Clinically Important. Bold text indicates a critical outcome.

Figure 17. Results Summary: Electro-acupuncture Versus Control

Outcome	6	12
Geriatric Depression Scale	●	●
Pittsburgh Sleep Quality index	●	●
Stair climb time	●	●
WOMAC Pain	●	

Key: ●=Not Significant; ●=Possibly Clinically Important.
Bold text indicates a critical outcome.

Figure 18. Results Summary: Swedish Massage Therapy and Ultrasound Versus Control

		Week						
Outcome		4	8	12	16	26	36	52
Swedish Massage Therapy	50 foot walk time		●		●			
	VAS Pain		●		●			
	WOMAC Function		●		●			
	WOMAC Total		●		●			
	WOMAC Pain		●		●			
	WOMAC Stiffness		●		●			
Ultrasound	Walk speed (m/min)		●					●
	Lequesne index	●	●					●
	VAS Pain	●	●					●

Key: ●=Not Significant; ●=Statistically Significant; ●=Clinically Significant; ●=Possibly Clinically Important;

●=Significant But Not Clinically Important.

Bold text indicates a critical outcome.

Figure 19. Results Summary: Pulsed Electrical Stimulation

Outcome	Week 4	8	26
Patient Global Assessment of Disease Activity			●
Physician overall assessment		●	
SF-36 Mental			●
Human activity profile maximum activity			●
Human activity profile adjusted activity			●
Daily accelerometer count			●
Daily resting time, minutes			●
Daily light activity, minutes			●
Daily moderate activity, minutes			●
Daily hard activity, minutes			●
Pain on passive motion	●		
VAS Pain		●	
VAS Function		●	
Morning stiffness		●	
Tenderness	●		
Physician's overall assessment	●		

Key: ●=Not Significant; ●=Statistically Significant. Bold text indicates a critical outcome.

Figure 20. Results Summary: Electromagnetic Fields

		Week	
Outcome		4	6.4
Pulsed Electromagnetic Field	Pain on passive motion	●	
	Tenderness	●	
	Physician's overall assessment	●	
Therapeutic Application of Modulated Electro Magnetic Field (TAMMEF) Versus Extremely Low Frequency Electromagnetic Field Therapy	Complete reduction of pain		●
	Lequesne index: Total recovery of articular function		●

Key: ●=Not Significant; ●=Statistically Significant.

Bold text indicates a critical outcome.

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 86. Quality and Applicability: Acupuncture Versus Control

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Berman (1999)	WOMAC Pain	4	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	WOMAC Pain	4	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	Lequesne index	4	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	Lequesne index	8	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	Lequesne index	12	●	◐	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Berman (1999)	WOMAC Pain	8	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	WOMAC Pain	12	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	WOMAC Function	4	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	WOMAC Function	8	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (1999)	WOMAC Function	12	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Berman (2004)	6 minute walk distance	8	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman	6 minute walk	26	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
(2004)	distance															
Berman (2004)	6 minute walk distance	8	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	6 minute walk distance	26	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	WOMAC Pain	8	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	WOMAC Pain	14	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	WOMAC Pain	26	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	WOMAC Function	4	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Berman (2004)	WOMAC Function	8	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	WOMAC Function	14	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Berman (2004)	WOMAC Function	26	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Sandgee (2002)	50 foot walk time	4	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Sandgee (2002)	Lequesne index	4	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Suarez-Almazor (2010)	SF-12 Physical Health	4	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Suarez-Almazor (2010)	SF-12 Physical Health	6	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)	SF-12 Physical Health	13	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)	SF-12 Mental Health	4	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)	SF-12 Mental Health	6	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)	SF-12 Mental Health	13	●	◐	●	●	●	●	●	●	High	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Suarez-Almazor (2010)*	WOMAC Pain	4	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)*	WOMAC Pain	6	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)*	WOMAC Pain	13	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)*	WOMAC Function	4	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Suarez-Almazor (2010)*	WOMAC Function	6	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Suarez-Almazor (2010)*	WOMAC Function	13	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Taechaarpornkul (2009)	WOMAC Pain	13	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Taechaarpornkul (2009)	Cox-2 consumption	5	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Taechaarpornkul (2009)	Cox-2 consumption	13	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Taechaarpornkul (2009)*	WOMAC Pain	5	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Taechaarpornkul (2009)*	WOMAC Function	5	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Taecharpornkul (2009)*	WOMAC Function	13	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
VAS (2004)	PLQC- Negative Mood	13	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
VAS (2004)	PLQC- Physical capability	13	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
VAS (2004)	PLQC- Psychological Functioning	13	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
VAS (2004)	PLQC- Social Functioning	13	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
VAS (2004)	PLQC- Social Well-Being	13	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
VAS (2004)	NSAID consumption	13	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
VAS (2004)	VAS Pain	13	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Weiner (2004)	WOMAC Pain	6	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Witt (2005)	SF-36 Physical Health	8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Williamson (2007)	OKS	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	OKS	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	OKS	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	50m walk(s)	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Williamson (2007)	50m walk(s)	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	50m walk(s)	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	Post-op stay (days)	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	VAS (cm)	Williamson (2007)	●	●	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	VAS (cm)	Williamson (2007)	●	●	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	VAS (cm)	Williamson (2007)	●	●	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson	HAD Anxiety	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
(2007)																
Williamson (2007)	HAD Anxiety	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	HAD Anxiety	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	HAD Depression	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	HAD Depression	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate
Williamson (2007)	HAD Depression	Williamson (2007)	●	◐	●	○	●	●	●	●	High	○	○	●	●	Moderate

Table 87. Quality and Applicability: Periosteal Stimulation Therapy

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Weiner (2004)	WOMAC Pain	6	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Weiner (2004)	Geriatric Depression Scale	6	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Weiner (2004)	Geriatric Depression Scale	12	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Weiner (2004)	Pittsburgh Sleep Quality index	6	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Weiner (2004)	Pittsburgh Sleep Quality index	12	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Weiner (2004)	Stair climb time	6	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Weiner (2004)	Stair climb time	12	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 88. Quality and Applicability: Pulsed Electrical and Electromagnetic Therapy

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Fary (2011)	Patient Global Assessment of Disease Activity	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	SF-36 Mental	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	Human activity profile maximum activity	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	Human activity profile adjusted activity	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	Daily accelerometer count	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	Daily resting time, minutes	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Fary (2011)	Daily light activity, minutes	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	Daily moderate activity, minutes	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Fary (2011)	Daily hard activity, minutes	26	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Trock (1994)	Pain on passive motion	4 weeks after treatment completion	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Trock (1994)	Tenderness	4 weeks after treatment completion	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Trock (1994)	Physician overall assessment	4 weeks after treatment	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
		completion														
Zizic (1995)	VAS Pain % change	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zizic (1995)	VAS Function % change	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zizic (1995)	Percent change adjusted mean physician evaluation (VAS)	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zizic (1995)	At least 15 minute improvement in morning stiffness	8	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Battisti (2004)	Complete reduction of pain	6.4	●	◐	○	●	○	●	●	●	Moderate	●	○	●	●	Moderate
Battisti (2004)	Lequesne index: Total recovery of articular function	6.4	●	◐	○	●	○	●	●	●	Moderate	●	○	●	●	Moderate

Table 89. Quality and Applicability: TENS, Interferential Current, and Short Wave Diathermy

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
4	VAS Pain TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	VAS Pain IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	VAS Pain SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	VAS Pain TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	VAS Pain IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	VAS Pain SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	VAS Pain TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	VAS Pain IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
26	VAS Pain SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Nottingham Health Profile-Pain TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Nottingham Health Profile-Pain IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Nottingham Health Profile-Pain SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Nottingham Health Profile-Pain TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Nottingham Health Profile-Pain IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Nottingham Health Profile-Pain SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	Nottingham Health Profile-Pain TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	Nottingham Health Profile-Pain IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
26	Nottingham Health Profile-Pain SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Timed walk TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Timed walk IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Timed walk SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Timed walk TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Timed walk IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Timed walk SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	Timed walk TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	Timed walk IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Duration (Weeks)	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
26	Timed walk SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Nottingham Health Profile: Physical TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Nottingham Health Profile: Physical IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
4	Nottingham Health Profile: Physical SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Nottingham Health Profile: Physical TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Nottingham Health Profile: Physical IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
13	Nottingham Health Profile: Physical SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	Nottingham Health Profile: Physical TENS		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
26	Nottingham Health Profile: Physical IFC		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate
26	Nottingham Health Profile: Physical SWD		●	◐	○	●	●	○	●	●	Moderate	○	○	○	●	Moderate

Note 1 TENS= Transcutaneous electrical nerve stimulation; IFC=Interferential current; SWD=Short Wave Diathermy

Table 90. Swedish Massage Therapy Versus Usual Care

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Perlman (2006)	50 foot walk time	8	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	50 foot walk time	16	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	VAS Pain	8	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	VAS Pain	16	●	○	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Function	8	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Function	16	●	○	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Total	8	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Total	16	●	○	○	○	○	○	●	●	Low	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Perlman (2006)	WOMAC Pain	8	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Pain	16	●	○	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Stiffness	8	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Perlman (2006)	WOMAC Stiffness	16	●	○	○	○	○	○	●	●	Low	○	○	●	●	Moderate

Table 91. Ultrasonic Wave Plus Exercise Versus Exercise Alone

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Huang (2005)	Walk speed (m/min)	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2005)	Lequesne index	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2005)	VAS Pain	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2005)	Walk speed (m/min)	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2005)	Lequesne index	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2005)	VAS Pain	52	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2005)	Walk speed (m/min)	8	●	●	●	○	●	●	●	○	Moderate	○	○	●	●	Moderate
Yang (2011)	VAS Pain	4	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Duration (Weeks)</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Yang (2011)	Lequesne index	4	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

FINDINGS

Table 92. Acupuncture Versus Control: Pain

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Berman (2004)	WOMAC Pain	336	Yes	4	Acupuncture	Sham acupuncture	-0.08 (-0.29, 0.14)	No	True negative	High
Suarez-Almazor (2010)	WOMAC Pain	301	Yes	4	Traditional Chinese acupuncture	Sham	-0.05 (-0.27, 0.18)	No	True negative	High
Taechaarpornkul (2009)	WOMAC Pain	66	Unclear	5	Six point Chinese acupuncture	Two point Chinese acupuncture	-0.08 (-0.57, 0.40)	No	Inconclusive	High
Suarez-Almazor (2010)	WOMAC Pain	301	Yes	6	Traditional Chinese acupuncture	Sham	-0.18 (-0.40, 0.05)	No	Inconclusive	High
Berman (2004)	WOMAC Pain	330	Yes	8	Acupuncture	Sham acupuncture	-0.14 (-0.35, 0.08)	No	True negative	High
Berman (2004)	WOMAC Pain	315	Yes	14	Acupuncture	Sham acupuncture	-0.24 (-0.46, -0.01)	Favors electro-acupuncture	Possibly clinically significant	High
Taechaarpornkul (2009)	WOMAC Pain	66	Unclear	13	Six point Chinese acupuncture	Two point Chinese acupuncture	-0.29 (-0.77, 0.20)	No	Inconclusive	High
Suarez-Almazor (2010)	WOMAC Pain	301	Yes	13	Traditional Chinese acupuncture	Sham	-0.05 (-0.28, 0.18)	No	True negative	High

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
VAS (2004)	VAS Pain	97	Yes	13	Acupuncture	Placebo	-1.31 (-1.75, -0.87)	Favors acupuncture	Possibly clinically significant	Moderate
Berman (2004)	WOMAC Pain	283	Yes	26	Acupuncture	Sham acupuncture	-0.23 (-0.47, 0.00)	No	Inconclusive	High
Williamson (2007)	VAS Pain	121	Yes	7	Acupuncture	Usual care	-.232 (-.59 , .125)	No	Not clinically important	High
Williamson (2007)	VAS Pain	121	Yes	12	Acupuncture	Usual care	-.301 (-.66 ,.058)	No	Not clinically important	High
Williamson (2007)	VAS Pain	121	Yes	12 post TKA surgery	Acupuncture	Usual care	-.382 (-.741, -.022)	Favors acupuncture	Not clinically important	High

Table 93. Acupuncture Versus Control: Function

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Sandgee (2002)	50 foot walk time	91	Unclear	4	Electro-acupuncture	Sham	0.41 (-0.01, 0.82)	No	N/A	Moderate

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Williamson (2007)	50m walk time(s)	121	Unclear	7	Acupuncture	Usual care	-0.16 (-0.52 ,0.2)	No	Unclear	High
Williamson (2007)	50m walk time(s)	121	Unclear	12	Acupuncture	Usual care	-0.15 (-0.51 ,0.20)	No	Unclear	High
Williamson (2007)	50m walk time(s)	121	Unclear	12 post TKA surgery	Acupuncture	Usual care	0.35 (-0.01 ,0.71)	No	Unclear	High
Berman (2004)	6 minute walk distance	319	Unclear	8	Acupuncture	Sham	-0.02 (-0.24, 0.20)	No	N/A	High
Berman (2004)	6 minute walk distance	265	Unclear	26	Acupuncture	Sham	-0.13 (-0.37, 0.11)	No	N/A	High
Berman (2004)	6 minute walk distance	252	Unclear	8	Acupuncture	Education	0.26 (-0.00, 0.52)	No	N/A	High
Berman (2004)	6 minute walk distance	211	Unclear	26	Acupuncture	Education	0.27 (-0.01, 0.56)	No	N/A	High
Williamson (2007)	Oxford Knee Score	121	Unclear	7	Acupuncture	Usual care	-0.442 (-0.803 , -0.081)	Favors acupuncture	Unclear	High
Williamson (2007)	Oxford Knee Score	121	Unclear	12	Acupuncture	Usual care	-0.356 (-0.72 ,0.004)	No	Unclear	High
Williamson (2007)	Oxford Knee Score	121	Unclear	12 post TKA surgery	Acupuncture	Usual care	-0.13 (-0.49 ,0.22)	No	Unclear	High

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Suarez-Almazor (2010)	SF-12 Mental Health	301	Unclear	4	Traditional Chinese acupuncture	Sham	0.08 (-0.14, 0.31)	No	N/A	High
Suarez-Almazor (2010)	SF-12 Mental Health	301	Unclear	6	Traditional Chinese acupuncture	Sham	0.15 (-0.08, 0.38)	No	N/A	High
Suarez-Almazor (2010)	SF-12 Mental Health	301	Unclear	13	Traditional Chinese acupuncture	Sham	0.08 (-0.15, 0.31)	No	N/A	High
Suarez-Almazor (2010)	SF-12 Physical Health	301	Unclear	4	Traditional Chinese acupuncture	Sham	-0.03 (-0.26, 0.19)	No	N/A	High
Suarez-Almazor (2010)	SF-12 Physical Health	301	Unclear	6	Traditional Chinese acupuncture	Sham	-0.07 (-0.30, 0.15)	No	N/A	High
Suarez-Almazor (2010)	SF-12 Physical Health	301	Unclear	13	Traditional Chinese acupuncture	Sham	0.11 (-0.12, 0.33)	No	N/A	High
Berman (2004)	WOMAC Function	336	Yes	4	Acupuncture	Sham acupuncture	-0.18 (-0.39, 0.04)	No	Inconclusive	High
Berman (2004)	WOMAC Function	330	Yes	8	Acupuncture	Sham	-0.27 (-0.49, -0.06)	Favors electro-acupuncture	Possibly clinically significant	High

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Berman (2004)	WOMAC Function	315	Yes	14	Acupuncture	Sham acupuncture	-0.23 (-0.45, -0.01)	Favors electro-acupuncture	Possibly clinically significant	High
Berman (2004)	WOMAC Function	283	Yes	26	Acupuncture	Sham acupuncture	-0.21 (-0.44, 0.03)	No	Inconclusive	High
Suarez-Almazor (2010)	WOMAC Function	301	Yes	4	Traditional Chinese acupuncture	Sham	-0.10 (-0.33, 0.12)	No	True negative	High
Suarez-Almazor (2010)	WOMAC Function	301	Yes	6	Traditional Chinese acupuncture	Sham	-0.10 (-0.33, 0.12)	No	True negative	High
Suarez-Almazor (2010)	WOMAC Function	301	Yes	13	Traditional Chinese acupuncture	Sham	-0.05 (-0.28, 0.18)	No	True negative	High
Taechaarpornkul (2009)	WOMAC Function	66	Unclear	5	Six point Chinese acupuncture	Two point Chinese acupuncture	-0.05 (-0.53, 0.43)	No	Inconclusive	High
Taechaarpornkul (2009)	WOMAC Function	66	Unclear	13	Six point Chinese acupuncture	Two point Chinese acupuncture	-0.39 (-0.88, 0.09)	No	Inconclusive	High

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Vas (2004)	Profile of quality of life in the chronically ill (PQLC): Negative Mood	97	Unclear	13	Acupuncture	Sham	0.14 (-0.26, 0.54)	No	N/A	Moderate
Vas(2004)	PQLC: Physical Capability	97	Unclear	13	Acupuncture	Sham	0.40 (-0.01, 0.80)	No	No	Moderate
Vas (2004)	PLQC- Psychological Functioning	97	Unclear	13	Acupuncture	Sham	0.39 (-0.01, 0.79)	No	N/A	Moderate
Vas (2004)	PLQC- Social Functioning	97	Unclear	13	Acupuncture	Sham	0.16 (-0.24, 0.56)	No	N/A	Moderate
Vas (2004)	PLQC: Social Well-Being	97	Unclear	13	Acupuncture	Sham	0.00 (-0.40, 0.40)	No	N/A	Moderate

Table 94. Acupuncture Versus Usual Care: Hospital Anxiety and Depression Score

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Williamson (2007)	HAD Anxiety	121	Unclear	7	Acupuncture	Usual care	-0.026 (-0.382 ,0.33)	No	Unclear	High
Williamson (2007)	HAD Anxiety	121	Unclear	12	Acupuncture	Usual care	0.084 (-0.27 ,0.44)	No	Unclear	High
Williamson (2007)	HAD Anxiety	121	Unclear	12 post TKA surgery	Acupuncture	Usual care	0.082 (-0.27 ,0.439)	No	Unclear	High
Williamson (2007)	HAD Depression	121	Unclear	7	Acupuncture	Usual care	-0.079 (-0.436 ,0.28)	No	Unclear	High
Williamson (2007)	HAD Depression	121	Unclear	12	Acupuncture	Usual care	-0.121 (-0.48 ,0.236)	No	Unclear	High
Williamson (2007)	HAD Depression	121	Unclear	12 post TKA surgery	Acupuncture	Usual care	-0.409 (-0.77 ,0.05)	Favors acupuncture	Unclear	High

Table 95. Acupuncture Versus Control: Lequesne Index

Study	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Berman (1999)	336	Yes	4	Acupuncture	Usual care	-0.68 (-1.16, -0.21)	Favors acupuncture	N/A	Moderate
Sandgee (2002)	73	Yes	4	Electro-acupuncture	Sham	-0.70 (-1.12, -0.27)	Favors electro-acupuncture	N/A	Moderate
Berman (1999)	301	Yes	8	Acupuncture	Usual care	-0.98 (-1.47, -0.49)	Favors acupuncture	N/A	Moderate
Berman (1999)	66	Unclear	12	Acupuncture	Usual care	-0.80 (-1.28, -0.32)	Favors acupuncture	N/A	Moderate

Table 96. Acupuncture Versus Control: Consumption of Concomitant Medication

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Taechaarpornkul (2009)	66	Cox-2 consumption	Unclear	5	6 point acupuncture	2 point acupuncture	0.10 (-0.38, 0.58)	No	N/A	High
Taechaarpornkul (2009)	66	Cox-2 consumption	Unclear	13	6 point acupuncture	2 point acupuncture	-0.16 (-0.64, 0.33)	No	N/A	High
VAS (2004)	97	NSAID consumption	Yes	13	Acupuncture	Sham	-0.74 (-1.15, -0.33)	Favors acupuncture	N/A	Moderate

Table 97. Periosteal Stimulation Therapy Versus Regular Acupuncture (Weiner 2007)

Outcome	N	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
WOMAC Pain	88	Yes	6	Periosteal stimulation therapy	Regular acupuncture	-0.53 (-0.96, -0.11)	Favors PST	Possibly clinically important	High

Outcome	N	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Geriatric Depression Scale	88	Unclear	6	Periosteal stimulation therapy	Regular acupuncture	0.01 (-0.40, 0.43)	No	N/A	High
Geriatric Depression Scale	88	Unclear	12	Periosteal stimulation therapy	Regular acupuncture	0.10 (-0.32, 0.52)	No	N/A	High
Pittsburgh Sleep Quality index	88	Unclear	6	Periosteal stimulation therapy	Regular acupuncture	-0.10 (-0.52, 0.31)	No	N/A	High
Pittsburgh Sleep Quality index	88	Unclear	12	Periosteal stimulation therapy	Regular acupuncture	0.09 (-0.32, 0.51)	No	N/A	High
Stair climb time	88	Unclear	6	Periosteal stimulation therapy	Regular acupuncture	-0.03 (-0.45, 0.39)	No	N/A	High
Stair climb time	88	Unclear	12	Periosteal stimulation therapy	Regular acupuncture	0.22 (-0.20, 0.64)	No	N/A	High

Table 98. TENS, Interferential Current, and Short Wave Diathermy Versus Sham (Atamaz et al., 2012)

Treatment	Outcome	N	Sufficient Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
TENS	VAS Pain	74	Yes	4	TENS	Sham	0.191 (-0.266, 0.648)	No	True negative	Moderate
	VAS Pain	74	Yes	12	TENS	Sham	0.175 (-0.281, 0.632)	No	True negative	Moderate
	VAS Pain	74	Yes	26	TENS	Sham	0.009 (-0.447, 0.464)	No	True negative	Moderate
	Nottingham Health Profile: Pain	74	Unclear	4	TENS	Sham	-0.136 (-0.593, 0.32)	No	Unclear	Moderate
	Nottingham Health Profile: Pain	74	Unclear	12	TENS	Sham	0.015 (-0.44, 0.471)	No	Unclear	Moderate
	Nottingham Health Profile: Pain	74	Unclear	26	TENS	Sham	0.027 (-0.429, 0.483)	No	Unclear	Moderate
	Timed walk	74	Unclear	4	TENS	Sham	-0.153 (-0.609, 0.304)	No	Unclear	Moderate
	Timed walk	74	Unclear	12	TENS	Sham	-0.025 (-0.48, 0.431)	No	Unclear	Moderate
	Timed walk	74	Unclear	26	TENS	Sham	-0.121 (-0.578, 0.335)	No	Unclear	Moderate

Treatment	Outcome	N	Sufficient Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Nottingham Health Profile: Physical	74	Unclear	4	TENS	Sham	-0.086 (-0.542, 0.37)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	74	Unclear	12	TENS	Sham	0.015 (-0.441, 0.47)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	74	Unclear	26	TENS	Sham	-0.051 (-0.507, 0.405)	No	Unclear	Moderate
Interferential Current	VAS Pain	66	Yes	4	Interferential current	Sham	-0.398 (-0.886, 0.09)	No	True negative	Moderate
	VAS Pain	66	Yes	12	Interferential current	Sham	-0.459 (-0.949, 0.031)	No	True negative	Moderate
	VAS Pain	66	Yes	26	Interferential current	Sham	-0.514 (-1.005, -0.022)	No	True negative	Moderate
	Nottingham Health Profile: Pain	66	Unclear	4	Interferential current	Sham	-0.311 (-0.798, 0.175)	No	Unclear	Moderate

Treatment	Outcome	N	Sufficient Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Nottingham Health Profile: Pain	66	Unclear	12	Interferential current	Sham	-0.207 (-0.691, 0.278)	No	Unclear	Moderate
	Nottingham Health Profile: Pain	66	Unclear	26	Interferential current	Sham	-0.288 (-0.774, 0.198)	No	Unclear	Moderate
	Timed walk	66	Unclear	4	Interferential current	Sham	-0.143 (-0.627, 0.341)	No	Unclear	Moderate
	Timed walk	66	Unclear	12	Interferential current	Sham	0.064 (-0.419, 0.548)	No	Unclear	Moderate
	Timed walk	66	Unclear	26	Interferential current	Sham	-0.143 (-0.627, 0.341)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	66	Unclear	4	Interferential current	Sham	-0.193 (-0.677, 0.292)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	66	Unclear	12	Interferential current	Sham	-0.179 (-0.664, 0.305)	No	Unclear	Moderate

Treatment	Outcome	N	Sufficient Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Nottingham Health Profile: Physical	66	Unclear	26	Interferential current	Sham	-0.047 (-0.531, 0.436)	No	Unclear	Moderate
Short Wave Diathermy	VAS Pain	63	Yes	4	Short wave diathermy	Sham	-0.168 (-0.663, 0.327)	No	True negative	Moderate
	VAS Pain	63	Yes	12	Short wave diathermy	Sham	-0.078 (-0.572, 0.416)	No	True negative	Moderate
	VAS Pain	63	Yes	26	Short wave diathermy	Sham	0.085 (-0.409, 0.579)	No	True negative	Moderate
	Nottingham Health Profile: Pain	63	Unclear	4	Short wave diathermy	Sham	-0.321 (-0.818, 0.176)	No	Unclear	Moderate
	Nottingham Health Profile: Pain	63	Unclear	12	Short wave diathermy	Sham	-0.245 (-0.741, 0.251)	No	Unclear	Moderate
	Nottingham Health Profile: Pain	63	Unclear	26	Short wave diathermy	Sham	-0.353 (-0.851, 0.145)	No	Unclear	Moderate
	Timed walk	63	Unclear	4	Short wave diathermy	Sham	-0.048 (-0.542, 0.446)	No	Unclear	Moderate

Treatment	Outcome	N	Sufficient Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Timed walk	63	Unclear	12	Short wave diathermy	Sham	-0.172 (-0.667, 0.323)	No	Unclear	Moderate
	Timed walk	63	Unclear	26	Short wave diathermy	Sham	-0.311 (-0.808, 0.186)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	63	Unclear	4	Short wave diathermy	Sham	-0.173 (-0.668, 0.322)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	63	Unclear	12	Short wave diathermy	Sham	0.044 (-0.45, 0.538)	No	Unclear	Moderate
	Nottingham Health Profile: Physical	63	Unclear	26	Short wave diathermy	Sham	-.055 (-.439, .549)	No	Unclear	Moderate

Table 99. Swedish Massage Therapy Versus Usual Care (Perlman 2006)

Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
50 foot walk time	68	Yes	8	Swedish massage therapy	Waitlist control	-0.51 (-0.99, -0.02)	Favors massage therapy	N/A	Low
50 foot walk time	68	Unclear	16	Swedish massage therapy	Waitlist control	-0.40 (-0.88, 0.08)	No	N/A	Low
VAS Pain	68	Yes	8	Swedish massage therapy	Waitlist control	-0.86 (-1.36, -0.36)	Favors massage therapy	Possibly clinically important	Low
VAS Pain	68	No	16	Swedish massage therapy	Waitlist control	-0.04 (-0.51, 0.44)	No	Inconclusive	Low
WOMAC Function	68	Yes	8	Swedish massage therapy	Waitlist control	-0.78 (-1.27, -0.28)	Favors massage therapy	Possibly clinically important	Low
WOMAC Function	68	No	16	Swedish massage therapy	Waitlist control	-0.13 (-0.60, 0.35)	No	Inconclusive	Low
WOMAC Total	68	Yes	8	Swedish massage therapy	Waitlist control	-0.84 (-1.34, -0.35)	Favors massage therapy	Possibly clinically important	Low
WOMAC Total	68	No	16	Swedish massage therapy	Waitlist control	-0.84 (-1.34, -0.35)	No	Inconclusive	Low

Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
WOMAC Pain	68	Yes	8	Swedish massage therapy	Waitlist control	-0.94 (-1.44, -0.44)	Favors massage therapy	Clinically Significant	Low
WOMAC Pain	68	No	16	Swedish massage therapy	Waitlist control	-0.22 (-0.70, 0.25)	No	Inconclusive	Low
WOMAC Stiffness	68	Yes	8	Swedish massage therapy	Waitlist control	-0.67 (-1.16, -0.18)	Favors massage therapy	Possibly clinically important	Low
WOMAC Stiffness	68	No	16	Swedish massage therapy	Waitlist control	-0.14 (-0.62, 0.33)	No	Inconclusive	Low

Table 100. Ultrasound Versus Control

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Huang (2005)	70	Walk speed (m/min)	Yes	8	Isotonic exercise plus ultrasonic wave therapy	Isotonic exercise only	1.66 (1.12, 2.21)	Favors isotonic exercise plus ultrasonic wave therapy	N/A	Moderate
Huang (2005)	70	Lequesne index	Yes	8	Isotonic exercise plus ultrasonic wave therapy	Isotonic exercise only	-1.67 (-2.22, -1.12)	Favors isotonic exercise plus ultrasonic wave therapy	N/A	Moderate
Huang (2005)	70	VAS Pain	Yes	8	Isotonic exercise plus ultrasonic wave therapy	Isotonic exercise only	-0.16 (-0.63, 0.31)	No	True negative	Moderate

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Huang (2005)	70	Walk speed (m/min)	Yes	52	Isotonic exercise plus ultrasonic wave therapy	Isotonic exercise only	1.34 (0.82, 1.86)	Favors isotonic exercise plus ultrasonic wave therapy	N/A	Moderate
Huang (2005)	70	Lequesne index	Yes	52	Isotonic exercise plus ultrasonic wave therapy	Isotonic exercise only	-1.49 (-2.03, -0.96)	Favors isotonic exercise plus ultrasonic wave therapy	N/A	Moderate
Huang (2005)	70	VAS Pain	Yes	52	Isotonic exercise plus ultrasonic wave therapy	Isotonic exercise only	-0.89 (-1.38, -0.39)	Favors isotonic exercise plus ultrasonic wave therapy	Possibly clinically important	Moderate
Yang (2011)	100	VAS Pain	Yes	4	Ultrasound	Placebo	1.081 (0.66 ,1.50)	Ultrasound	Unclear	Moderate

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Yang (2011)	100	Lequesne index curative effect	Yes	4	Ultrasound	Placebo	0.877 (0.47 ,1.29)	Ultrasound	Unclear	Moderate

Table 101. Pulsed Electrical and Electromagnetic Therapy

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Fary (2011)	70	Global Assessment of Disease Activity	Unclear	26	Pulsed electrical stimulation	Placebo	-0.125 (-0.595 ,0.344)	No	Unclear	Low
Fary (2011)	70	SF-36 Mental	Unclear	26	Pulsed electrical stimulation	Placebo	0.136 (-0.333 ,0.606)	No	Inconclusive	Low
Fary (2011)	70	Human activity profile maximum activity	Unclear	26	Pulsed electrical stimulation	Placebo	-0.268 (-0.739 ,0.203)	No	Unclear	Low

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Fary (2011)	70	Human activity profile adjusted activity	Unclear	26	Pulsed electrical stimulation	Placebo	-0.039 (-0.508 ,0.43)	No	Unclear	Low
Fary (2011)	70	Daily accelerometer count	Unclear	26	Pulsed electrical stimulation	Placebo	0.34 (-0.133 ,0.812)	No	Unclear	Low
Fary (2011)	70	Daily resting time, minutes	Unclear	26	Pulsed electrical stimulation	Placebo	-0.182 (-0.651 ,0.288)	No	Unclear	Low
Fary (2011)	70	Daily light activity, minutes	Unclear	26	Pulsed electrical stimulation	Placebo	-0.03 (-0.499 ,0.439)	No	Unclear	Low
Fary (2011)	70	Daily moderate activity, minutes	Unclear	26	Pulsed electrical stimulation	Placebo	0.291 (-0.18 ,0.762)	No	Unclear	Low
Fary (2011)	70	Daily hard activity, minutes	Unclear	26	Pulsed electrical stimulation	Placebo	0.11 (-0.36, 0.58)	No	Unclear	Low
Trock (1994)	72	Pain on passive motion	Unclear	4 weeks after treatment	Pulsed electromagnetic fields	Placebo	0.469 (0 ,0.939)	No	Unclear	High
Trock (1994)	72	Tenderness	Unclear	4 weeks after treatment	Pulsed electromagnetic fields	Placebo	0.518 (0.047 ,0.989)	Favors pulsed electromagnetic fields	Unclear	High

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Trock (1994)	73	Physician overall assessment	Unclear	4 weeks after treatment	Pulsed electromagnetic fields	Placebo	0.526 (0.058 ,0.995)	Favors pulsed electromagnetic fields	Unclear	High
Battisti (2004)	60	Complete reduction of pain	Unclear	6.4	Therapeutic Application of Modulated Electro Magnetic Field (TAMMEF)	Extremely low frequency electromagnetic field	OR=2.74 (0.63, 11.82)	No	Unclear	Moderate
Battisti (2004)	60	Lequesne index: Total recovery of articular function	Unclear	6.4	Therapeutic Application of Modulated Electro Magnetic Field (TAMMEF)	Extremely low frequency electromagnetic field	OR=1.35 (0.46, 3.97)	No	Unclear	Moderate
Zizic (1995)	71	At least 15 minute improvement in morning stiffness	Unclear	8	Pulsed electrical stimulation	Sham	OR=2.70 (0.97, 7.51)	No	Unclear	Moderate
Zizic (1995)	71	VAS Pain % change	Unclear	8	Pulsed electrical stimulation	Sham	Mean difference=12.29 (p=.04)	Favors pulsed electrical stimulation	Unclear	Moderate
Zizic (1995)	71	VAS Function % change	Unclear	8	Pulsed electrical stimulation	Sham	Mean difference=10.83 (p=.045)	Favors pulsed electrical stimulation	Unclear	Moderate

Study	N	Outcome	Power	Weeks	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Zizic (1995)	71	Percent change adjusted mean physician evaluation (VAS)	Unclear	8	Pulsed electrical stimulation	Sham	Mean difference=14.64 (p=.023)	Favors pulsed electrical stimulation	Unclear	Moderate

Figure 21. Acupuncture: WOMAC pain in MID Units

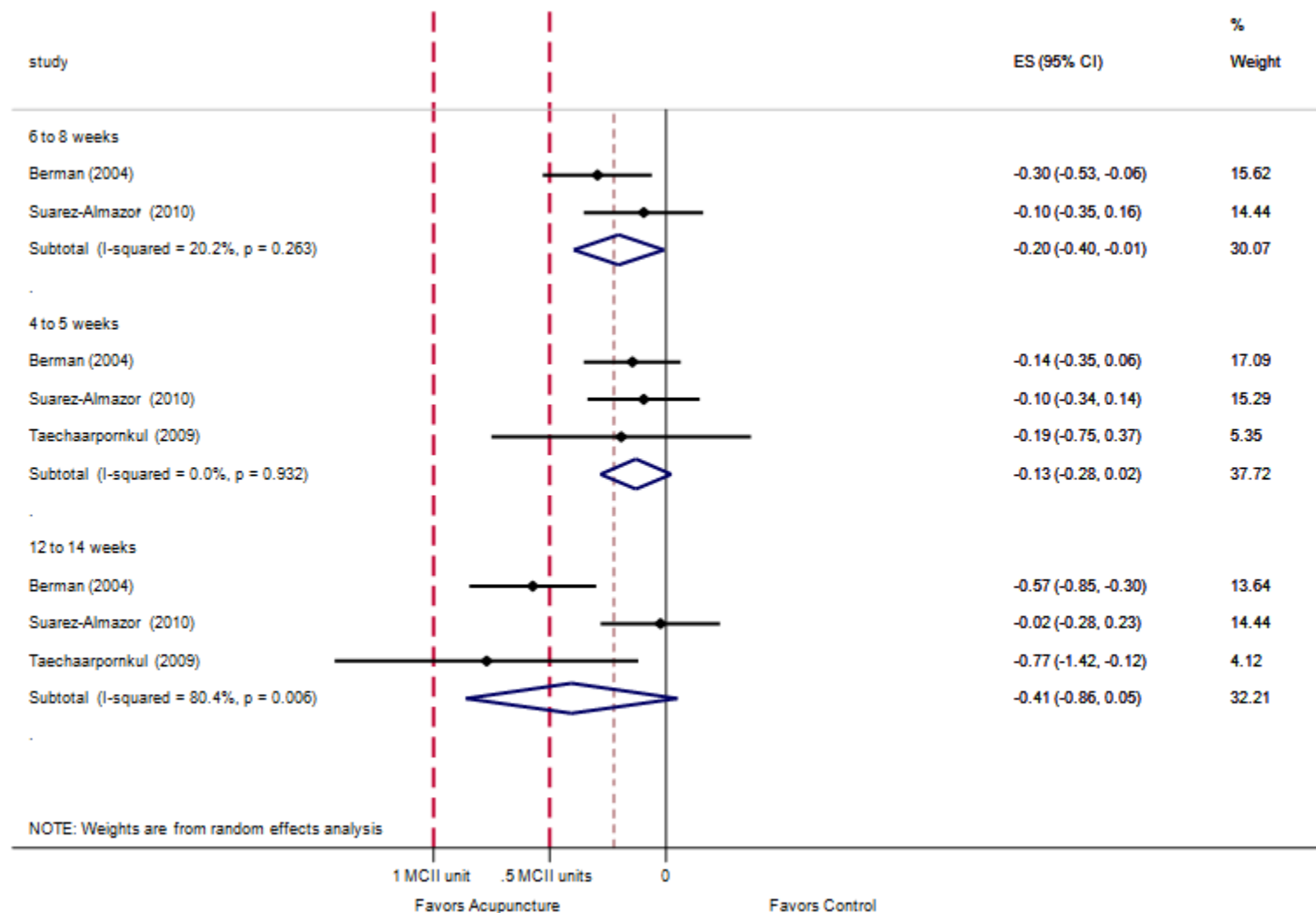


Figure 22. Acupuncture: WOMAC Function in MID Units

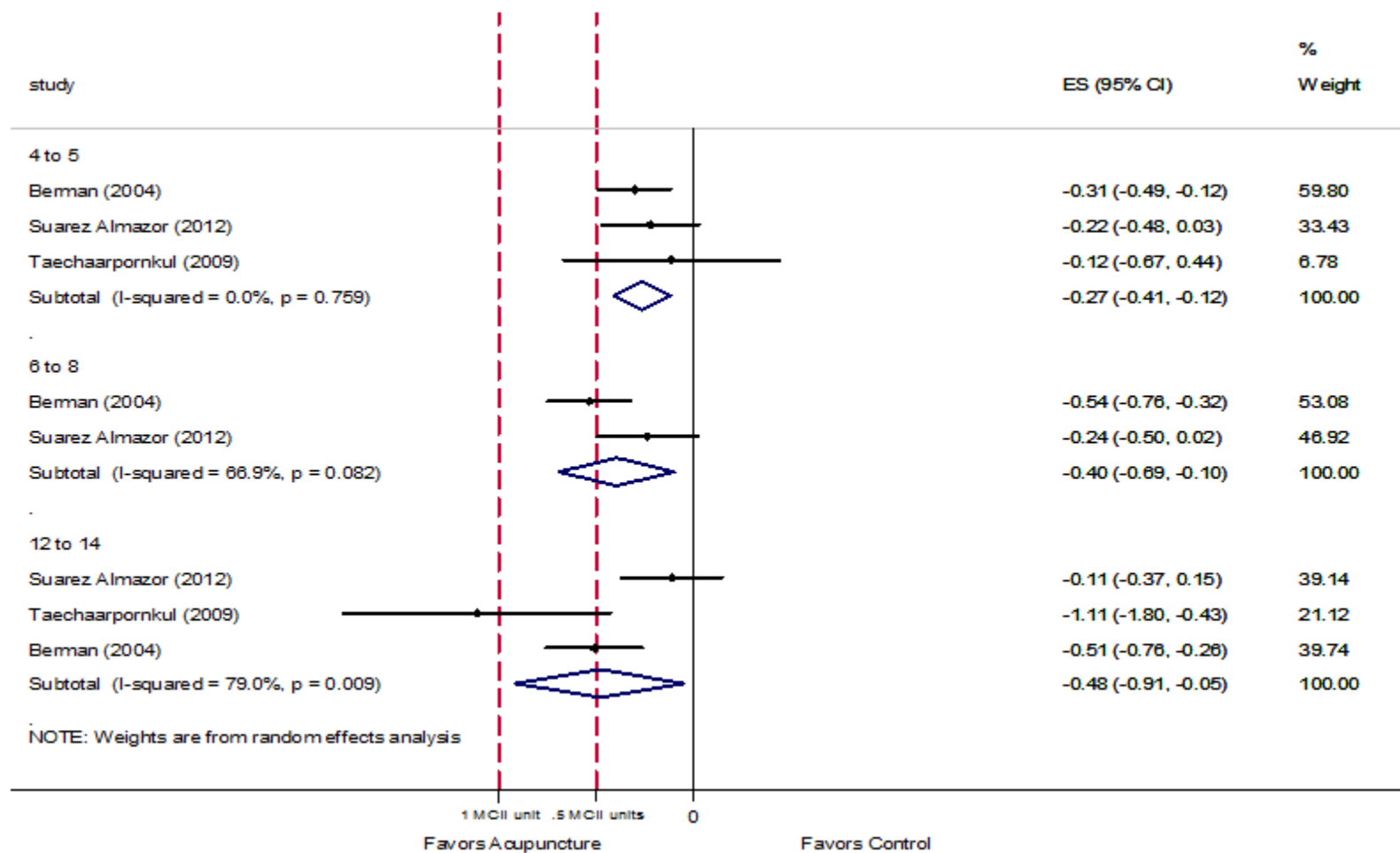
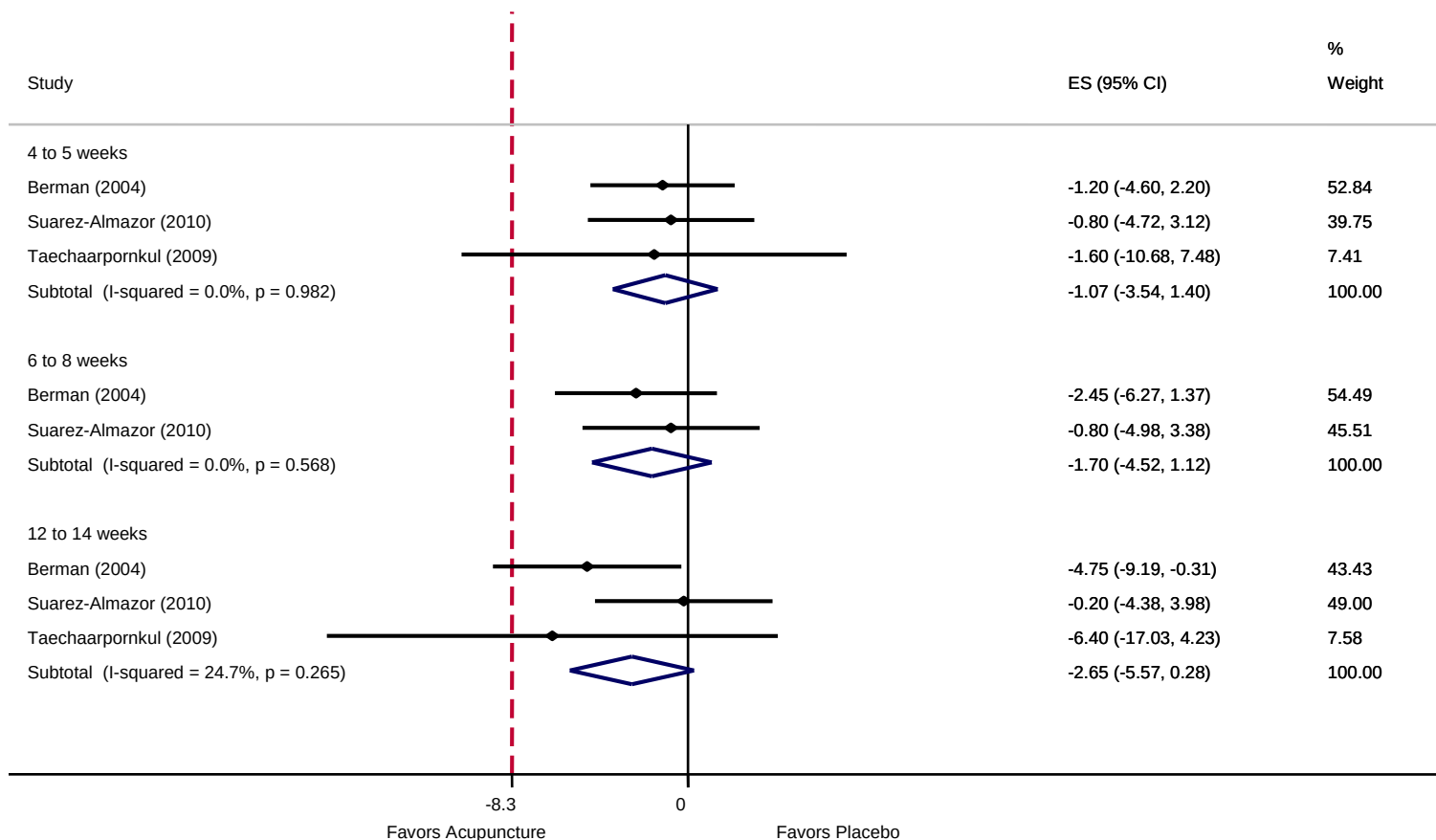
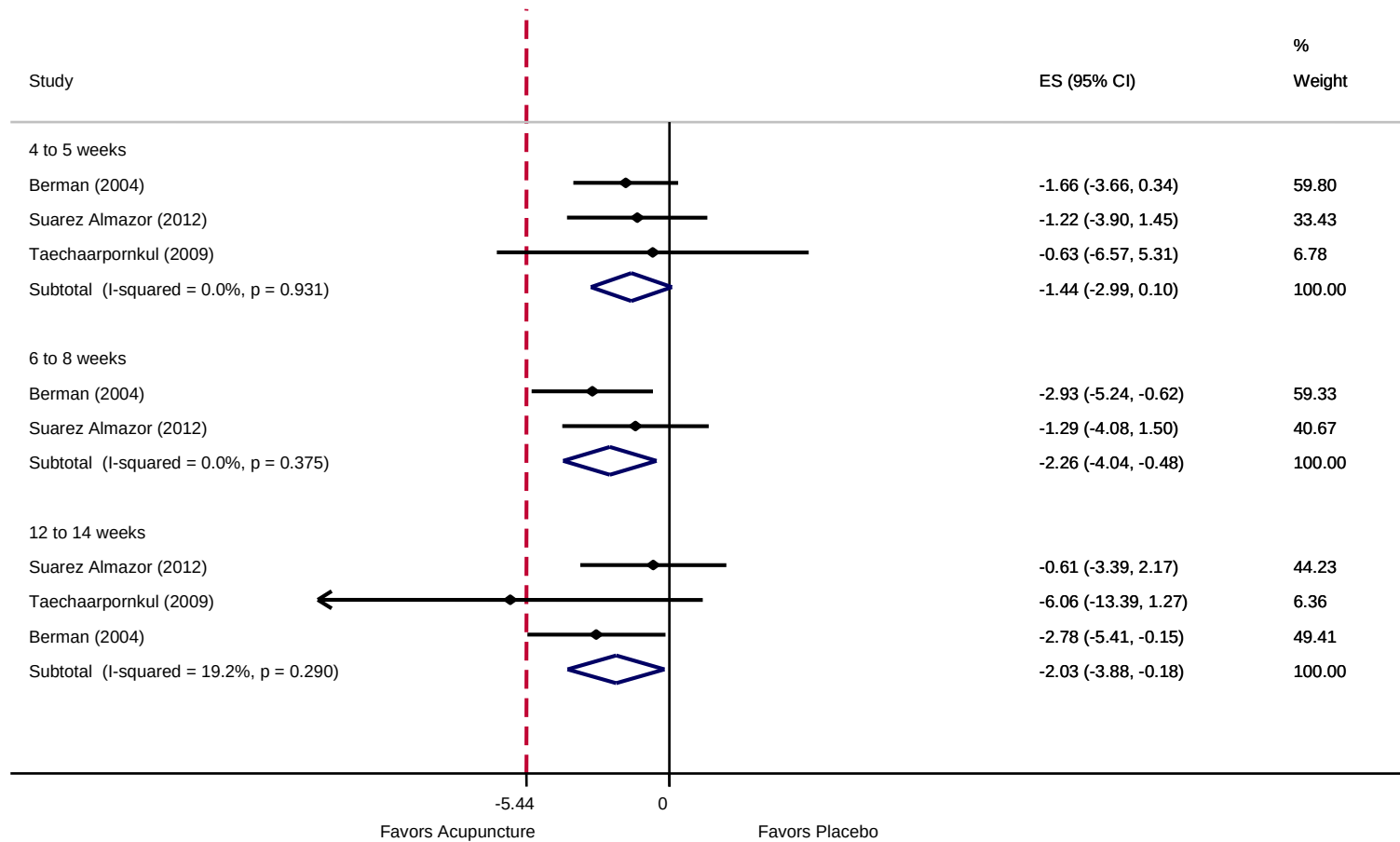


Figure 23. Acupuncture Versus Placebo: WOMAC Pain (1999)



The red line indicates the MCII

Figure 24. Acupuncture Versus Control: WOMAC Function



The red line indicates the MCII

RECOMMENDATION 4

We are unable to recommend for or against the use of a valgus directing force brace (medial compartment unloader) for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

This recommendation is based on three separate studies; one high-strength study⁷⁸ compared a valgus producing brace plus usual care to a neoprene sleeve brace plus usual care and to usual care alone. A second high-strength study compared a valgus directing force brace to a lateral wedge foot orthotic.⁷⁹ The third study of moderate-strength compared a valgus directing force brace plus usual care to usual care alone.⁸⁰ Therapies were compared with respect to how much they improved pain, stiffness, self-reported functional capacity, and physical performance measures (observed walking distance and number of stairs climbed in 30 seconds). Improvement using the valgus producing brace was not consistently significant across the four studies. For all statistically significant comparisons, the clinical significance of the improvements in pain and physical function were unclear.

Based on a lack of appropriate studies, the use of a valgus directing force brace was not evaluated.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 102-Table 104](#), [Table 105-Table 107](#)

There were two high-^{78;79} and one moderate-⁸⁰ quality randomized controlled trials that comprised the evidence for this recommendation. Two studies compared braces plus usual care to usual care alone.^{78;80} One RCT compared bracing to insoles.⁷⁹ One of the three studies had a potential for investigator bias. No other quality domains were flawed in any of the included studies.

APPLICABILITY

Relevant Tables: [Table 102-Table 104](#), [Table 105-Table 107](#)

In all three included studies, there was uncertainty whether the treatment administration and the study participants were representative of clinical practice. The Kirkley et al.⁷⁸ study was the only study that did not use all enrolled patients in their final analysis. Also,

the Van Raaij et al.⁷⁹ study was the only one with compliance and adherence measures that were not similar to regular practice.

FINAL STRENGTH OF EVIDENCE

All studies had high quality and moderate applicability that resulted in in high strength of evidence ratings.

Table 102. Quality and Applicability Summary: Brace Versus Usual Care

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Kirkley (1999)	WOMAC Pain	6 months	High	Moderate	High
Kirkley (1999)	WOMAC Function	6 months	High	Moderate	High
Kirkley (1999)	WOMAC Stiffness	6 months	High	Moderate	High
Kirkley (1999)	WOMAC Total	6 months	High	Moderate	High
Kirkley (1999)	VAS Pain on 6 minute walk	6 months	High	Moderate	High
Kirkley (1999)	VAS Pain on stair climb	6 months	High	Moderate	High
Kirkley (1999)	6 minute walk distance	6 months	High	Moderate	High
Kirkley (1999)	Number of stairs climbed in 30 seconds	6 months	High	Moderate	High
Kirkley (1999)	MACTAR	6 months	High	Moderate	High
Kirkley (1999)	Clinical success rate	6 months	High	Moderate	High
Brouwer (2006)	VAS Pain	3 months	Moderate	Moderate	Moderate
Brouwer (2006)	VAS Pain	6 months	Moderate	Moderate	Moderate
Brouwer (2006)	VAS Pain	1 year	Moderate	Moderate	Moderate
Brouwer (2006)	Hospital for Special Surgery: Function	3 months	Moderate	Moderate	Moderate
Brouwer (2006)	Hospital for Special Surgery: Function	6 months	Moderate	Moderate	Moderate
Brouwer (2006)	Hospital for Special Surgery: Function	1 year	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Brouwer (2006)	Walk distance (km)	3 months	Moderate	Moderate	Moderate
Brouwer (2006)	Walk distance (km)	6 months	Moderate	Moderate	Moderate
Brouwer (2006)	Walk distance (km)	1 year	Moderate	Moderate	Moderate
Brouwer (2006)	EQ-5D	3 months	Moderate	Moderate	Moderate
Brouwer (2006)	EQ-5D	6 months	Moderate	Moderate	Moderate
Brouwer (2006)	EQ-5D	1 year	Moderate	Moderate	Moderate

Table 103. Quality and Applicability Summary: Brace Versus Sleeve

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Kirkley (1999)	WOMAC Pain	6 months	High	Moderate	High
Kirkley (1999)	WOMAC Function	6 months	High	Moderate	High
Kirkley (1999)	WOMAC Stiffness	6 months	High	Moderate	High
Kirkley (1999)	WOMAC Total	6 months	High	Moderate	High
Kirkley (1999)	VAS Pain on 6 minute walk	6 months	High	Moderate	High
Kirkley (1999)	VAS Pain on stair climb	6 months	High	Moderate	High
Kirkley (1999)	6 minute walk distance	6 months	High	Moderate	High
Kirkley (1999)	Number of stairs climbed in 30 seconds	6 months	High	Moderate	High
Kirkley (1999)	MACTAR	6 months	High	Moderate	High
Kirkley (1999)	Clinical success rate	6 months	High	Moderate	High

Table 104. Quality and Applicability Summary: Brace Versus Insoles

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Van Raaij	VAS Pain	6 months	High	Moderate	High

RESULTS

Relevant Tables: [Figure 25-Figure 26](#), [Table 108-Table 113](#)

Two out of the three studies compared braces combined with usual care to usual care alone. Brouwer et al.⁸⁰ included a patient population with Ahlback grades of 1-2. Kirkley et al.⁷⁸ included patients with Kellgren and Lawrence grades of 1-4. In the Brouwer et al. study usual care consisted of education, analgesics (as needed) and physical therapy (as needed). In the Kirkley et al. study, usual care consisted of an educational pamphlet and as needed acetaminophen. Participants who were already taking NSAIDs before the study were allowed to continue using them.

There was inconclusive evidence regarding the efficacy of knee bracing. Kirkley et al.⁷⁸ found that patients in the brace group reported significantly better scores on the WOMAC subscales (pain, function, stiffness, total), VAS pain on waking, VAS pain on climbing stairs, and the MACTAR tests than the group who received only acetaminophen and an educational pamphlet. Kirkley et al. found nonsignificant differences for distance walked in 6 minutes, and number of stairs climbed in 30 seconds. Brouwer et al.⁸⁰ found statistically nonsignificant differences between the brace group and the usual care group (education, analgesic as needed, and physical therapy as needed) at three, six and 12 months, in VAS pain, knee function and quality of life. Although, walking distance was found to be significantly greater in the treatment group than the control group at each follow up period.

Kirkley et al.⁷⁸ also compared the unloader brace to the neoprene sleeve. For all pain outcomes, the brace was significantly more effective than the sleeve. However, there was no statistically significant difference between the two treatments for self reported functioning, functional tasks, WOMAC Stiffness or WOMAC Total ([Figure 26](#)).

Van Raaij et al.⁷⁹ compared the effectiveness of bracing to foot insoles. The authors found that VAS pain was significantly lessened in the brace group than the insole group.

Figure 25. Results Summary: Brace Versus Usual Care

	13	Week 26	52
VAS Pain	●	●	●
Walking distance	●	●	●
HSS Function	●	●	●
EQ-5D	●	●	●
1cm improvement on VAS Pain after 6 minute walk			●
VAS Pain on 30 second stair climb improvement			●
VAS Pain on 6 minute walk- improvement			●
WOMAC Pain improvement			●
30 second stair climb improvement			●
6 minute walk distance- improvement			●

MACTAR improvement	●
WOMAC Function improvement	●
WOMAC Stiffness improvement	●
WOMAC Total improvement	●

Key: ●=Not Significant; ●=Statistically Significant

Figure 26. Results Summary: Brace vs. Sleeve and Insoles

Treatment	Control	Outcome	Week 26
Brace	Sleeve	WOMAC Pain improvement	●
		VAS Pain on 6 minute walk improvement	●
		VAS Pain on 30 second stair climb improvement	●
		1cm improvement on VAS Pain after 6 minute walk	●
		WOMAC Function improvement	●
		MACTAR improvement	●
		6 minute walk distance improvement	●
		30 second stair climb improvement	●
		WOMAC Stiffness improvement	●
		WOMAC Total improvement	●
Brace	Insole	VAS Pain	●

Key: ●=Not Significant; ●=Statistically Significant in Favor of Treatment

EVIDENCE TABLES AND FIGURES

QUALITY AND APPLICABILITY

Table 105. Quality and Applicability: Brace Versus Usual Care

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Kirkley (1999)	WOMAC Pain	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	WOMAC Function	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	WOMAC Stiffness	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	WOMAC Total	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	VAS Pain on 6 minute walk	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	VAS Pain on stair climb	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome									Quality					Applicability Study
		Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias		Participants	Intervention and Expertise	Compliance and Adherence	Analysis	
Kirkley (1999)	6 minute walk distance	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	Number of stairs climbed in 30 seconds	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	MACTAR	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	Clinical success rate	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Brouwer (2006)	VAS Pain 13 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	VAS Pain 26 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	VAS Pain 52 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	Hospital for Special Surgery: Function 13 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Brouwer (2006)	Hospital for Special Surgery: Function 26 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	Hospital for Special Surgery: Function 52 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	Walk distance (km) 13 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	Walk distance (km) 26 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	Walk distance (km) 52 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	EQ-5D 13 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	EQ-5D 26 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Brouwer (2006)	EQ-5D 52 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 106. Quality and Applicability: Unloader Brace Versus Neoprene Sleeve

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Kirkley (1999)	WOMAC Pain	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	WOMAC Function	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	WOMAC Stiffness	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	WOMAC Total	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	VAS Pain on 6 minute walk	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	VAS Pain on stair climb	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	6 minute walk distance	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	Number of stairs climbed in 30 seconds	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	<i>Quality</i>	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Kirkley (1999)	MACTAR	●	◐	●	●	●	●	●	○	High	○	○	●	○	Moderate
Kirkley (1999)	Clinical success rate	●	●	●	●	●	●	●	○	High	○	○	●	○	Moderate

Table 107. Quality and Applicability: Braces Versus Insoles

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Van-Raaij (2010)	VAS Pain	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Van-Raaij (2010)	WOMAC Function	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

FINDINGS

Table 108. Brace Plus Usual Care Versus Usual Care: Pain

Study	Outcome	N	Power	Week	Severity	Avg. BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (1999)	1cm improvement on VAS Pain after 6 minute walk	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	OR=8.59 (2.94, 25.12)	Favors brace	N/A	High
Brouwer (2006)	VAS Pain	117	Unclear	13	Ahlback 1-2	28.5	Brace	Usual care	MD= -0.73(-1.62, .16)	No	True negative	High
Brouwer (2006)	VAS Pain	117	Unclear	26	Ahlback 1-2	28.5	Brace	Usual care	MD=-0.58(-1.48, .32)	No	True negative	High
Brouwer (2006)	VAS Pain	117	Unclear	52	Ahlback 1-2	28.5	Brace	Usual care	MD=-0.81(-1.76, .14)	No	True negative	High
Kirkley (1999)	VAS Pain on 30 second stair climb improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD=21.5 (p<.001)	Favors brace	Unclear	High

Study	Outcome	N	Power	Week	Severity	Avg. BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (1999)	VAS Pain on 6 minute walk-improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 18.9 (p<.001)	Favors brace	Unclear	High
Kirkley (1999)	WOMAC Pain improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 2.26 (p<.001)	Favors brace	Unclear	High

Table 109. Brace Plus Usual Care Versus Usual Care: Functional Tasks

Study	Outcome	N	Power	Week	Severity	Avg. BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (1999)	30 second stair climb improvement	74	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD=16.21	No	N/A	High
Kirkley (1999)	6 minute walk distance-improvement	74	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 4.1 meters	No	N/A	High
Brouwer (2006)	Walking distance	117	Yes	13	Ahlback 1-2	28.5	Brace	Usual care	MD=1.21 (.12, 2.28)	Favors brace	N/A	High
Brouwer (2006)	Walking distance	117	Unclear	26	Ahlback 1-2	28.5	Brace	Usual care	MD=0.79 (-.4, 1.98)	No	N/A	High
Brouwer (2006)	Walking distance	117	Yes	52	Ahlback 1-2	28.5	Brace	Usual care	MD=1.34 (.05, 2.63)	Favors brace	N/A	High

Table 110. Brace Plus Usual Care Versus Usual Care: Function

Study	Outcome	N	Power	Week	Severity	Avg. BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Brouwer (2006)	HSS Function	117	Yes	13	Ahlback 1-2	28.5	Brace	Usual care	MD=3.5 (-.24, 7.24)	No	N/A	High
Brouwer (2006)	HSS Function	117	Yes	26	Ahlback 1-2	28.5	Brace	Usual care	MD=3.2 (-.58, 6.98)	No	N/A	High
Brouwer (2006)	HSS Function	117	Yes	52	Ahlback 1-2	28.5	Brace	Usual care	MD=3 (-1.05, 7.05)	No	N/A	High
Kirkley (1999)	MACTAR improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 11.6 (p=.017)	Favors brace	N/A	High
Kirkley (1999)	WOMAC Function improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 6.54 (p=.001)	Favors brace	Unclear	High

Table 111. Brace plus Usual Care Versus Usual Care: Other Outcomes

Outcome type	Study	Outcome	N	Power	Week	Severity	Avg. BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
WOMAC Stiffness	Kirkley (1999)	WOMAC Stiffness improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 1.47 (p<.001)	Favors brace	Unclear	High
WOMAC Total	Kirkley (1999)	WOMAC Total improvement	74	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Usual care	MD= 10.28 (p<.001)	Favors brace	Unclear	High
Quality of Life	Brouwer (2006)	EQ-5D	117	Unclear	13	Ahlback 1-2	28.5	Brace	Usual care	MD=0.03 (-.05, .12)	No	N/A	High
	Brouwer (2006)	EQ-5D	117	Unclear	26	Ahlback 1-2	28.5	Brace	Usual care	MD=0.01 (-.08, .1)	No	N/A	High
	Brouwer (2006)	EQ-5D	117	Unclear	52	Ahlback 1-2	28.5	Brace	Usual care	MD=0.01 (-.08, .1)	No	N/A	High

Table 112. Brace Versus Neoprene Sleeve

Outcome Type	Study	Outcome	N	Power	Week	Severity	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Sig	Strengt h Of evidenc e
Pain	Kirkley (1999)	WOMAC Pain	77	Yes	26	Kellgren and Lawrence Grade 1-4	Not Reported (NR)	Unloader brace	Neoprene sleeve	MD=1.204 (P.045)	Favors brace	Unclear	High
	Kirkley (1999)	VAS Pain on 6 minute walk	77	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD= (p=.021)	Favors brace	Unclear	High
	Kirkley (1999)	VAS Pain on 30 second stair climb	77	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=12.3 (p=.016)	Favors brace	Unclear	High
	Kirkley (1999)	1cm on VAS Pain after 6 minute walk	77	Yes	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	OR= 1.95 (0.79, 4.85)	Favors brace	N/A	High

Outcome Type	Study	Outcome	N	Power	Week	Severity	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Sig	Strength Of evidence
Function (Self-Reported)	Kirkley (1999)	WOMAC Function	77	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=3.532 (P=.081)	No	Unclear	High
	Kirkley (1999)	MACTAR	77	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=16.1 (P=.174)	No	N/A	High
Function Task	Kirkley (1999)	6 minute walk distance	77	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=26.9 m (NS)	No	N/A	High
	Kirkley (1999)	30 second stair climb	77	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=5.59 Steps (NS)	No	N/A	High

Outcome Type	Study	Outcome	N	Power	Week	Severity	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Sig	Strength Of evidence
WOMAC Stiffness	Kirkley (1999)	WOMAC Stiffness	77	Unclear	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=.524 (P=.91)	No	Unclear	High
WOMAC Total	Kirkley (1999)	WOMAC Total	77	Sufficient	26	Kellgren and Lawrence Grade 1-4	NR	Unloader brace	Neoprene sleeve	MD=5.26 (P=.062)	No	Unclear	High

Table 113. Braces Versus Insoles

Study	Outcome	N	Power	Week	Severity	BMI	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Van Raaij (2010)	VAS Pain	117	Yes	26	K-L Grade 1-4	29.2	Brace	Insole	-.82 (-1.247, -.39)	Favors brace	Possibly clinically important	High

RECOMMENDATION 5

We cannot suggest that lateral wedge insoles be used for patients with symptomatic medial compartment osteoarthritis of the knee.

Strength of Recommendation: Moderate

Description: A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

RATIONALE

This recommendation is based on five studies. Four studies, one of high-strength⁸¹ and three of moderate-strength, compared outcomes using lateral wedge insoles to neutral insoles.⁸²⁻⁸⁴ No significant changes in pain, self-reported physical function, or Patient Global Assessment scores were seen between the two types of insoles. A fifth low-strength study compared urethane lateral wedge insoles to rubber lateral insoles, and found a statistically significant improvement in Lequesne score for urethane insoles, but this outcome was of uncertain clinical significance.⁸⁵

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 114-Table 115](#), [Table 117](#)

There were four studies that compared lateral wedge insoles to neutral insoles. Bennell et al.⁸¹ was of high strength; Baker et al.,⁸² Maillefert et al.⁸³ and Pham et al.⁸⁴ were moderate strength. Group assignment was not flawed in the Baker et al. and Bennell et al. studies^{81;82}. The equality of treatment groups at baseline was acceptable in the Bennell et al.⁸¹ study. The treatment integrity was a problem in the studies by Maillefert et al.⁸³ and Pham et al.⁸⁴ due to the use of concomitant NSAIDs. There was potential for investigator bias in the Baker et al. and Bennell et al.^{81;82} studies. No lateral wedge insole studies had problems with the validity of the outcomes measurements.

Toda et al.⁸⁵ compared Lequesne index scores of rubber to urethane insoles. This low strength study was flawed in the group assignment, comparability, investigator bias and blinding domains.

APPLICABILITY

Relevant Tables: [Table 114-Table 115](#), [Table 117](#)

Moderate applicability ratings were given to all studies. The delivery of treatment interventions might not have been representative of clinical practice in the studies. In four out of five studies, participants might not have been representative of the osteoarthritis of the knee patient population.^{81;83-85} All enrolled patients were included in the final analyses of each study. Compliance and adherence were typical of clinical practice in the studies by Toda et al. and Bennell et al.^{81;85}

FINAL STRENGTH OF EVIDENCE

The moderate quality and moderate applicability ratings were the reasons four out of five studies were rated as moderate strength of evidence. One of the four studies had moderate quality but low applicability and received a low strength of evidence rating.

Table 114. Quality and Applicability Summary: Lateral Wedge Insole

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Baker (2007)	WOMAC Pain	6 weeks	Moderate	Moderate	Moderate
Bennell (2011)	Health related quality of life	1 year	High	Moderate	High
Bennell (2011)	Number of daily steps	1 year	High	Moderate	High
Bennell (2011)	Physical activity scale or elderly (0-400)	1 year	High	Moderate	High
Bennell (2011)	WOMAC Function	1 year	High	Moderate	High
Bennell (2011)	WOMAC Function	1 year	High	Moderate	High
Maillefert (2001)	Analgesics taken in past 3 months	6 months	Moderate	Moderate	Moderate
Maillefert (2001)	NSAIDS taken in past 3 months	6 months	Moderate	Moderate	Moderate
Maillefert (2001)	WOMAC Pain	13 weeks	Moderate	Moderate	Moderate
Maillefert (2001)	WOMAC Stiffness	13 weeks	Moderate	Moderate	Moderate
Bennell (2011)	WOMAC Stiffness	1 year	High	Moderate	High
Pham(2004)	Global assessment	24 weeks	Moderate	Moderate	Moderate

Table 115. Quality and Applicability Summary: Rubber Versus Urethane Insole

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Toda (2004)	Lequesne index	4 weeks	Moderate	Moderate	Moderate

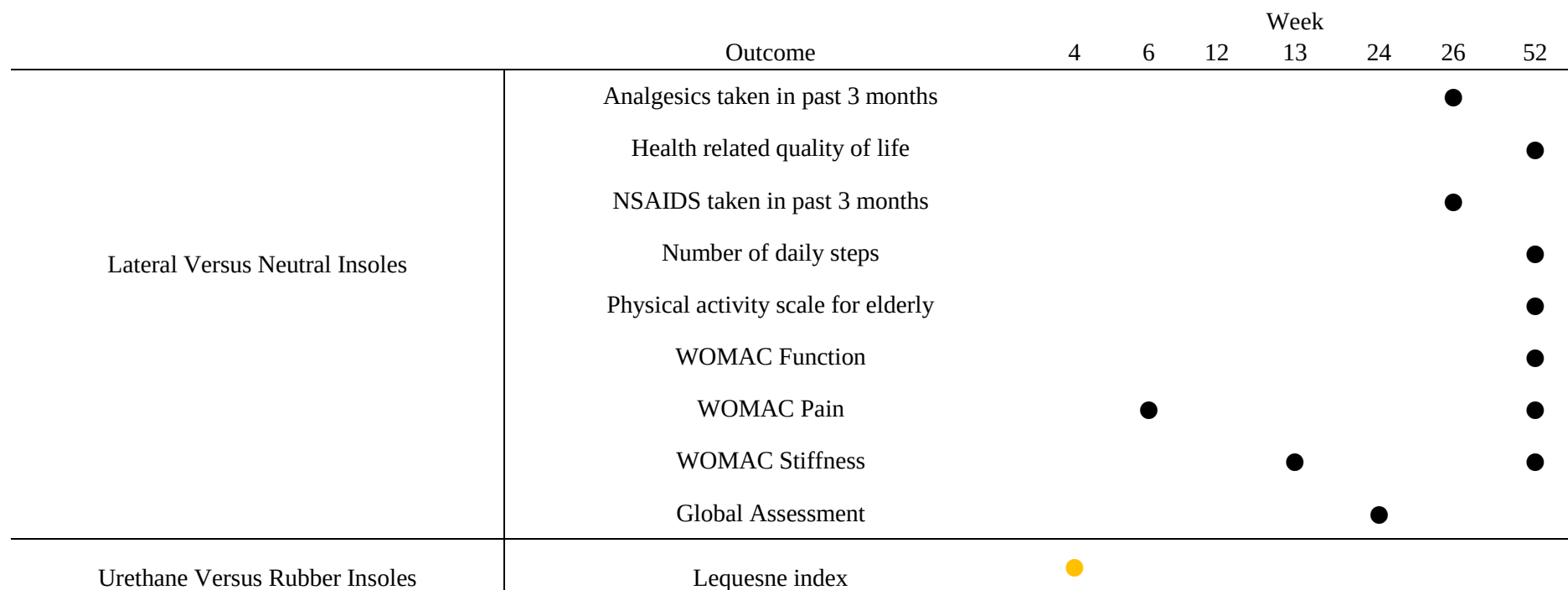
RESULTS

Relevant Tables: [Figure 27-Figure 30](#), [Table 118-Table 120](#)

There were 11 outcomes that compared lateral wedge insoles to neutral insoles. None of the differences in outcomes between treatment groups were statistically significant.

Toda et al.⁸⁵ found that participants who wore urethane insoles reported better Lequesne index scores than those who wore rubber insoles (see [Figure 27](#) for a summary of the results).

Figure 27. Results Summary: Foot Orthotics



Key: ●=Not Significant; ●=Statistically Significant in Favor of Urethane Insoles

EVIDENCE TABLES AND FIGURES

QUALITY AND APPLICABILITY

Table 116. Quality and Applicability: Lateral Wedge Insole

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Baker (2007)	WOMAC Pain	●	●	●	●	○	●	●	○	Moderate	●	○	○	●	Moderate
Maillefert (2001)	13 week WOMAC Stiffness	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Toda (2004)	Lequesne index	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Bennell (2011)	Health related quality of life	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bennell (2011)	WOMAC Pain	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bennell (2011)	WOMAC Function	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bennell (2011)	WOMAC Stiffness	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Bennell (2011)	Physical activity scale for elderly (0-400)	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bennell (2011)	Number of daily steps	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maillefert (2001)	NSAIDS taken in past 3 months	●	◐	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Maillefert (2001)	NSAIDS taken in past 3 months	●	◐	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Pham(2004)	Global Assessment	●	◐	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate

Table 117 Quality and Applicability: Rubber versus Urethane Insoles

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	<i>Quality</i>	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	<i>Applicability Study</i>
Baker (2007)	WOMAC Pain	●	●	●	●	○	●	●	○	Moderate	●	○	○	●	Moderate

FINDINGS

Table 118. Lateral Wedge versus Neutral Insoles: Critical Outcomes

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Custom/Not Custom	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Baker (2007)	WOMAC Pain	86	Yes	6	Lateral wedge	Neutral insole	Not custom	-0.05 (-0.47, 0.38)	No	Inconclusive	Moderate
Bennell(2011)	WOMAC Pain	179	Yes	52	Lateral wedge	Neutral insole	Not custom	0.15 (-0.15, 0.44)	No	N/A	High
Bennell(2011)	Health related quality of life	179	Unclear	52	Lateral wedge	Neutral insole	Not custom	0.08 (-0.17, 0.42)	No	N/A	High
Bennell(2011)	WOMAC Function	179	Yes	52	Lateral wedge	Neutral insole	Not custom	0.07 (-0.22, 0.36)	No	True negative	High

Table 119. Lateral Wedge versus Neutral Insoles: other outcomes

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Custom/Not Custom	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bennell(2011)	Physical activity scale for elderly (0-400)	179	Unclear	52	Lateral Wedge insole	Neutral insole	Not custom	-0.1 (-0.39, 0.19)	No	N/A	High

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Custom/Not Custom	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bennell(2011)	Number of daily steps	179	Unclear	52	Lateral Wedge insole	Neutral insole	Not custom	0.2 (-0.09, 0.49)	No	N/A	High
Bennell(2011)	WOMAC Stiffness	179	Yes	52	Lateral Wedge insole	Neutral insole	Not custom	0.2 (-0.13, 0.46)	No	True negative	High
Maillefert (2001)	WOMAC Stiffness	147	Yes	13	Lateral Wedge insole	Neutral insole	Custom	0.20 (-0.13, 0.52)	No	Inconclusive	Low
Maillefert (2001)	Analgesics taken in past 3 months	147	Yes	26	Lateral Wedge insole	Neutral insole	Custom	-.059(-.37, .26)	No	N/A	Low
Maillefert (2001)	NSAIDS taken in past 3 months	147	Yes	26	Lateral Wedge insole	Neutral insole	Custom	-.19(-.5, .12)	No	N/A	Low
Pham(2004)	Patient Global Assessment of Disease Activity	156	Unclear	24	Lateral Wedge insole	Neutral insole	Custom	.05 (-0.27, 0.36)	No	N/A	Moderate

Table 120. Urethane Versus Rubber Insole (Both With Subtalar Strapping)

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Custom/Not Custom	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Toda (2008)	Lequesne index	84	Yes	4	Lateral urethane insole	Lateral rubber insole	Not custom	-0.44 (-0.01, -0.88)	Favors urethane	N/A	Moderate

Figure 28. Lateral Wedge Insole Versus Neutral Insoles: Critical Outcomes

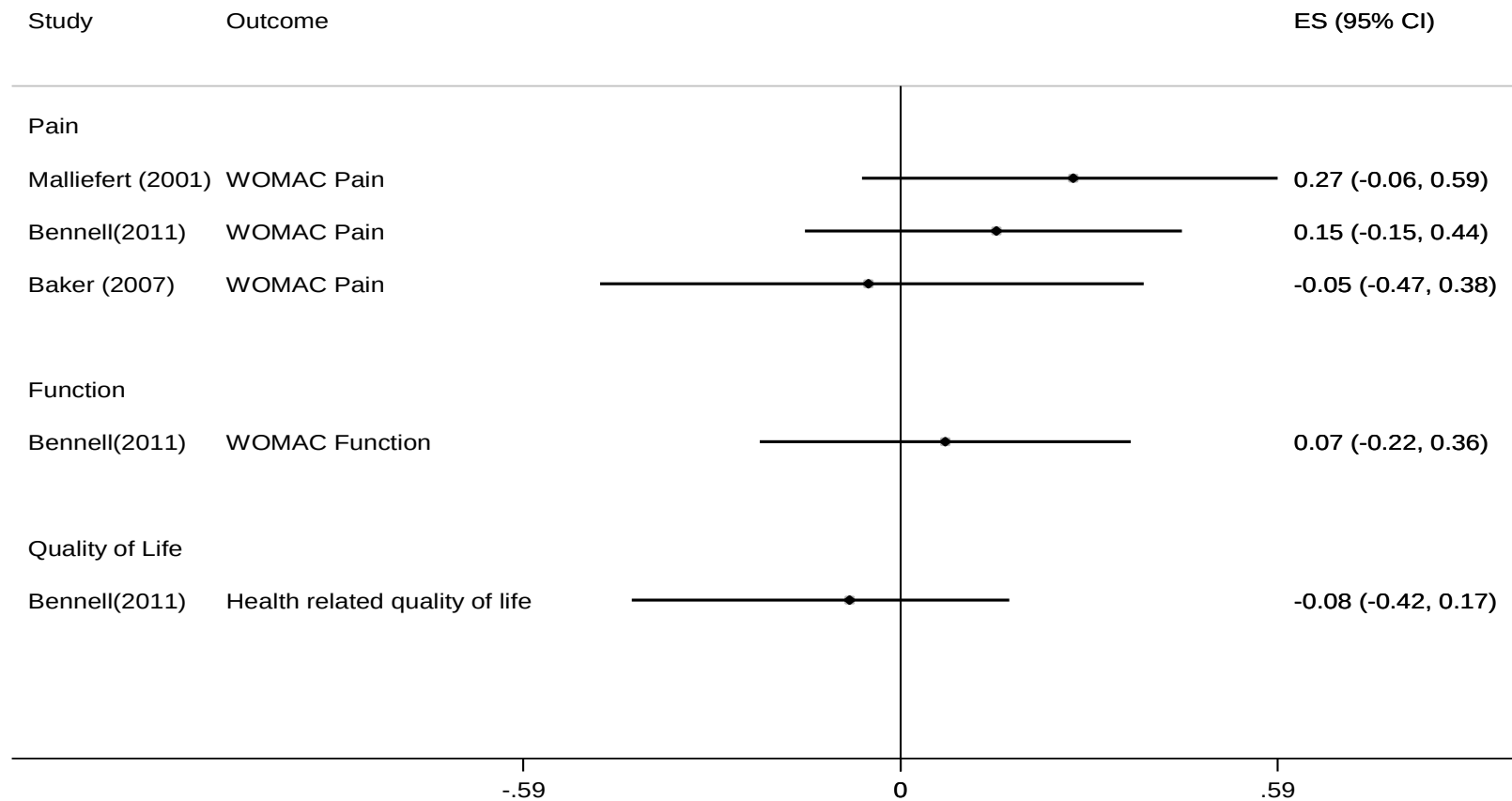


Figure 29. Lateral Wedge Insoles Versus Neutral Insoles: Other Outcomes

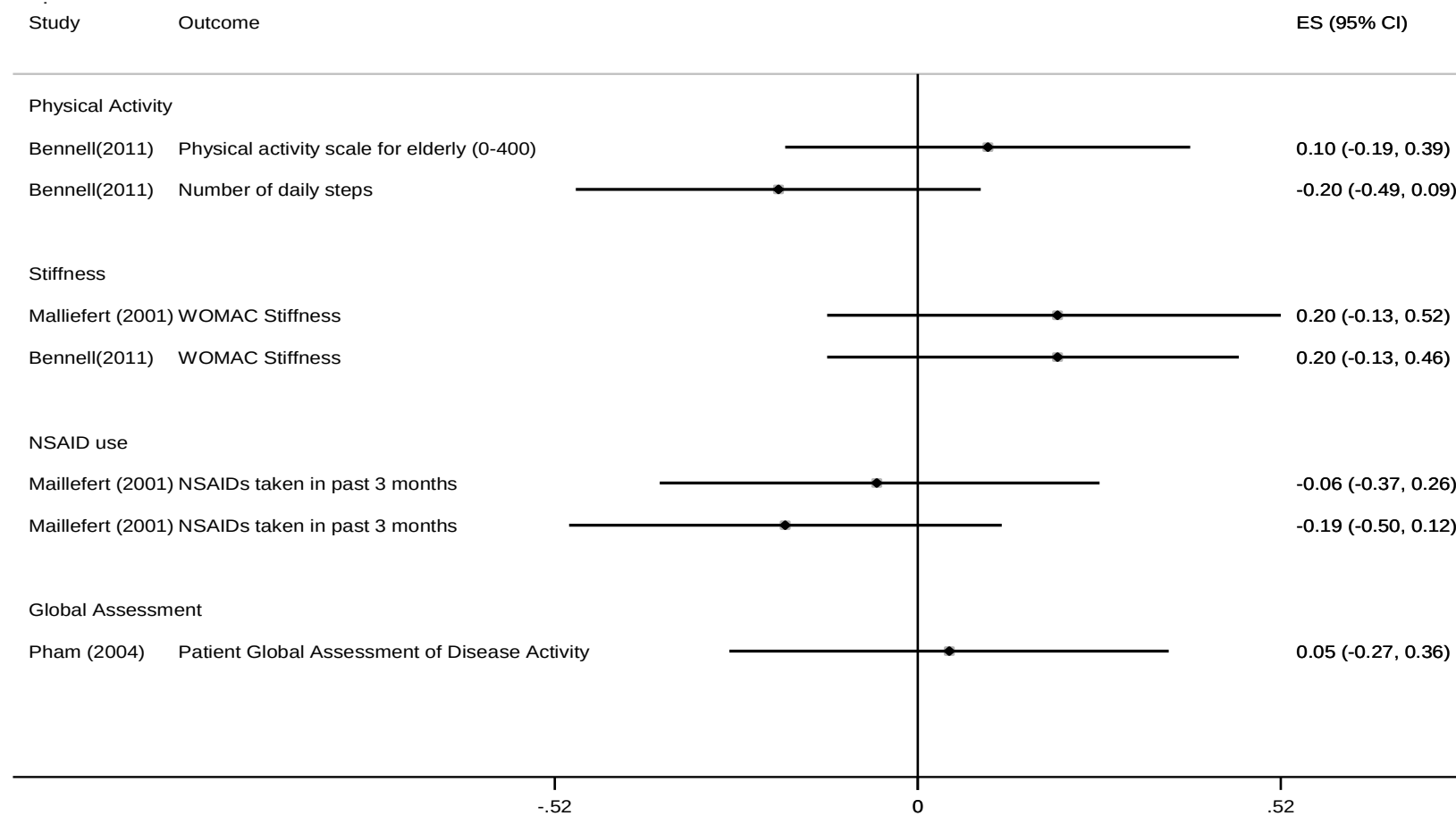
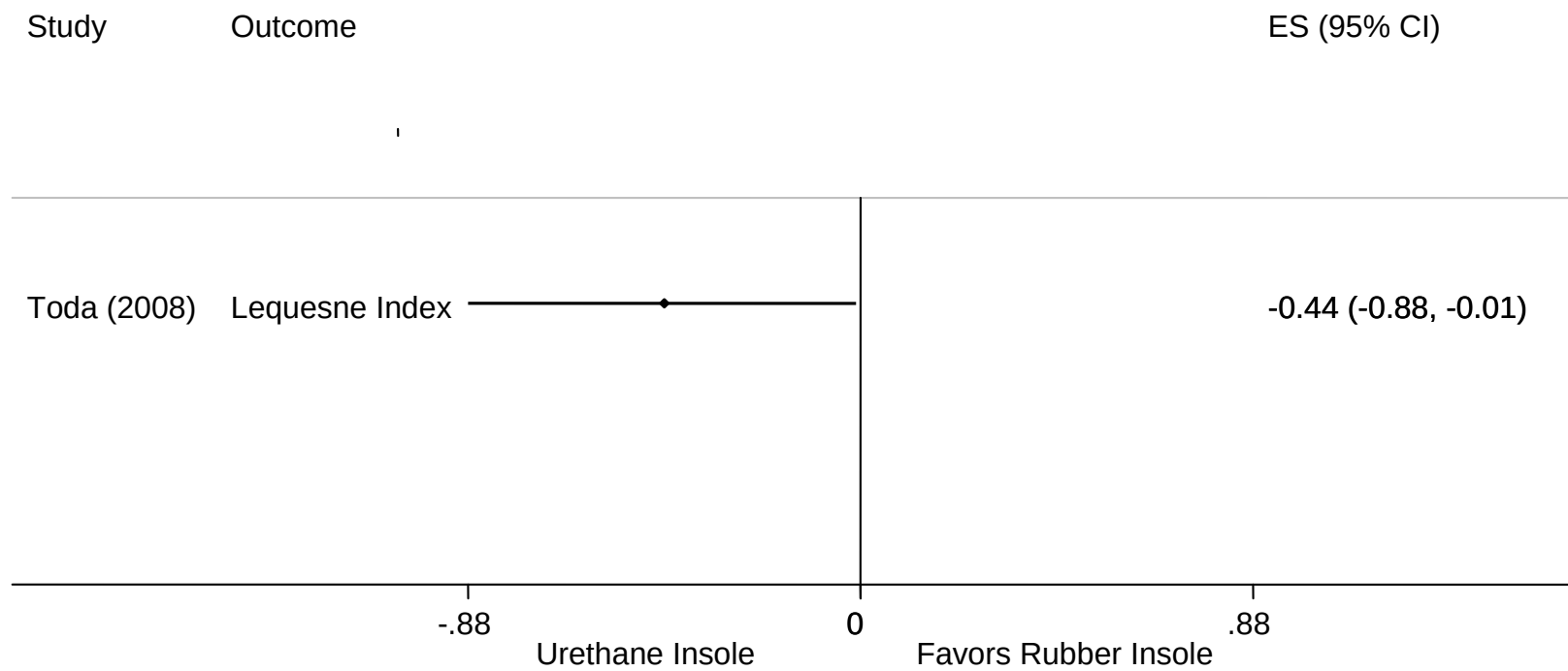


Figure 30. Urethane Versus Rubber Insoles



RECOMMENDATION 6

We cannot recommend using glucosamine and chondroitin for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RATIONALE

Twenty-one studies were included as evidence for this recommendation; all were prospective. Twelve focused on glucosamine alone, eight on chondroitin sulfate alone, and one (Clegg et. al⁸⁶) assessed both. Sixteen were of moderate-strength and five were of high-strength.

Among the studies, eleven of 52 outcomes were statistically significant in favor of glucosamine when compared to placebo. WOMAC pain and function subscales scores and VAS pain were the critical outcomes and were not associated with statistical significance at any treatment duration period. When meta-analyses were run for WOMAC pain, function, stiffness and total subscale scores, all meta-analyses showed that the overall effect of glucosamine compared to placebo was not statistically significant.

Two studies compared glucosamine to active treatments. Glucosamine was compared to reparagen⁸⁷ (a poly-herbal supplement), and enzymatic hydrolyzed collagen.⁸⁸ Glucosamine was found to have no significant effect on pain compared to these treatments.

[Figure 33](#) presents the meta-analysis results comparing chondroitin sulfate to placebo in pain scores on the VAS. The weighted mean difference revealed that scores were 11.89 points lower in the chondroitin group than in the placebo group. However, the difference was not clinically important.

At this time, both glucosamine and chondroitin sulfate have been extensively studied. Despite the availability of the literature, there is essentially no evidence that minimum clinically important outcomes have been achieved compared to placebo, whether evaluated alone or in combination. The strength of the recommendation is based on lack of efficacy, not on potential harm.

One of our search terms was nutraceuticals and we initially maintained a broad focus. However, the original guidance was to evaluate methylsulfonylmethane, omega-3, gelatin, vitamin D, dimethylsulfoxide, antioxidants, and coenzyme Q10. The general term was intended to guide the search of the specific terms. Additionally, the evidence for nutraceuticals was variable and could not be easily summarized. Two moderate-strength studies^{89;90} comparing ginger extract to placebo arose in the included evidence. The only

improvement in pain associated with both statistical significance and clinical importance was measured using WOMAC stiffness. Clinical importance could not be determined for four other pain measures, or they did not meet the minimum clinically important improvement threshold. The findings on outcomes of function were contradictory and low in count, which rendered them inconclusive. Glycosaminoglycan polysulfuric acid (GAGPS)⁹¹ produced a true negative finding statistically and clinically, and gubitung was associated with higher WOMAC total scores than glucosamine in a non-control matched study where clinical importance could not be determined.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 121](#)-[Table123](#)

Twenty one studies were included as evidence for this recommendation. Schnitzer et al. was the only study that was not prospective. Fifteen studies were flawed in the group assignment domain. The studies and outcomes were all blinded. Ten studies were flawed in group comparability. With the exception of studies by Cibere et al.⁹² and Mazierez et al.,⁹³ treatment integrity was maintained. Three studies did not have investigator bias as a concern, and all studies used valid outcome measurement instruments. In all, there were five high quality studies, one low quality study and 15 moderate quality studies included in this recommendation.

APPLICABILITY

Relevant Tables: [Table 121](#)-[Table123](#)

Seventeen studies enrolled patients who might not have been representative of the osteoarthritis of the knee population. Treatment administration was atypical of regular clinical practice in all studies and compliance and adherence were typical in 18 out of 21 studies. Finally, five studies did not include all enrolled patients in the final analyses.

FINAL STRENGTH OF EVIDENCE

All strength of evidence ratings were the same as the quality ratings since every outcome was of moderate applicability.

Table 121. Quality and Applicability Summary: Dietary Supplements

Study	Outcome	Quality	Applicability	Strength of Evidence
Bourgeois (1998)	VAS Pain (1200mg) 6 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	VAS Pain (400mg tid) 6 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	VAS Pain (1200mg) 13 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	VAS Pain (400mg tid) 13 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	Lequesne index (1200mg) 6 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	Lequesne index (400mg tid) 6 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	Lequesne index (1200mg) 13 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	Lequesne index (400mg tid) 13 weeks	Moderate	Moderate	Moderate
Bourgeois (1998)	VAS Pain (1200mg) 6 weeks	Moderate	Moderate	Moderate
Bucsi and Poor (1998)	VAS Pain 1 month	Moderate	Moderate	Moderate
Bucsi and Poor (1998)	VAS Pain 3 months	Moderate	Moderate	Moderate
Bucsi and Poor (1998)	VAS Pain 6 months	Moderate	Moderate	Moderate
Cibere (2004)	WOMAC Pain on walking	High	Moderate	High

Study	Outcome	Quality	Applicability	Strength of Evidence
Cibere (2004)	WOMAC Pain	High	Moderate	High
Cibere (2004)	WOMAC Function	High	Moderate	High
Cibere (2004)	WOMAC Stiffness	High	Moderate	High
Cibere (2004)	WOMAC Total	High	Moderate	High
Clegg (2006)	WOMAC Pain	Moderate	Moderate	Moderate
Clegg (2006)	Health Assessment Questionnaire-Pain	Moderate	Moderate	Moderate
Clegg (2006)	WOMAC Function	Moderate	Moderate	Moderate
Clegg (2006)	HAQ Alternative Disability	Moderate	Moderate	Moderate
Clegg (2006)	WOMAC Stiffness	Moderate	Moderate	Moderate
Clegg (2006)	WOMAC Total	Moderate	Moderate	Moderate
Clegg (2006)	Acetaminophen consumption	Moderate	Moderate	Moderate
Clegg (2006)	Patient Global Assessment of Response to Therapy	Moderate	Moderate	Moderate
Clegg (2006)	Patient Global Assessment of Disease Status	Moderate	Moderate	Moderate
Clegg (2006)	Physician Global Assessment of Disease Status	Moderate	Moderate	Moderate
Das (2000)	Lequesne index 4 weeks	Moderate	Moderate	Moderate
Das (2000)	Lequesne index 8 weeks	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Das (2000)	Lequesne index 13 weeks	Moderate	Moderate	Moderate
Das (2000)	Patient Global Assessment 4 weeks	Moderate	Moderate	Moderate
Das (2000)	Patient Global Assessment 8 weeks	Moderate	Moderate	Moderate
Giordano (2009)	Daily consumption of NSAIDS 4 weeks	Moderate	Moderate	Moderate
Giordano (2009)	Daily consumption of NSAIDS 8 weeks	Moderate	Moderate	Moderate
Giordano (2009)	Daily consumption of NSAIDS 12 weeks	Moderate	Moderate	Moderate
Giordano (2009)	Daily consumption of NSAIDS 16 weeks	Moderate	Moderate	Moderate
Giordano (2009)	Daily consumption of NSAIDS 20 weeks	Moderate	Moderate	Moderate
Giordano (2009)	Daily consumption of NSAIDS 24 weeks	Moderate	Moderate	Moderate
Houpt (1999)	WOMAC Pain	Moderate	Moderate	Moderate
Houpt (1999)	WOMAC Function	Moderate	Moderate	Moderate
Houpt (1999)	WOMAC Stiffness	Moderate	Moderate	Moderate
Houpt (1999)	WOMAC Total	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Hughes (2002)	WOMAC Pain	High	Moderate	High
Hughes (2002)	WOMAC Function	High	Moderate	High
Hughes (2002)	WOMAC Stiffness	High	Moderate	High
Kahan (2009)	Patient Global Assessment 26 weeks	High	Moderate	High
Kahan (2009)	Physician Global Assessment 26 weeks	High	Moderate	High
Mazieres (2001)	VAS Effect of OAK on Daily Living	Moderate	Moderate	Moderate
Mazieres (2001)	Change in Lequesne index	Moderate	Moderate	Moderate
Mazieres (2001)	VAS Pain with Activity	Moderate	Moderate	Moderate
Mazieres (2001)	Change in VAS Pain at rest	Moderate	Moderate	Moderate
Mazieres (2006)	VAS Pain during activity 4 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	VAS Pain during activity 12 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	VAS Pain during activity 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Lequesne index 4 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Lequesne index 12 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Lequesne index 24 weeks	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Mazieres (2006)	Change in pain at rest (VAS; 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Patient Global Assessment 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Physician Global Assessment 3.1 (2.7) 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Consumption of analgesics 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Days requiring NSAIDS 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Mental SF-12 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Physical SF-12 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	OARSI Responders 24 weeks	Moderate	Moderate	Moderate
Mazieres (2006)	Adverse Events 24 weeks	Moderate	Moderate	Moderate
McAlindon (2004)	WOMAC Pain	High	Moderate	High
McAlindon (2004)	WOMAC Function	High	Moderate	High
McAlindon (2004)	WOMAC Stiffness	High	Moderate	High
McAlindon (2004)	WOMAC Total	High	Moderate	High
Moller (2010)	VAS Pain 1 month	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Moller (2010)	VAS Pain 2 months	Moderate	Moderate	Moderate
Moller (2010)	VAS Pain 3 months	Moderate	Moderate	Moderate
Moller (2010)	Lequesne index 1 month	Moderate	Moderate	Moderate
Moller (2010)	Lequesne index 2 months	Moderate	Moderate	Moderate
Moller (2010)	Lequesne index 3 months	Moderate	Moderate	Moderate
Moller (2010)	SF-36 Mental Function	Moderate	Moderate	Moderate
Moller (2010)	SF-36 Physical Function	Moderate	Moderate	Moderate
Noack (1994)	Lequesne index 4 weeks	Moderate	Moderate	Moderate
Noack (1994)	Responder (3pt reduction in Lequesne and positive investigator global assessment) 4 weeks	Moderate	Moderate	Moderate
Noack (1994)	Gastrointestinal disturbances 4 weeks	Moderate	Moderate	Moderate
Noack (1994)	Pruritus or skin reaction 4 weeks	Moderate	Moderate	Moderate
Noack (1994)	Headache 4 weeks	Moderate	Moderate	Moderate
Noack (1994)	Circulatory disturbances 4 weeks	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Noack (1994)	Total adverse events 4 weeks	Moderate	Moderate	Moderate
Pavelka (2002)	WOMAC Total	Moderate	Moderate	Moderate
Pavelka (2002)	Lequesne index	Moderate	Moderate	Moderate
Rindone (2000)	VAS Walking Pain week 4	Moderate	Moderate	Moderate
Rindone (2000)	VAS Walking Pain week 8	Moderate	Moderate	Moderate
Rindone (2000)	VAS Resting Pain week 4	Moderate	Moderate	Moderate
Rindone (2000)	VAS Resting Pain week 8	Moderate	Moderate	Moderate
Trc (2010)	VAS improvement 20mm	Moderate	Moderate	Moderate
Trc (2010)	WOMAC Total 15 or more points	Moderate	Moderate	Moderate
Trc (2010)	VAS Pain	Moderate	Moderate	Moderate
Trc (2010)	VAS typical or average pain	Moderate	Moderate	Moderate
Trc (2010)	VAS Pain level at its best	Moderate	Moderate	Moderate
Trc (2010)	VAS Pain level at its worst	Moderate	Moderate	Moderate
Uebelhart (2004)	VAS Pain 3 months	High	Moderate	High
Uebelhart (2004)	VAS Pain 6 months	High	Moderate	High
Uebelhart (2004)	VAS Pain 9 months	High	Moderate	High
Uebelhart (2004)	VAS Pain 12 months	High	Moderate	High

Study	Outcome	Quality	Applicability	Strength of Evidence
Uebelhart (2004)	Lequesne index 3 months	High	Moderate	High
Uebelhart (2004)	Lequesne index 6 months	High	Moderate	High
Uebelhart (2004)	Lequesne index 9 months	High	Moderate	High
Uebelhart (2004)	Lequesne index 12 months	High	Moderate	High
Pavelka (2010)	WOMAC Total week 4	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Total week 8	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Total week 12	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Total week 24	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Total week 32	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Stiffness week 4	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Stiffness week 8	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Stiffness week 12	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Stiffness week 24	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Stiffness week 32	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Pain week 4	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Pain week 8	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Pain week 12	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Pain week 24	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Pain week 32	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Function week 4	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Function week 8	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Pavelka (2010)	WOMAC Function week 12	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Function week 24	Moderate	Moderate	Moderate
Pavelka (2010)	WOMAC Function week 32	Moderate	Moderate	Moderate
Pavelka (2010)	Pain on movement (VAS) week 4	Moderate	Moderate	Moderate
Pavelka (2010)	Pain on movement (VAS) week 8	Moderate	Moderate	Moderate
Pavelka (2010)	Pain on movement (VAS) week 12	Moderate	Moderate	Moderate
Pavelka (2010)	Pain on movement (VAS) week 24	Moderate	Moderate	Moderate
Pavelka (2010)	Pain on movement (VAS) week 32	Moderate	Moderate	Moderate
Pavelka (2010)	Lequesne index week 4	Moderate	Moderate	Moderate
Pavelka (2010)	Lequesne index week 8	Moderate	Moderate	Moderate
Pavelka (2010)	Lequesne index week 12	Moderate	Moderate	Moderate
Pavelka (2010)	Lequesne index week 24	Moderate	Moderate	Moderate
Pavelka (2010)	Lequesne index week 32	Moderate	Moderate	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 4	Moderate	Moderate	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 8	Moderate	Moderate	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 12	Moderate	Moderate	Moderate

Study	Outcome	Quality	Applicability	Strength of Evidence
Pavelka (2010)	Rescue medication, mean tablets/day week 24	Moderate	Moderate	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 32	Moderate	Moderate	Moderate
Pavelka (2010)	VAS Pain at rest week 4	Moderate	Moderate	Moderate
Pavelka (2010)	VAS Pain at rest week 8	Moderate	Moderate	Moderate
Pavelka (2010)	VAS Pain at rest week 12	Moderate	Moderate	Moderate
Pavelka (2010)	VAS Pain at rest week 24	Moderate	Moderate	Moderate
Pavelka (2010)	VAS Pain at rest week 32	Moderate	Moderate	Moderate
Rai (2004)	Lequesne index week 52	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Figure 31-Figure 41](#), [Table 124-Table 143](#)

Eleven out of 52 outcomes were statistically significant in favor of glucosamine when compared to placebo (see [Figure 31](#)). WOMAC pain, WOMAC function, and VAS pain were the critical outcomes. None were associated with statistical significance at any time duration ([Figure 31](#)).

Meta-analyses were run for WOMAC pain, WOMAC function, WOMAC stiffness and WOMAC total. All meta-analyses showed statistically insignificant differences between glucosamine and placebo ([Figures 38-41](#)).

Two studies compared glucosamine to active treatments. Glucosamine was compared to reparaGen⁸⁷ and enzymatic hydrolyzed collagen (EHC).⁸⁸ It was found to have no statistically significant effect on pain compared to reparaGen.

Enzymatic hydrolyzed collagen (EHC) was compared to glucosamine sulfate by Trc et al.⁸⁸ All pain outcomes were statistically significant in favor of EHC. However, two outcomes—VAS pain and VAS pain at its worst—were not clinically important.

[Figure 32](#) presents a summary of the results for chondroitin sulfate. Twenty four out of 64 outcomes were significantly higher for chondroitin over placebo. The critical outcomes presented in the studies were pain and function. Pain was significantly lower in the glucosamine group for 12 out of 22 outcomes. Of those 12, four outcomes were

clinically important and six were possibly clinically important. No statistically significant results were found for any functional outcome.

[Figure 33](#) presents the meta-analysis results comparing VAS chondroitin sulfate to placebo in VAS pain scores. The weighted mean difference revealed that VAS pain was 11.89 points lower in the chondroitin group than in the placebo group. However, the difference was not clinically important.

Pavelka et al.⁹⁴ compared piascledine (avocado soybean unsaponifiable) to chondroitin sulfate. The authors measured WOMAC total and subscale scores, as well as VAS pain, Lequesne index, and concomitant medication use at four, eight, 12, 24 and 32 weeks. None of the 40 outcomes were associated with significant differences between treatment groups.

Two studies compared combined chondroitin and glucosamine to placebo. Only two of 11 outcomes were statistically significant in favor of the treatment group. However, one study by Clegg et al.⁸⁶ also did a subgroup analysis stratified by severity. For the moderate to severe osteoarthritis subgroup, the authors found the treatment group to have significantly higher odds of being OARSI responders. Moderate to severe osteoarthritic patients were more likely to achieve 20% to 50% reductions in WOMAC pain scores than those who received a placebo. The outcomes were not statistically significant in the total sample or in the mild severity subgroup.

Figure 31. Results Summary: Glucosamine Versus Placebo

	4 weeks	8 weeks	12 weeks	16 weeks	13 weeks	20 weeks	24 weeks	26 weeks	3 years
WOMAC Pain		○	○				○	○○	
Walking Pain	○	○						○	○
WOMAC Stiffness		○	○				○	○○	
WOMAC Function		○	○				○	○○	
WOMAC Total		○	○				○	○	● ○
VAS Pain	○	○							
Lequesne index	○ ○	●			○				●
HAQ Disability							○○		
HAQ Pain							○○		
Daily consumption of additional Medications	●	●	●	●		●	● ○		
Patient Global Assessment	○	○					● ○ ○		

	4 weeks	8 weeks	12 weeks	16 weeks	13 weeks	20 weeks	24 weeks	26 weeks	3 years
responder (3pt reduction in Lequesne and positive investigator global assessment)									
Gastrointestinal disturbances									
Pruritus or skin reaction									
Headache									
Circulatory disturbances									
Total adverse events									

***Each shape represents the result of one study at each time period.**



Insignificant treatment effect



Possibly clinically significant in favor of Glucosamine



Statistically significant in favor of Glucosamine

Figure 32. Results Summary: Chondroitin Sulfate Versus Placebo

Outcome/Duration	4 weeks	6 weeks	8 weeks	12 weeks	13 weeks	24 weeks	26 weeks	39 weeks	52 weeks
VAS Pain	○ ●	● ●	●	● ●	○ ● ● ○	○ ●	○	●	●
VAS Pain with activity	○			○	●	○			
WOMAC Pain						○			
HAQ Pain						○			
VAS effect of OAK on daily living					○				
WOMAC Function						○			
SF-36 Mental Function						○ ○			
SF-12 Mental Function						○			
SF-12 Physical Function						○			
HAQ Alternative Disability						○			
WOMAC Stiffness						○			
WOMAC Total						○			
Lequesne index	● ○	● ●	●	○ ●	○ ● ● ○	○	○	○	○

Outcome/Duration	4 weeks	6 weeks	8 weeks	12 weeks	13 weeks	24 weeks	26 weeks	39 weeks	52 weeks
Additional analgesic use	○			○		●○○○			
Walk time	○			○		○			
Patient Global Assessment						○●○	●		
Physician Global Assessment						○○	●		
OARSI Responders						●			
Adverse events						○			

***Note: each shape represents a finding from one study at each time point**

- Indicates a statistically insignificant treatment effect between Chondroitin Sulfate and control.
- Indicates a statistically significant treatment effect in favor of Chondroitin Sulfate.
- Indicates a possibly clinically significant treatment effect in favor of Chondroitin Sulfate.
- Indicates a clinically significant treatment effect in favor of Chondroitin Sulfate.
- Statistically significant, but not clinically important effect in favor of Chondroitin Sulfate

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 122. Quality And Applicability: Glucosamine Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Cibere (2004)	WOMAC Pain on Walking	●	◐	●	●	●	○	●	●	High	○	○	●	●	Moderate
Cibere (2004)	WOMAC Pain	●	○	●	●	●	○	●	●	High	○	○	●	●	Moderate
Cibere (2004)	WOMAC Function	●	○	●	●	●	○	●	●	High	○	○	●	●	Moderate
Cibere (2004)	WOMAC Stiffness	●	○	●	●	●	○	●	●	High	○	○	●	●	Moderate
Cibere (2004)	WOMAC Total	●	○	●	●	●	○	●	●	High	○	○	●	●	Moderate
Clegg (2006)	WOMAC Pain	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Clegg (2006)	WOMAC Stiffness	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	WOMAC Function	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Normalized WOMAC	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	HAQ Alternative Disability	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	HAQ Pain	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Patient Global Assessment of Response to Therapy	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Patient Global Assessment of Disease Status	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Clegg (2006)	Physician Global Assessment of Disease Status	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Hughes (2002)	WOMAC Pain	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Hughes (2002)	WOMAC Function	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Hughes (2002)	WOMAC Stiffness	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Rindone (2000)	VAS Walking Pain week 4	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Rindone (2000)	VAS Walking Pain week 8	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Rindone (2000)	VAS Resting Pain week 4	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Rindone (2000)	VAS Resting Pain week 8	●	●	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Pavelka (2002)	WOMAC Total	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2002)	Lequesne index	●	◐	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
McAlindon (2004)	WOMAC Pain	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
McAlindon (2004)	WOMAC Function	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
McAlindon (2004)	WOMAC Stiffness	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
McAlindon (2004)	WOMAC Total	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Houpt (1999)	WOMAC Pain	●	○	○	●	○	●	●	○	Moderate	●	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Houpt (1999)	WOMAC Function	●	●	○	●	○	●	●	○	Moderate	●	○	●	○	Moderate
Houpt (1999)	WOMAC Stiffness	●	○	○	●	○	●	●	○	Moderate	●	○	●	○	Moderate
Houpt (1999)	WOMAC Total	●	○	○	●	○	●	●	○	Moderate	●	○	●	○	Moderate
Trc (2010)	VAS improvement 20mm	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Trc (2010)	WOMAC Total 15mm improvement	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Trc (2010)	VAS Pain	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Trc (2010)	VAS typical or	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
	average pain														
Trc (2010)	VAS Pain level at its best	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Trc (2010)	VAS Pain level at its worst	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Giordano (2009)	Daily consumption of NSAIDS 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Giordano (2009)	Daily consumption of NSAIDS 8 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Giordano (2009)	Daily consumption of NSAIDS 12 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Giordano (2009)	Daily consumption of NSAIDS 16 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Giordano (2009)	Daily consumption of NSAIDS 20 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Giordano (2009)	Daily consumption of NSAIDS 24 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Noack (1994)	Lequesne index 4 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Noack (1994)	Responder (3pt reduction in Lequesne and positive investigator global assessment) 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Noack (1994)	Gastrointestinal disturbances 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Noack (1994)	Pruritus or skin reaction 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Noack (1994)	Headache 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Noack (1994)	Circulatory disturbances 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Noack (1994)	Total adverse events 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Das (2000)	Lequesne index 4 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Das (2000)	Lequesne index 8 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Das (2000)	Lequesne index 13 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Das (2000)	Patient Global Assessment 4 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Das (2000)	Patient Global Assessment 8 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Rai (2004)	Lequesne index week 52	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Reginster (2001)	WOMAC Total week 156	●	●	●	●	○	●	●	●	High	○	○	○	●	Moderate
Reginster (2001)	WOMAC Pain week 156	●	●	●	●	○	●	●	●	High	○	○	○	●	Moderate

Table 123. Quality and Applicability: Chondroitin

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bourgeois (1998)	VAS Pain (1200mg) 6 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bourgeois (1998)	VAS Pain (400mg tid) 6 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bourgeois (1998)	VAS Pain (1200mg) 13 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bourgeois (1998)	VAS Pain (400mg tid) 13 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bourgeois (1998)	Lequesne index (1200mg) 6 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Clegg (2006)	WOMAC Pain	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	WOMAC Stiffness	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	WOMAC Function	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Normalized WOMAC	●	●	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	HAQ Alternative Disability	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	HAQ Pain	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Patient Global Assessment of Response to	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
	Therapy														
Clegg (2006)	Patient Global Assessment of Disease Status	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Physician Global Assessment of Disease Status	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Clegg (2006)	Acetaminophen consumption	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Mazieres (2006)	VAS Pain during activity 4 weeks	●	●	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	VAS Pain during activity 12 weeks	●	●	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Mazieres (2006)	VAS Pain during activity 24 weeks	●	●	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Lequesne index 4 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Lequesne index 12 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Lequesne index 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	VAS change in pain at rest 24 weeks	●	●	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Patient Global Assessment 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Physician Global Assessment 3.1 (2.7) 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Mazieres (2006)	Consumption of analgesics 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	days requiring NSAIDS 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Mental SF-12 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Physical SF-12 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	OARSI Responders 24 weeks	●	●	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Mazieres (2006)	Adverse events 24 weeks	●	◐	○	●	●	○	●	○	Moderate	○	○	○	●	Moderate
Bourgeois (1998)	Lequesne index (400mg tid) 6 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bourgeois (1998)	Lequesne index (1200mg) 13 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bourgeois (1998)	Lequesne index (400mg tid) 13 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bucsi and Poor (1998)	VAS Pain 1 month	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bucsi and Poor (1998)	VAS Pain 3 months	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Bucsi and Poor (1998)	VAS Pain 6 months	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mazieres	VAS effect of OAK	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
(2001)	on daily living														
Mazieres (2001)	Change in Lequesne index	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Mazierez (2001)	VAS Pain with Activity	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Mazierez (2001)	Change in VAS Pain at Rest	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Moller (2010)	VAS Pain 1 month	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Moller (2010)	VAS Pain 2 months	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Moller (2010)	VAS Pain 3 months	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Moller (2010)	Lequesne index 1 month	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Moller (2010)	Lequesne index 2 months	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Moller (2010)	Lequesne index 3 months	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Moller(2010)	SF-36 Mental Function	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Moller(2010)	SF-36 Physical Function	●	○	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Uebelhart (2004)	VAS Pain 3 months	●	●	○	●	●	●	●	○	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Uebelhart (2004)	VAS Pain 6 months	●	●	○	●	●	●	●	○	High	○	○	●	●	Moderate
Uebelhart (2004)	VAS Pain 9 months	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Uebelhart (2004)	VAS Pain 12 months	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Uebelhart (2004)	Lequesne index 3 months	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Uebelhart (2004)	Lequesne index 6 months	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Uebelhart (2004)	Lequesne index 9 months	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Uebelhart (2004)	Lequesne index 12 months	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bourgeois (1998)	VAS Pain (1200mg) 6 weeks	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kahan (2003)	Patient Global Assessment 26 weeks	●	●	●	●	●	●	●	○	High	○	○	○	●	Moderate
Kahan (2003)	Physician Global Assessment 26 weeks	●	◐	●	●	●	●	●	○	High	○	○	○	●	Moderate
Pavelka (2010)	WOMAC Total week 4	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Total week 8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Pavelka (2010)	WOMAC Total week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Total week 24	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Total week 32	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Stiffness week 4	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Stiffness week 8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Stiffness week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Pavelka (2010)	WOMAC Stiffness week 24	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Stiffness week 32	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Pain week 4	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Pain week 8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Pain week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Pain week 24	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Pavelka (2010)	WOMAC Pain week 32	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Function week 4	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Function week 8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Function week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Function week 24	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	WOMAC Function week 32	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Pavelka (2010)	Pain on movement (VAS) week 4	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Pain on movement (VAS) week 8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Pain on movement (VAS) week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Pain on movement (VAS) week 24	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Pain on movement (VAS) week 32	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Lequesne index week 4	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Pavelka (2010)	Lequesne index week 8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Lequesne index week 12	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Lequesne index week 24	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Lequesne index week 32	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 4	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
	week 8														
Pavelka (2010)	Rescue medication, mean tablets/day week 12	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 24	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day week 32	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	VAS Pain at rest week 4	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Pavelka (2010)	VAS Pain at rest week 8	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	VAS Pain at rest week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	VAS Pain at rest week 24	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2010)	VAS Pain at rest week 32	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

FINDINGS

Table 124. Glucosamine Versus Placebo: Pain

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Cibere (2004)	WOMAC Pain on walking	137	Unclear	26	Glucosamine Sulfate	Placebo	.13 (-.21,.47)	No	N/A	High
Cibere (2004)	WOMAC Pain	137	No	26	Glucosamine Sulfate	Placebo	.03 (-.31,.36)	No	Inconclusive	High
Hughes (2002)	WOMAC Pain	75	Unclear	26	Glucosamine Sulfate	Placebo	.06 (-.39, .52)	No	Inconclusive	High
Rindone (2000)	VAS Walking Pain	98	Yes	4	Glucosamine	Placebo	.08 (-.32, .48)	No	N/A	Moderate
Rindone (2000)	VAS Walking Pain	98	Yes	8	Glucosamine	Placebo	.00 (-.4, .4)	No	N/A	Moderate
Rindone (2000)	VAS Resting Pain	98	Yes	4	Glucosamine	Placebo	-.08 (-.47, .32)	No	N/A	Moderate
Rindone (2000)	VAS Resting Pain	98	Yes	8	Glucosamine	Placebo	-.08 (-.48, .32)	No	N/A	Moderate
McAlindon (2004)	WOMAC Pain	205	Yes	12	Glucosamine Sulfate/Glucosamine HCL	Placebo	-.14 (-.41, .14)	No	Inconclusive	High
Reginster (2001)	WOMAC Pain	212	Yes	156	Glucosamine Sulfate	Placebo	-.21 (-.48, .06)	No	Inconclusive	High
Houpt	WOMAC Pain	98	No	8	Glucosamine HCL	Placebo	-.12 (-.52, .27)	No	Inconclusive	Moderate

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Clegg (2006)	WOMAC Pain	630	Yes	24	Glucosamine	Placebo	0.03 (-0.13,0.18)	No	True negative	Moderate
Clegg (2006)	Health Assessment Questionnaire-Pain	630	Yes	24	Glucosamine	Placebo	0.03 (-0.13, .18)	No	True negative	Moderate

Table 125. Glucosamine Versus Placebo: Function

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
McAlindon (2004)	WOMAC Function	205	Yes	12	Glucosamine Sulfate/Glucosamine HCL	Placebo	.06 (-.21, .34)	No	Negative	High
Hughes (2002)	WOMAC Function	75	Unclear	26	Glucosamine Sulfate	Placebo	.11(-.34, .57)	No	Inconclusive	High
Cibere (2004)	WOMAC Function	137	No	26	Glucosamine Sulfate	Placebo	-.02 (-.32, .35)	No	Negative	High
Houpt (1999)	WOMAC Function	98	Yes	8	Glucosamine HCL	Placebo	-.08 (-.48, .32)	No	Inconclusive	Moderate

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Clegg (2006)	WOMAC Function	630	Yes	24	Glucosamine	Placebo	0.01 (-0.14, 0.17)	No	True negative	Moderate
Clegg (2006)	HAQ Alternative Disability Score	630	Yes	24	Glucosamine	Placebo	-0.06 (-0.21, 0.1)	No	Unclear	Moderate

Table 126. Glucosamine Versus Placebo: WOMAC Stiffness

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Cibere (2004)	WOMAC Function	137	No	26	Glucosamine Sulfate	Placebo	-.09(-.42, .25)	No	Inconclusive	High
Hughes (2002)	WOMAC Stiffness	75	Unclear	26	Glucosamine Sulfate	Placebo	.14(-.32, .59)	No	Inconclusive	High
McAlindon (2004)	WOMAC Stiffness	205	Yes	12	Glucosamine Sulfate/Glucosamine HCL	Placebo	-.06(-.34, .21)	No	Negative	High
Houpt (1999)	WOMAC Stiffness	98	No	8	Glucosamine HCL	Placebo	-.19(-.59, .21)	No	Inconclusive	Moderate
Clegg (2006)	WOMAC Stiffness	630	Yes	24	Glucosamine	Placebo	0.03 (-0.12, 0.19)	No	True negative	Moderate

Table 127. Glucosamine Versus Placebo: WOMAC Total

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2002)	WOMAC Total	203	Yes	156	Glucosamine Sulfate	Placebo	-.35(-.63, -.08)	Favors Glucosamine Sulfate	Possibly clinically important	Moderate
Cibere (2004)	WOMAC Total	137	No	26	Glucosamine Sulfate	Placebo	.01(-.33, .34)	No	Negative	High
McAlindon (2004)	WOMAC Total	205	Yes	12	Glucosamine Sulfate/ Glucosamine HCL	Placebo	.00	No	Negative	High
Houpt	WOMAC Total	98	No	8	Glucosamine HCL	Placebo	-.10(-.50, .30)	No	Inconclusive	Moderate
Reginster (2001)	WOMAC Total	212	yes	156	Glucosamine Sulfate	Placebo	-.19 (-.46, .08)	No	Inconclusive	High
Clegg (2006)	WOMAC Total	630	Yes	24	Glucosamine	Placebo	0.03 (-0.13, 0.18)	No	True negative	Moderate

Table 128. Glucosamine Versus Placebo: Other Outcomes

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2002)	Lequesne index	101	Yes	156	Glucosamine Sulfate	Placebo	-.42(-.70, -.14)	Favors GS	N/A	Moderate
Noack (1994)	Lequesne index	252	Unclear	4	Glucosamine Sulfate	Placebo	-0.2 (-0.44, 0.05)	No	N/A	Moderate
Das (2000)	Lequesne index	72	Unclear	4	Glucosamine HCL plus Sodium Chondroitin plus Manganese Ascorbate	Placebo	-.23(-.695, .235)	No	N/A	Moderate
Das (2000)	Lequesne index	72	Unclear	8	Glucosamine HCL plus Sodium Chondroitin plus Manganese Ascorbate	Placebo	-.55(-1.02, -.075)	Yes	N/A	Moderate
Das (2000)	Lequesne index	72	Unclear	13	Glucosamine HCL plus Sodium Chondroitin plus Manganese Ascorbate	Placebo	-.44(-.907, .031)	No	N/A	Moderate

Study	Outcome	N	Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Clegg (2006)	Patient Global Assessment of Response to Therapy	630	Yes	24	Glucosamine	Placebo	2.9 (2.68, 3.12)	Yes	Unclear	Moderate
Clegg (2006)	Patient Global Assessment of Disease Status	630	Unclear	24	Glucosamine	Placebo	0.05 (-0.11, 0.2)	No	Unclear	Moderate
Clegg (2006)	Physician Global Assessment of Disease Status	630	Unclear	24	Glucosamine	Placebo	0.1 (-0.06, 0.26)	No	Unclear	Moderate
Clegg (2006)	Number of 500-mg tablets of Acetaminophen	630	Unclear	24	Glucosamine	Placebo	-0.06 (-0.21, 0.1)	No	Unclear	Moderate

Table 129 Glucosamine HCL Plus Sodium Chondroitin Plus Manganese Ascorbate Versus Placebo: Patient Global Assessment

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Das (2000)	Patient Global Assessment	72	Yes	4	Glucosamine HCL plus Sodium Chondroitin plus Manganese Ascorbate	Placebo	-.07(-.534, .394)	No	True negative	Moderate
Das (2000)	Patient Global Assessment	72	Yes	8	Glucosamine HCL plus Sodium Chondroitin plus Manganese Ascorbate	Placebo	-.294(-.76, .173)	No	True negative	Moderate

Table 130. Glucosamine Versus Placebo: NSAID Consumption

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Novack (1994)	Daily consumption of NSAIDS	60	Unclear	4	Glucosamine	Placebo	-0.55 (-1.07, -0.04)	Favors Glucosamine	N/A	Moderate
Novack (1994)	Daily consumption of NSAIDS	60	Unclear	8	Glucosamine	Placebo	-0.9 (-1.43, -0.37)	Favors Glucosamine	N/A	Moderate

Novack (1994)	Daily consumption of NSAIDS	60	Unclear	12	Glucosamine	Placebo	-1.24 (-1.79, -0.68)	Favors Glucosamine	N/A	Moderate
Novack (1994)	Daily consumption of NSAIDS	60	Unclear	16	Glucosamine	Placebo	-1.13 (-1.68, -0.58)	Favors Glucosamine	N/A	Moderate
Novack (1994)	Daily consumption of NSAIDS	60	Unclear	20	Glucosamine	Placebo	-1.14 (-1.69, -0.59)	Favors Glucosamine	N/A	Moderate
Novack (1994)	Daily consumption of NSAIDS	60	Unclear	24	Glucosamine	Placebo	-0.82 (-1.35, -0.29)	Favors Glucosamine	N/A	Moderate

Table 131. Glucosamine Versus Placebo: Adverse Events

Study	Outcome	N	Power to Detect MCII	week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Noack (1994)	Gastrointestinal disturbances	246	Unclear	4	Glucosamine	Placebo	OR=.83 (.24, 2.78)	No	N/A	Moderate
Noack (1994)	Pruritus or Skin reaction	249	Unclear	4	Glucosamine	Placebo	OR=.328 (.03, 3.19)	No	N/A	Moderate
Noack (1994)	Headache	250	Unclear	4	Glucosamine	Placebo	OR=1(.14, 7.21)	No	N/A	Moderate
Noack (1994)	Circulatory disturbances	250	Unclear	4	Glucosamine	Placebo	OR=.2(.009, 4.14)	No	N/A	Moderate
Noack (1994)	Total adverse events	239	Unclear	4	Glucosamine	Placebo	OR=.59 (.24, 1.48)	No	N/A	Moderate

Table 132. Glucosamine Versus Reparagen: Pain

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Mehta (2007)	20% decrease in WOMAC Pain and 10mm decrease in VAS Pain	95	Unclear	8	Glucosamine Sulfate	Reparagen	OR .88 (.37 ,2.08)	No	N/A	Moderate
Mehta (2007)	20% decrease in WOMAC Pain	95	Unclear	8	Glucosamine Sulfate	Reparagen	OR=.67 (.25 , 1.79)	No	N/A	Moderate

Table 133. Glucosamine Versus Enzymatic Hydrolyzed Collagen

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Trc (2010)	VAS improvement 20mm	93	Yes	12	Glucosamine Sulfate	Enzymatic hydrolyzed collagen	OR= 0.27 (0.12, 0.65)	Favors enzymatic hydrolyzed collagen	N/A	Moderate
Trc (2010)	WOMAC Total 15 or more points	91	Yes	12	Glucosamine Sulfate	Enzymatic hydrolyzed collagen	OR= 0.29 (0.10, 0.83)	Favors enzymatic hydrolyzed collagen	N/A	Moderate
Trc (2010)	VAS Pain	93	Yes	12	Glucosamine Sulfate	Enzymatic hydrolyzed collagen	0.85 (0.42 ,1.27)	Favors enzymatic hydrolyzed collagen	Possibly clinically important	Moderate
Trc (2010)	VAS typical or average pain	93	Yes	12	Glucosamine Sulfate	Enzymatic hydrolyzed collagen	0.56 (0.14 ,0.97)	Favors enzymatic hydrolyzed collagen	Not clinically important	Moderate
Trc (2010)	VAS Pain level at its best	93	Yes	12	Glucosamine Sulfate	Enzymatic hydrolyzed collagen	0.43 (0.02 ,0.85)	Favors enzymatic hydrolyzed collagen	Not clinically important	Moderate
Trc (2010)	VAS Pain level at its worst	93	Yes	12	Glucosamine Sulfate	Enzymatic hydrolyzed collagen	0.83 (0.41 ,1.26)	Favors enzymatic hydrolyzed collagen	Possibly clinically important	Moderate

Table 134. Chondroitin Sulfate Versus Placebo: Pain

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bourgeois (1998)	VAS Pain	84	Yes	6	Chondroitin Sulfate (1200mg qd)	Placebo	-0.85 (-1.30, -0.40)	Favors CS	Possibly clinically significant	Moderate
Bourgeois (1998)	VAS Pain	87	Yes	6	Chondroitin Sulfate (400mg tid)	Placebo	-0.72 (-1.15, -0.28)	Favors CS	Not clinically significant	Moderate
Bourgeois (1998)	VAS Pain	84	Yes	13	Chondroitin Sulfate (1200mg qd)	Placebo	-0.90 (-1.35, -0.45)	Favors CS	Possibly clinically significant	Moderate
Bourgeois (1998)	VAS Pain	87	Yes	13	Chondroitin Sulfate (400mg tid)	Placebo	-0.89 (-1.33, -0.45)	Favors CS	Possibly clinically significant	Moderate
Moller (2010)	VAS Pain	116	Yes	4	Chondroitin Sulfate	Placebo	-2.58 (-3.08, -2.09)	Favors CS	Clinically important	Moderate
Moller (2010)	VAS Pain	116	Yes	8	Chondroitin Sulfate	Placebo	-1.99(-2.44, -1.54)	Favors CS	Clinically important	Moderate
Moller (2010)	VAS Pain	116	Yes	12	Chondroitin Sulfate	Placebo	-4.15(-4.80, -3.5)	Favors CS	Clinically important	Moderate
Bucsi and Poor (1998)	VAS Pain	85	Yes	4	Chondroitin Sulfate	Placebo	-.28(-.71, .15)	No	N/A	Moderate
Bucsi and Poor (1998)	VAS Pain	85	Yes	12	Chondroitin Sulfate	Placebo	-.64 (-1.07, -.20)	Favors CS	Possibly clinically significant	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bucsi and Poor (1998)	VAS Pain	85	Yes	24	Chondroitin Sulfate	Placebo	-.92 (-1.37 , -.47)	Favors CS	Clinically important	Moderate
Uebelhart (2004)	VAS Pain	110	Yes	13	Chondroitin Sulfate	Placebo	-.26 (-.63 , .12)	No	True negative	High
Uebelhart (2004)	VAS Pain	110	Yes	26	Chondroitin Sulfate	Placebo	-.28(-.65 , .10)	No	N/A	High
Uebelhart (2004)	VAS Pain	110	Yes	39	Chondroitin Sulfate	Placebo	-.45(-.83 , -.07)	Favors CS	Possibly clinically significant	High
Uebelhart (2004)	VAS Pain	110	Yes	52	Chondroitin Sulfate	Placebo	-.42(-.79 , -.04)	Favors CS	Possibly clinically significant	High
Mazieres (2001)	VAS Pain with activity	130	Yes	13	Chondroitin Sulfate	Placebo	-.38 (-.73 , -.03)	Favors CS	Not clinically important	Moderate
Mazieres (2001)	Change in VAS Pain at rest	130	Yes	13	Chondroitin Sulfate	Placebo	-.25(-.6 , .09)	No	True negative	Moderate
Mazieres (2006)	VAS Pain during activity	153	Yes	4	Chondroitin Sulfate	Placebo	-0.14 (-0.36, 0.09)	No	True negative	Moderate
Mazieres (2006)	VAS Pain during activity	153	Yes	12	Chondroitin Sulfate	Placebo	-0.09 (-0.31, 0.13)	No	True negative	Moderate
Mazieres (2006)	VAS Pain during activity	153	Yes	24	Chondroitin Sulfate	Placebo	-0.21 (-0.44, 0.01)	No	True negative	Moderate
Mazieres (2006)	VAS Pain	153	Yes	24	Chondroitin Sulfate	Placebo	-0.14 (-0.36, 0.09)	No	True negative	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Clegg (2006)	WOMAC Pain	631	Yes	24	Chondroitin Sulfate	Placebo	0.02 (-0.14, 0.18)	No	True negative	Moderate
Clegg (2006)	HAQ Pain Score	631	Unclear	24	Chondroitin Sulfate	Placebo	0.04 (-0.11, 0.2)	No	Unclear	Moderate

Table 135. Chondroitin Sulfate Versus Placebo: Function

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Mazieres (2001)	VAS effect of OAK on daily living	130	Unclear	12.85	Chondroitin Sulfate	Placebo	-.24 (-.59, .10)	No	N/A	Moderate
Moller(2010)	SF-36 Mental Function	129	Unclear	24	Chondroitin Sulfate	Placebo	-.07(-.43, .30)	No	N/A	Moderate
Mazieres (2006)	SF-12 Physical Function	24	Yes	24	Chondroitin Sulfate	Placebo	0.08 (-0.14, 0.31)	No	N/A	Moderate
Mazieres (2006)	SF-36 Mental Function	24	Yes	24	Chondroitin Sulfate	Placebo	0.21 (-0.02, 0.43)	No	N/A	Moderate
Bucsi (1998)	Walk time	85	Unclear	4	Chondroitin Sulfate	Placebo	-0.20 (-0.63, 0.23)	No	N/A	Moderate
Bucsi (1998)	Walk time	85	Unclear	12	Chondroitin Sulfate	Placebo	-0.17 (-0.60, 0.26)	No	N/A	Moderate
Bucsi (1998)	Walk time	85	Unclear	24	Chondroitin Sulfate	Placebo	-0.33 (-0.76, 0.10)	No	N/A	Moderate

Clegg (2006)	WOMAC Function	631	Yes	24	Chondroitin Sulfate	Placebo	-0.02 (-0.18, 0.13)	No	True negative	Moderate
Clegg (2006)	HAQ Alternative Disability	631	Unclear	24	Chondroitin Sulfate	Placebo	-0.03 (-0.18, 0.13)	No	Unclear	Moderate

Table 136. Chondroitin Sulfate Versus Placebo: WOMAC Stiffness

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Clegg (2006)	WOMAC Stiffness	631	Yes	24	Chondroitin Sulfate	Placebo	0.1 (-0.06, 0.26)	No	True negative	Moderate

Table 137. Chondroitin Sulfate Versus Placebo: WOMAC Total

Study	Outcome	N	Power to Detect MCII	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Clegg (2006)	WOMAC Total	631	Yes	24	Chondroitin Sulfate	Placebo	0.04 (-0.12, 0.2)	No	True negative	Moderate

Table 138. Chondroitin Sulfate Versus Placebo: Lequesne Index

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Mazieres (2001)	Change in Lequesne index	130	Yes	13	Chondroitin Sulfate	Placebo	-.27(-.62, .07)	No	N/A	Moderate
Uebelhart (2004)	Lequesne index	110	Yes	13	Chondroitin Sulfate	Placebo	-.15(-.53, .22)	No	N/A	High
Uebelhart (2004)	Lequesne index	110	Yes	26	Chondroitin Sulfate	Placebo	-.21(-.59, .16)	No	N/A	High
Uebelhart (2004)	Lequesne index	110	Yes	39	Chondroitin Sulfate	Placebo	-.26(-.63, .12)	No	N/A	High
Uebelhart (2004)	Lequesne index	110	Yes	52	Chondroitin Sulfate	Placebo	-.32(-.69, .06)	No	N/A	High
Moller (2010)	Lequesne index	110	Yes	4	Chondroitin Sulfate	Placebo	.66(.29, 1.04)	Favors Placebo	N/A	Moderate
Moller (2010)	Lequesne index	110	Yes	8	Chondroitin Sulfate	Placebo	-2.24(-2.70, -1.77)	Favors CS	N/A	Moderate
Moller (2010)	Lequesne index	110	Yes	12	Chondroitin Sulfate	Placebo	-3.50(-4.08, -2.91)	Favors CS	N/A	Moderate
Mazieres (2006)	Lequesne index	4	Yes	4	Chondroitin Sulfate	Placebo	-0.04 (-0.26, 0.19)	No	N/A	Moderate
Mazieres (2006)	Lequesne index	12	Yes	12	Chondroitin Sulfate	Placebo	-0.03 (-0.25, 0.19)	No	N/A	Moderate
Mazieres (2006)	Lequesne index	24	Yes	24	Chondroitin Sulfate	Placebo	-0.14 (-0.37, 0.08)	No	N/A	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bourgeois (1998)	Lequesne index	84	Yes	6	Chondroitin Sulfate (1200mg qd)	Placebo	-0.66 (-1.10, -0.22)	Favors CS	N/A	Moderate
Bourgeois (1998)	Lequesne index	87	Yes	6	Chondroitin Sulfate (400mg tid)	Placebo	-0.78 (-1.21, -0.34)	Favors CS	N/A	Moderate
Bourgeois (1998)	Lequesne index	84	Yes	13	Chondroitin Sulfate (1200mg qd)	Placebo	-0.84 (-1.28, -0.39)	Favors CS	N/A	Moderate
Bourgeois (1998)	Lequesne index	87	Yes	13	Chondroitin Sulfate (400mg tid)	Placebo	-0.84 (-1.28, -0.40)	Favors CS	N/A	Moderate

Table 139. Chondroitin Versus Placebo: Additional Analgesic Use

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bucsi (1998)	Paracetamol consumption	85	Unclear	4	Chondroitin Sulfate	Placebo	-0.20 (-0.63, 0.22)	No	Unclear	Moderate
Bucsi (1998)	Paracetamol consumption	85	Unclear	12	Chondroitin Sulfate	Placebo	-0.20 (-0.63, 0.23)	No	Unclear	Moderate
Bucsi (1998)	Paracetamol consumption	85	Unclear	24	Chondroitin Sulfate	Placebo	-0.44 (-0.88, -.01)	Favors Chondroitin Sulfate	Unclear	Moderate
Mazieres (2006)	Analgesic consumption	4	Yes	24	Chondroitin Sulfate	Placebo	0 (-0.22, 0.22)	No	N/A	Moderate
Mazieres (2006)	Number of days NSAIDS were taken	12	Yes	24	Chondroitin Sulfate	Placebo	-0.1 (-0.33, 0.12)	No	N/A	Moderate
Clegg (2006)	Acetaminophen consumption	631	Yes	24	Chondroitin Sulfate	Placebo	0.05 (-0.1, 0.21)	No	Unclear	Moderate

Table 140. Chondroitin Sulfate Versus Placebo: Other Outcomes

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Mazieres (2006)	Patient Global Assessment	307	Unclear	24	Chondroitin Sulfate	Placebo	0.2 (-0.03, 0.42)	No	True negative	Moderate
Mazieres (2006)	Physician Global Assessment	307	Unclear	24	Chondroitin Sulfate	Placebo	0.21 (-0.01, 0.43)	No	N/A	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Mazieres (2006)	OARSI Responders	307	Yes	24	Chondroitin Sulfate	Placebo	OR= 1.67 (1.05, 2.67)	Favors Chondroitin Sulfate	Unclear	Moderate
Mazieres (2006)	Adverse Events	307	Unclear	24	Chondroitin Sulfate	Placebo	OR=.98 (.63,1.54)	No	N/A	Moderate
Kahan (2009)	Patient Global Assessment	622	Yes	26	Chondroitin Sulfate	Placebo	0.18 (0.02, 0.34)	Favors Chondroitin Sulfate	Not Clinically important	High
Kahan (2009)	Physician Global Assessment	622	Unclear	26	Chondroitin Sulfate	Placebo	0.16 (0.01, 0.32)	Favors Chondroitin Sulfate	N/A	High
Clegg (2006)	Patient Global Assessment of Response to Therapy	631	Yes	24	Chondroitin Sulfate	Placebo	2.95 (2.73, 3.18)	Yes	Unclear	Moderate
Clegg (2006)	Patient Global Assessment of Disease Status	631	Yes	24	Chondroitin Sulfate	Placebo	0.05 (-0.11, 0.2)	No	Unclear	Moderate
Clegg (2006)	Physician Global Assessment of Disease Status	631	Yes	24	Chondroitin Sulfate	Placebo	0.04 (-0.12, 0.19)	No	Unclear	Moderate

Table 141. Chondroitin Sulfate Plus Glucosamine Versus Placebo

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Rai (2004)	Lequesne index	50	Yes	52	Chondroitin Sulfate plus Glucosamine	Placebo	Mean Difference=7.78 (p<.01)	Yes	Unclear	Moderate
Clegg (2006)	WOMAC Pain	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.13 (-0.28, 0.03)	No	True negative	Moderate
Clegg (2006)	WOMAC Stiffness	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.05 (-0.21, 0.1)	No	True negative	Moderate
Clegg (2006)	WOMAC Function	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.14 (-0.29, 0.02)	No	True negative	Moderate
Clegg (2006)	Normalized WOMAC	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.11 (-0.27, 0.04)	No	True negative	Moderate
Clegg (2006)	HAQ Alternative Disability	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.11 (-0.26, 0.05)	No	Unclear	Moderate
Clegg (2006)	HAQ Pain	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.15 (-0.3, 0.01)	No	Unclear	Moderate
Clegg (2006)	Patient Global Assessment of Response to Therapy	631	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	2.9 (2.67, 3.12)	Yes	Unclear	Moderate

Clegg (2006)	Patient Global Assessment of Disease Status	631	Unclear	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.08 (-0.23, 0.08)	No	Unclear	Moderate
Clegg (2006)	Physician Global Assessment of Disease Status	631	Unclear	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.04 (-0.2, 0.12)	No	Unclear	Moderate
Clegg (2006)	Acetaminophen consumption	631	Unclear	24	Chondroitin Sulfate plus Glucosamine	Placebo	-0.06 (-0.21, 0.1)	No	Unclear	Moderate

Table 142. Chondroitin Sulfate Plus Glucosamine: Stratified By Severity (Clegg 2006)

Severity Subgroup	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Odds Ratio	Sig	Strength of Evidence
Mild (WOMAC Pain 5-12)	20% WOMAC decrease	558	Unclear	24	Chondroitin Sulfate plus Glucosamine	Placebo	1.13 (0.8, 1.59)	No	Moderate
	OMERACT-OARSI Response	488	Unclear	24	Chondroitin Sulfate plus Glucosamine	Placebo	1.16 (0.81, 1.67)	No	Moderate
	50% decrease in WOMAC Pain score	488	Unclear	24	Chondroitin Sulfate plus Glucosamine	Placebo	0.99 (0.69, 1.41)	No	Moderate
Moderate to Severe (WOMAC > 12)	20% WOMAC decrease	142	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	3.2 (1.53, 6.69)	No	Moderate
	OMERACT-OARSI response	142	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	3.18 (1.56, 6.46)	No	Moderate

Severity Subgroup	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Odds Ratio	Sig	Strength of Evidence
	50% decrease in WOMAC Pain score	142	Yes	24	Chondroitin Sulfate plus Glucosamine	Placebo	2.28 (1.16, 4.51)	No	Moderate

Table 143. Piascledine Versus Chondroitin Sulfate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	WOMAC Total	357	Yes	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.09 (-0.12, 0.3)	No	True negative	Moderate
Pavelka (2010)	WOMAC Total	357	Yes	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.09 (-0.12, 0.3)	No	True negative	Moderate
Pavelka (2010)	WOMAC Total	357	Yes	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.09 (-0.12, 0.3)	No	True negative	Moderate
Pavelka (2010)	WOMAC Total	357	Yes	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.08 (-0.12, 0.29)	No	True negative	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	WOMAC Total	357	Yes	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.08 (-0.13, 0.28)	No	True negative	Moderate
Pavelka (2010)	WOMAC Stiffness	357	Yes	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.03 (-0.17, 0.24)	No	True negative	Moderate
Pavelka (2010)	WOMAC Stiffness	357	Yes	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.06 (-0.14, 0.27)	No	True negative	Moderate
Pavelka (2010)	WOMAC Stiffness	357	Yes	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.04 (-0.17, 0.25)	No	True negative	Moderate
Pavelka (2010)	WOMAC Stiffness	357	Yes	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.03 (-0.18, 0.23)	No	True negative	Moderate
Pavelka (2010)	WOMAC Stiffness	357	Yes	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.12 (-0.09, 0.33)	No	True negative	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	WOMAC Pain	357	Yes	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.1 (-0.11, 0.3)	No	True negative	Moderate
Pavelka (2010)	WOMAC Pain	357	Yes	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.1 (-0.11, 0.31)	No	True negative	Moderate
Pavelka (2010)	WOMAC Pain	357	Yes	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.06 (-0.15, 0.26)	No	True negative	Moderate
Pavelka (2010)	WOMAC Pain	357	Yes	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.1 (-0.1, 0.31)	No	True negative	Moderate
Pavelka (2010)	WOMAC Pain	357	Yes	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.08 (-0.12, 0.29)	No	True negative	Moderate
Pavelka (2010)	WOMAC Function	357	Yes	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.09 (-0.12, 0.3)	No	True negative	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	WOMAC Function	357	Yes	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.09 (-0.12, 0.29)	No	True negative	Moderate
Pavelka (2010)	WOMAC Function	357	Yes	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.1 (-0.11, 0.31)	No	True negative	Moderate
Pavelka (2010)	WOMAC Function	357	Yes	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.08 (-0.13, 0.29)	No	True negative	Moderate
Pavelka (2010)	WOMAC Function	357	Yes	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.07 (-0.14, 0.27)	No	True negative	Moderate
Pavelka (2010)	Pain on movement (VAS)	357	Yes	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.17 (-0.04, 0.38)	No	True negative	Moderate
Pavelka (2010)	Pain on movement (VAS)	357	Yes	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.09 (-0.12, 0.3)	No	True negative	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	Pain on movement (VAS)	357	Yes	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.11 (-0.1, 0.32)	No	True negative	Moderate
Pavelka (2010)	Pain on movement (VAS)	357	Yes	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.1 (-0.1, 0.31)	No	True negative	Moderate
Pavelka (2010)	Pain on movement (VAS)	357	Yes	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.02 (-0.19, 0.23)	No	True negative	Moderate
Pavelka (2010)	Lequesne index	357	Unclear	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.08 (-0.13, 0.29)	No	Unclear	Moderate
Pavelka (2010)	Lequesne index	357	Unclear	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.04 (-0.17, 0.24)	No	Unclear	Moderate
Pavelka (2010)	Lequesne index	357	Unclear	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0 (-0.21, 0.21)	No	Unclear	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	Lequesne index	357	Unclear	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.03 (-0.18, 0.24)	No	Unclear	Moderate
Pavelka (2010)	Lequesne index	357	Unclear	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0 (-0.21, 0.21)	No	Unclear	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day	357	Unclear	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.03 (-0.18, 0.24)	No	Unclear	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day	357	Unclear	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.03 (-0.18, 0.24)	No	Unclear	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day	357	Unclear	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.02 (-0.19, 0.23)	No	Unclear	Moderate
Pavelka (2010)	Rescue medication, mean tablets/day	357	Unclear	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0 (-0.21, 0.21)	No	Unclear	Moderate

Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD (Odds Ratio When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2010)	Rescue medication, mean tablets/day	357	Unclear	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	-0.01 (-0.22, 0.2)	No	Unclear	Moderate
Pavelka (2010)	Pain at rest (VAS)	357	Yes	4	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.1 (-0.11, 0.31)	No	True negative	Moderate
Pavelka (2010)	Pain at rest (VAS)	357	Yes	8	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.13 (-0.08, 0.33)	No	True negative	Moderate
Pavelka (2010)	Pain at rest (VAS)	357	Yes	12	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.16 (-0.04, 0.37)	No	True negative	Moderate
Pavelka (2010)	Pain at rest (VAS)	357	Yes	24	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.03 (-0.17, 0.24)	No	True negative	Moderate
Pavelka (2010)	Pain at rest (VAS)	357	Yes	32	Avocado soybean unsaponifiable (Piascledine)	Chondroitin Sulfate	0.01 (-0.2, 0.22)	No	True negative	Moderate

Figure 33. Chondroitin Sulfate Versus Placebo: VAS Pain

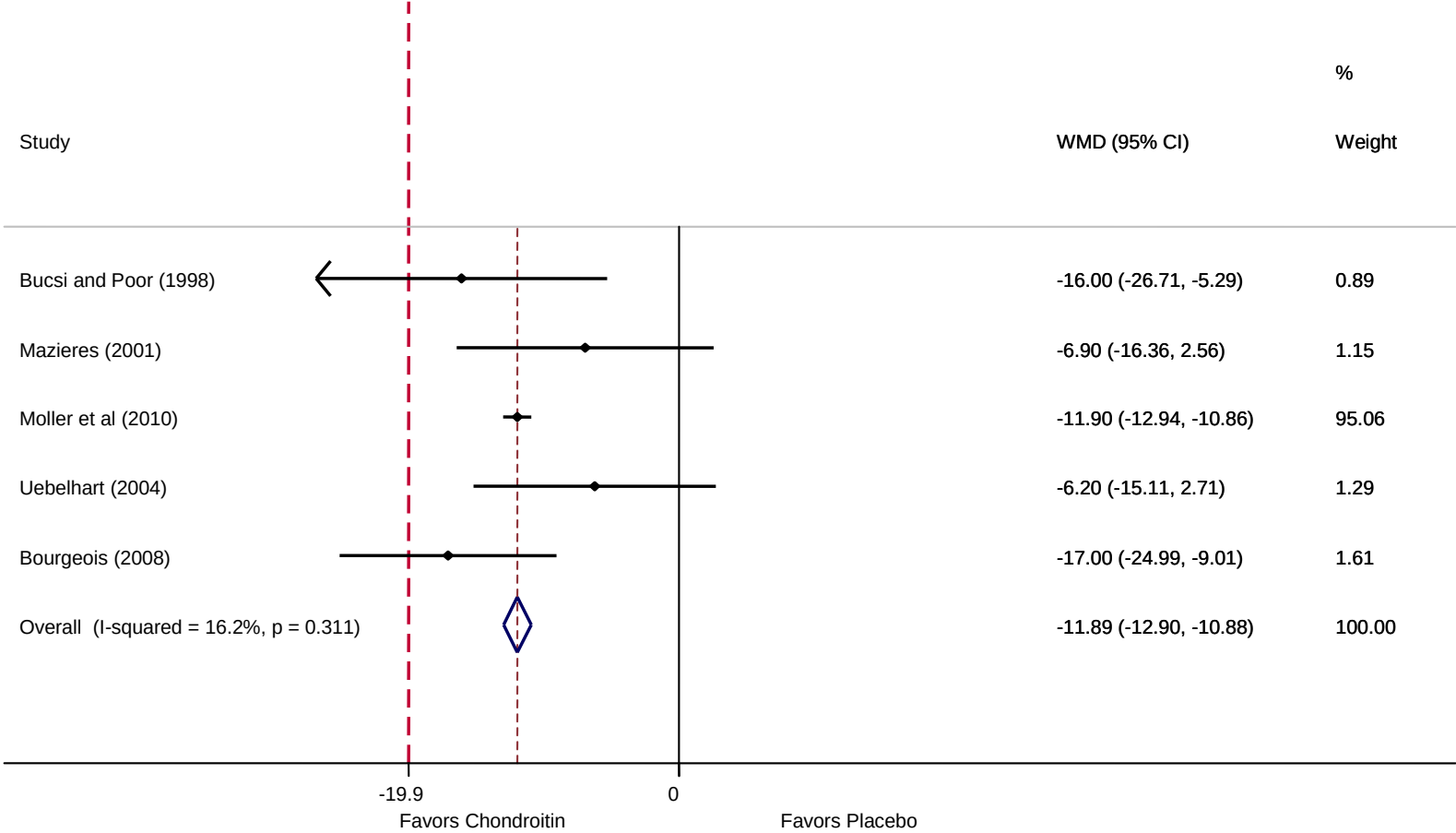


Figure 34. Glucosamine Versus Placebo: WOMAC Pain in MID Units

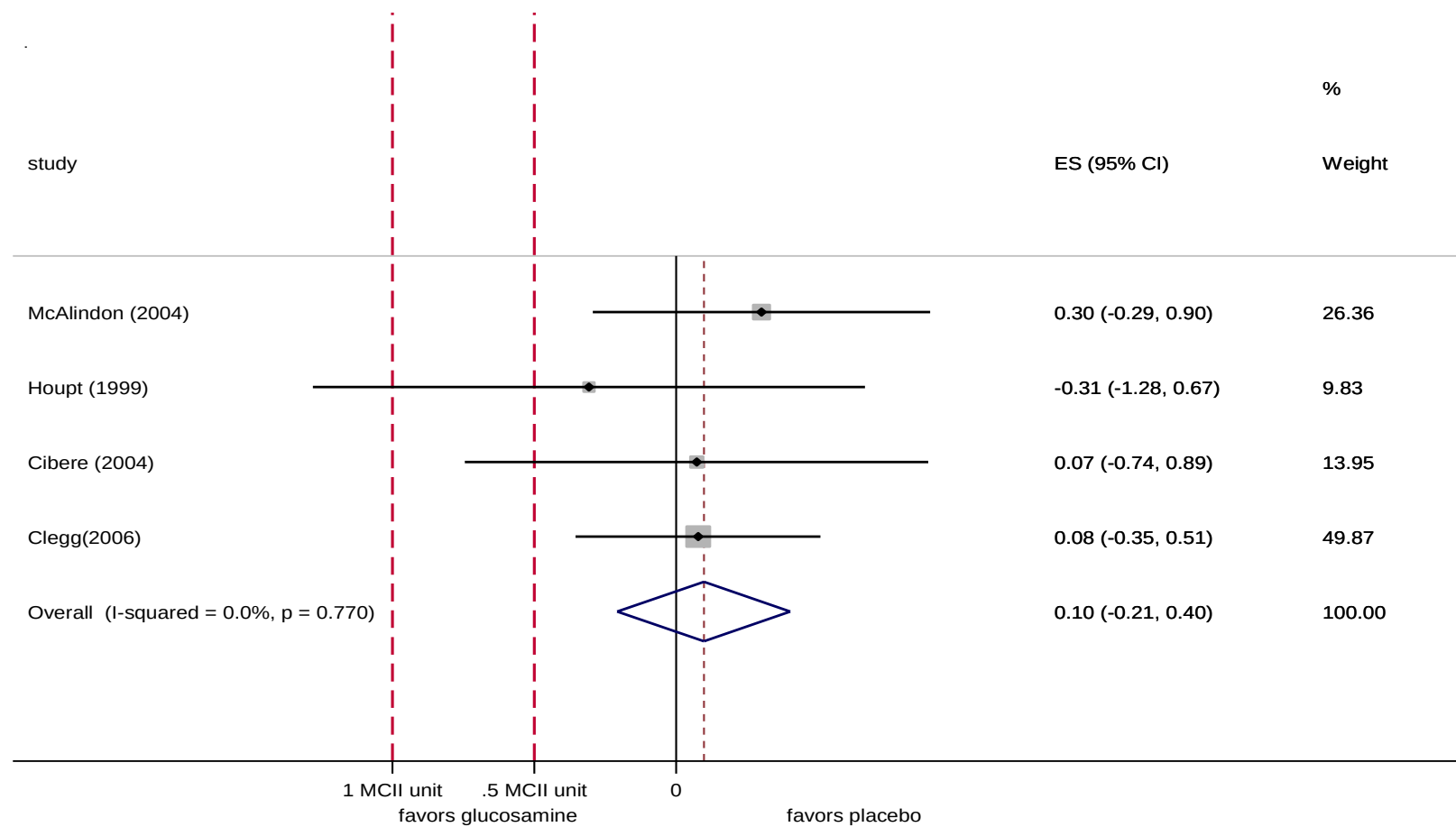


Figure 35. Glucosamine Versus Placebo: WOMAC Function in MID Units

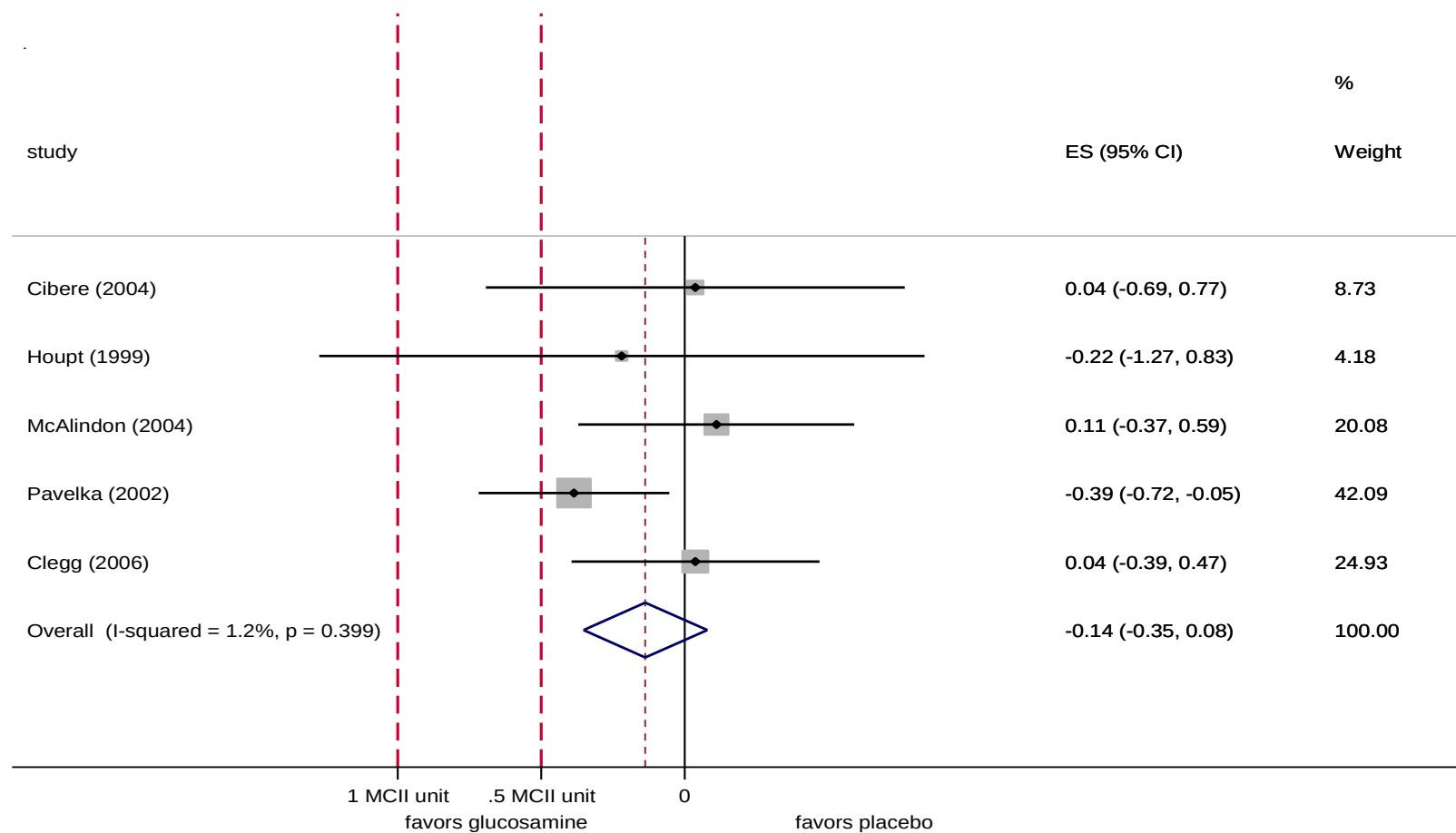


Figure 36. Glucosamine Versus Placebo: WOMAC Stiffness in MID Units

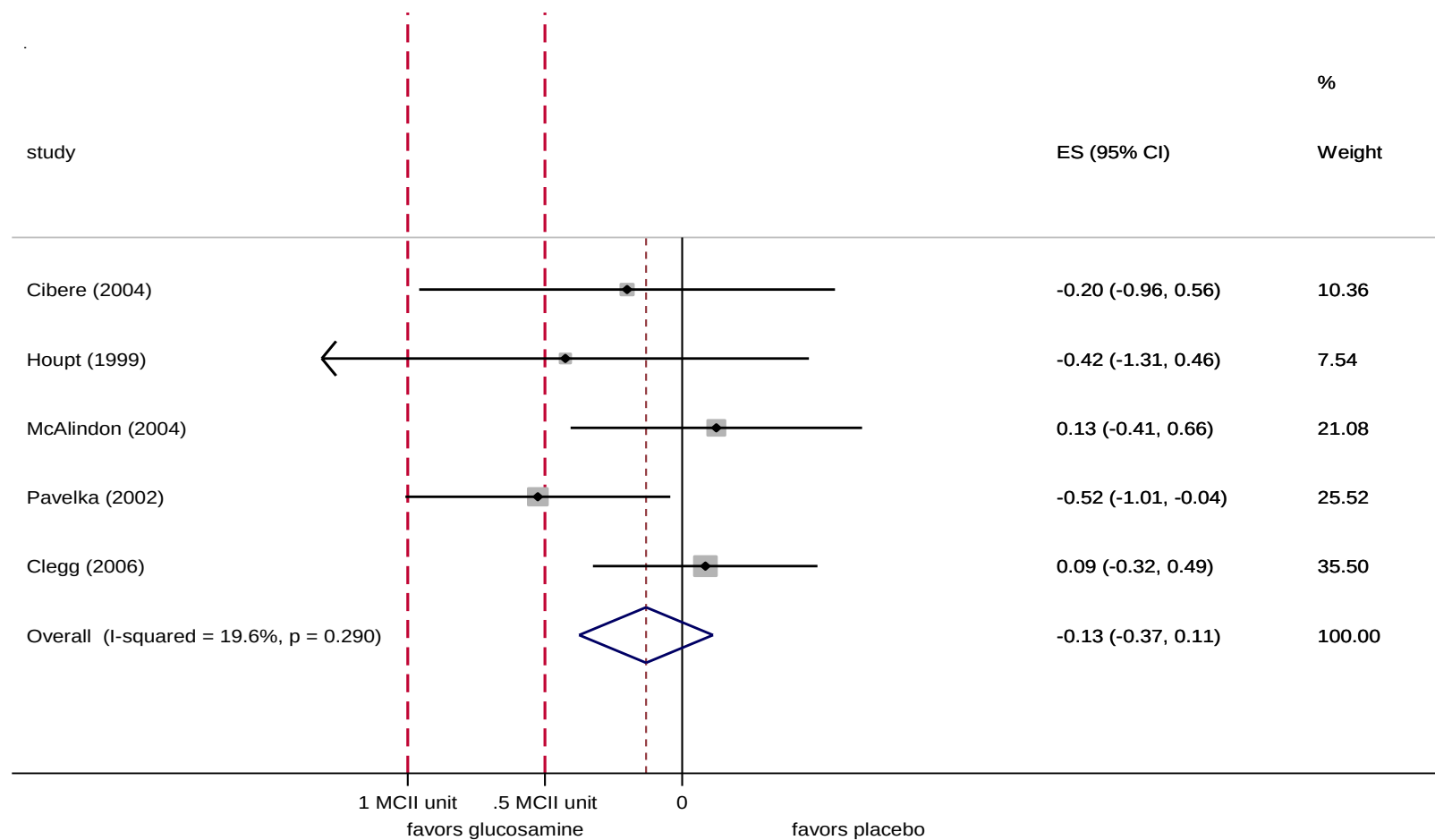


Figure 37. Glucosamine Versus Placebo: WOMAC Total in MID Units

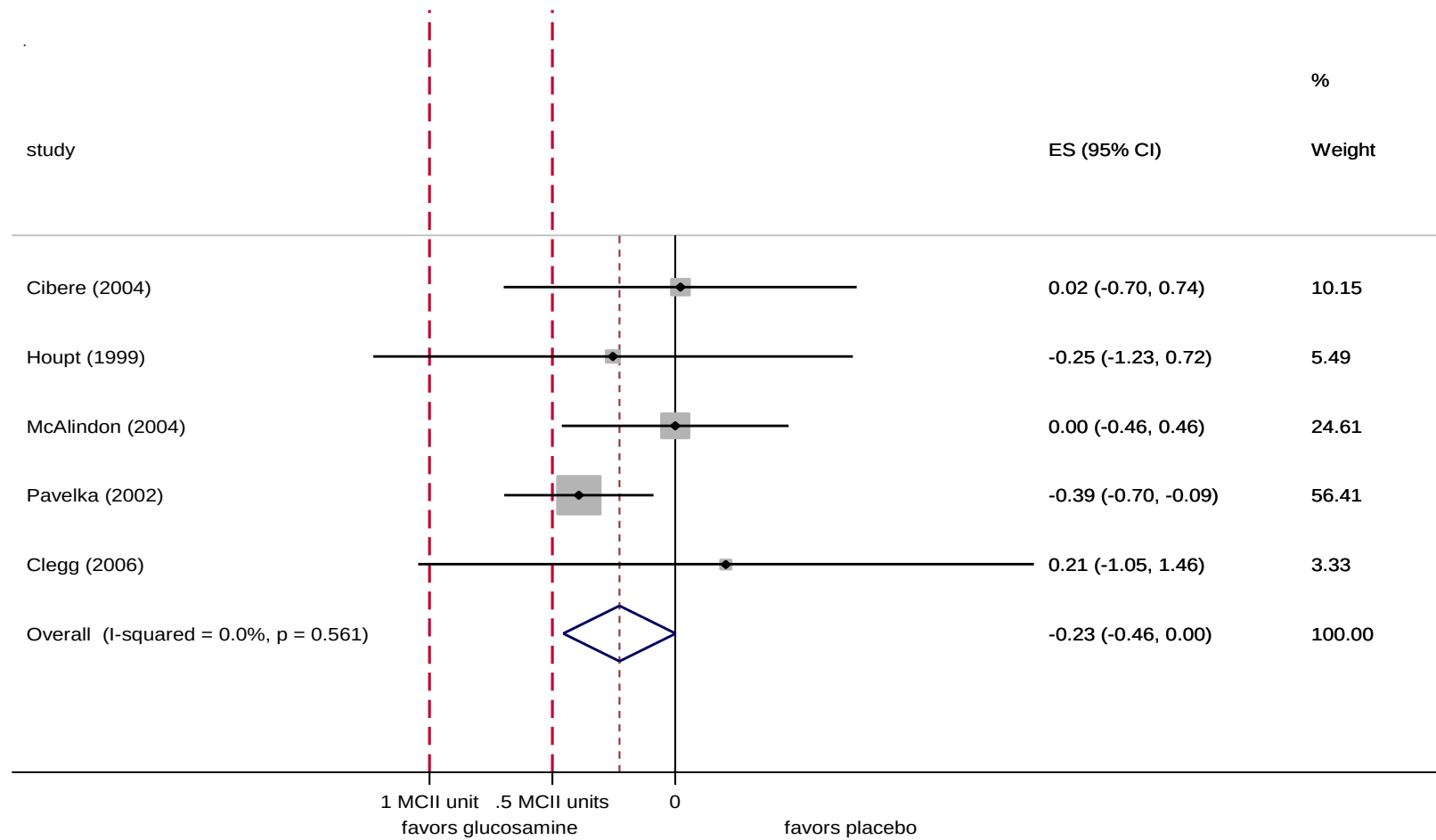
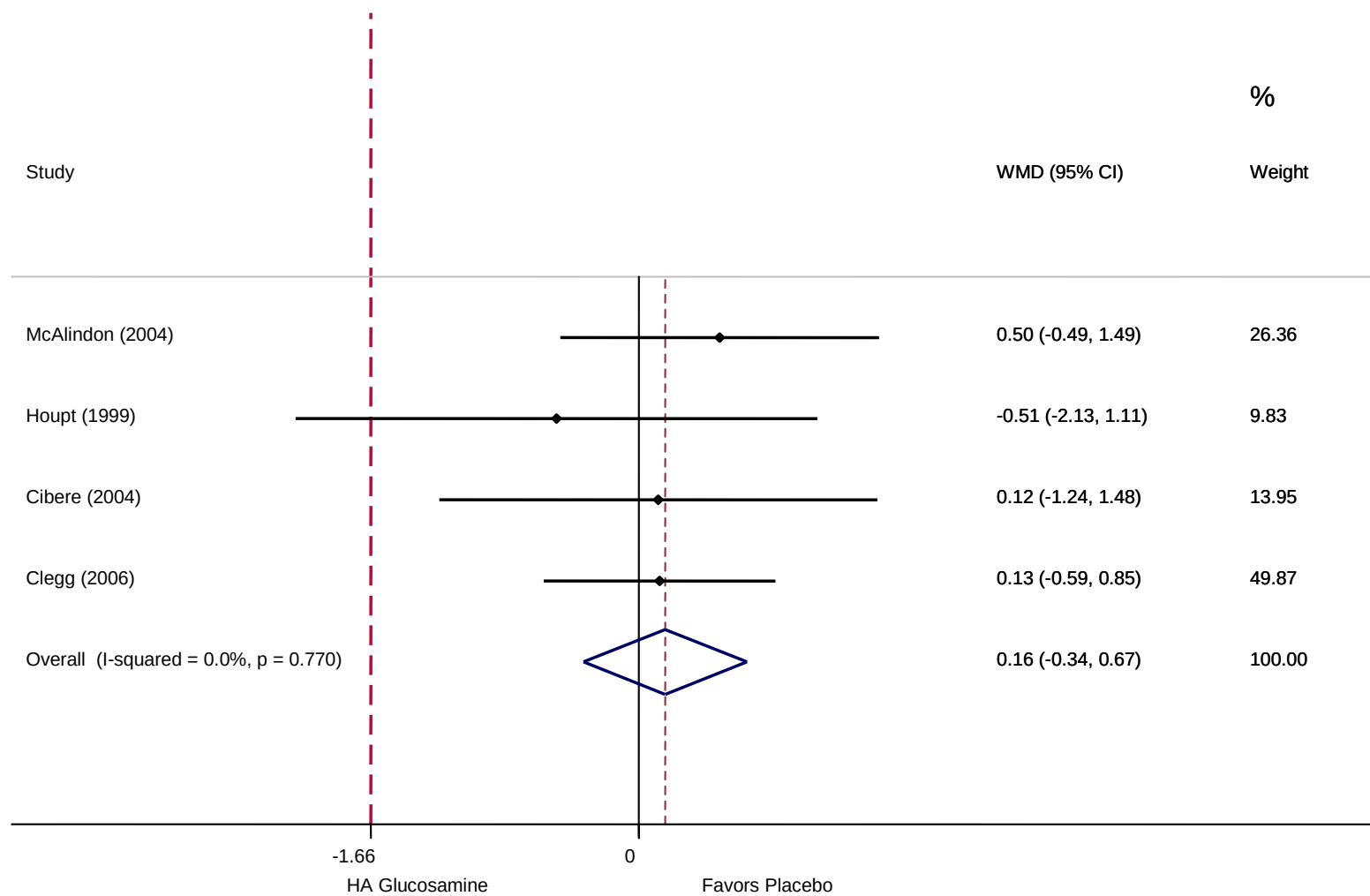


Figure 38. Glucosamine Versus Placebo: WOMAC Pain



The red line indicates the MCII

Figure 39. Glucosamine Versus Placebo: WOMAC Function

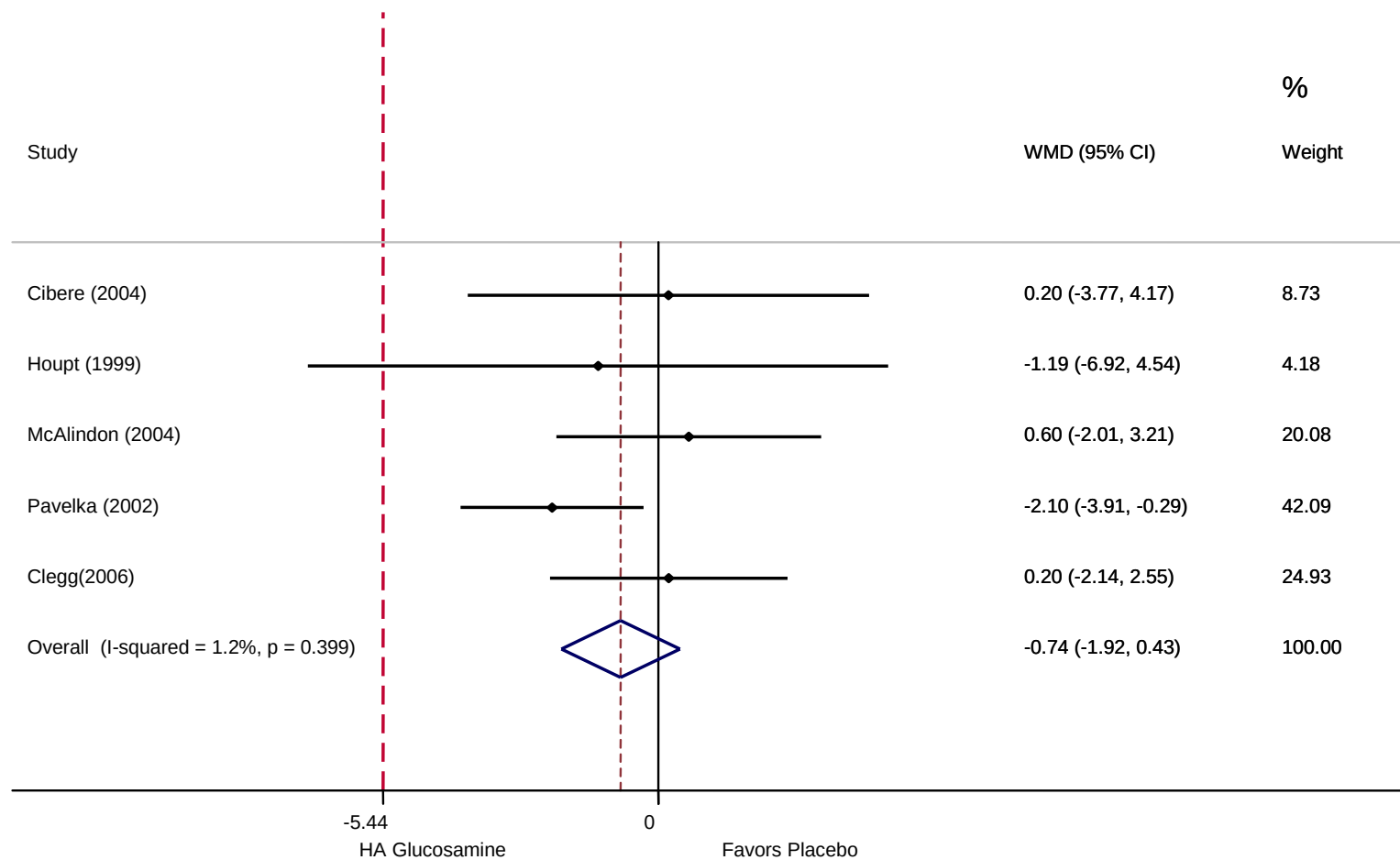
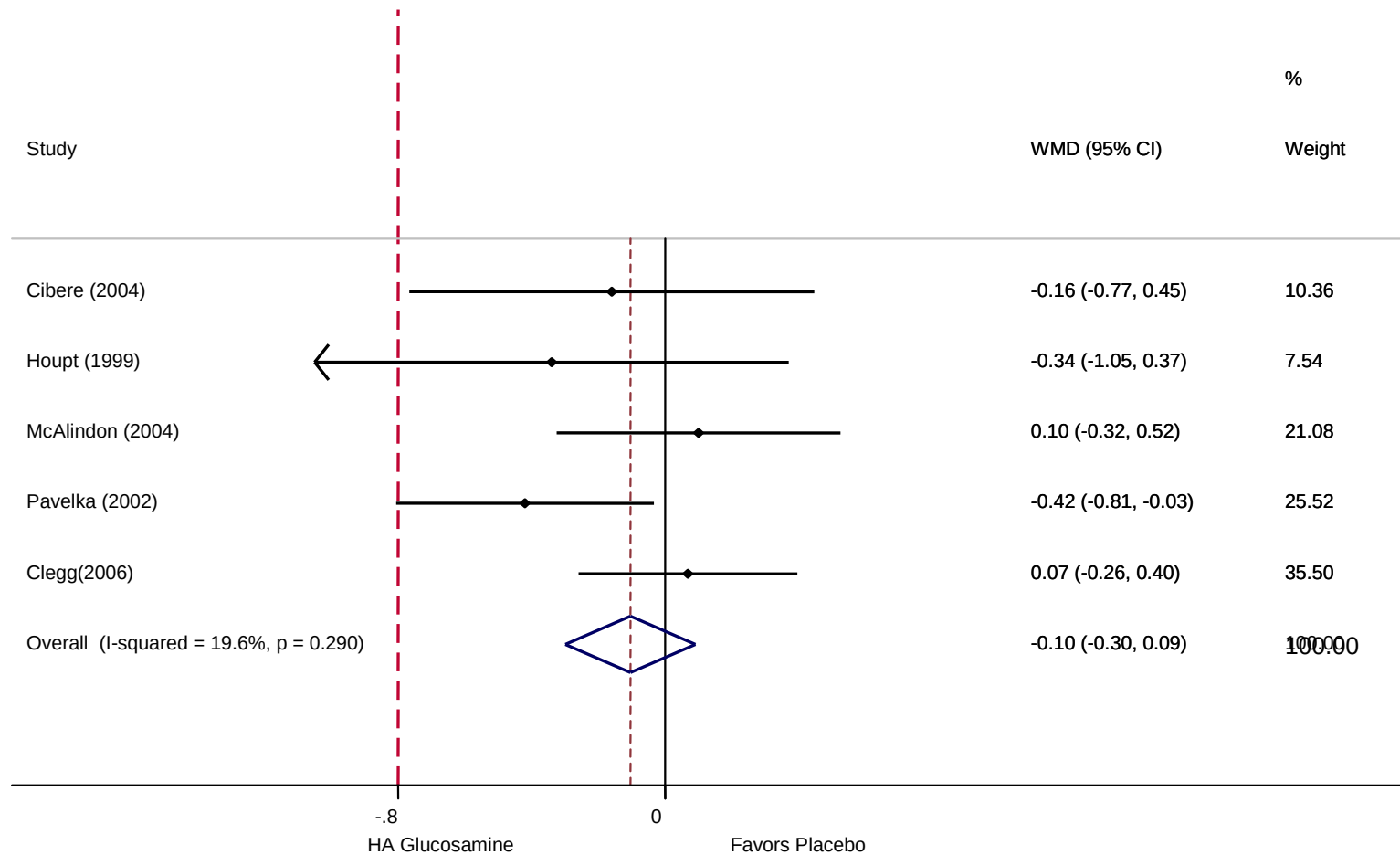
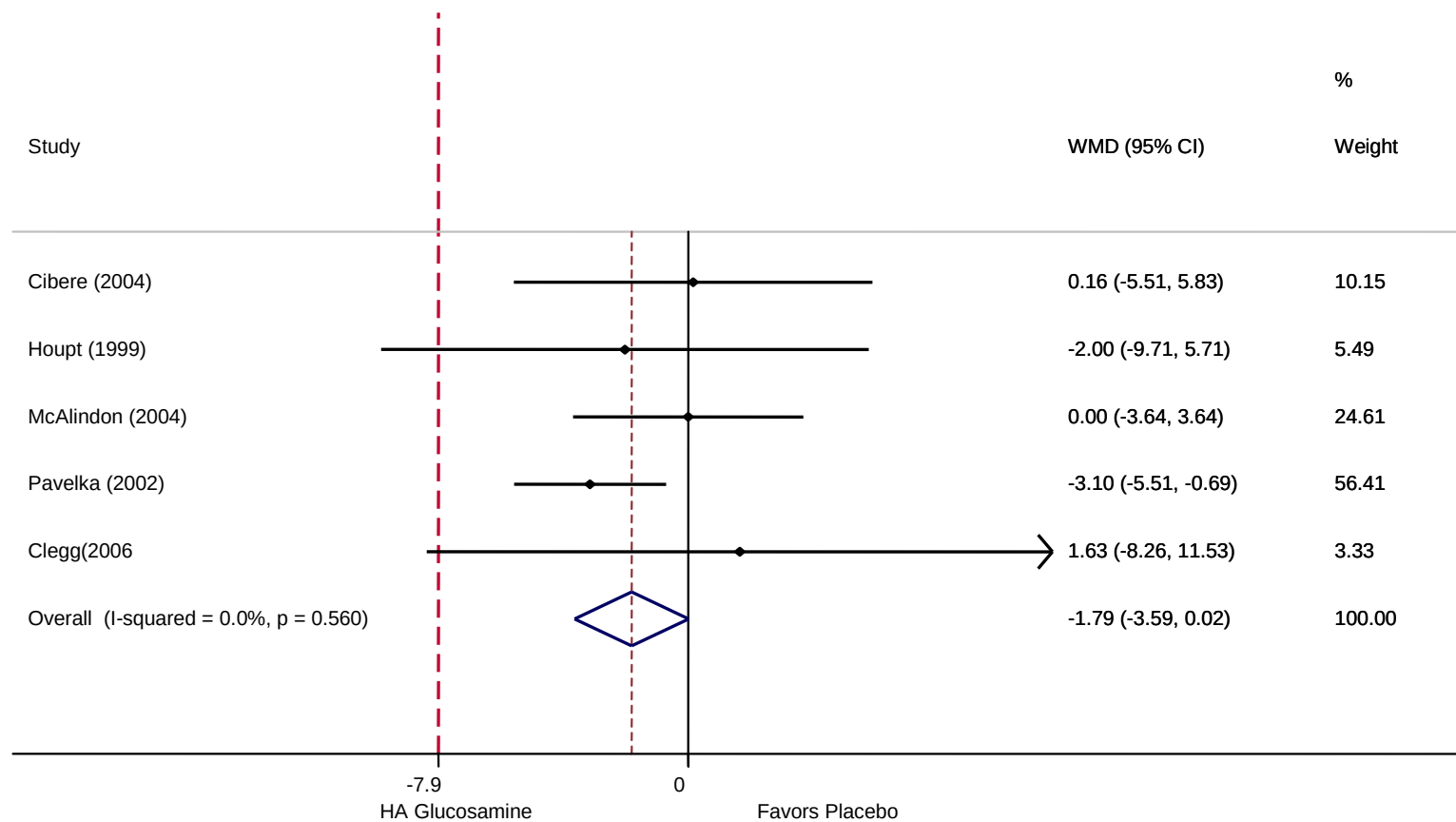


Figure 40. Glucosamine Versus Placebo: WOMAC Stiffness



The red line indicates the MCII

Figure 41. Glucosamine Versus Placebo: WOMAC Total



RECOMMENDATION 7A

We recommend nonsteroidal anti-inflammatory drugs (NSAIDs; oral or topical) or Tramadol for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm and/or that the quality of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RECOMMENDATION 7B

We are unable to recommend for or against the use of acetaminophen, opioids, or pain patches for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

This recommendation included studies of both selective (cyclo-oxygenase-2, COX-2 inhibitors) and non-selective NSAIDs. The endorsement for NSAIDs was based on 202 favorable outcomes from 19 studies comparing either the selective, non-selective or topical analgesics to placebo. Twelve studies were of selective NSAIDs, four were of non-selective oral NSAIDs, and six were of topical NSAIDs. (Three studies compared multiple types of analgesics to placebo.) Three were high-strength studies, 14 were moderate, and two were of low-strength. The moderate and low strength studies were included because they examined different outcomes than the high strength articles. Out of 202 total outcomes, 171 were statistically significant in favor of the experimental group. Fifteen outcomes were above the MCII threshold and 63 outcomes were possibly clinically significant. The remaining outcomes were neither statistically nor clinically significant.

Two high- and three moderate- strength studies examining the various outcome measures in this recommendation compared tramadol to placebo. They included outcome measurements with follow up periods that ranged from 8 to 13 weeks in duration. Ten of 14 outcomes were statistically significant in favor of the treatment group. Two statistically significant outcomes (WOMAC pain and stiffness subscale scores) were possibly clinically significant and the other eight outcomes could not be evaluated. Fishman et al.⁹⁵ did not find any statistically significant improvements in pain efficacy between tramadol contramid doses of 100mg, 200mg and 300mg. Beaulieu et al.⁹⁶ found similar treatment effects in tramadol and diclofenac in using WOMAC pain, stiffness and function subscale scales.

The recommendation on acetaminophen was downgraded from level B (i.e. Moderate) in the 2008 edition of the guideline to inconclusive in our current guideline. As opposed to the selection criteria previously used, our current systematic review examined acetaminophen separately and found only one relevant study that tested it against placebo (Miceli-Richard et al.⁹⁷). Their study found no statistical significance or minimum clinically important improvement to patients compared to placebo. In addition, their findings and the previous clinical guideline were based on the usage of a maximum of 4000 mg of acetaminophen per day, and there has been a recent change to a dosage not to exceed 3000 mg per day; see: [FDA Acetaminophen Dosage Announcement](#).

The work group realizes that many practitioners prefer to start with acetaminophen prior to NSAIDs due to the side effect profile of NSAIDs. However, we found it unreasonable to recommend a treatment that does not show benefit over placebo.

Our literature review found no relevant studies meeting our inclusion criteria on opioids or pain patches for the treatment of knee osteoarthritis.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 144](#), [Table 148-Table 154](#)

To summarize, this recommendation included 731 outcomes from 52 studies of which 107 outcomes were rated as high quality, 571 were moderate, and 53 were of low quality. The study by Schnitzer et al.⁹⁸ was retrospective and evaluated 20 outcomes that were flawed in the hypothesis and blinding domains. One other study with six outcomes was not sufficiently blinded.⁹⁹ Forty-seven studies and 624 outcomes were flawed in the group assignment domain. Twenty-nine studies were flawed in terms of group comparability, and five studies had treatment integrity flaws. There were no flaws in how outcomes were measured in any of the studies. The potential for investigator bias was present in all but one study.

APPLICABILITY

Relevant Tables: [Table 144](#), [Table 148-Table 154](#)

All included studies in this recommendation was of moderate applicability. The enrolled patients in 48 of the 52 studies may not have been representative of the osteoarthritis of the knee population seen in clinical practice. Also, the treatment intervention was administered in a manner not consistent with clinical practice in all of the studies. Since 675 out of 731 outcomes were measured on an intent-to-treat basis, a sufficient percentage of enrolled patients were included in the final analysis.

FINAL STRENGTH OF EVIDENCE

Every study was assigned a moderate applicability rating. The strength of evidence ratings were the same as the quality ratings. A total of 107 outcomes had high strength of evidence, 571 had moderate strength, and 53 had low ratings.

Table 144. Quality and Applicability Summary: Analgesics

Study	Outcome	Weeks	Comparison	Quality	Applicability	Strength of Evidence
Astorga (1991)	Time to walk 50ft	4	Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Astorga (1991)	Time to walk 50ft	6	Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Astorga (1991)	Time to walk 50ft	8	Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Astorga (1991)	Morning stiffness	4	Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Astorga (1991)	Morning stiffness	6	Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Astorga (1991)	Morning stiffness	8	Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate

Astorga (1991)	Morning stiffness		Etodolac 300mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Function	52	Tenidap 120mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Pain	52	Tenidap 40mg versus Tenidap 120mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Pain	52	Tenidap 40mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Pain	52	Tenidap 120mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Stiffness	52	Tenidap 40mg versus Tenidap 120mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Stiffness	52	Tenidap 40mg versus Piroxicam 20mg	Moderate	Moderate	Moderate

Ayral (2003)	Change in WOMAC averaged VAS Stiffness	52	Tenidap 120mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Total	52	Tenidap 40mg versus Tenidap 120mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Total	52	Tenidap 40mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Total	52	Tenidap 120mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Physician Global Assessment	52	Tenidap 120mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Physician Global Assessment	52	Tenidap 40mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Patient Global Assessment	52	Tenidap 120mg versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ayral (2003)	Patient Global	52	Tenidap 40mg	Moderate	Moderate	Moderate

	Assessment		versus Placebo			
Ayral (2003)	Physician Global Assessment	52	Tenidap 40mg versus Tenidap 120mg	Moderate	Moderate	Moderate
Ayral (2003)	Patient Global Assessment	52	Tenidap 40mg versus vehicle control	Moderate	Moderate	Moderate
Babul (2004)	WOMAC Function	12	Tramadol ER versus Placebo	Moderate	Moderate	Moderate
Babul (2004)	Patient Global Assessment	12	Tramadol ER versus Placebo	Moderate	Moderate	Moderate
Babul (2004)	VAS	12	Tramadol ER versus Placebo	Moderate	Moderate	Moderate
Babul (2004)	WOMAC Pain	12	Tramadol ER versus Placebo	Moderate	Moderate	Moderate
Babul (2004)	WOMAC Stiffness	12	Tramadol ER versus Placebo	Moderate	Moderate	Moderate
Baer (2005)	WOMAC Function	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	High	Moderate	High
Baer (2005)	WOMAC Pain	6	Pennsaid (topical Diclofenac solution) versus	High	Moderate	High

			vehicle control solution			
Baer (2005)	WOMAC Pain on walking	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	High	Moderate	High
Baer (2005)	WOMAC Stiffness	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	High	Moderate	High
Barthel (2009)	Weeks with no rescue drug	12	Diclofenac sodium 1% gel in DMSO versus DMSO vehicle	Moderate	Moderate	Moderate
Barthel (2009)	Weeks with no rescue drug	12	Diclofenac sodium 1% gel in DMSO versus DMSO vehicle	Moderate	Moderate	Moderate
Beaulieu (2008)	WOMAC Stiffness	6	CR Tramadol versus SR Diclofenac	Moderate	Moderate	Moderate
Beaulieu (2008)	WOMAC Function	6	CR Tramadol versus SR Diclofenac	Moderate	Moderate	Moderate

Beaulieu (2008)	Mean change in WOMAC Pain	6	Tramadol versus Diclofenac	Moderate	Moderate	Moderate
Bellamy (1993)	WOMAC Function	12	Tenoxicam versus Diclofenac	Moderate	Moderate	Moderate
Bellamy (1993)	WOMAC Pain	12	Tenoxicam versus Diclofenac	Moderate	Moderate	Moderate
Bellamy (1993)	WOMAC Stiffness	12	Tenoxicam versus Diclofenac	Moderate	Moderate	Moderate
Bookman (2004)	Mean WOMAC Stiffness (Likert)	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	Mean WOMAC Pain (Likert)	4	Topical Diclofenac versus Placebo gel	High	Moderate	High
Bookman (2004)	Mean WOMAC Function (Likert)	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	Acetaminophen consumption	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	Acetaminophen consumption	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	Acetaminophen	4	Topical Diclofenac versus	Moderate	Moderate	Moderate

	consumption		vehicle control			
Bookman (2004)	Acetaminophen consumption	4	Topical Diclofenac versus Placebo	Moderate	Moderate	Moderate
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus vehicle control	High	Moderate	High

Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Stiffness	4	Topical Diclofenac versus Placebo	High	Moderate	High
Bookman (2004)	WOMAC Stiffness	4	Topical Diclofenac versus vehicle control	High	Moderate	High
Chubick (1987)	Improvement in morning weight-bearing pain	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	Moderate	Moderate	Moderate

Chubick (1987)	Improvement in afternoon weight-bearing pain	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	Moderate	Moderate	Moderate
Chubick (1987)	Improvement in night pain	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	Moderate	Moderate	Moderate
Chubick (1987)	Improvement in tenderness	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	Moderate	Moderate	Moderate
Dick (1992)	Time to walk 50ft	6	Etodolac 300mg x2 versus Piroxicam 20mg	Moderate	Moderate	Moderate
Dick (1992)	Morning stiffness	6	Etodolac 300mg x2 versus Piroxicam 20mg	Moderate	Moderate	Moderate
Ehrich (1999)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 125mg versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate

Ehrich (1999)	WOMAC Function	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Evcik (2003)	Health assessment questionnaire	26	Tenoxicam versus Placebo	Low	Moderate	Low
Evcik (2003)	Lequesne Index	26	Tenoxicam versus Placebo	Low	Moderate	Low
Evcik (2003)	VAS ascending stairs	26	Tenoxicam versus Placebo	Low	Moderate	Low
Evcik (2003)	VAS descending stairs	26	Tenoxicam versus Placebo	Low	Moderate	Low
Evcik (2003)	VAS Walking	26	Tenoxicam versus Placebo	Low	Moderate	Low
Evcik (2003)	VAS at rest	26	Tenoxicam versus Placebo	Low	Moderate	Low
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid versus Placebo	High	Moderate	High
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid versus Placebo	High	Moderate	High
Fishman (2007)	WOMAC Pain, percent improvement from	12	Tramadol Contramid versus	High	Moderate	High

	baseline		Placebo			
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid 100mg versus Tramadol Contramid 200mg	High	Moderate	High
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid 100mg versus Tramadol Contramid 300mg	High	Moderate	High
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid 200mg versus Tramadol Contramid 300mg	High	Moderate	High
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 400mg versus Placebo	Low	Moderate	Low
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 200mg versus Placebo	Low	Moderate	Low
Fleischmann (2006)	VAS Pain improvement	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	VAS Pain improvement	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Pain	13	Lumiracoxib versus Placebo	Low	Moderate	Low

Fleischmann (2006)	WOMAC Pain	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 200mg versus Celecoxib 200mg	Low	Moderate	Low
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 400mg versus Celecoxib 200mg	Low	Moderate	Low
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 200mg versus Lumiracoxib 400mg	Low	Moderate	Low
Fleischmann (2006)	Physician Global Assessment	13	Celecoxib (Cox- 2) versus Placebo	Low	Moderate	Low
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 200mg versus Placebo	Low	Moderate	Low
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 400mg versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Function	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Function	13	Lumiracoxib versus Placebo	Low	Moderate	Low

Fleischmann (2006)	VAS Pain improvement	13	Celecoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Pain	13	Celecoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Stiffness	13	Kumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOMAC Total	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	WOAMC Total	13	Lumiracoxib versus Placebo	Low	Moderate	Low
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 200mg versus Celecoxib 200mg	Low	Moderate	Low
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 400mg versus Celecoxib 200mg	Low	Moderate	Low
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 200mg versus Lumiracoxib 400mg	Low	Moderate	Low
Fleischmann (2006)	Adverse events	13	Lumiracoxib 200mg versus	Moderate	Moderate	Moderate

Celecoxib 200mg						
Fleischmann (2006)	Adverse events	13	Lumiracoxib 400mg versus Celecoxib 200mg	Moderate	Moderate	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 200mg versus Lumiracoxib 400mg	Moderate	Moderate	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 400mg versus Placebo	Moderate	Moderate	Moderate
Fleischmann (2001)	WOMAC Function	13	Tramadol versus Placebo	High	Moderate	High
Fleischmann (2001)	WOMAC Pain	13	Tramadol versus Placebo	High	Moderate	High
Fleischmann (2001)	WOMAC Stiffness	13	Tramadol versus Placebo	High	Moderate	High
Gibofsky (2003)	WOMAC Function	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Function	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate

Gibofsky (2003)	VAS Pain on walking improvement	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	VAS Pain on walking improvement	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Pain	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Pain	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Stiffness	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Stiffness	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Function improvement	6	Celecoxib 200mg versus Rofecoxib	Moderate	Moderate	Moderate
Gibofsky (2003)	VAS Pain on walking improvement	6	Celecoxib 200mg versus Rofecoxib	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Pain improvement	6	Celecoxib 200mg versus Rofecoxib	Moderate	Moderate	Moderate
Gibofsky (2003)	WOMAC Stiffness	6	Celecoxib 200mg versus Rofecoxib	Moderate	Moderate	Moderate

improvement						
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Adverse events	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Aceclofenac	Moderate	Moderate	Moderate
Gibofsky (2003)	Any adverse event	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Aceclofenac	Moderate	Moderate	Moderate
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Aceclofenac	Moderate	Moderate	Moderate
Gibofsky (2003)	Patient Global Assessment	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Patient Global Assessment	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Physician Global Assessment	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Physician Global	6	Rofecoxib 25mg	Moderate	Moderate	Moderate

	Assessment		versus Placebo			
Gibofsky (2003)	Patient Global Assessment of Response to Treatment	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Gibofsky (2003)	Patient Global Assessment	6	Celecoxib 200mg versus Rofecoxib 25mg	Moderate	Moderate	Moderate
Gibofsky (2003)	Physician Global Assessment	6	Celecoxib 200mg versus Rofecoxib 25mg	Moderate	Moderate	Moderate
Goregaonkar (2009)	Gastritis	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Goregaonkar (2009)	Abdominal pain	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Goregaonkar (2009)	Dizziness	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Goregaonkar	Drowsiness	4	Lornoxicam 8mg versus Diclofenac	Moderate	Moderate	Moderate

(2009)			50mg			
Goregaonkar (2009)	Headache	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Goregaonkar (2009)	Nausea/Vomiting	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Goregaonkar (2009)	Diarrhea	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Goregaonkar (2009)	GI Events	4	Lornoxicam 8mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 60mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 10mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 60mg	High	Moderate	High

Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 10mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 10mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 10mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 30mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 30mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 60mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 10mg	High	Moderate	High
Gottesdiener	Patient Global Assessment of	6	Etoricoxib 5mg versus Etoricoxib	High	Moderate	High

(2002)	Disease Status		30mg			
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 10mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 10mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 30mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 5mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 10mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 30mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Global Assessment of Disease Status	6	Etoricoxib 60mg versus Etoricoxib 90mg	High	Moderate	High

Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 10mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment	6	Etoricoxib 10mg versus Etoricoxib 90mg	High	Moderate	High

Response						
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 60mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 10mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 30mg	High	Moderate	High
Gottesdiener	Physician Assessment of	6	Etoricoxib 5mg versus Etoricoxib	High	Moderate	High

(2002)	Treatment Response		60mg			
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 60mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 90mg	High	Moderate	High
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 60mg versus Etoricoxib 90mg	High	Moderate	High

Herrera (2007)	WOMAC Function	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	Moderate	Moderate	Moderate
Herrera (2007)	VAS Pain	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	Moderate	Moderate	Moderate
Herrera (2007)	WOMAC Pain	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	Moderate	Moderate	Moderate
Herrera (2007)	WOMAC Stiffness	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	Moderate	Moderate	Moderate
Herrera (2007)	WOMAC Total	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	Moderate	Moderate	Moderate
Karbowski (1991)	Time to walk 50ft	6	Etodolac 300mg versus Indomethacin 50mg	Moderate	Moderate	Moderate
Karbowski (1991)	Morning stiffness	6	Etodolac 300mg versus Indomethacin	Moderate	Moderate	Moderate

50mg						
Kivits (2002)	VAS Pain improvement	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain improvement	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain improvement	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain improvement	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain improvement	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain improvement	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC	12	Valdecoxib	Moderate	Moderate	Moderate

	Stiffness		versus Placebo			
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 5mg versus Naproxen	Moderate	Moderate	Moderate

			500mg			
Kivits (2002)	Accidental injury	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate

Kivits (2002)	Diarrhea	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Headache	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Headache	12	Valdecoxib 10mg versus Naproxen	Moderate	Moderate	Moderate

			500mg			
Kivits (2002)	Headache	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate

Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	12	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	6	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	12	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	6	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	12	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	6	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC	6	Valdecoxib 10mg versus Naproxen	Moderate	Moderate	Moderate

	Stiffness		10mg			
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib 10mg versus Naproxen 10mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib 20mg versus Naproxen 20mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib 20mg versus Naproxen 20mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib 10mg versus Naproxen 10mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib 10mg versus Naproxen 10mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib 20mg versus Naproxen 20mg	Moderate	Moderate	Moderate

Kivits (2002)	WOMAC Total	12	Valdecoxib 20mg versus Naproxen 20mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib 5mg versus Naproxen 5mg	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 5mg versus Naproxen	Moderate	Moderate	Moderate

			500mg			
Kivits (2002)	Constipation	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate

Kivits (2002)	Dyspepsia	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Headache	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Headache	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Headache	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 10mg versus Naproxen	Moderate	Moderate	Moderate

			500mg			
Kivits (2002)	Myalgia	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 10mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 5mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Abdominal Pain	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate

Kivits (2002)	Accidental Injury	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Headache	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 20mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Kivits (2002)	Upper respiratory	12	Valdecoxib 20mg versus Naproxen	Moderate	Moderate	Moderate

tract infections			500mg			
Kivits (2004)	Acid reflux	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Naproxen	High	Moderate	High
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Placebo	High	Moderate	High
Kivits (2004)	Dyspepsia	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Epigastric discomfort	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	GI events	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Heartburn	6	Rofecoxib 12.5mg versus Nabumetone	High	Moderate	High

			1000mg			
Kivits (2004)	Nausea	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	Moderate	Moderate	Moderate
Kivits (2004)	At least one adverse event	6	Nabumetone 1000 versus Placebo	High	Moderate	High
Kivits (2004)	Acid reflux	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Naproxen	High	Moderate	High
Kivits (2004)	Dyspepsia	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High

Kivits (2004)	Epigastric discomfort	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	GI events	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Heartburn	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Nausea	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Acid reflux	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Naproxen	High	Moderate	High

Kivits (2004)	Dyspepsia	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Epigastric discomfort	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	GI events	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Heartburn	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Nausea	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	High	Moderate	High
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 10mg (Cox-2) versus Placebo	Moderate	Moderate	Moderate

Kivits (2002)	Physician Global Assessment	12	Valdecoxib 10mg (Cox-2) versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 20mg (Cox-2) versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 20mg (Cox-2) versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 5mg (Cox-2) versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 5mg (Cox-2) versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	VAS Pain	6	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	6	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Stiffness	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	WOMAC Total	6	Naproxen versus	Moderate	Moderate	Moderate

Placebo						
Kivits (2002)	WOMAC Total	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	6	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Kivits (2002)	physician Global Assessment	6	Valdecoxib 10mg versus Naproxen	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 10mg versus Naproxen	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 20mg versus Naproxen	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 20mg versus Naproxen	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 5mg versus Naproxen	Moderate	Moderate	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 5mg versus Naproxen	Moderate	Moderate	Moderate
Kivits (2004)	Patient Global Assessment of Response to Treatment	6	Rofecoxib versus Placebo	High	Moderate	High

Kivits (2004)	Patient Global Assessment of Response to Treatment	6	Nabumetone versus Placebo	High	Moderate	High
Kivits (2004)	Patient Assessment of Treatment Response (good or excellent)	6	Rofecoxib 12.5mg versus Nabumetone	High	Moderate	High
Kogstad (1981)	Sequence A ability to walk (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	Moderate	Moderate	Moderate
Kogstad (1981)	Sequence B ability to walk (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	Moderate	Moderate	Moderate
Kogstad (1981)	Sequence A pain at night (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	Moderate	Moderate	Moderate
Kogstad (1981)	Sequence B pain at night (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	Moderate	Moderate	Moderate
Kogstad (1981)	Sequence A pain on movement (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	Moderate	Moderate	Moderate
Kogstad (1981)	Sequence B pain on movement	4	Piroxicam 20mg versus Naproxen	Moderate	Moderate	Moderate

	(VAS)		250mg			
La Montagna (1998)	Present pain index	12	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
La Montagna (1998)	Present pain index	24	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
La Montagna (1998)	Visual analogue scale	12	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
La Montagna (1998)	Visual analogue scale	24	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
Lee (1985)	Adverse events	6	High dose diflunisal (NSAID) versus Placebo	Moderate	Moderate	Moderate
Lee (1985)	Adverse events	6	Low dose diflunisal (NSAID) versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	Physician Global Assessment of	13	Celecoxib 200mg	Moderate	Moderate	Moderate

	Disease		versus Placebo			
Lehmann (2005)	Physician Global Assessment of Disease	13	Lumiracoxib 100mg versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib (Cox-2) with loading dose versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Pain	13	Lumiracoxib (Cox-2) with loading dose versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	VAS Pain improvement	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Pain	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Pain	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate

Lehmann (2005)	WOMAC Function improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Function improvement	13	Lumiracoxib 100mg versus Celecoxib	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Function improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	VAS Pain improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Pain improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib 100mg versus Celecoxib	Moderate	Moderate	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate

Lehmann (2005)	WOMAC Pain improvement	13	Lumiracoxib 100mg versus Celecoxib	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Pain improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Stiffness improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Stiffness improvement	13	Lumiracoxib 100mg versus Celecoxib	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Stiffness improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Total	13	Celecoxib 100mg versus Lumiracoxib with loading dose	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib 100mg versus Celecoxib	Moderate	Moderate	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib 100mg versus	Moderate	Moderate	Moderate

			Lumiracoxib with loading dose			
Lehmann (2005)	Physician Global Assessment of Disease	13	Lumiracoxib 100mg versus Celecoxib 200mg	Moderate	Moderate	Moderate
Lehmann (2005)	Patient Global Assessment of Disease	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	Patient Global Assessment of Disease	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Lehmann (2005)	Patient Global Assessment of Disease	13	Lumiracoxib versus Celecoxib	Moderate	Moderate	Moderate
Liang (2003))	Change in Lequesne index	4	Etodolac Sustained-Release 400mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
Lohmander (2005)	Patient Assessment of Treatment Response	6	Naproxcinod versus Naproxen	Low	Moderate	Low
Lohmander (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod versus Placebo	Low	Moderate	Low

Lohmander (2005)	Patient Global Assessment of Response to Treatment	6	Naproxen versus Placebo	Low	Moderate	Low
Lohmander (2005)	Adverse events	6	Naproxcinod 750mg versus Piroxicam	Moderate	Moderate	Moderate
Lohmander (2005)	Adverse events	6	Naproxcinod 750mg versus Placebo	Moderate	Moderate	Moderate
Lohmander (2005)	Adverse events	6	Naproxen 500mg versus Placebo	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	4	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	8	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	16	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	20	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	24	Diacerein versus Piroxicam	Moderate	Moderate	Moderate

Louthrenoo (2007)	WOMAC Pain	4	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Pain	8	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Pain	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Pain	16	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Pain	20	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Pain	24	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	4	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	8	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	16	Diacerein versus Piroxicam	Moderate	Moderate	Moderate

Louthrenoo (2007)	Paracetamol intake pills per day	20	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	24	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	SF-36 sum score	16	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	SF-36 sum score	24	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Stiffness	4	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Stiffness	8	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Stiffness	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Stiffness	16	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Stiffness	20	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Stiffness	24	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo	WOMAC Total	4	Diacerein versus	Moderate	Moderate	Moderate

(2007)			Piroxicam			
Louthrenoo (2007)	WOMAC Total	8	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Total	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Total	16	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Total	20	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Total	24	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Upper respiratory infection	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Dyspepsia	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Diarrhea	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Abdominal pain	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Bowel motility disorders	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo	Constipation	12	Diacerein versus	Moderate	Moderate	Moderate

(2007)			Piroxicam			
Louthrenoo (2007)	Nausea	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Hypertension	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Myalgia	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Arthropathy	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Oedema	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	Dizziness	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	4	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	8	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Louthrenoo (2007)	WOMAC Function	12	Diacerein versus Piroxicam	Moderate	Moderate	Moderate
Luyten (2007)	WOMAC	24	Continuous Celecoxib versus Intermittent Celecoxib	Moderate	Moderate	Moderate

Luyten (2007)	WOMAC Stiffness	24	Continuous Celecoxib versus Intermittent Celecoxib	Moderate	Moderate	Moderate
Luyten (2007)	WOMAC Total	24	Continuous Celecoxib versus Intermittent Celecoxib	Moderate	Moderate	Moderate
Luyten (2007)	WOMAC Pain	24	Continuous Celecoxib versus Intermittent Celecoxib	Moderate	Moderate	Moderate
Luyten (2007)	WOMAC Stiffness	24	Continuous Celecoxib versus Intermittent Celecoxib	Moderate	Moderate	Moderate
Luyten (2007)	WOMAC Total	24	Continuous Celecoxib versus Intermittent Celecoxib	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne functional index	4	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne functional index	8	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate

Lücker (1994)	Lequesne Functional index	12	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
Lücker (1994)	VAS Pain	4	Nimesulide 100mg versus Etodolac	Moderate	Moderate	Moderate
Lücker (1994)	VAS Pain	8	Nimesulide 100mg versus Etodolac	Moderate	Moderate	Moderate
Lücker (1994)	VAS Pain	12	Nimesulide 100mg versus Etodolac	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne index	4	Nimesulide 100mg versus Etodolac	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne index	8	Nimesulide 100mg versus Etodolac	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne index	12	Nimesulide 100mg versus Etodolac	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne functional index	4	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
Lücker (1994)	Lequesne	8	Nimesulide 100mg versus	Moderate	Moderate	Moderate

Functional index			Etodolac 300mg			
Lücker (1994)	Lequesne Functional index	12	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
Lücker (1994)	VAS Pain (10cm)	4	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
Lücker (1994)	VAS Pain (10cm)	8	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
Lücker (1994)	VAS Pain (10cm)	12	Nimesulide 100mg versus Etodolac 300mg	Moderate	Moderate	Moderate
McKenna (2001)	Alt increased	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Anaemia	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Back pain	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Constipation	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate

McKenna (2001)	Diarrhea	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Dizziness	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Dyspepsia	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Flatulence	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Headache	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Accidental injury	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Myalgia	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Nausea	6	Celecoxib 100mg versus Diclofenac 50mg	Moderate	Moderate	Moderate
McKenna (2001)	Peripheral	6	Celecoxib 100mg versus Diclofenac	Moderate	Moderate	Moderate

	Oedema		50mg			
McKenna (2001)	Nausea	6	Rofecoxib 25mg versus Naproxcinod 125mg	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Function	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	VAS Pain improvement	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Pain	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Stiffness	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Total	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	Patient Global Assessment	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	Patient Global Assessment	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	Patient Global Assessment	6	Celecoxib versus Diclofenac	Moderate	Moderate	Moderate
McKenna (2001)	Physician Global Assessment	6	Celecoxib (Cox- 2) versus Placebo	Moderate	Moderate	Moderate

McKenna (2001)	WOMAC Function improvement	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	VAS Pain	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Pain	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Stiffness	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Total	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	Physician Global Assessment	6	Diclofenac versus Placebo	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Function	6	Celecoxib 100mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Pain	6	Celecoxib 100mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
McKenna (2001)	VAS Pain	6	Celecoxib 100mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
McKenna (2001)	WOMAC Stiffness	6	Celecoxib 100mg versus Diclofenac	Moderate	Moderate	Moderate

100mg						
McKenna (2001)	WOMAC Total	6	Celecoxib 100mg versus Diclofenac 100mg	Moderate	Moderate	Moderate
McKenna (2001)	Physician Global Assessment	6	Celecoxib versus Diclofenac (NSAID)	Moderate	Moderate	Moderate
Micelli (2004)	VAS Pain	6	Acetaminophen versus Placebo	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	4	Eltenac gel 0.3% versus Eltenac gel 0.1%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	5	Eltenac gel 0.3% versus Eltenac gel 0.1%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 0.3% versus Eltenac gel 0.1%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	4	Eltenac gel 1% versus Eltenac gel 0.3%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	4	Eltenac gel 1% versus Eltenac gel 0.1%	Moderate	Moderate	Moderate

Ottillinger (2001)	VAS Pain	5	Eltenac gel 1% versus Eltenac gel 0.3%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	5	Eltenac gel 1% versus Eltenac gel 0.1%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 1% versus Eltenac gel 0.3%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 1% versus Eltenac gel 0.1%	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	4	Eltenac gel 0.1% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	5	Eltenac gel 0.1% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 0.1% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	4	Eltenac gel 0.3% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	5	Eltenac gel 0.3% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 0.3% versus Placebo gel	Moderate	Moderate	Moderate

Ottillinger (2001)	VAS Pain	4	Eltenac gel 1% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	5	Eltenac gel 1% versus Placebo gel	Moderate	Moderate	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 1% versus Placebo gel	Moderate	Moderate	Moderate
Queiros (1990)	Mean pain at night (1 to 4)	4	Piroxicam 20mg versus Oxaprozin 1200mg	Moderate	Moderate	Moderate
Queiros (1990)	Mean pain on walking in the evening (1 to 21)	4	Piroxicam 20mg versus Oxaprozin 1200mg	Moderate	Moderate	Moderate
Queiros (1990)	Mean pain on walking in the morning (1 to 21)	4	Piroxicam 20mg versus Oxaprozin 1200mg	Moderate	Moderate	Moderate
Roth (2004)	WOMAC Function	12	Topical Diclofenac versus vehicle control	High	Moderate	High
Roth (2004)	WOMAC Pain	12	Topical Diclofenac versus vehicle control	High	Moderate	High
Roth (2004)	WOMAC Pain on walking	12	Topical Diclofenac versus vehicle control	High	Moderate	High

Roth (2004)	WOMAC Stiffness	12	Topical Diclofenac versus vehicle control	High	Moderate	High
Roth (2004)	Patient Global Assessment	12	Topical Diclofenac versus Placebo	High	Moderate	High
Rother (2007)	WOMAC Function	6	Topical Ketoprofen versus Celecoxib	Moderate	Moderate	Moderate
Rother (2007)	WOMAC Function	6	Topical Ketoprofen versus Placebo	Moderate	Moderate	Moderate
Rother (2007)	WOMAC Function	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Rother (2007)	WOMAC Pain	6	Topical Ketoprofen versus Celecoxib	Moderate	Moderate	Moderate
Rother (2007)	WOMAC Pain	6	Topical Ketoprofen versus Placebo	Moderate	Moderate	Moderate
Rother (2007)	WOMAC Pain	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Total	12	Naproxen versus Placebo	Moderate	Moderate	Moderate

Schnitzer (1999)	Minimum effective Naproxen dose	8	Tramadol versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Celecoxib 200mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Celecoxib 200mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Rofecoxib 12.5mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Abdominal pain	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	Low	Moderate	Low

Schnitzer (2005)	Abdominal pain	6	Acetaminophen 4000mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Abdominal pain		Acetaminophen 4000mg versus Celecoxib 200mg	Low	Moderate	Low
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Rofecoxib 12.5mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Celecoxib 200mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Celecoxib 200mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Diarrhea	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Diarrhea	6	Acetaminophen 4000mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Diarrhea		Acetaminophen 4000mg versus Celecoxib 200mg	Low	Moderate	Low

Schnitzer (2005)	Headache	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Headache	6	Acetaminophen 4000mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Lower extremity edema	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Lower extremity edema	6	Acetaminophen 4000mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Nausea	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Nausea	6	Acetaminophen 4000mg versus Rofecoxib 25mg	Low	Moderate	Low
Schnitzer (2005)	Upper respiratory infection	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	Low	Moderate	Low
Schnitzer (2005)	Upper respiratory	6	Acetaminophen 4000mg versus	Low	Moderate	Low

infection		Rofecoxib 25mg				
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 125mg versus Naproxcinod 375mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Naproxcinod 750mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 125mg versus Naproxcinod 750mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 375mg versus Naproxcinod 750mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 375mg versus Naproxcinod 750mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment	6	Naproxcinod 125mg versus	Moderate	Moderate	Moderate

	Response		Naproxen 500mg			
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 375mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 375mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 750mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 750mg versus Naproxen 500mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod 125mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Placebo	Moderate	Moderate	Moderate

Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod 375mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 375mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod 750mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 750mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxen 500mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxen 500mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease responders	6	Rofecoxib 25mg versus Naproxcinod 125mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Global Assessment of	6	Rofecoxib 25mg versus	Moderate	Moderate	Moderate

	Disease responders		Naproxcinod 375mg			
Schnitzer (2005)	Patient Global Assessment of Disease responders	6	Rofecoxib 25mg versus Naproxcinod 750mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response (Good or Excellent)	6	Rofecoxib 25mg versus Naproxcinod 125mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response (Good or Excellent)	6	Rofecoxib 25mg versus Naproxcinod 375mg	Moderate	Moderate	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response (Good or Excellent)	6	Rofecoxib 25mg versus Naproxcinod 750mg	Moderate	Moderate	Moderate
Schnitzer (2009)	Patient Assessment of Treatment Response	4	Rofecoxib 12.5mg versus Rofecoxib 25mg	Moderate	Moderate	Moderate
Schnitzer (2009)	Physician Assessment of Treatment	4	Rofecoxib 12.5mg versus	Moderate	Moderate	Moderate

Response			Rofecoxib 25mg			
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Function	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Pain	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate

Schnitzer (2010)	WOMAC Pain	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Total	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Total	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Function	13	Naproxcinod versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod 375mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod 750mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain during walking	13	Naproxcinod 375mg versus	Moderate	Moderate	Moderate

	improvement		Placebo			
Schnitzer (2010)	VAS Pain during walking	13	Naprociod 750mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Pain	13	Naproxcinod 375mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Pain	13	Naprociod 750mg versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2009)	WOMAC Function	4	Rofecoxib 12.5mg versus Rofecoxib	Moderate	Moderate	Moderate
Schnitzer (2009)	WOMAC Pain	4	Rofecoxib 12.5mg versus Rofecoxib	Moderate	Moderate	Moderate
Schnitzer (2009)	WOMAC Stiffness	4	Rofecoxib 12.5mg versus Rofecoxib	Moderate	Moderate	Moderate
Schnitzer (2010)	Rescue Acetaminophen	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	SF-36 MCS improvement	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Function	12	Naproxen versus	Moderate	Moderate	Moderate

	improvement		Placebo			
Schnitzer (2010)	VAS Pain	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Schnitzer (2010)	WOMAC Pain	12	Naproxen versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Physician Global Assessment of Disease	13	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Physician Global Assessment of Disease	13	Lumiracoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Physician Global Assessment of Disease	13	Lumiracoxib 400mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Function	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Function	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Function	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate

Tannenbaum (2004)	VAS Pain improvement	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	VAS Pain improvement	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	VAS Pain improvement	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Pain	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Pain	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Pain	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Stiffness	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Total	13	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	WOMAC Total	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate

Tannenbaum (2004)	WOMAC Total	13	Lumiracoxib versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Patient Global Assessment of Disease	13	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Patient Global Assessment of Disease	13	Lumiracoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Patient Global Assessment of Disease	13	Lumiracoxib 400mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Adverse events	13	Celecoxib 100mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Adverse events	13	Lumiracoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Tannenbaum (2004)	Adverse events	13	Lumiracoxib 400mg versus Placebo	Moderate	Moderate	Moderate
Torri (1994)	WOMAC averaged VAS Pain	12	Aceclofenac versus Piroxicam	Moderate	Moderate	Moderate
Tyson (1980)	Linear analogue pain scale	8	Benoxaprofen versus Ibuprofen	Moderate	Moderate	Moderate

Tyson (1980)	Linear analogue pain scale	12	Benoxaprofen versus Ibuprofen	Moderate	Moderate	Moderate
Tyson (1980)	Linear analogue pain scale	16	Benoxaprofen versus Ibuprofen	Moderate	Moderate	Moderate
Williams (2000)	WOMAC Function	6	Celecoxib 200mg QD versus Placebo	Moderate	Moderate	Moderate
Williams (2000)	Lequesne Index	6	Celecoxib 100mg BID versus Placebo	Moderate	Moderate	Moderate
Williams (2000)	Lequesne Index	6	Celecoxib 200mg QD versus Placebo	Moderate	Moderate	Moderate
Williams (2000)	Lequesne Index	6	Celecoxib 200mg versus Celecoxib 100mg bid	Moderate	Moderate	Moderate
Williams (2000)	WOMAC Total	6	Celecoxib 200mg versus Celecoxib	Moderate	Moderate	Moderate
Williams (2000)	Patient Global Assessment	6	Celecoxib 200mg versus Celecoxib 100mg	Moderate	Moderate	Moderate
Williams (2000)	Lequesne Index	6	Celecoxib 100mg BID versus Placebo	Moderate	Moderate	Moderate

Williams (2000)	Lequesne Index	6	Celecoxib 200mg QD versus Placebo	Moderate	Moderate	Moderate
Williams (2000)	Lequesne Index	6	Celecoxib 200mg versus Celecoxib 100mg bid	Moderate	Moderate	Moderate
Williams (2000)	Patient Global Assessment	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Williams (2000)	Patient Global Assessment	6	Celecoxib 100mg versus Placebo	Moderate	Moderate	Moderate
Williams (2000)	Patient Global Assessment	6	Celecoxib 100 versus Celecoxib 200mg	Moderate	Moderate	Moderate
Williams (2001)	Patient Global Assessment	6	Celecoxib 100mg versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Patient Global Assessment	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Lequesne Index	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Lequesne Index	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Lequesne Index	6	Celecoxib 100mg BID versus Celecoxib 200mg	Low	Moderate	Low

			qd			
Williams (2001)	Adverse events	6	Celecoxib 100mg versus Celecoxib 200mg	Moderate	Moderate	Moderate
Williams (2001)	Adverse events	6	Celecoxib 100mg versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Adverse events	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Zheng (2006)	VAS Pain on walking improvement	12	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	VAS Pain on walking		Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	WOMAC Total VAS improvement	12	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	WOMAC Total		Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	Pain on walking	4	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	Pain on walking	8	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	Pain on walking	12	Diacerein versus	Moderate	Moderate	Moderate

Diclofenac						
Zheng (2006)	Pain on walking	16	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	WOMAC Total	4	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	WOMAC Total	8	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	WOMAC Total	12	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	WOMAC Total	16	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	Adverse events	16	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Zheng (2006)	GI adverse events	16	Diacerein versus Diclofenac	Moderate	Moderate	Moderate
Bradely (1993)	HAQ Disability improvement	4	Ibuprofen 300mg versus Ibuprofen 600mg	Moderate	Moderate	Moderate
Bradely (1993)	Health Assessment Questionnaire improvement	4	Ibuprofen 300mg versus Ibuprofen 600	Moderate	Moderate	Moderate
Bradely (1993)	Walk time (sec)	4	Ibuprofen 300mg versus Ibuprofen	Moderate	Moderate	Moderate

	improvement		600mg			
Burch (2007)	Improvement in pain intensity numerical rating scale	12	Tramadol Contramid OAD versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Physician Global Assessment of Disease	6	Rofecoxib 125mg versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Physician Global Assessment of Disease	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Physician Global Assessment of Response to Treatment	6	Rofecoxib 125mg versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Physician Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	WOMAC Function	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	WOMAC Pain	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	VAS Pain improvement	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate

Ehrich (1999)	VAS Pain improvement	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	WOMAC Stiffness	6	Rofecoxib versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Patient Global Assessment of Disease	6	Rofecoxib 125mg versus Placebo	Moderate	Moderate	Moderate
Ehrich (1999)	Patient Global Assessment of Disease	6	Rofecoxib 25mg versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Function	8	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Function	16	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Function	20	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Function	24	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Pain	8	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Pain	12	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Pain	16	Diacerein versus	Moderate	Moderate	Moderate

Placebo						
Pavelka (2007)	WOMAC Pain	20	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Pain	24	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Stiffness	4	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Stiffness	8	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Stiffness	16	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Stiffness	20	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Stiffness	24	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	Paracetamol intake pills per day	4	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	Paracetamol intake pills per day	8	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	Paracetamol intake pills per	12	Diacerein versus Placebo	Moderate	Moderate	Moderate

	day					
Pavelka (2007)	Paracetamol intake pills per day	16	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	Paracetamol intake pills per day	20	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	Paracetamol intake pills per day	24	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Total	4	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Total	8	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Total	16	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Total	20	Diacerein versus Placebo	Moderate	Moderate	Moderate
Pavelka (2007)	WOMAC Total	24	Diacerein versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Lequesne Index	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Lequesne Index	6	Celecoxib versus	Moderate	Moderate	Moderate

Placebo						
Williams (2001)	WOMAC Total	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	WOMAC Total	6	Celecoxib versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Lequesne Index	6	Celecoxib 100mg BID versus Celecoxib 200mg qd	Moderate	Moderate	Moderate
Williams (2001)	WOMAC Total	6	Celecoxib 100mg BID versus Celecoxib 200mg qd	Moderate	Moderate	Moderate
Williams (2001)	Physician Global Assessment	6	Celecoxib 100mg versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	Physician Global Assessment	6	Celecoxib 200mg versus Placebo	Moderate	Moderate	Moderate
Williams (2001)	physician Global Assessment	6	Celecoxib 100mg versus Celecoxib 200mg	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Table 145](#), [Table 155-Table165](#), [Figure 47-Figure 80](#)

There were 126 outcomes in which Cox-2 inhibitors were compared to placebo. Cox-2 inhibitors were significantly superior to placebo in 114 outcomes. Of these significant outcomes, 43 were at least possibly clinically important, 38 were of unknown clinical importance, and 33 were not clinically significant.

The critical outcomes were function and stiffness. Nine of 10 functional outcomes were improved in patients who received Cox-2's. One functional outcome was clinically important and eight were possibly clinically important. Nine of 15 stiffness-related outcomes were at least possibly clinically important in favor of Cox-2's. An additional two outcomes were statistically significant but not clinically important.

There was little difference in the efficacies of Cox-2 inhibitors. Out of 88 total outcomes, 24 were statistically significant. However, 23 out of 24 significant outcomes were between high versus lower doses of the same Cox-2's. Only one of 21 critical outcomes was statistically significant in favor of one Cox-2 over another (WOMAC stiffness; Celecoxib over Rofecoxib).

NSAIDs were compared to placebo based on 35 outcomes, of which 31 were statistically significant in favor of the treatment. Seventeen of these outcomes were at least possibly clinically important, and nine were of unknown clinical importance. An additional nine outcomes were statistically significant in favor of NSAIDs but not clinically important.

Pain, function and stiffness were the critical outcomes included in the studies that compared NSAIDs to placebo. All 17 pain outcomes were statistically significant, eight of which were at least possibly clinically important. All three stiffness outcomes were possibly clinically significant in favor of NSAIDs. Three of seven functional outcomes were statistically significant indicating improvement in the treatment group.

There was little difference in the efficacies between various NSAIDs. Thirteen of 91 outcomes were statistically significant endorsing one NSAID over another ([table 158](#))

Thirty-two outcomes compared topical NSAIDs to a placebo/vehicle control solution. Eighteen of 32 were statistically significant indicating improvement in the treatment group. The critical outcomes were pain, function and stiffness. Twelve of 21 pain outcomes were lessened significantly in the treatment group. Three of four stiffness-related outcomes and the single functional outcome significantly favored topical NSAIDs over placebo.

Two studies compared topical NSAIDs to active treatments. Otillinger et al.¹⁰⁰ found no significant differences in VAS pain scores at 4, 5 and 6 weeks between eltenac .1%, .3% and 1% gels. Rother et al.¹⁰¹ found insignificant differences in pain and function between Celecoxib and topical Ketoprofen.

NSAIDs and Cox-2 inhibitors appeared to be of similar efficacy. Three of 44 outcomes favored Cox-2s over NSAIDs, and only one outcome favored NSAIDs. Pain, stiffness and function were the included critical outcomes. None were statistically significant between the two drug classifications.

Diacerein (interleukin) was compared to placebo based on 25 outcomes. Sixteen outcomes were significantly superior in the treatment group; 13 were possibly clinically important and three were of unknown clinical importance. Ten of 14 critical outcomes (pain, stiffness, and function) were significantly improved in patients who received Diacerein compared to those who received placebo.

Forty-four outcomes compared interleukins to NSAIDs. The evidence was mixed on whether one treatment was superior to the other. Twenty-seven outcomes were not statistically significant, 12 endorsed interleukins and five favored NSAIDs.

Five studies evaluating 14 outcomes compared Tramadol to placebo. Ten were significantly improved in the treatment group. Five of seven pain outcomes showed Tramadol to be superior over placebo. One of two functional outcomes and one of two stiffness outcomes were statistically significant indicating benefit of Tramadol over placebo.

Fishman et al.⁹⁵ compared WOMAC pain scores for 100mg, 200mg and 300mg doses of Tramadol. There were no significant differences by dose.

One study found that VAS pain scores were not significantly different between acetaminophen and placebo.⁹⁷ Acetaminophen was compared to NSAIDs based on ten outcomes and Cox-2s based on six. Four outcomes significantly favored NSAIDs over acetaminophen but one was not clinically important. Four of six outcomes were superior in patients who received Cox-2s, and two outcomes were significantly better in the acetaminophen group.

Network Meta Analysis

Network meta-analyses were conducted for the following outcomes: pain, WOMAC function, WOMAC stiffness, WOMAC total, and adverse events. [Figures 42](#) through [46](#) illustrate conceptual path models of each network meta-analysis that examine direct and indirect treatment comparisons.

[Figures 47](#) through [80](#) are forest plots summarizing the results of all network meta-analyses separated according to drug comparison and outcome (pain, function, stiffness, WOMAC total, and adverse events). For example, there is a separate plot for the results of Cox-2s versus NSAIDs, Cox-2s versus Cox-2s, NSAIDs versus NSAIDs. Other plots contain comparisons of Cox-2s and NSAIDs to interleukins and Tramadol.

Consistency checks for all network meta-analyses can be found in Appendix XIII. All pairwise effects were statistically compared to indirect treatment effects using the back calculation method described by Dias et al. No indirect effects of any outcome were found to be significantly different than the direct effects in the pairwise meta-analyses.

All Cox-2 inhibitors were significantly more effective than placebo for pain. The NSAIDs Aceclofenac, Diclofenac, Naproxen, Naproxcinod, topical Diclofenac and topical Ketoprofen showed statistically significant benefit for pain. Topical Etenac, Aceclofenac, Tenidap and Tenoxicam produced lower pain scores than placebo treatment, but they did not reach statistical significance. Patients who received the opioid Tramadol had significantly lower pain scores than those in the placebo group. Diacerein (an interleukin) did not have a statistically significant benefit on pain compared to placebo assignment.

All active treatments showed similar efficacy in terms of pain relief. As can be seen in [Figures 48](#) through [52](#), there were only two significant treatment comparisons for pain. Patients treated with Rofecoxib reported significantly lower pain scores than Celecoxib and Tenoxicam patients.

Tramadol, Cox-2 inhibitors, and most all NSAIDs produced possibly clinically important improvements in WOMAC function scores relative to placebo. Two of six NSAIDs, Piroxicam and Tenidap, were associated with better function scores than scores based on placebo, but the differences were not statistically significant. Diacerein were not associated with significantly different function scores than placebo.

The active treatments showed similar efficacy for improving WOMAC function scores (see [Figures 54](#) to [58](#)). There were four significant active treatment comparisons. Naproxen produced WOMAC function scores that were significantly higher than all associated with Cox-2 inhibitors and topical Ketoprofen. The differences were possibly clinically important.

Analgesics were less successful in treating stiffness related to knee osteoarthritis than they were for improving pain and function. NSAIDs, interleukins and Tramadol did not produce significantly lower WOMAC stiffness scores than placebo. Two of four Cox-2 inhibitors, Celecoxib and Rofecoxib, had possibly clinically important improvements in stiffness compared to placebo. When each active treatment was compared to one another in the network meta-analysis, there were not any significant differences found in WOMAC stiffness scores.

All WOMAC total scores for Cox-2 inhibitors, NSAIDs, opioids and interleukins were significantly better than all placebo scores. Each drug treatment effect was possibly clinically important since their confidence intervals contained the MCII. There were no statistically significant differences in overall WOMAC scores for any of the active treatments.

Adverse Events

The odds of experiencing adverse events were similar between treatment arms in the network meta-analysis. Pairwise analyses were used to compare specific types of adverse events between analgesics. While the overall occurrence of Gastrointestinal Events are not significantly lower for Cox-2's than for NSAIDs, patients who received Cox-2 inhibitors were significantly less likely to experience abdominal pain, constipation or

dyspepsia ([see figure 75](#)). For non gastrointestinal events, there were no significant differences between Cox-2's and NSAIDs ([figure 76](#)).

Patients who received Acetaminophen did not have significantly different odds of experiencing any specific adverse event than patients who received Celecoxib ([figure 77](#)). Rofecoxib 12.5mg had lesser odds of causing abdominal pain and headaches ([figure 78](#)). Compared to Acetaminophen, those who received Rofecoxib 25mg had significantly lesser odds of experiencing diarrhea and abdominal pain, but greater odds of Lower Extremity Edema ([figure 79](#)).

[Figure 80](#) presents a comparison of the likelihood of specific adverse events between Acetaminophen (4000mg) and Ibuprofen (1200 and 4000mg). There were no statistically significant differences between the treatments.

Figure 42. Network Meta-Analysis Model: Pain

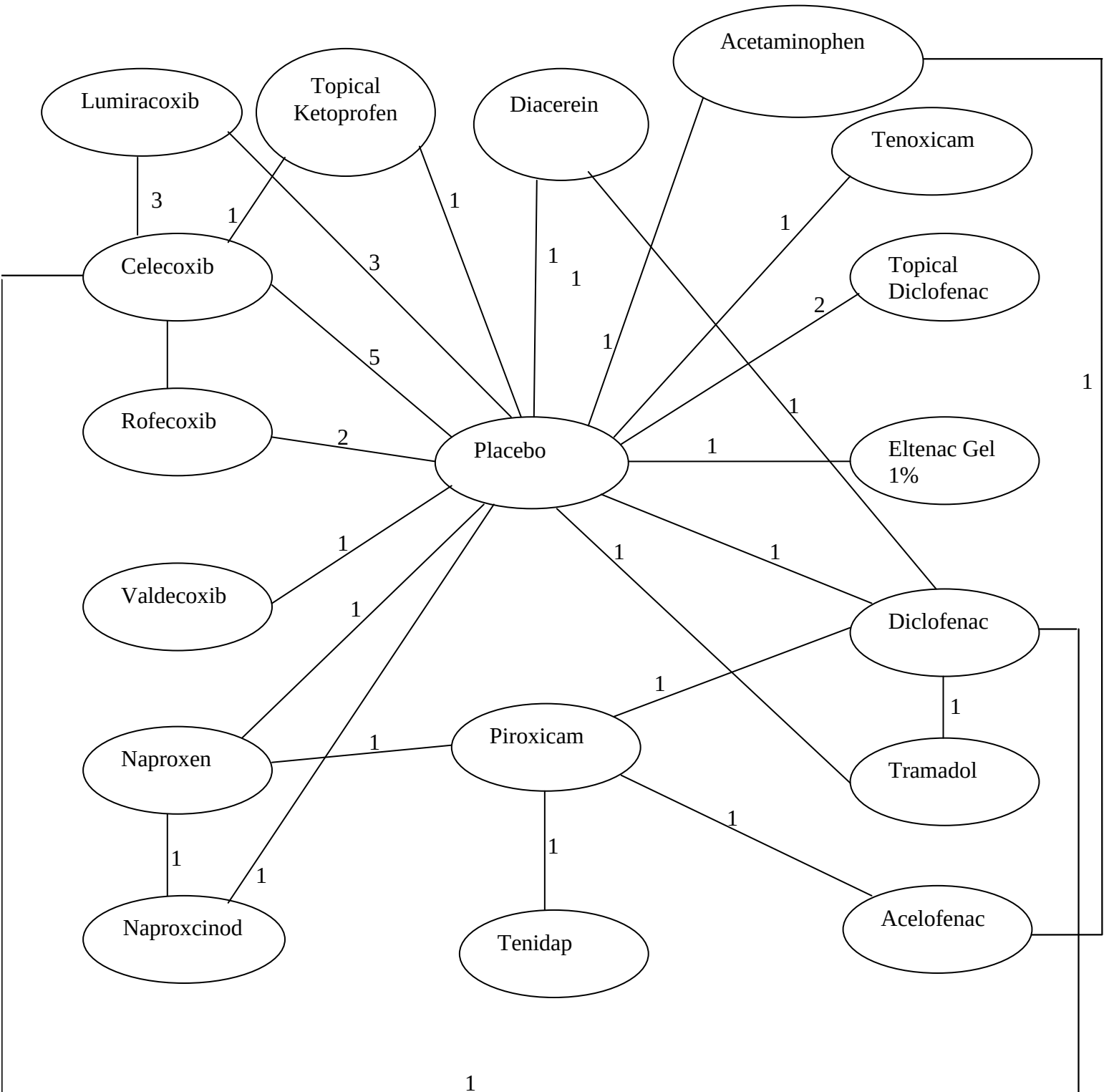


Figure 43. Network Meta-Analysis Model: WOMAC Function

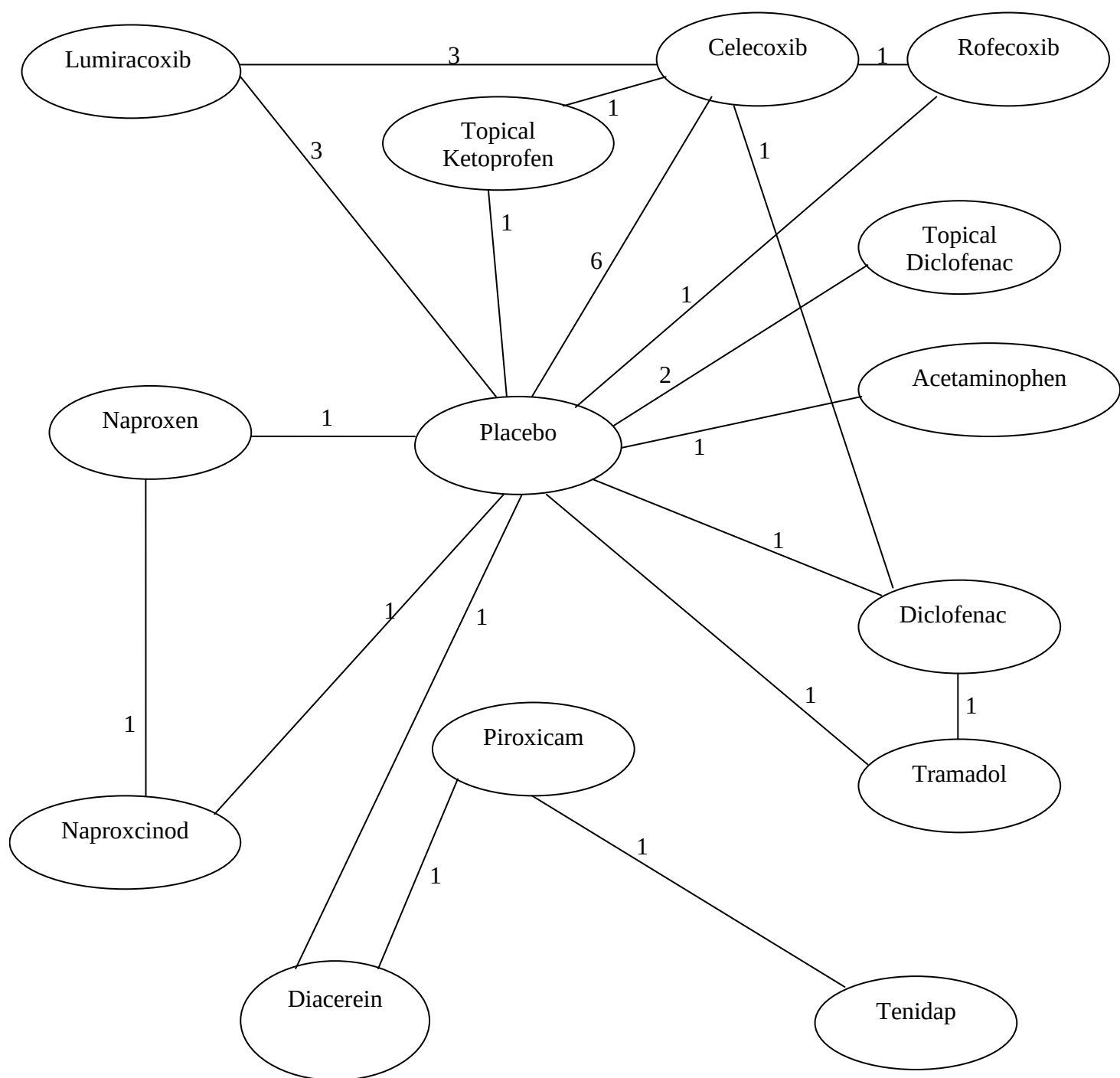


Figure 44. Network Meta-Analysis Model: WOMAC Stiffness

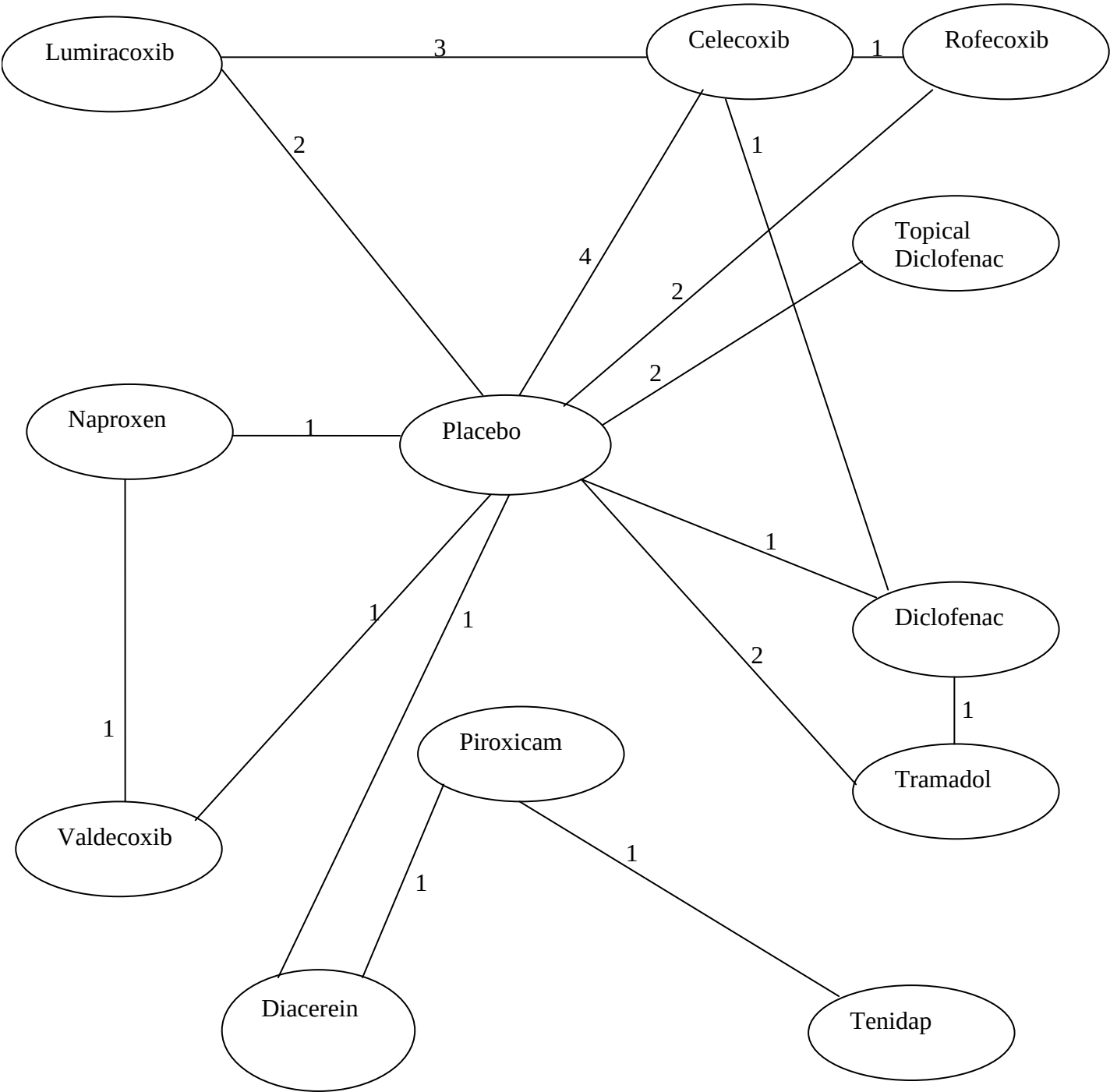
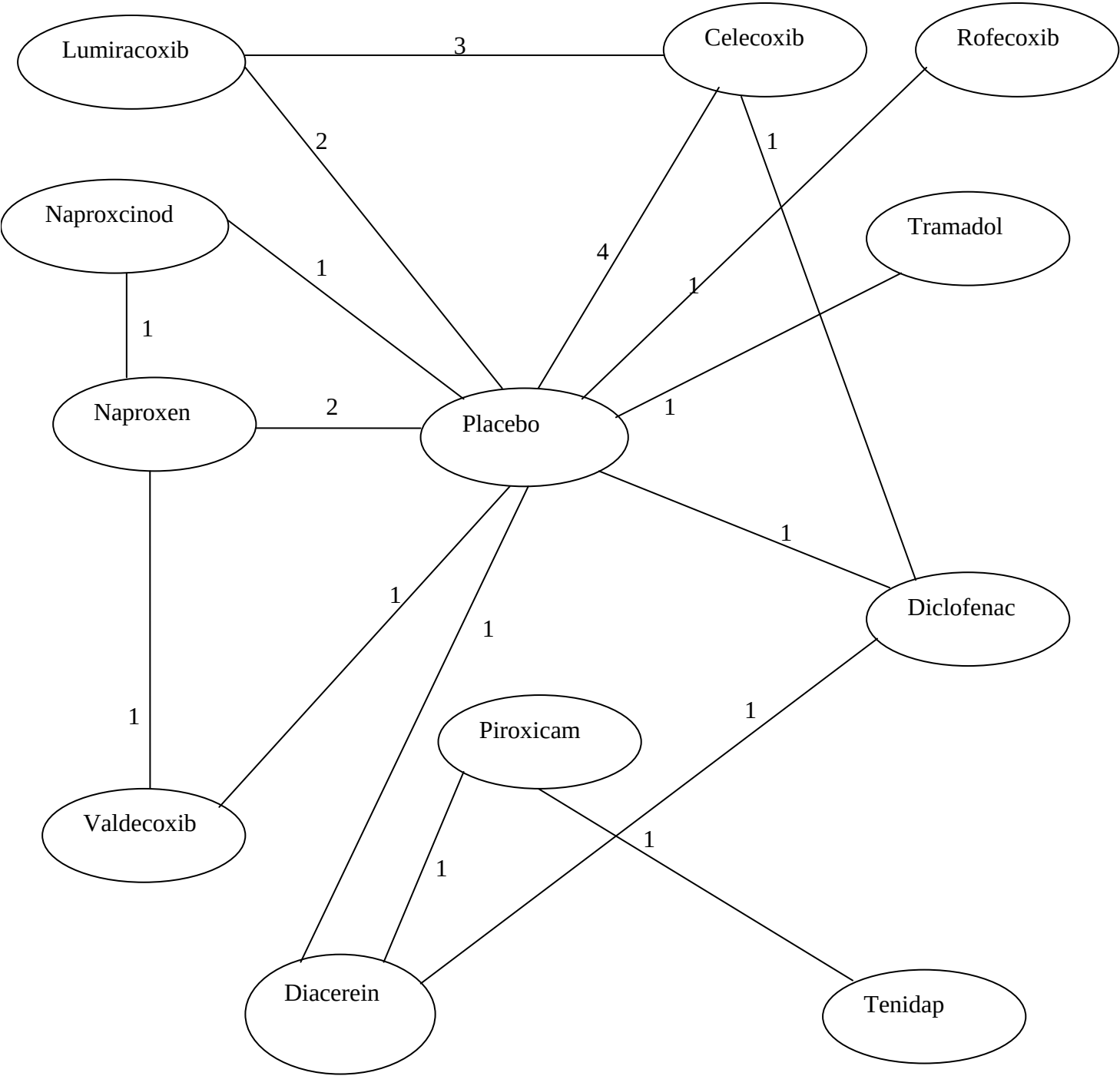


Figure 45. Network Meta-Analysis Model: WOMAC Total



Events Figure 46. Network Meta-Analysis Model: Adverse Events

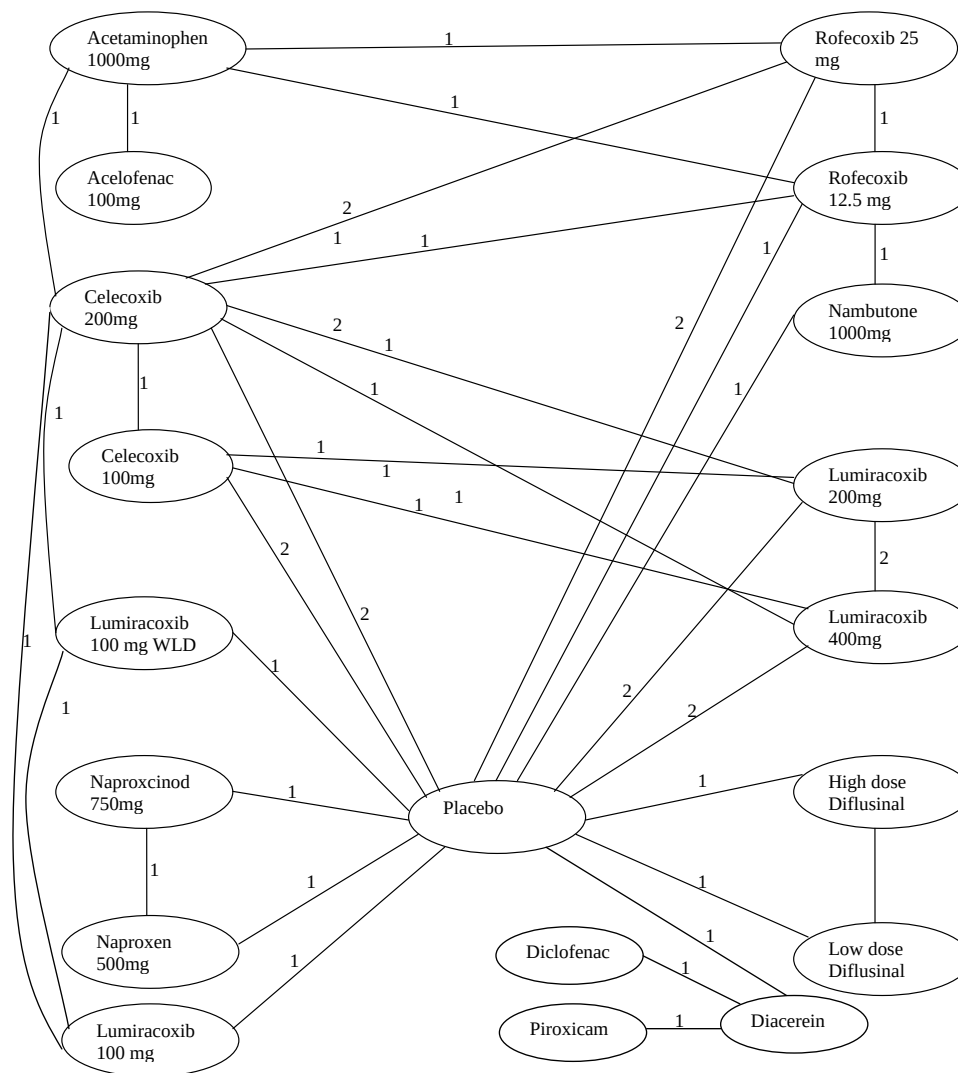


Table 145. Network Meta-Analysis: Statistically Significant Treatment Comparisons

Comparison	Outcome
Rofecoxib over Tenoxicam	Pain
Rofecoxib over Celecoxib	Pain
Naproxen over Lumiracoxib	Function
Naproxen over Celecoxib	Function
Naproxen over Rofecoxib	Function
Naproxen over Topical Ketoprofen	Function

Table 146. Results Summary: Drug Treatments Versus Placebo (Patient and Physician Assessments)

Study	Patient Global Assessment *	Physician Global Assessment	Patient Global Assessment of Disease Status	Physician Global Assessment of Disease Status	Patient Global Assessment of Treatment Response	Physician Global Assessment of Treatment Response
Celecoxib	○ ○ ○ ● ● ●	● ● ● ● ● ● ○	● ●	● ●		
Lumiracoxib	○ ○	● ●	● ● ●	● ● ●		
Rofecoxib	●	○	● ● ●	● ●	● ● ●	● ●
Valdecoxib		● ● ● ● ● ○				
Diclofenac Topical	○	●				
Diclofenac	○					
Naproxen		● ●	● ●		● ●	
Orgotein					● ●	
Naproxcinod			● ● ○		● ● ○	
○ Statistically, but not clinically significant (only Patient Global Assessment has an MCII) ● Statistically Significant, but outcome has no MCII ● Possibly clinically significant ● Clinically Significant						

Table 147. Statistically Significant Active Treatment Comparisons: Global Assessments

Outcome	Favors	Comparison
Patient Global Assessment	Aceclofenac	Paracetamol (Not Clinically Significant)
Patient Global Assessment	Celecoxib 200mg	Celecoxib 100mg (Clinically Significant)
Patient Global Assessment	Lumiracoxib200mg	Lumiracoxib 400mg(Clinically Significant)
Physician Global Assessment	Aceclofenac	Paracetamol
Physician Global Assessment	Diclofenac (NSAID)	Celecoxib (Cox-2)
Physician Global Assessment	Celecoxib 200mg	Celecoxib 100mg
Patient Global Assessment Of Disease	Etoricoxib 60mg Or 90mg	Etoricoxib 30mg Or Less
Physician Assessment Of Treatment Response	Etoricoxib 60mg Or 90mg	Etoricoxib 30mg Or Less
Patient Assessment Of Treatment Response	Rofecoxib	Acetaminophen
Physician Assessment Of Treatment Response	Rofecoxib	Acetaminophen

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY
Table 148. Quality and Applicability: Cox-2

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Ehrich (1999)	Physician Global Assessment of Disease	6	Rofecoxib 125mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	Physician Global Assessment of Disease	6	Rofecoxib 25mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	Physician Global Assessment of Response to Treatment	6	Rofecoxib 125mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Ehrich (1999)	Physician Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	WOMAC Function	6	Rofecoxib versus Placebo	●	○	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	WOMAC Pain	6	Rofecoxib versus Placebo	●	○	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	VAS Pain improvement	6	Rofecoxib versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	VAS Pain improvement	6	Rofecoxib versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Ehrich (1999)	WOMAC Stiffness	6	Rofecoxib versus Placebo	●	○	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 125mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	Patient Global Assessment of Disease	6	Rofecoxib 125mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	Patient Global Assessment of Disease	6	Rofecoxib 25mg versus Placebo	●	●	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 400mg versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 200mg versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	VAS Pain improvement	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	VAS Pain improvement	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Pain	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2006)	WOMAC Pain	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 200mg versus Celecoxib 200mg	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 400mg versus Celecoxib 200mg	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	Patient Global Assessment	13	Lumiracoxib 200mg versus Lumiracoxib 400mg	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2006)	Physician Global Assessment	13	Celecoxib (Cox-2) versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 200mg versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 400mg versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Function	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Function	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2006)	VAS Pain improvement	13	Celecoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Pain	13	Celecoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Total	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Fleischmann (2006)	WOMAC Total	13	Lumiracoxib versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 200mg versus Celecoxib 200mg	●	●	○	●	○	○	●	○	Low	○ ○ ● ●		Moderate
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 400mg versus Celecoxib 200mg	●	●	○	●	○	○	●	○	Low	○ ○ ● ●		Moderate
Fleischmann (2006)	Physician Global Assessment	13	Lumiracoxib 200mg versus Lumiracoxib 400mg	●	●	○	●	○	○	●	○	Low	○ ○ ● ●		Moderate
Gibofsky (2003)	WOMAC Function	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ○		Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gibofsky (2003)	WOMAC Function	6	Rofecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	VAS Pain on walking improvement	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	VAS Pain on walking improvement	6	Rofecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	WOMAC Pain	6	Rofecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	WOMAC Pain	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	WOMAC Stiffness	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gibofsky (2003)	WOMAC Stiffness	6	Rofecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	WOMAC Function improvement	6	Celecoxib 200mg versus Rofecoxib	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	VAS Pain on walking improvement	6	Celecoxib 200mg versus Rofecoxib	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	WOMAC Pain improvement	6	Celecoxib 200mg versus Rofecoxib	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gibofsky (2003)	WOMAC Stiffness improvement	6	Celecoxib 200mg versus Rofecoxib	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Patient Global Assessment	6	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Patient Global Assessment	6	Rofecoxib 25mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Physician Global Assessment	6	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Physician Global Assessment	6	Rofecoxib 25mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gibofsky (2003)	Patient Global Assessment of Response to Treatment	6	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Patient Global Assessment	6	Celecoxib 200mg versus Rofecoxib 25mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Physician Global Assessment	6	Celecoxib 200mg versus Rofecoxib 25mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 60mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 10mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 10mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 10mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 10mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 30mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 30mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Global Assessment of Disease	6	Etoricoxib 60mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 10mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence Analysis	Applicability Study
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○ ○ ● ●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 10mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○ ○ ● ●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○ ○ ● ●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 10mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○ ○ ● ●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 30mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 5mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 10mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Global Assessment of Disease	6	Etoricoxib 30mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Physician Global Assessment of Disease Patient	6	Etoricoxib 60mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Assessment of Treatment Response Patient	6	Etoricoxib 5mg versus Etoricoxib 10mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Assessment of Treatment Response Patient	6	Etoricoxib 5mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Assessment of Treatment Response Patient	6	Etoricoxib 5mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 60mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Patient Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 10mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 30mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 60mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 5mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 10mg versus Etoricoxib 90mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 30mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gottesdiener (2002)	Physician Assessment of Treatment Response	6	Etoricoxib 60mg versus Etoricoxib 90mg	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Kivits (2002)	VAS Pain improvement	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	VAS Pain improvement	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	VAS Pain improvement	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	VAS Pain improvement	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	VAS Pain improvement	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	VAS Pain improvement	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	WOMAC Total	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 10mg (Cox-2) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 10mg (Cox-2) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 20mg (Cox-2) versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 20mg (Cox-2) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 5mg (Cox-2) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 5mg (Cox-2) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivitz (2004)	Patient Global Assessment of Response to Treatment	6	Rofecoxib versus Placebo	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	Physician Global Assessment of Disease	13	Celecoxib 200mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	Physician Global Assessment of Disease	13	Lumiracoxib 100mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib (Cox-2) with loading dose versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Pain	13	Lumiracoxib (Cox-2) with loading dose versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	VAS Pain improvement	13	Celecoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Pain	13	Celecoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Pain	13	Lumiracoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	WOMAC Function improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Function improvement	13	Lumiracoxib 100mg versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Function improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	VAS Pain improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Pain improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib 100mg versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	VAS Pain improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Pain improvement	13	Lumiracoxib 100mg versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Pain improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	WOMAC Stiffness improvement	13	Celecoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Stiffness improvement	13	Lumiracoxib 100mg versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Stiffness improvement	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	WOMAC Total	13	Celecoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib 100mg versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	WOMAC Total	13	Lumiracoxib 100mg versus Lumiracoxib with loading dose	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lehmann (2005)	Physician Global Assessment of Disease	13	Lumiracoxib 100mg versus Celecoxib 200mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	Patient Global Assessment of Disease	13	Celecoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	Patient Global Assessment of Disease	13	Lumiracoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lehmann (2005)	Patient Global Assessment of Disease	13	Lumiracoxib versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence Analysis	Applicability Study
Luyten (2007)	WOMAC	24	Continuous Celecoxib versus Intermittent Celecoxib	●	◐	○	●	●	○	●	○	Moderate	○ ○ ● ●	Moderate
Luyten (2007)	WOMAC Stiffness	24	Continuous Celecoxib versus Intermittent Celecoxib	●	◐	○	●	●	○	●	○	Moderate	○ ○ ● ●	Moderate
Luyten (2007)	WOMAC Total	24	Continuous Celecoxib versus Intermittent Celecoxib	●	◐	○	●	●	○	●	○	Moderate	○ ○ ● ●	Moderate
Mckenna (2001)	WOMAC Function	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Mckenna (2001)	VAS Pain improvement	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	WOMAC Pain	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	WOMAC Stiffness	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	WOMAC Total	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	Patient Global Assessment	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Mckenna (2001)	Physician Global Assessment	6	Celecoxib (Cox-2) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease	6	Rofecoxib 25mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Rofecoxib 25mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Celecoxib 200mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Celecoxib 200mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Rofecoxib 12.5mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2009)	Patient Assessment of Treatment Response	4	Rofecoxib 12.5mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2009)	Physician Assessment of Treatment Response	4	Rofecoxib 12.5mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2010)	WOMAC Function	13	Naproxcinod versus Placebo	●	○	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2010)	WOMAC Pain	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	WOMAC Pain	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	WOMAC Total	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2010)	WOMAC Total	13	Naproxcinod versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2009)	WOMAC Function	4	Rofecoxib 12.5mg versus Rofecoxib	●	○	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2009)	WOMAC Pain	4	Rofecoxib 12.5mg versus	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2009)	WOMAC Stiffness	4	Rofecoxib 12.5mg versus	●	○	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	Physician Global Assessment of Disease	13	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	Physician Global Assessment of Disease	13	Lumiracoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Tannenbaum (2004)	Physician Global Assessment of Disease	13	Lumiracoxib 400mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Function	13	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Function	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Function	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	VAS Pain improvement	13	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Tannenbaum (2004)	VAS Pain improvement	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	VAS Pain improvement	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Pain	13	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Pain	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Pain	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Stiffness	13	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Tannenbaum (2004)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Stiffness	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Total	13	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Total	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	WOMAC Total	13	Lumiracoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Tannenbaum (2004)	Patient Global Assessment of Disease	13	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	Patient Global Assessment of Disease	13	Lumiracoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Tannenbaum (2004)	Patient Global Assessment of Disease	13	Lumiracoxib 400mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	WOMAC Function	6	Celecoxib 200mg QD versus Placebo	●	○	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2000)	Lequesne index	6	Celecoxib 100mg BID versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Lequesne index	6	Celecoxib 200mg QD versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Lequesne index	6	Celecoxib 200mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	WOMAC Total	6	Celecoxib 100mg bid versus Celecoxib 200mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2000)	Patient Global Assessment	6	Celecoxib 200mg versus Celecoxib 100mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Lequesne index	6	Celecoxib versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Lequesne index	6	Celecoxib versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	WOMAC Total	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	WOMAC Total	6	Celecoxib versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2001)	Lequesne index	6	Celecoxib 100mg BID versus Celecoxib 200mg qd	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	WOMAC Total	6	Celecoxib 100mg BID versus Celecoxib 200mg qd	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Patient Global Assessment	6	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Patient Global Assessment	6	Celecoxib 100mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2000)	Patient Global Assessment	6	Celecoxib 100 versus Celecoxib 200mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Patient Global Assessment	6	Celecoxib 100mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Patient Global Assessment	6	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Physician Global Assessment	6	Celecoxib 100mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2001)	Physician Global Assessment	6	Celecoxib 200mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Physician Global Assessment	6	Celecoxib 100mg versus Celecoxib 200mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Ehrich (1999)	WOMAC Function	6	Rofecoxib versus Placebo	●	○	○	●	●	○	●	○	Moderate	○	○	●	●	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 200mg versus Celecoxib 200mg	●	●	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2006)	Adverse events	13	Lumiracoxib 400mg versus Celecoxib 200mg	●	●	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 200mg versus Lumiracoxib 400mg	●	●	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 200mg versus Placebo	●	◐	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate
Fleischmann (2006)	Adverse events	13	Lumiracoxib 400mg versus Placebo	●	◐	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Gibofsky (2003)	Adverse events	6	Rofecoxib 25mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Gibofsky (2003)	Any adverse event	6	Aceclofenac Rofecoxib 25mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Abdominal pain	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Accidental injury	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Diarrhea	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Dyspepsia	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Flatulence	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Headache	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Headache	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Headache	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Myalgia	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Nausea	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2004)	Acid reflux	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Naproxen	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Placebo	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence Analysis	Applicability Study
Kivits (2004)	Dyspepsia	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	● ○ ● ●	Moderate
Kivits (2004)	Epigastric discomfort	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	● ○ ● ●	Moderate
Kivits (2004)	GI events	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	● ○ ● ●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence Analysis	Applicability Study
Kivits (2004)	Heartburn	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	● ○ ● ●	Moderate
Kivits (2004)	Nausea	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	● ○ ● ●	Moderate
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	● ○ ● ●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Abdominal pain	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Abdominal pain	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Abdominal pain		Acetaminophen 4000mg versus Celecoxib 200mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Rofecoxib 12.5mg versus Rofecoxib 12.5mg Celecoxib 200mg	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Rofecoxib 25mg versus Celecoxib 200mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Rofecoxib 200mg versus Rofecoxib 25mg	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Diarrhea	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Diarrhea	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Diarrhea		Acetaminophen 4000mg versus Celecoxib 200mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Headache	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Headache	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Lower extremity edema	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Lower extremity edema	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Nausea	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Schnitzer (2005)	Nausea	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Upper respiratory infection	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○ ○ ● ●		Moderate
Schnitzer (2005)	Upper respiratory infection	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	◐	○	○	○	●	●	○	Low	○ ○ ● ●		Moderate
Tannenbaum (2004)	Adverse events	13	Celecoxib 100mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○ ● ●		Moderate
Tannenbaum (2004)	Adverse events	13	Lumiracoxib 200mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○ ● ●		Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Tannenbaum (2004)	Adverse events	13	Lumiracoxib 400mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Lequesne index	6	Celecoxib 100mg BID versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Lequesne index	6	Celecoxib 200mg QD versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2000)	Lequesne index	6	Celecoxib 200mg versus Celecoxib 100mg bid	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2001)	Lequesne index	6	Celecoxib versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Lequesne index	6	Celecoxib versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Lequesne index	6	Celecoxib 100mg BID versus Celecoxib 200mg qd	●	◐	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Williams (2001)	Adverse events	6	Celecoxib 100mg versus Celecoxib 200mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Williams (2001)	Adverse events	6	Celecoxib 100mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Williams (2001)	Adverse events	6	Celecoxib 200mg versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

Table 149. Quality and Applicability: NSAIDs Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Astorga (1991)	Time to walk 50ft	4	Etodolac 300mg versus Piroxicam 20mg	●	◐	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate
Astorga (1991)	Time to walk 50ft	6	Etodolac 300mg versus Piroxicam 20mg	●	◐	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate
Astorga (1991)	Time to walk 50ft	8	Etodolac 300mg versus Piroxicam 20mg	●	◐	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ●: Moderate power												
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Astorga (1991)	Morning stiffness	4	Etodolac 300mg versus Piroxicam 20mg	●	●	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate
Astorga (1991)	Morning stiffness	6	Etodolac 300mg versus Piroxicam 20mg	●	●	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate
Astorga (1991)	Morning stiffness	8	Etodolac 300mg versus Piroxicam 20mg	●	●	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate
Astorga (1991)	Morning stiffness	Final follow up	Etodolac 300mg versus Piroxicam 20mg	●	●	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ●: Moderate power													
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Goregaonkar (2009)	Gastritis	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate
Goregaonkar (2009)	Abdominal pain	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate
Goregaonkar (2009)	Dizziness	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate
Goregaonkar (2009)	Drowsiness	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ●: Moderate power													
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Goregaonkar (2009)	Headache	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate
Goregaonkar (2009)	Nausea/Vomiting	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate
Goregaonkar (2009)	Diarrhea	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate
Goregaonkar (2009)	GI events	4	Lornoxicam 8mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Ayral (2003)	Change in WOMAC averaged VAS Function	52	Tenidap 120mg versus Piroxicam 20mg	●	○	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Pain	52	Tenidap 40mg versus Tenidap 120mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Pain	52	Tenidap 40mg versus Piroxicam 20mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Pain	52	Tenidap 120mg versus Piroxicam 20mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Ayral (2003)	Change in WOMAC averaged VAS Stiffness	52	Tenidap 40mg versus Tenidap 120mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Stiffness	52	Tenidap 40mg versus Piroxicam 20	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Stiffness	52	Tenidap 120mg versus Piroxicam 20	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Ayral (2003)	Change in WOMAC averaged VAS Total	52	Tenidap 40mg versus Tenidap 120mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate		
Ayral (2003)	Change in WOMAC averaged VAS Total	52	Tenidap 40mg versus Piroxicam 20	●	●	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Ayral (2003)	Change in WOMAC averaged VAS Total	52	Tenidap 120mg versus Piroxicam 20	●	●	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Bellamy (1993)	WOMAC Function	12	Tenoxicam versus Diclofenac	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Bellamy (1993)	WOMAC Pain	12	Tenoxicam versus Diclofenac	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																		
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Bellamy (1993)	WOMAC Stiffness	12	Tenoxicam versus Diclofenac	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate	
Bradely (1993)	HAQ Disability improvement	4	Ibuprofen 300 versus Ibuprofen 600mg	●	●	○	●	○	●	●	●		Moderate	○	○	●	●	Moderate
Bradely (1993)	Health Assessment Questionnaire improvement	4	Ibuprofen 300mg versus Ibuprofen 600	●	●	○	●	○	●	●	●		Moderate	○	○	●	●	Moderate
Bradely (1993)	Walk time (sec) improvement	4	Ibuprofen 300mg versus Ibuprofen 600	●	●	○	●	○	●	●	●		Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Chubick (1987)	Improvement in morning weight-bearing pain	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate		
Chubick (1987)	Improvement in afternoon weight-bearing pain	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Chubick (1987)	Improvement in night pain	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Chubick (1987)	Improvement in tenderness	4	Sulindac 300-400mg Qd versus Sulindac 300-400mg Bid	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate		
Dick (1992)	Time to walk 50ft	6	Etodolac 300mgx2 versus Piroxicam 20mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Dick (1992)	Morning stiffness	6	Etodolac 300mgx2 versus Piroxicam 20mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Evcik (2003)	Health Assessment Questionnaire	26	Tenoxicam versus Placebo	●	◐	○	○	○	●	●	○	Low	●	○	●	○	Moderate
Evcik (2003)	Lequesne index	26	Tenoxicam versus Placebo	●	◐	○	○	○	●	●	○		●	○	●	○	Moderate
Evcik (2003)	VAS Ascending stairs	26	Tenoxicam versus Placebo	●	●	○	○	○	●	●	○		●	○	●	○	Moderate
Evcik (2003)	VAS Descending stairs	26	Tenoxicam versus Placebo	●	●	○	○	○	●	●	○		●	○	●	○	Moderate
Evcik (2003)	VAS Walking	26	Tenoxicam versus Placebo	●	●	○	○	○	●	●	○		●	○	●	○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Evciik (2003)	VAS at rest	26	Tenoxicam versus Placebo	●	●	○	○	○	●	●	○	Low	●	○	●	○	Moderate
Herrera (2007)	WOMAC Function	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●	●
Herrera (2007)	VAS	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrera (2007)	WOMAC Pain	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Herrera (2007)	WOMAC Stiffness	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrera (2007)	WOMAC Total	4	Diclofenac Cr 100mg versus Diclofenac Ir 50mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Karbowski (1991)	Time to walk 50ft	6	Etodolac 300mg versus Indomethacin 50mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Karbowski (1991)	Morning stiffness	6	Etodolac 300mg versus Indomethacin 50mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	VAS Pain	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	VAS Pain	6	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	6	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	6	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Total	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kogstad (1981)	Sequence A ability to walk (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Kogstad (1981)	Sequence B ability to walk (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Kogstad (1981)	Sequence A pain at night (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Kogstad (1981)	Sequence B pain at night (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kogstad (1981)	Sequence A pain on movement (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Kogstad (1981)	Sequence B pain on movement (VAS)	4	Piroxicam 20mg versus Naproxen 250mg	●	●	○	●	○	●	●	○		Moderate	○	○	●	
La Montagna (1998)	Present Pain index	12	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
La Montagna (1998)	Present Pain index	24	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
La Montagna (1998)	Adverse events	12	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
La Montagna (1998)	VAS	24	Piroxicam-Beta-Cyclodextrin 20mg versus Diclofenac 100mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ◐: Moderate power															
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Liang (2003)	Change in Lequesne index	4	Etodolac Sustained-Release 400mg versus Diclofenac 50mg Nimesulide 100mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate		
Lücker (1994)	Lequesne Functional index	4	versus Etodolac 300mg Nimesulide 100mg	●	◐	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate
Lücker (1994)	Lequesne Functional index	8	versus Etodolac 300mg	●	◐	○	●	●	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Lücker (1994)	Lequesne Functional index	12	Nimesulide 100mg versus Etodolac 300mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Lücker (1994)	Lequesne Functional index	4	Nimesulide 100mg versus Etodolac 300mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Lücker (1994)	Lequesne Functional index	8	Nimesulide 100mg versus Etodolac 300mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Lücker (1994)	Lequesne Functional index	12	Nimesulide 100mg versus Etodolac 300mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Lücker (1994)	VAS Pain 10cm	4	Nimesulide 100mg versus Etodolac 300mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Lücker (1994)	VAS Pain 10cm	8	Nimesulide 100mg versus Etodolac 300mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Lücker (1994)	VAS Pain 10cm	12	Nimesulide 100mg versus Etodolac 300mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Luyten (2007)	WOMAC Pain	24	Continuous Celecoxib versus Intermittent Celecoxib	●	◐	○	●	●	○	●	○		Moderate	○	○	●		●	Moderate
Luyten (2007)	WOMAC Stiffness	24	Continuous Celecoxib versus Intermittent Celecoxib	●	◐	○	●	●	○	●	○		Moderate	○	○	●		●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ●: Moderate power												
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Luyten (2007)	WOMAC Total	24	Continuous Celecoxib versus Intermittent Celecoxib	●	◐	○	●	●	○	●	○	Moderate	○ ○	●	●	Moderate
Mckenna (2001)	WOMAC Function improvement	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Mckenna (2001)	VAS Pain	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Mckenna (2001)	WOMAC Pain	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Mckenna (2001)	WOMAC Stiffness	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																		
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Mckenna (2001)	WOMAC Total	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate	
Queiros (1990)	Mean pain at night (1 to 4)	4	Piroxicam 20mg versus Oxaprozin 1200mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●	○	Moderate
Queiros (1990)	Mean pain on walking in the evening (1 to 21)	4	Piroxicam 20mg versus Oxaprozin 1200mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●	○	Moderate
Queiros (1990)	Mean pain on walking in the morning (1 to 21)	4	Piroxicam 20mg versus Oxaprozin 1200mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●	○	Moderate
Schnitzer	WOMAC Total	12	Naproxen versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	Rescue Acetaminophen	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	SF-36 MCS improvement	13	Naproxcinod versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	WOMAC Function	13	Naproxcinod versus Placebo	●	○	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	VAS Pain at rest improvement	13	Naproxcinod 375mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2010)	VAS Pain at rest improvement	13	Naprocinod 750mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	13	Naproxcinod 375mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	VAS Pain during walking	13	Naprocinod 750mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	WOMAC Pain	13	Naproxcinod 375mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	WOMAC Pain	13	Naprocinod 750mg versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2010)	Rescue Acetaminophen	12	Naproxen versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	SF-36 MCS improvement	12	Naproxen versus Placebo	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	WOMAC Function improvement	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	VAS Pain	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Schnitzer (2010)	VAS Pain during walking improvement	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2010)	WOMAC Pain	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Tyson (1980)	Linear analogue pain scale	8	Benoxaprofen versus Ibuprofen	●	◐	○	●	○	●	●	○	Moderate	● ○ ● ●			Moderate
Tyson (1980)	Linear analogue pain scale	12	Benoxaprofen versus Ibuprofen	●	◐	○	●	○	●	●	○	Moderate	● ○ ● ●			Moderate
Tyson (1980)	Linear analogue pain scale	16	Benoxaprofen versus Ibuprofen	●	◐	○	●	○	●	●	○	Moderate	● ○ ● ●			Moderate
Bookman (2004)	WOMAC Stiffness (Likert)	4	Topical Diclofenac versus Placebo	●	○	●	●	●	●	●	○	High	○ ○ ● ●			Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Bookman (2004)	Mean WOMAC Pain (Likert)	4	Topical Diclofenac versus Placebo gel	●	○	●	●	●	●	●	○	High	○ ○ ● ●			Moderate
Bookman (2004)	Mean WOMAC Function (Likert)	4	Topical Diclofenac versus vehicle control	●	○	●	●	●	●	●	○	High	○ ○ ● ●			Moderate
Bookman (2004)	Acetaminophen consumption	4	Topical Diclofenac versus vehicle control	●	◐	●	●	●	●	●	○	High	○ ○ ● ●			Moderate
Bookman (2004)	Acetaminophen consumption	4	Topical Diclofenac versus Placebo	●	◐	●	●	●	●	●	○	High	○ ○ ● ●			Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Barthel (2009)	Weeks with no rescue drug	12	Diclofenac sodium 1% gel in DMSO versus DMSO vehicle Topical	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate		
Bookman (2004)	Acetaminophen consumption	4	Diclofenac versus vehicle control Topical	●	◐	○	●	○	●	●	○		Moderate	○	○	○		●	Moderate
Bookman (2004)	Acetaminophen consumption	4	Diclofenac versus Placebo	●	◐	○	●	○	●	●	○			Moderate	○	○		○	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Barthel (2009)	Weeks with no rescue drug	12	Diclofenac sodium 1% gel in DMSO versus DMSO vehicle Topical Diclofenac	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Roth (2004)	WOMAC Function	12	Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Baer (2005)	WOMAC Function	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	●	●	●	●	●	●	●	○	High	○ ○	● ●	●	Moderate
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○ ○	● ●	●	Moderate
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○ ○	● ●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Rother (2007)	WOMAC Function	6	topical Ketoprofen versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate		
Rother (2007)	WOMAC Function	6	topical Ketoprofen versus Placebo	●	●	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Rother (2007)	WOMAC Function	6	Celecoxib versus Placebo	●	●	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate		

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Bookman (2004)	WOMAC Function	4	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate		
Roth (2004)	WOMAC Pain	12	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○		High	○	○	●		●	Moderate
Roth (2004)	WOMAC Pain on walking	12	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○		High	○	○	●		●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Baer (2005)	WOMAC Pain	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	●	●	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Baer (2005)	WOMAC Pain on walking	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	●	●	●	●	●	●	●	○	High	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ●: Moderate power												
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Otillinger (2001)	VAS Pain	4	Eltenac gel 0.3% versus Eltenac gel 0.1%	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	5	Eltenac gel 0.3% versus Eltenac gel 0.1%	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	6	Eltenac gel 0.3% versus Eltenac gel 0.1%	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	4	Eltenac gel 1% versus Eltenac gel 0.3%	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

				○: Domain flaws present ●: Moderate power													
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Ottilinger (2001)	VAS Pain	4	Eltenac gel 1% versus Eltenac gel 0.1%	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Ottilinger (2001)	VAS Pain	5	Eltenac gel 1% versus Eltenac gel 0.3%	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Ottilinger (2001)	VAS Pain	5	Eltenac gel 1% versus Eltenac gel 0.1%	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Ottilinger (2001)	VAS Pain	6	Eltenac gel 1% versus Eltenac gel 0.3%	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Otillinger (2001)	VAS Pain	6	Eltenac gel 1% versus Eltenac gel 0.1%	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	4	Eltenac gel 0.1% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	5	Eltenac gel 0.1% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	6	Eltenac gel 0.1% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate
Otillinger (2001)	VAS Pain	4	Eltenac gel 0.3% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Ottillinger (2001)	VAS Pain	5	Eltenac gel 0.3% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 0.3% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Ottillinger (2001)	VAS Pain	4	Eltenac gel 1% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Ottillinger (2001)	VAS Pain	5	Eltenac gel 1% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Ottillinger (2001)	VAS Pain	6	Eltenac gel 1% versus Placebo gel	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○ ○ ● ●			Moderate
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○ ○ ● ●			Moderate
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○ ○ ● ●			Moderate
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○ ○ ● ●			Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Rother (2007)	WOMAC Pain	6	Topical Ketoprofen versus Celecoxib	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Rother (2007)	WOMAC Pain	6	Topical Ketoprofen versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Rother (2007)	WOMAC Pain	6	Celecoxib versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Bookman (2004)	WOMAC Pain	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Bookman (2004)	WOMAC Pain on walking	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Roth (2004)	WOMAC Stiffness	12	Topical Diclofenac versus vehicle control	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Baer (2005)	WOMAC Stiffness	6	Pennsaid (topical Diclofenac solution) versus vehicle control solution	●	●	●	●	●	●	●	○	High	○ ○	● ●	●	Moderate
Bookman (2004)	WOMAC Stiffness	4	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○ ○	● ●	●	Moderate
Bookman (2004)	WOMAC Stiffness	4	Topical Diclofenac versus vehicle control	●	◐ *	●	●	●	●	●	○	High	○ ○	● ●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Torri (1994)	WOMAC averaged VAS Pain	12	Aceclofenac versus Piroxicam	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Ayral (2003)	Physician Global Assessment	52	Tenidap 120mg versus Piroxicam 20mg	●	◐	○	●	○	●	●	○		Moderate	○	○	○		●	●
Ayral (2003)	Physician Global Assessment	52	Tenidap 40mg versus Piroxicam 20mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Ayral (2003)	Patient Global Assessment	52	Tenidap 120mg versus Piroxicam 20mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Ayral (2003)	Patient Global Assessment	52	Tenidap 40mg versus Placebo	●	◐	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Ayral (2003)	Physician Global Assessment	52	Tenidap 40mg versus Tenidap 120mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Ayral (2003)	Patient Global Assessment	52	Tenidap 40mg versus vehicle control	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2004)	At least one adverse event	6	nabumetone 1000 versus Placebo	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	Physician Global Assessment	6	Naproxen versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	12	Naproxen versus Placebo	●	●	○	●	●	●	●	○		Moderate	○	○	●	●
Kivitz (2004)	Patient Global Assessment of Response to Treatment	6	Nabumetone versus Placebo	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Lee (1985)	Adverse events	6	High dose diflunisal (NSAID) versus Placebo	●	●	○	●	●	●	●	○		Moderate	○	○	●	○

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Lee (1985)	Adverse events	6	Low dose diflunisal (NSAID) versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Lohmander (2005)	Patient Assessment of Treatment Response	6	Naproxcinod versus Naproxen	●	●	○	●	○	○	●	○	Low	○	○	●	○	Moderate
Lohmander (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod versus Placebo	●	●	○	●	○	○	●	○	Low	○	○	●	○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lohmander (2005)	Patient Global Assessment of Response to Treatment	6	Naproxen versus Placebo	●	●	○	●	○	○	●	○	Low	○ ○ ● ○			Moderate
Lohmander (2005)	Adverse events	6	Naproxcinod 750mg versus Piroxicam	●	●	○	●	○	○	●	○	Moderate	○ ○ ● ○			Moderate
Lohmander (2005)	Adverse events	6	Naproxcinod 750mg versus Placebo	●	◐	○	●	○	○	●	○	Moderate	○ ○ ● ○			Moderate
Lohmander (2005)	Adverse events	6	Naproxen 500mg versus Placebo	●	◐	○	●	○	○	●	○	Moderate	○ ○ ● ○			Moderate
Mckenna (2001)	Patient Global Assessment	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○	Moderate	○ ○ ● ●			Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
McKenna (2001)	Alt increased	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Anaemia	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Back pain	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Constipation	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
McKenna (2001)	Diarrhea	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Dizziness	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Dyspepsia	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Flatulence	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
McKenna (2001)	Headache	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Accidental injury	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Myalgia	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
McKenna (2001)	Nausea	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
McKenna (2001)	Peripheral Oedema	6	Celecoxib 100mg versus Diclofenac 50mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	Physician Global Assessment	6	Diclofenac versus Placebo	●	●	○	●	●	●	●	○		Moderate	○	○	●	
Roth(2004)	Patient Global Assessment	12	Topical Diclofenac versus Placebo	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 125mg versus Naproxcinod 375mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Naproxcinod 750mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 125mg versus Naproxcinod 750mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 375mg versus Naproxcinod 750mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 375mg versus Naproxcinod 750mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Naproxen 500mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 125mg versus Naproxen 500mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 375mg versus Naproxen 500mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 375mg versus Naproxen 500mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 750mg versus Naproxen 500mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Naproxcinod 750mg versus Naproxen 500mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod 125mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Placebo	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 125mg versus Placebo	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod 375mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 375mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxcinod 750mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxcinod 750mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Schnitzer (2005)	Patient Global Assessment of Response to Treatment	6	Naproxen 500mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease Status	6	Naproxen 500mg versus Placebo	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

Table 150. Quality and Applicability: Cox-2s Versus NSAIDs

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

<i>Study</i>	<i>Outcome</i>	<i>Week</i>	<i>Comparison</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Aceclofenac	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gibofsky (2003)	Adverse events	6	Celecoxib 200mg versus Aceclofenac	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Kivits (2002)	VAS Pain	12	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	VAS Pain	6	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	VAS Pain	12	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	VAS Pain	6	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	VAS Pain	12	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	VAS Pain	6	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib 10mg versus Naproxen 10mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib 10mg versus Naproxen 10mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib 20mg versus Naproxen 20mg	●	●	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib 20mg versus Naproxen 20mg	●	●	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Kivits (2002)	WOMAC Stiffness	12	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Kivits (2002)	WOMAC Stiffness	6	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib 10mg versus Naproxen 10mg	●	●	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	WOMAC Total	6	Valdecoxib 10mg versus Naproxen 10mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib 20mg versus Naproxen 20mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	WOMAC Total	12	Valdecoxib 20mg versus Naproxen 20mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	WOMAC Total	12	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	WOMAC Total	6	Valdecoxib 5mg versus Naproxen 5mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	Abdominal pain	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	Accidental injury	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Accidental injury	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Kivits (2002)	Constipation	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Kivits (2002)	Constipation	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Kivits (2002)	Diarrhea	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Kivits (2002)	Diarrhea	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	Dyspepsia	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Dyspepsia	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Flatulence	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Headache	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Headache	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Headache	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Myalgia	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Myalgia	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	Nausea	12	Valdecoxib 10mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 5mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence Analysis			Applicability Study	
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 10mg versus Naproxen 500mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 5mg versus Naproxen 500mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Abdominal pain	12	Valdecoxib 20mg versus Naproxen 500mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Accidental injury	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Constipation	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Diarrhea	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Dyspepsia	12	Valdecoxib 20mg versus Naproxen 500mg	●	●	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Flatulence	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Headache	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2002)	Myalgia	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Nausea	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Upper respiratory tract infections	12	Valdecoxib 20mg versus Naproxen 500mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2004)	Acid reflux	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Naproxen	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Dyspepsia	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Epigastric discomfort	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2004)	GI events	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Heartburn	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Nausea	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Acid reflux	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	At least one adverse event	6	Rofecoxib 12.5mg versus Naproxen	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Dyspepsia	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence	Analysis	Applicability Study
Kivits (2004)	Epigastric discomfort	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	● ○ ● ●	●	Moderate
Kivits (2004)	GI events	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	● ○ ● ●	●	Moderate
Kivits (2004)	Heartburn	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	● ○ ● ●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivits (2004)	Nausea	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2004)	Vomiting	6	Rofecoxib 12.5mg versus Nabumetone 1000mg	●	◐	●	●	●	●	●	○	High	●	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 10mg versus Naproxen	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 10mg versus Naproxen	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 20mg versus Naproxen	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 20mg versus Naproxen	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	6	Valdecoxib 5mg versus Naproxen	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate
Kivits (2002)	Physician Global Assessment	12	Valdecoxib 5mg versus Naproxen	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kivitz (2004)	Patient Assessment of Treatment Response (Good or Excellent)	6	Rofecoxib 12.5mg versus Nabumetone	●	●	●	●	●	●	●	○	High	●	○	●	●	Moderate
Lücker (1994)	VAS Pain	4	Nimesulide 100mg versus Etodolac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Lücker (1994)	VAS Pain	8	Nimesulide 100mg versus Etodolac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Lücker (1994)	VAS Pain	12	Nimesulide 100mg versus Etodolac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Lücker (1994)	Lequesne index	4	Nimesulide 100mg versus Etodolac	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	○	Moderate
Lücker (1994)	Lequesne index	8	Nimesulide 100mg versus Etodolac	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	○	Moderate
Lücker (1994)	Lequesne index	12	Nimesulide 100mg versus Etodolac	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	○	Moderate
Mckenna (2001)	Patient Global Assessment	6	Celecoxib versus Diclofenac	●	◐	○	●	●	●	●	○	Moderate	○ ○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
McKenna (2001)	Nausea	6	Rofecoxib 25mg versus Naproxcinod 125mg	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate		
Mckenna (2001)	WOMAC Function	6	Celecoxib 100mg versus Diclofenac 100mg	●	●	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate
Mckenna (2001)	WOMAC Pain	6	Celecoxib 100mg versus Diclofenac 100mg	●	●	○	●	●	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Mckenna (2001)	VAS Pain	6	Celecoxib 100mg versus Diclofenac 100mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	WOMAC Stiffness	6	Celecoxib 100mg versus Diclofenac 100mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Mckenna (2001)	WOMAC Total	6	Celecoxib 100mg versus Diclofenac 100mg	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Mckenna (2001)	Physician Global Assessment	6	Celecoxib versus Diclofenac (NSAID)	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease responders	6	Rofecoxib 25mg versus Naproxcinod 125mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Global Assessment of Disease responders	6	Rofecoxib 25mg versus Naproxcinod 375mg	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Schnitzer (2005)	Patient Global Assessment of Disease responders	6	Rofecoxib 25mg versus Naproxcinod 750mg	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response (Good or Excellent)	6	Rofecoxib 25mg versus Naproxcinod 125mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Schnitzer (2005)	Patient Assessment of Treatment Response (Good or Excellent)	6	Rofecoxib 25mg versus Naproxcinod 375mg	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response (good or excellent)	6	Rofecoxib 25mg versus Naproxcinod 750mg	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

Table 151. Quality and Applicability: Acetaminophen Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

flaws present																			
●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Gualda (2007)	Physician Global Assessment	6	Paracetamol versus Aceclofenac 100mg	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate		
Gualda (2007)	Patient Global Assessment	6	Paracetamol 1000mg versus aceclofenac 100mg	●	●	●	●	●	●	●	○		High	○	○	●		●	Moderate
Gualda (2007)	Adverse events	6	Paracetamol 1000mg versus Celecoxib 200mg	●	○	●	●	●	●	●	○		High	○	○	●		●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ●: Moderate power																		
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Acetaminophen 4000mg versus Rofecoxib 12.5mg	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate	
Schnitzer (2009)	Physician Assessment of Treatment Response	4	Acetaminophen 1300mg versus Rofecoxib 25mg	●	●	○	●	○	●	●	○		Moderate	○	○	●	○	Moderate
Schnitzer (2009)	Physician Assessment of Treatment Response	4	Acetaminophen 1300mg versus Rofecoxib 12.5mg	●	●	○	●	○	●	●	○		Moderate	○	○	●	○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																		
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Acetaminophen 1000mg versus Rofecoxib 12.5mg	○	◐	○	○	○	●	●	○	Low	○	○	●	●	Moderate	
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	●	○	○	○	●	●	○		Low	○	○	●	●	Moderate
Schnitzer (2005)	Patient Assessment of Treatment Response	6	Acetaminophen 4000mg versus Rofecoxib 25mg	○	●	○	○	○	●	●	○		Low	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Abdominal pain	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Abdominal pain	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Constipation	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Constipation	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Diarrhea	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Diarrhea	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Dizziness	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Dizziness	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Dyspepsia	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Dyspepsia	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Flatulence	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Flatulence	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Headache	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Headache	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Nausea	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Schnitzer (2009)	Nausea	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Schnitzer (2009)	Pain	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Schnitzer (2009)	Pain	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Peripheral edema	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Peripheral edema	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Abdominal pain	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Schnitzer (2009)	Abdominal pain	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate		
Schnitzer (2009)	Constipation	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○		Moderate	○	○	●		○	Moderate
Schnitzer (2009)	Constipation	4	Acetaminophen ER 1300mg versus Rofecoxib 25mg	●	◐	○	●	○	●	●	○			Moderate	○	○		●	

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																		
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study		
Schnitzer (2009)	Diarrhea	4	Acetaminophen ER 1300mg versus Rofecoxib 12.5mg	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate	
Schnitzer (2005)	Any clinical adverse event, VACT2	6	Acetaminophen 1000mg versus Rofecoxib 25mg	○	●	○	○	○	●	●	○		Low	○	○	●	●	Moderate
Schnitzer (2009)	Patient Assessment of Treatment Response	4	Acetaminophen ER versus Diclofenac	●	●	○	●	○	●	●	○		Moderate	○	○	●	○	Moderate
Micelli (2004)	VAS Pain	6	Acetaminophen versus Placebo	●	◐	○	●	○	●	●	●		Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Bradely (1991)	HAQ Disability	4	Acetaminophen versus Ibuprofen	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Bradely (1991)	HAQ Disability	4	Acetaminophen versus Ibuprofen	●	◐	○	●	○	●	●	●		○	○	●	●	Moderate
Bradely (1991)	Health Assessment Questionnaire	4	Acetaminophen versus Ibuprofen	●	◐	○	●	○	●	●	●		○	○	●	●	Moderate
Bradely (1991)	Health Assessment Questionnaire	4	Acetaminophen versus Ibuprofen	●	◐	○	●	○	●	●	●		○	○	●	●	Moderate
Bradely (1991)	Walk time (sec) improvement	4	Acetaminophen versus Ibuprofen	●	◐	○	●	○	●	●	●		○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Bradely (1991)	Walk time (sec)	4	Acetaminophen versus Ibuprofen	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Gualda (2007)	VAS Pain	6	Paracetamol versus Aceclofenac	●	●	●	●	●	●	●	○		High	○	○	●	●
Micelli (2004)	VAS Pain	6	Acetaminophen versus Placebo	●	◐	○	●	○	●	●	●	Moderate		○	○	●	●

Table 152. Quality and Applicability: Interleukin Versus Control

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	investigator bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	WOMAC Function	4	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Function	8	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Function	12	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Function	16	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Function	20	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	WOMAC Function	24	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Pain	4	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Pain	8	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Pain	12	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Pain	16	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Pain	20	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	WOMAC Pain	24	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	4	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	8	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	12	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	16	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Paracetamol intake pills per day	20	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	Paracetamol intake pills per day	24	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	SF-36 sum score	16	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	SF-36 sum score	24	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Stiffness	4	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Stiffness	8	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Stiffness	12	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	WOMAC Stiffness	16	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Stiffness	20	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Stiffness	24	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Total	4	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Total	8	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Total	12	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	WOMAC Total	16	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Total	20	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Total	24	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Upper respiratory infection	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Dyspepsia	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Diarrhea	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	Abdominal pain	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Bowel motility disorders	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Constipation	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Nausea	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Hypertension	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Myalgia	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Louthrenoo (2007)	Arthropathy	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Oedema	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	Dizziness	12	Diacerein versus Piroxicam	●	◐	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Pavelka (2007)	WOMAC Function	8	Diacerein versus Placebo	●	○	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Function	16	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Function	20	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Pavelka (2007)	WOMAC Function	24	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Pain	8	Diacerein versus Placebo	●	○	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Pain	12	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Pain	16	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Pain	20	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Pain	24	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Pavelka (2007)	WOMAC Stiffness	4	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Stiffness	8	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Stiffness	16	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Stiffness	20	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Stiffness	24	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	Paracetamol intake pills per day	4	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Pavelka (2007)	Paracetamol intake pills per day	8	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	Paracetamol intake pills per day	12	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	Paracetamol intake pills per day	16	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	Paracetamol intake pills per day	20	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	Paracetamol intake pills per day	24	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Total	4	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Pavelka (2007)	WOMAC Total	8	Diacerein versus Placebo	●	○	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Total	16	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Total	20	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2007)	WOMAC Total	24	Diacerein versus Placebo	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Zheng (2006)	VAS Pain on walking improvement	12	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Zheng (2006)	VAS Pain on walking	12 to 16	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Zheng (2006)	WOMAC Total VAS improvement	12	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Zheng (2006)	WOMAC Total	12 to 16	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Zheng (2006)	Pain on walking	4	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	Pain on walking	8	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Zheng (2006)	Pain on walking	12	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	Pain on walking	16	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	WOMAC Total	4	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	WOMAC Total	8	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	WOMAC Total	12	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	WOMAC Total	16	Diacerein versus Diclofenac	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Zheng (2006)	Adverse events	16	Diacerein versus Diclofenac	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Zheng (2006)	GI adverse events	16	Diacerein versus Diclofenac	●	◐	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Louthrenoo (2007)	WOMAC Function	4	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Function	8	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate
Louthrenoo (2007)	WOMAC Function	12	Diacerein versus Piroxicam	●	●	○	●	○	●	●	○	Moderate	○	○	○	●	Moderate

Table 153. Quality and Applicability: Tramadol Versus Control

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Babul (2004)	WOMAC Function	12	Tramadol ER versus Placebo	●	●	○	●	○	●	●	○	Moderate	○ ○ ● ●			Moderate
Babul (2004)	Patients' global	12	Tramadol ER versus Placebo	●	●	○	●	○	●	●	○	Moderate	○ ○ ● ●			Moderate
Babul (2004)	VAS	12	Tramadol ER versus Placebo	●	●	○	●	○	●	●	○	Moderate	○ ○ ● ●			Moderate
Babul (2004)	WOMAC Pain	12	Tramadol ER versus Placebo	●	●	○	●	○	●	●	○	Moderate	○ ○ ● ●			Moderate
Babul (2004)	WOMAC Stiffness	12	Tramadol ER versus Placebo	●	●	○	●	○	●	●	○	Moderate	○ ○ ● ●			Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

○: Domain flaws present ●: Moderate power																			
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study			
Beaulieu (2008)	WOMAC Stiffness	6	CR Tramadol versus SR Diclofenac	●	○	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate		
Beaulieu (2008)	WOMAC Function	6	CR Tramadol versus SR Diclofenac	●	○	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Beaulieu (2008)	Mean change in WOMAC Pain	6	Tramadol versus Diclofenac	●	○	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate
Burch (2007)	Improvement in pain intensity numerical rating scale	12	Tramadol Contramid OAD versus Placebo	●	●	○	●	○	●	●	○		Moderate	○	○	●		●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid versus Placebo	●	◐	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid versus Placebo	●	◐	●	●	●	●	●	○	High	○ ○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid versus Placebo	●	●	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid 100mg versus Tramadol Contramid 200mg	●	◐	●	●	●	●	●	○	High	○ ○	●	●	Moderate

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid 100mg versus Tramadol Contramid 300mg	●	◐	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Fishman (2007)	WOMAC Pain, percent improvement from baseline	12	Tramadol Contramid 200mg versus Tramadol Contramid 300mg	●	◐	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Fleischmann (2001)	WOMAC Function	13	Tramadol versus Placebo	●	●	●	●	●	●	●	○	High	○ ○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Fleischmann (2001)	WOMAC Pain	13	Tramadol versus Placebo	●	●	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Fleischmann (2001)	WOMAC Stiffness	13	Tramadol versus Placebo	●	●	●	●	●	●	●	○	High	○ ○	●	●	Moderate
Schnitzer (1999)	Minimum effective Naproxen dose	8	Tramadol versus Placebo	●	◐	○	●	○	●	●	○	Moderate	○ ○	●	●	Moderate

Table 154. Quality and Applicability: Orgotein Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

○: Domain flaws present																	
●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
McIlwain (1989)	Patient Assessment of Treatment Response	12	Orgotein 8mg x3 versus Orgotein 16 mg x 3	●	●	○	●	●	●	●	○	Moderate	○	○	○	●	Moderate

FINDINGS

Table 155. Cox-2s Versus Placebo

Type	Study	Outcome	N	Sufficie nt Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Clinical Significance
	Fleischmann (2006)	WOMAC Function	693	Yes	13	Lumiracoxib	Placebo	-0.48571	-0.64572	-0.3257	Lumiracoxib	Possibly clinically significant
	Fleischmann (2006)	WOMAC Function	694	Yes	13	Lumiracoxib	Placebo	-0.46178	-0.62153	-0.30203	Lumiracoxib	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Function	724	Yes	13	Celecoxib	Placebo	-0.25686	-0.41168	-0.10203	Celecoxib	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Function	730	Yes	13	Lumiracoxib	Placebo	-0.29966	-0.45437	-0.14496	Lumiracoxib	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Function	734	Yes	13	Lumiracoxib	Placebo	-0.28331	-0.43772	-0.1289	Lumiracoxib	Possibly clinically significant
	Gibofsky (2003)	WOMAC Function	285	Yes	6	Celecoxib	Placebo	-0.48333	-0.7322	-0.23446	Celecoxib	Possibly clinically significant
	Gibofsky (2003)	WOMAC Function	286	Yes	6	Rofecoxib	Placebo	-0.40069	-0.64833	-0.15305	Rofecoxib	Possibly clinically significant
	Mckenna (2001)	WOMAC Function	399	Yes	6	Celecoxib	Placebo	-0.39924	-0.59745	-0.20104	Celecoxib	Possibly clinically significant

	Williams (2000)	WOMAC Function	453	No	6	Celecoxib 200mg QD	Placebo	0.00481 1	-0.1794	0.18902 2	NS	True negative
	Ehrich (1999)	WOMAC Function	145	No	6	Rofecoxib	Placebo	-1.11169	-1.46213	-0.76126	Rofecoxib	Clinically significant
Lequesne index	Williams (2001)	Lequesne index	484	Unclear	6	Celecoxib	Placebo	-43.2659	-46.0084	-40.5234	Celecoxib	Unclear
	Williams (2001)	Lequesne index	474	Unclear	6	Celecoxib	Placebo	-37.7525	-40.1724	-35.3325	Celecoxib	Unclear
	Williams (2000)	Lequesne index	462	Unclear	6	Celecoxib 100mg BID	Placebo	-0.32841	-0.51202	-0.1448	Celecoxib 100mg BID	Unclear
	Williams (2000)	Lequesne index	453	Unclear	6	Celecoxib 200mg QD	Placebo	-0.39366	-0.57966	-0.20766	Celecoxib 200mg QD	Unclear
	Fleischmann (2006)	VAS Pain improvement	693	Yes	13	Lumiracoxib	Placebo	-0.26685	-0.42542	-0.10828	Lumiracoxib	Not clinically significant
	Fleischmann (2006)	VAS Pain improvement	694	Yes	13	Lumiracoxib	Placebo	-0.31161	-0.47035	-0.15288	Lumiracoxib	Not clinically significant
	Fleischmann (2006)	WOMAC Pain	693	Yes	13	Lumiracoxib	Placebo	-0.34431	-0.50329	-0.18533	Lumiracoxib	Possibly clinically significant
	Fleischmann (2006)	WOMAC Pain	694	Yes	13	Lumiracoxib	Placebo	-0.3443	-0.50322	-0.18538	Lumiracoxib	Possibly clinically significant
	Fleischmann (2006)	VAS Pain improvement	675	Yes	13	Celecoxib	Placebo	-0.22358	-0.38303	-0.06413	Celecoxib	Not clinically significant
	Fleischmann (2006)	WOMAC Pain	675	Yes	13	Celecoxib	Placebo	-0.29674	-0.45653	-0.13695	Celecoxib	Possibly clinically significant

	Tannenbaum (2004)	VAS Pain improvement	724	Yes	13	Celecoxib	Placebo	-0.21425	-0.3689	-0.0596	Celecoxib	Not clinically significant
	Tannenbaum (2004)	VAS Pain improvement	730	Yes	13	Lumiracoxib	Placebo	-0.18623	-0.34046	-0.03199	Lumiracoxib	Not clinically significant
	Tannenbaum (2004)	VAS Pain improvement	734	Yes	13	Lumiracoxib	Placebo	-0.3032	-0.45771	-0.14869	Lumiracoxib	Not clinically significant
	Tannenbaum (2004)	WOMAC Pain	724	Yes	13	Celecoxib	Placebo	-0.18402	-0.33857	-0.02947	Celecoxib	Not clinically significant
	Tannenbaum (2004)	WOMAC Pain	730	Yes	13	Lumiracoxib	Placebo	-0.19301	-0.34727	-0.03876	Lumiracoxib	Not clinically significant
	Tannenbaum (2004)	WOMAC Pain	734	Yes	13	Lumiracoxib	Placebo	-0.21031	-0.36442	-0.0562	Lumiracoxib	Not clinically significant
	Gibofsky (2003)	VAS Pain on walking improvement	285	Yes	6	Celecoxib	Placebo	-0.39492	-0.64272	-0.14712	Celecoxib	Not clinically significant
	Gibofsky (2003)	VAS Pain on walking improvement	286	Yes	6	Rofecoxib	Placebo	-0.32077	-0.56762	-0.07392	Rofecoxib	Not clinically significant

	Lehmann (2005)	VAS Pain improvement	844	Yes	13	Lumiracoxib (Cox-2) with loading dose	Placebo	-0.19962	-0.33488	-0.06435	Lumiracoxib (Cox-2) with loading dose	Not clinically significant
	Lehmann (2005)	WOMAC Pain	844	Yes	13	Lumiracoxib (Cox-2) with loading dose	Placebo	-0.17771	-0.31291	-0.04251	Lumiracoxib (Cox-2) with loading dose	Not clinically significant
	Gibofsky (2003)	WOMAC Pain	286	Yes	6	Rofecoxib	Placebo	-0.49078	-0.73953	-0.24204	Rofecoxib	Possibly clinically significant
	Lehmann (2005)	VAS Pain improvement	844	Yes	13	Celecoxib	Placebo	-0.21819	-0.35352	-0.08286	Celecoxib	Not clinically significant
	Lehmann (2005)	VAS Pain improvement	844	Yes	13	Lumiracoxib	Placebo	-0.22578	-0.36115	-0.09042	Lumiracoxib	Not clinically significant
	Lehmann (2005)	WOMAC Pain	844	Yes	13	Celecoxib	Placebo	-0.23041	-0.36579	-0.09503	Celecoxib	Not clinically significant
	Lehmann (2005)	WOMAC Pain	844	Yes	13	Lumiracoxib	Placebo	-0.22332	-0.35867	-0.08796	Lumiracoxib	Not clinically significant
	Gibofsky (2003)	WOMAC Pain	285	Yes	6	Celecoxib	Placebo	-0.51629	-0.76562	-0.26697	Celecoxib	Possibly clinically significant
	Kivits (2002)	VAS Pain improvement	406	Yes	6	Valdecoxib	Placebo	-0.24767	-0.44297	-0.05237	Valdecoxib	Not clinically significant
	Kivits (2002)	VAS Pain improvement	410	Yes	6	Valdecoxib	Placebo	-0.21281	-0.40695	-0.01867	Valdecoxib	Not clinically significant

	Kivits (2002)	VAS Pain improvement	406	Yes	6	Valdecoxib	Placebo	-0.29993	-0.49558	-0.10428	Valdecoxib	Not clinically significant
	Kivits (2002)	VAS Pain improvement	406	Yes	12	Valdecoxib	Placebo	-0.18084	-0.37579	0.01411 ₇	NS	True negative
	Kivits (2002)	VAS Pain improvement	410	Yes	12	Valdecoxib	Placebo	-0.18939	-0.38342	0.00464 ₁	NS	True negative
	Kivits (2002)	VAS Pain improvement	406	Yes	12	Valdecoxib	Placebo	-0.28608	-0.48164	-0.09053	Valdecoxib	Not clinically significant
	Mckenna (2001)	VAS Pain improvement	399	Yes	6	Celecoxib	Placebo	-0.41988	-0.6183	-0.22147	Celecoxib	Not clinically significant
	Mckenna (2001)	WOMAC Pain	399	Yes	6	Celecoxib	Placebo	-0.38937	-0.58748	-0.19125	Celecoxib	Possibly clinically significant
	Ehrich (1999)	WOMAC Pain	145	No	6	Rofecoxib	Placebo	-1.0773	-1.42626	-0.72833	Rofecoxib	Clinically significant
	Ehrich (1999)	VAS Pain improvement	145	Yes	6	Rofecoxib	Placebo	-1.12278	-1.4737	-0.77187	Rofecoxib	Possibly clinically significant
	Ehrich (1999)	VAS Pain improvement	145	Yes	6	Rofecoxib	Placebo	-0.96188	-1.30623	-0.61754	Rofecoxib	Possibly clinically significant
WOMAC Stiffness	Fleischmann (2006)	WOMAC Stiffness	693	Yes	13	Lumiracoxib	Placebo	-0.36238	-0.52148	-0.20329	Lumiracoxib	Possibly clinically significant

	Fleischmann (2006)	WOMAC Stiffness	694	Yes	13	Lumiracoxib	Placebo	-0.27036	-0.42889	-0.11184	Lumiracoxib	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Stiffness	724	Yes	13	Celecoxib	Placebo	-0.17976	-0.3343	-0.02523	Celecoxib	Not clinically significant
	Tannenbaum (2004)	WOMAC Stiffness	730	Yes	13	Lumiracoxib	Placebo	-0.17263	-0.32682	-0.01843	Lumiracoxib	Not clinically significant
	Tannenbaum (2004)	WOMAC Stiffness	734	Yes	13	Lumiracoxib	Placebo	0	-0.15373	0.153728	NS	True negative
	Gibofsky (2003)	WOMAC Stiffness	285	Yes	6	Celecoxib	Placebo	-4.92792	-5.40363	-4.45221	Celecoxib	Clinically significant
	Gibofsky (2003)	WOMAC Stiffness	286	Yes	6	Rofecoxib	Placebo	-4.22771	-4.65426	-3.80116	Rofecoxib	Clinically significant
	Kivits (2002)	WOMAC Stiffness	406	Yes	6	Valdecoxib	Placebo	-0.12676	-0.32151	0.067988	NS	True negative
	Kivits (2002)	WOMAC Stiffness	410	Yes	6	Valdecoxib	Placebo	-0.23077	-0.42501	-0.03653	Valdecoxib	Possibly clinically significant
	Kivits (2002)	WOMAC Stiffness	406	Yes	6	Valdecoxib	Placebo	-0.23541	-0.43064	-0.04018	Valdecoxib	Possibly clinically significant
	Kivits (2002)	WOMAC Stiffness	406	Yes	12	Valdecoxib	Placebo	-0.11881	-0.31353	0.075918	NS	True negative
	Kivits (2002)	WOMAC Stiffness	410	Yes	12	Valdecoxib	Placebo	-0.16668	-0.36061	0.027253	NS	True negative
	Kivits (2002)	WOMAC Stiffness	406	Yes	12	Valdecoxib	Placebo	-0.1964	-0.39143	-0.00137	Valdecoxib	Possibly clinically significant

	Mckenna (2001)	WOMAC Stiffness	399	Yes	6	Celecoxib	Placebo	-0.39911	-0.59732	-0.2009	Celecoxib	Possibly clinically significant
	Ehrich (1999)	WOMAC Stiffness	145	No	6	Rofecoxib	Placebo	-1.09593	-1.44569	-0.74617	Rofecoxib	Clinically significant
WOMAC Total	Fleischmann (2006)	WOMAC Total	693	Yes	13	Lumiracoxib	Placebo	-0.47107	-0.63096	-0.31119	Lumiracoxib	Possibly clinically significant
	Fleischmann (2006)	WOMAC Total	694	Yes	13	Lumiracoxib	Placebo	-0.45161	-0.61127	-0.29194	Lumiracoxib	Possibly clinically significant
	Schnitzer (2010)	WOMAC Total	343	Yes	13	Naproxcinod	Placebo	-0.30757	-0.52305	-0.09209	Naproxcinod	Possibly clinically significant
	Schnitzer (2010)	WOMAC Total	333	Yes	13	Naproxcinod	Placebo	-0.35554	-0.57386	-0.13722	Naproxcinod	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Total	724	Yes	13	Celecoxib	Placebo	-0.25129	-0.40609	-0.09649	Celecoxib	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Total	730	Yes	13	Lumiracoxib	Placebo	-0.28334	-0.43797	-0.12872	Lumiracoxib	Possibly clinically significant
	Tannenbaum (2004)	WOMAC Total	734	Yes	13	Lumiracoxib	Placebo	-0.28217	-0.43657	-0.12776	Lumiracoxib	Possibly clinically significant
	Lehmann (2005)	WOMAC Total	844	Yes	13	Lumiracoxib	Placebo	-0.22095	-0.3563	-0.08561	Lumiracoxib	Not clinically significant

	Lehmann (2005)	WOMAC Total	844	Yes	13	Lumiracoxib	Placebo	-0.20165	-0.33693	-0.06638	Lumiracoxib	Not clinically significant
	Kivits (2002)	WOMAC Total	406	Yes	12	Valdecoxib	Placebo	-0.17728	-0.37222	0.017656	NS	True negative
	Kivits (2002)	WOMAC Total	410	Yes	12	Valdecoxib	Placebo	-0.20345	-0.39754	-0.00935	Valdecoxib	Not clinically significant
	Kivits (2002)	WOMAC Total	406	Yes	12	Valdecoxib	Placebo	-0.19789	-0.39292	-0.00286	Valdecoxib	Not clinically significant
	Kivits (2002)	WOMAC Total	406	Yes	6	Valdecoxib	Placebo	-0.13774	-0.33253	0.057042	NS	True negative
	Kivits (2002)	WOMAC Total	410	Yes	6	Valdecoxib	Placebo	-0.2076	-0.40172	-0.01348	Valdecoxib	Possibly clinically significant
	Kivits (2002)	WOMAC Total	406	Yes	6	Valdecoxib	Placebo	-0.24111	-0.43638	-0.04585	Valdecoxib	Possibly clinically significant
	Williams (2001)	WOMAC Total	484	Yes	6	Celecoxib	Placebo	-5.10879	-5.47781	-4.73978	Celecoxib	Clinically significant
	Williams (2001)	WOMAC Total	474	Yes	6	Celecoxib	Placebo	-5.59231	-5.9926	-5.19203	Celecoxib	Clinically significant
	Mckenna (2001)	WOMAC Total	399	Yes	6	Celecoxib	Placebo	-0.41279	-0.61113	-0.21445	Celecoxib	Possibly clinically significant
Global Assessment	Williams (2000)	Patient Global Assessment	453	Yes	6	Celecoxib 200mg	Placebo	-0.33159	-0.51707	-0.14611	Celecoxib 200mg	Not clinically significant

	Fleischmann (2006)	Patient Global Assessment	694	Yes	13	Lumiracoxib 400mg	Placebo	-0.34539	-0.50432	-0.18646	Lumiracoxib 400mg	Not clinically significant
	Fleischmann (2006)	Patient Global Assessment	693	Yes	13	Lumiracoxib 200mg	Placebo	-0.32586	-0.48473	-0.16699	Lumiracoxib 200mg	Not clinically significant
	Mckenna (2001)	Patient Global Assessment	399	Yes	6	Celecoxib	Placebo	-0.4335	-0.63206	-0.23495	Celecoxib	Not clinically significant
	Williams (2000)	Patient Global Assessment	462	Yes	6	Celecoxib 100mg	Placebo	-0.32841	-0.51202	-0.1448	Celecoxib 100mg	Not clinically significant
	Williams (2001)	Patient Global Assessment	484	Yes	6	Celecoxib 100mg	Placebo	-3.06211	-3.32529	-2.79893	Celecoxib 100mg	Clinically significant
	Williams (2001)	Patient Global Assessment	474	Yes	6	Celecoxib 200mg	Placebo	-6.11409	-6.54443	-5.68376	Celecoxib 200mg	Clinically significant
	Gibofsky (2003)	Patient Global Assessment	285	Yes	6	Celecoxib 200mg	Placebo	OR=2.50	1.47	4.26	Celecoxib 200mg	Clinically significant

	Gibofsky (2003)	Patient Global Assessment	286	Yes	6	Rofecoxib 25mg	Placebo	OR=2.04	1.2	3.49	Rofecoxib 25mg	Clinically significant
	Fleischmann (2006)	Physician Global Assessment	675	Yes	13	Celecoxib (Cox-2)	Placebo	-0.25204	-0.41161	-0.09247	Celecoxib (Cox-2)	Unclear
	Fleischmann (2006)	Physician Global Assessment	693	Yes	13	Lumiracoxib 200mg	Placebo	-0.35846	-0.51753	-0.1994	Lumiracoxib 200mg	Unclear
	Fleischmann (2006)	Physician Global Assessment	694	Yes	13	Lumiracoxib 400mg	Placebo	-0.34115	-0.50005	-0.18224	Lumiracoxib 400mg	Unclear
	Kivits (2002)	Physician Global Assessment	410	Yes	6	Valdecoxib 10mg (Cox-2)	Placebo	-0.2834	-0.47797	-0.08883	Valdecoxib 10mg (Cox-2)	Unclear
	Kivits (2002)	Physician Global Assessment	410	Yes	12	Valdecoxib 10mg (Cox-2)	Placebo	-0.28799	-0.48259	-0.09338	Valdecoxib 10mg (Cox-2)	Unclear
	Kivits (2002)	Physician Global Assessment	406	Unclear	6	Valdecoxib 20mg (Cox-2)	Placebo	-0.19324	-0.38825	0.001769	NS	Unclear

	Kivits (2002)	Physician Global Assessment	406	Yes	12	Valdecoxib 20mg (Cox-2)	Placebo	-0.22194	-0.4171	-0.02679	Valdecoxib 20mg (Cox-2)	Unclear
	Kivits (2002)	Physician Global Assessment	406	Yes	6	Valdecoxib 5mg (Cox-2)	Placebo	-0.22375	-0.41892	-0.02859	Valdecoxib 5mg (Cox-2)	Unclear
	Kivits (2002)	Physician Global Assessment	406	Yes	12	Valdecoxib 5mg (Cox-2)	Placebo	-0.19912	-0.39416	-0.00408	Valdecoxib 5mg (Cox-2)	Unclear
	Mckenna (2001)	Physician Global Assessment	399	Yes	6	Celecoxib (Cox-2)	Placebo	-0.3884	-0.5865	-0.19029	Celecoxib (Cox-2)	Unclear
	Williams (2001)	Physician Global Assessment	484	Yes	6	Celecoxib 100mg	Placebo	-4.99222	-5.35479	-4.62964	Celecoxib 100mg	Unclear
	Williams (2001)	Physician Global Assessment	474	Yes	6	Celecoxib 200mg	Placebo	-6.65607	-7.1181	-6.19404	Celecoxib 200mg	Unclear
	Gibofsky (2003)	Physician Global Assessment	285	Yes	6	Celecoxib 200mg	Placebo	OR=1.9 9	1.19	3.33	Celecoxib 200mg	Unclear

	Gibofsky (2003)	Physician Global Assessment	286	Unclear	6	Rofecoxib 25mg	Placebo	OR=1.59	0.95	2.66	NS	Unclear
	Lehmann (2005)	Patient Global Assessment of Disease	844	Yes	13	Celecoxib	Placebo	-0.1617	-0.29685	-0.02655	Celecoxib	Unclear
	Lehmann (2005)	Patient Global Assessment of Disease	844	Yes	13	Lumiracoxib	Placebo	-0.25402	-0.3895	-0.11855	Lumiracoxib	Unclear
	Tannenbaum (2004)	Patient Global Assessment of Disease	724	Yes	13	Celecoxib 200mg	Placebo	-0.25907	-0.41391	-0.10424	Celecoxib 200mg	Unclear
	Tannenbaum (2004)	Patient Global Assessment of Disease	730	Yes	13	Lumiracoxib 200mg	Placebo	-0.28128	-0.43589	-0.12666	Lumiracoxib 200mg	Unclear
	Tannenbaum (2004)	Patient Global Assessment of Disease	734	Yes	13	Lumiracoxib 400mg	Placebo	-0.33077	-0.48544	-0.17611	Lumiracoxib 400mg	Unclear

	Ehrich (1999)	Patient Global Assessment of Disease	145	Yes	6	Rofecoxib 125mg	Placebo	-1.21037	-1.56523	-0.85551	Rofecoxib 125mg	Unclear
	Ehrich (1999)	Patient Global Assessment of Disease	145	Yes	6	Rofecoxib 25mg	Placebo	-1.03651	-1.38379	-0.68923	Rofecoxib 25mg	Unclear
	Schnitzer (2005)	Patient Global Assessment of Disease	202	yes	6	Rofecoxib 25mg	Placebo	OR=2.7 4	1.55	4.85	Rofecoxib 25mg	Unclear
	Ehrich (1999)	Physician Global Assessment of Disease	145	Yes	6	Rofecoxib 125mg	Placebo	-1.24218	-1.59853	-0.88583	Rofecoxib 125mg	Unclear
	Ehrich (1999)	Physician Global Assessment of Disease	145	Yes	6	Rofecoxib 25mg	Placebo	-1.04206	-1.38957	-0.69455	Rofecoxib 25mg	Unclear
	Lehmann (2005)	Physician Global Assessment of Disease	844	Yes	13	Celecoxib 200mg	Placebo	-0.22744	-0.36281	-0.09208	Celecoxib 200mg	Unclear

	Lehmann (2005)	Physician Global Assessment of Disease	844	Yes	13	Lumiracoxib 100mg	Placebo	-0.26683	-0.40236	-0.1313	Lumiracoxib 100mg	Unclear
	Tannenbaum	Physician Global Assessment of Disease	724	Yes	13	Celecoxib 200mg	Placebo	-0.19281	-0.34739	-0.03823	Celecoxib 200mg	Unclear
	Tannenbaum	Physician Global Assessment of Disease	730	Yes	13	Lumiracoxib 200mg	Placebo	-0.21671	-0.37105	-0.06237	Lumiracoxib 200mg	Unclear
	Tannenbaum	Physician Global Assessment of Disease	734	Yes	13	Lumiracoxib 400mg	Placebo	-0.24974	-0.404	-0.09548	Lumiracoxib 400mg	Unclear
	Ehrich (1999)	Patient Global Assessment of Response to Treatment	145	Yes	6	Rofecoxib 125mg	Placebo	-1.4568	-1.82405	-1.08955	Rofecoxib 125mg	Unclear

	Ehrich (1999)	Patient Global Assessment of Response to Treatment	145	Yes	6	Rofecoxib 25mg	Placebo	-1.21549	-1.57058	-0.86039	Rofecoxib 25mg	Unclear
	Schnitzer (2005)	Patient Global Assessment of Response to Treatment	202	Yes	6	Rofecoxib 25mg	Placebo	OR=	2.45844 7	8.00969 1	Rofecoxib 25mg	Unclear
	Kivitz (2004)	Patient Global Assessment of Response to Treatment	625	Yes	6	Rofecoxib	Placebo	OR=	2.34679 2	4.84210 9	Rofecoxib 12.5mg	Unclear
	Gibofsky (2003)	Patient Global Assessment of Response to Treatment	285	Yes	6	Celecoxib 200mg	Placebo	OR=1.9 9	1.19	3.33	Celecoxib 200mg	Unclear

	Gibofsky (2003)	Patient Global Assessme nt of Response to Treatment	286	Unclear	6	Rofecoxib 25mg	Placebo	OR=1.5 9	0.95	2.66	NS	Unclear
	Ehrich (1999)	Physician Global Assessme nt of Response to Treatment	145	Yes	6	Rofecoxib 125mg	Placebo	-1.20414	-1.55871	-0.84957	Rofecoxib 125mg	Unclear
	Ehrich (1999)	Physician Global Assessme nt of Response to Treatment	145	Yes	6	Rofecoxib 25mg	Placebo	-1.09595	-1.4457	-0.74619	Rofecoxib 25mg	Unclear

Table 156. Cox-2s Versus Cox-2s

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
Function	Gibofsky (2003)	WOMAC Function improvement	379	Yes	6	Celecoxib 200mg	Rofecoxib	-0.14	-0.34	0.06	NS	True negative
	Lehmann (2005)	WOMAC Function improvement	844	Yes	13	Celecoxib 100mg	Lumiracoxib with loading dose	0.01	-0.13	0.14	NS	True negative
	Lehmann (2005)	WOMAC Function improvement	844	Yes	13	Lumiracoxib 100mg	Celecoxib	-0.02	-0.15	0.12	NS	True negative
	Lehmann (2005)	WOMAC Function improvement	844	Yes	13	Lumiracoxib 100mg	Lumiracoxib with loading dose	-0.01	-0.14	0.13	NS	True negative
	Schnitzer (2009)	WOMAC Function	206	No	4	Rofecoxib 12.5mg	Rofecoxib	0.21	-0.07	0.48	NS	Inconclusive
Lequesne index	Williams (2000)	Lequesne index	453	Unclear	6	Celecoxib 200mg	Celecoxib 100mg bid	-0.07	-0.25	0.12	NS	Unclear
	Williams (2001)	Lequesne index	472	Unclear	6	Celecoxib 100mg BID	Celecoxib 200mg qd	0	-0.18	0.18	NS	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
Pain	Lehmann (2005)	VAS Pain improvement	844	Yes	13	Celecoxib 100mg	Lumiracoxib with loading dose	-0.02	-0.15	0.12	NS	True negative
	Luyten (2007)	WOMAC Pain	120	Unclear	24	Continuous Celecoxib	Intermittent Celecoxib	Mean difference=0	p>0.05	-	NS	Unclear
	Gibofsky (2003)	VAS Pain on walking improvement	379	Yes	6	Celecoxib 200mg	Rofecoxib	-0.08	-0.28	0.12	NS	True negative
	Gibofsky (2003)	WOMAC Pain improvement	379	Yes	6	Celecoxib 200mg	Rofecoxib	-0.02	-0.23	0.18	NS	True negative
	Lehmann (2005)	WOMAC Pain improvement	844	Yes	13	Celecoxib 100mg	Lumiracoxib with loading dose	-0.05	-0.19	0.08	NS	True negative
	Lehmann (2005)	VAS Pain improvement	844	Yes	13	Lumiracoxib 100mg	Celecoxib	-0.01	-0.14	0.13	NS	True negative

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Lehmann (2005)	VAS Pain improvement	844	Yes	13	Lumirac oxib 100mg	Lumirac oxib with loading dose	-0.03	-0.16	0.11	NS	True negative
	Lehmann (2005)	WOMAC Pain improvement	844	Yes	13	Lumirac oxib 100mg	Celecoxib	0	-0.13	0.13	NS	True negative
	Lehmann (2005)	WOMAC Pain improvement	844	Yes	13	Lumirac oxib 100mg	Lumirac oxib with loading dose	-0.05	-0.19	0.08	NS	True negative
	Schnitzer (2009)	WOMAC Pain	209	Yes	4	Rofecoxib 12.5mg	Rofecoxib	0.17	-0.1	0.44	NS	Inconclusive
Stiffness	Gibofsky (2003)	WOMAC Stiffness improvement	379	Yes	6	Celecoxib 200mg	Rofecoxib	-1	-1.21	-0.78	Celecoxib 200mg	Clinically significant
	Lehmann (2005)	WOMAC Stiffness improvement	844	Yes	13	Celecoxib 100mg	Lumirac oxib with loading dose	0	-0.13	0.13	NS	True negative
	Lehmann (2005)	WOMAC Stiffness improvement	844	Yes	13	Lumirac oxib 100mg	Celecoxib	-0.11	-0.25	0.02	NS	True negative

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Lehmann (2005)	WOMAC Stiffness improvement	844	Yes	13	Lumiracoxib 100mg	Lumiracoxib with loading dose	-0.11	-0.24	0.03	NS	True negative
	Schnitzer (2009)	WOMAC Stiffness	208	No	4	Rofecoxib 12.5mg	Rofecoxib	0.19	-0.08	0.47	NS	True negative
	Luyten (2007)	WOMAC Stiffness	120	Unclear	24	Continuous Celecoxib	Intermittent Celecoxib	Mean Difference = 0	p>0.05	-	NS	Unclear
WOMAC Total	Williams (2000)	WOMAC Total	453	Yes	6	Celecoxib 200mg	Celecoxib	0.04	-0.14	0.23	NS	True negative
	Williams (2001)	WOMAC Total	472	Yes	6	Celecoxib 100mg BID	Celecoxib 200mg qd	0.46	0.28	0.64	Celecoxib 200mg qd	Possibly clinically significant
	Lehmann (2005)	WOMAC Total	844	Yes	13	Celecoxib 100mg	Lumiracoxib with loading dose	0.01	-0.13	0.14	NS	True negative
	Lehmann (2005)	WOMAC Total	844	Yes	13	Lumiracoxib 100mg	Celecoxib	-0.03	-0.17	0.1	NS	True negative

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Lehmann (2005)	WOMAC Total	844	Yes	13	Lumiracoxib 100mg	Lumiracoxib with loading dose	-0.02	-0.16	0.11	NS	True negative
	Luyten (2007)	WOMAC Total	120	Unclear	24	Continuous Celecoxib	Intermittent Celecoxib	Mean Difference = 37	p>0.05	-	NS	Unclear
Global assessment	Williams (2000)	Patient Global Assessment	453	Unclear	6	Celecoxib 200mg	Celecoxib 100mg	0	-0.18	0.18	NS	True negative
	Fleischmann (2006)	Patient Global Assessment	906	Yes	13	Lumiracoxib 200mg	Celecoxib 200mg	-0.03	-0.16	0.1	NS	True negative
	Fleischmann (2006)	Patient Global Assessment	907	Yes	13	Lumiracoxib 400mg	Celecoxib 200mg	-0.05	-0.18	0.08	NS	True negative
	Williams (2000)	Patient Global Assessment	472	Yes	6	Celecoxib 100	Celecoxib 200mg	3.33	3.05	3.61	Celecoxib 200mg	Clinically significant

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Fleischmann (2006)	Patient Global Assessment	925	Yes	13	Lumiracoxib 200mg	Lumiracoxib 400mg	0.18	-0.11	0.15	NS	True negative
	Gibofsky (2003)	Patient Global Assessment	379	Unclear	6	Celecoxib 200mg	Rofecoxib 25mg	OR=1.223	0.816	1.833	NS	Unclear
	Fleischmann (2006)	Physician Global Assessment	906	Yes	13	Lumiracoxib 200mg	Celecoxib 200mg	-0.11	-0.24	0.02	NS	Unclear
	Fleischmann (2006)	Physician Global Assessment	907	Yes	13	Lumiracoxib 400mg	Celecoxib 200mg	-0.09	-0.22	0.04	NS	Unclear
	Fleischmann (2006)	Physician Global Assessment	925	Yes	13	Lumiracoxib 200mg	Lumiracoxib 400mg	-0.02	-0.15	0.11	NS	Unclear
	Williams (2001)	Physician Global Assessment	472	Yes	6	Celecoxib 100mg	Celecoxib 200mg	1.66	1.45	1.87	Celecoxib 200mg	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gibofsky (2003)	Physician Global Assessment	379	Unclear	6	Celecoxib 200mg	Rofecoxib 25mg	OR=1.249	0.833	1.87	NS	Unclear
	Lehmann (2005)	Patient Global Assessment of Disease	844	Yes	13	Lumiracoxib	Celecoxib	-0.09	-0.23	0.04	NS	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.01	-0.27	0.25	NS	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	-0.01	-0.27	0.25	NS	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.09	-0.18	0.36	NS	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Patient Global Assessment of Disease	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.36	0.1	0.62	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.27	0.01	0.53	Etoricoxib 90mg	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.1	-0.17	0.36	NS	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.37	0.1	0.63	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.28	0.01	0.54	Etoricoxib 90mg	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Patient Global Assessment of Disease	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.28	0.01	0.55	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.19	-0.08	0.46	NS	Unclear
	Gottesdiener (2002)	Patient Global Assessment of Disease	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.1	-0.36	0.17	NS	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	-0.01	-0.27	0.25	NS	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.09	-0.18	0.36	NS	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Physician Global Assessment of Disease	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.1	-0.17	0.36	NS	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.36	0.1	0.62	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.37	0.1	0.63	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.28	0.01	0.55	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.27	0.01	0.53	Etoricoxib 90mg	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Physician Global Assessment of Disease	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.28	0.01	0.54	Etoricoxib 90mg	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.19	-0.08	0.46	NS	Unclear
	Gottesdiener (2002)	Physician Global Assessment of Disease	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.1	-0.36	0.17	NS	Unclear
	Lehmann (2005)	Physician Global Assessment of Disease	844	Unclear	13	Lumiracoxib 100mg	Celecoxib 200mg	-0.04	-0.18	0.09	NS	Unclear
	Schnitzer (2009)	Patient Assessment of Treatment Response	209	Unclear	4	Rofecoxib 12.5mg	Rofecoxib 25mg	0.19	-0.08	0.46	NS	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Patient Assessment of Treatment Response	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	0.04	-0.22	0.29	NS	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.09	-0.17	0.36	NS	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.42	0.16	0.68	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.32	0.06	0.58	Etoricoxib 90mg	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Patient Assessment of Treatment Response	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.05	-0.21	0.32	NS	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.39	0.12	0.65	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.28	0.02	0.55	Etoricoxib 90mg	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.34	0.07	0.61	Etoricoxib 60mg	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Patient Assessment of Treatment Response	214	Unclear	6	Etoricoxi b 30mg	Etoricoxi b 90mg	0.23	-0.04	0.5	NS	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	224	Unclear	6	Etoricoxi b 60mg	Etoricoxi b 90mg	-0.1	-0.36	0.16	NS	Unclear
	Schnitzer (2005)	Patient Assessment of Treatment Response	782	Unclear	6	Celecoxi b 200mg	Rofecoxi b 12.5mg	OR= 1.051	0.78	1.416	NS	Unclear
	Schnitzer (2005)	Patient Assessment of Treatment Response	1050	Unclear	6	Celecoxi b 200mg	Rofecoxi b 25mg	OR= 0.827	0.649	1.054	NS	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Schnitzer (2005)	Patient Assessment of Treatment Response	786	Unclear	6	Rofecoxib 12.5mg	Rofecoxib 25mg	OR=0.786	0.584	1.059	NS	Unclear
	Gottesdiener (2002)	Patient Assessment of Treatment Response	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	0.04	-0.22	0.3	NS	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.09	-0.18	0.36	NS	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.05	-0.22	0.32	NS	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Physician Assessment of Treatment Response	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.37	0.11	0.63	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.33	0.07	0.59	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.28	0.01	0.55	Etoricoxib 60mg	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.31	0.05	0.57	Etoricoxib 90mg	Unclear

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors (NS=Not Significant)	Clinical Importance
	Gottesdiener (2002)	Physician Assessment of Treatment Response	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.27	0.01	0.53	Etoricoxib 90mg	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.23	-0.04	0.49	NS	Unclear
	Gottesdiener (2002)	Physician Assessment of Treatment Response	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.06	-0.32	0.2	NS	Unclear
	Schnitzer (2009)	Physician Assessment of Treatment Response	208	Unclear	4	Rofecoxib 12.5mg	Rofecoxib 25mg	0.17	-0.1	0.45	NS	Unclear

Table 157. NSAIDs Versus Placebo

Outcome Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=not Significant)	Clinical Importance
Additional Acetaminophen Use	Schnitzer (2010)	Rescue Acetaminophen	429	Unclear	12	Naproxen	Placebo	-0.28	-0.47	-0.09	Naproxen	Unclear
	Schnitzer (2010)	Rescue Acetaminophen	442	Unclear	13	Naproxen	Placebo	-0.22	-0.41	-0.03	Naproxen	Unclear
	Schnitzer (2010)	Rescue Acetaminophen	432	Unclear	13	Naproxen	Placebo	-0.53	-0.73	-0.33	Naproxen	Unclear
Function	Mckenna (2001)	WOMAC Function improvement	399	Yes	6	Diclofenac	Placebo	0.07	-0.15	0.29	Diclofenac	Possibly clinically significant
	Schnitzer (2010)	SF-36 MCS improvement	327	Unclear	12	Naproxen	Placebo	-0.52	-0.71	-0.33	NS	Unclear
	Schnitzer (2010)	WOMAC Function improvement	447	Yes	12	Naproxen	Placebo	-2	-2.55	-1.44	Naproxen	Possibly clinically significant
	Evcik (2003)	Health assessment questionnaire	76	Unclear	26	Tenoxicam	Placebo	0.11	-0.11	0.33	Tenoxicam	Unclear
	Schnitzer (2010)	SF-36 MCS improvement	337	Unclear	13	Naproxen	Placebo	0.09	-0.13	0.31	NS	Inconclusive
	Schnitzer (2010)	SF-36 MCS improvement	326	Unclear	13	Naproxen	Placebo	-0.03	-0.21	0.16	NS	Inconclusive
	Schnitzer (2010)	WOMAC Function	450	No	13	Naproxen	Placebo	-1.72	-2.25	-1.19		True negative
Lequesne index	Evcik (2003)	Lequesne index	76	Unclear	26	Tenoxicam	Placebo	-0.2	-0.39	0	Tenoxicam	Unclear

Pain	Kivits (2002)	VAS Pain	409	Yes	12	Naproxen	Placebo	-0.28	-0.48	-0.09	Naproxen	Not clinically significant
	Kivits (2002)	VAS Pain	409	Yes	6	Naproxen	Placebo	-0.48	-0.68	-0.28	Naproxen	Not clinically significant
	Mckenna (2001)	VAS Pain	399	Yes	6	Diclofenac	Placebo	-0.45	-0.64	-0.25	Diclofenac	Not clinically significant
	Mckenna (2001)	WOMAC Pain	399	Yes	6	Diclofenac	Placebo	-0.44	-0.66	-0.22	Diclofenac	Possibly clinically significant
	Schnitzer (2010)	VAS Pain	333	Yes	12	Naproxen	Placebo	-0.44	-0.66	-0.22	Naproxen	Not clinically significant
	Schnitzer (2010)	VAS Pain during walking improvement	333	Yes	12	Naproxen	Placebo	-1.68	-1.89	-1.46	Naproxen	Not clinically significant
	Schnitzer (2010)	WOMAC Pain	447	Yes	12	Naproxen	Placebo	-1.88	-2.42	-1.33	Naproxen	Clinically significant
	Evcik (2003)	VAS Ascending stairs	76	Yes	26	Tenoxicam	Placebo	-1.68	-2.21	-1.15	Tenoxicam	Clinically significant
	Evcik (2003)	VAS Descending stairs	76	Yes	26	Tenoxicam	Placebo	-1.36	-1.86	-0.86	Tenoxicam	Possibly clinically significant
	Evcik (2003)	VAS Walking	76	Yes	26	Tenoxicam	Placebo	-0.95	-1.42	-0.47	Tenoxicam	Possibly clinically significant
	Evcik (2003)	VAS At rest	76	Yes	26	Tenoxicam	Placebo	-0.25	-0.47	-0.04	Tenoxicam	Possibly clinically significant
	Schnitzer (2010)	VAS Pain at rest improvement	341	Yes	13	Naproxeno d 375mg	Placebo	-0.33	-0.55	-0.11	Naproxeno d	Not clinically significant

	Schnitzer (2010)	VAS Pain at rest improvement	330	Yes	13	Naproxcinod 750mg	Placebo	-0.28	-0.5	-0.06	Naproxcinod	Not clinically significant
	Schnitzer (2010)	VAS Pain during walking improvement	341	Yes	13	Naproxcinod 375mg	Placebo	-0.38	-0.6	-0.16	Naproxcinod	Not clinically significant
	Schnitzer (2010)	VAS Pain during walking	330	Yes	13	Naproxcinod 750mg	Placebo	-1.49	-1.7	-1.28	Naproxcinod	Not clinically significant
	Schnitzer (2010)	WOMAC Pain	461	Yes	13	Naproxcinod 375mg	Placebo	-1.55	-1.76	-1.34	Naproxcinod	Clinically significant
	Schnitzer (2010)	WOMAC Pain	450	Yes	13	Naproxcinod 750mg	Placebo	-0.22	-0.41	-0.02	Naproxcinod	Clinically significant
Stiffness	Kivits (2002)	WOMAC Stiffness	409	Yes	6	Naproxen	Placebo	-0.24	-0.44	-0.05	Naproxen	Possibly clinically significant
	Kivits (2002)	WOMAC Stiffness	409	Yes	12	Naproxen	Placebo	-0.57	-0.77	-0.37	Naproxen	Possibly clinically significant
	Mckenna (2001)	WOMAC Stiffness	399	Yes	6	Diclofenac	Placebo	-0.22	-0.42	-0.03	Diclofenac	Possibly clinically significant
WOMAC Total	Kivits (2002)	WOMAC Total	409	Yes	6	Naproxen	Placebo	-0.24	-0.43	-0.05	Naproxen	Possibly clinically significant
	Kivits (2002)	WOMAC Total	409	Yes	12	Naproxen	Placebo	-0.54	-0.74	-0.34	Naproxen	Possibly clinically significant
	Mckenna (2001)	WOMAC Total	399	Yes	6	Diclofenac	Placebo	-0.48	-0.7	-0.26	Diclofenac	Possibly clinically significant

	Schnitzer	WOMAC Total	332	Yes	12	Naproxen	Placebo	-0.28	-0.47	-0.09	Naproxen	Possibly clinically significant

Table 158. NSAIDs Versus NSAIDs

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
Function	Bradely (1993)	HAQ Disability	122	Unclear	4	Ibuprofen 300mg	Ibuprofen 600mg	-0.07	-0.42	0.29	NS	Unclear
	Bellamy (1993)	WOMAC Function	98	Unclear	12	Tenoxicam	Diclofenac	Mean difference =2.47	p>.05	-	NS	Unclear
	Ayral (2003)	WOMAC Function	416	No	52	Tenidap 120mg	Piroxicam 20mg	-0.07	-0.26	0.12	NS	Unclear
	Bradely (1993)	Health Assessment Questionnaire (HAQ)	122	Unclear	4	Ibuprofen 300mg	Ibuprofen 600	-0.06	-0.41	0.3	NS	Unclear
	Herrera (2007)	WOMAC Function	62	Unclear	4	Diclofenac CR 100mg	Diclofenac IR 50mg	Mean difference = 3.69	p>.05	-	NS	Unclear
	Schnitzer (2010)	WOMAC Function	455	Yes	13	Naproxcinod 750mg	Naproxen	0.12	-0.06	0.31	NS	True negative
	Schnitzer (2010)	WOMAC Function	465	Yes	13	Naproxcinod 375mg	Naproxen	0.18	0	0.36	NS	True negative

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Schnitzer (2010)	SF-36 MCS	369	Unclear	13	Naproxcinod 750mg	Naproxen	0.09	-0.11	0.3	NS	Unclear
	Schnitzer (2010)	SF-36 MCS	380	Unclear	13	Naproxcinod 375mg	Naproxen	0.11	-0.09	0.31	NS	Unclear
Function-Task	Bradely (1993)	Walk time (seconds)	122	Unclear	4	Ibuprofen 300mg	Ibuprofen 600	0.06	-0.3	0.41	NS	Unclear
	Kogstad (1981)	Sequence A ability to walk (VAS)	156	Yes	4	Piroxicam 20mg	Naproxen 250mg	-0.39	-0.71	-0.07	Piroxicam 20mg	Unclear
	Kogstad (1981)	Sequence B ability to walk (VAS)	142	Yes	4	Piroxicam 20mg	Naproxen 250mg	1.33	0.96	1.69	Naproxen 250mg	Unclear
	Karbowski (1991)	Time to walk 50ft	61	Unclear	6	Etodolac 300mg	Indomethacin 50mg	Mean Difference = 0.5	p>0.05	-	NS	Unclear
	Dick (1992)	Time to walk 50ft	116	Unclear	6	Etodolac 300mgx2	Piroxicam 20mg	Mean difference =-.1	p>0.05	-	NS	Unclear

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Astorga (1991)	Time to walk 50ft	220	Unclear	6	Etodolac 300mg	Piroxicam 20mg	Mean difference = -0.1	p>0.05	-	NS	Unclear
	Astorga (1991)	Time to walk 50ft	220	Unclear	6	Etodolac 300mg	Piroxicam 20mg	Mean difference = -.5	p>.05	-	NS	Unclear
	Astorga (1991)	Time to walk 50ft	220	Unclear	6	Etodolac 300mg	Piroxicam 20mg	Mean difference = -.2	p>.05	-	NS	Unclear
	Liang (2003)	Change in Lequesne index	64	Unclear	4	Etodolac sustained-release 400mg	Diclofenac 50mg	0.01	-0.48	0.5	NS	Unclear
	Kogstad (1981)	Sequence A pain at night (VAS)	156	Yes	4	Piroxicam 20mg	Naproxen 250mg	-0.78	-1.11	-0.45	Piroxicam 20mg	Not clinically significant
	Kogstad (1981)	Sequence B pain at night (VAS)	142	Yes	4	Piroxicam 20mg	Naproxen 250mg	0.78	0.44	1.12	Naproxen 250mg	Not clinically significant

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Tyson (1980)	Linear analogue pain scale	105	Unclear	8	Benoxaprofen	Ibuprofen	Mean difference = 37	p>0.05	-	NS	Unclear
	Tyson (1980)	Linear analogue pain scale	105	Unclear	12	Benoxaprofen	Ibuprofen	Mean Difference = -9.78	p<.05	-	Ibuprofen	Unclear
	Tyson (1980)	Linear analogue pain scale	105	Unclear	16	Benoxaprofen	Ibuprofen	Mean Difference = -5.53	p>.05	-	NS	Unclear
	Bellamy (1993)	WOMAC Pain	98	Unclear	12	Tenoxicam	Diclofenac	1.288	p>.05	-	NS	Unclear
	Ayral (2003)	WOMAC Pain	434	Yes	52	Tenidap 40mg	Tenidap 120mg	0.01	-0.17	0.2	NS	True negative
	Ayral (2003)	WOMAC Pain	437	Yes	52	Tenidap 40mg	Piroxicam 20mg	0.02	-0.17	0.21	NS	True negative
	Ayral (2003)	WOMAC Pain	427	Yes	52	Tenidap 120mg	Piroxicam 20mg	0.01	-0.18	0.2	NS	True negative
	Queiros (1990)	Pain at night (1 to 4)	60	Unclear	4	Piroxicam 20mg	Oxaprozin 1200mg	0	-0.51	0.51	NS	True negative
	Queiros (1990)	Walk pain in evening	60	Unclear	4	Piroxicam 20mg	Oxaprozin 1200mg	-0.31	-0.82	0.2	NS	True negative

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Queiros (1990)	Walk pain in the morning	60	Unclear	4	Piroxicam 20mg	Oxaprozin 1200mg	-0.37	-0.88	0.15	NS	True negative
	Kogstad (1981)	Sequence A pain on movement (VAS)	156	Yes	4	Piroxicam 20mg	Naproxen 250mg	-1	-1.33	-0.66	Piroxicam 20mg	Possibly clinically significant
	Kogstad (1981)	Sequence B pain on movement (VAS)	142	Yes	4	Piroxicam 20mg	Naproxen 250mg	0.99	0.65	1.34	Naproxen 250mg	Possibly clinically significant
	La Montagna (1998)	Present pain index	106	Unclear	12	Piroxicam-beta-cyclodextrin 20mg	Diclofenac 100mg	0.17	-0.21	0.56	NS	Unclear
	La Montagna (1998)	present pain index	106	Unclear	24	Piroxicam-beta-cyclodextrin 20mg	Diclofenac 100mg	0.2	-0.19	0.58	NS	Unclear
	La Montagna (1998)	VAS Pain	106	Unclear	12	Piroxicam-beta-cyclodextrin 20mg	Diclofenac 100mg	0.14	-0.24	0.53	NS	True negative

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	La Montagna (1998)	VAS Pain	106	Unclear	24	Piroxicam-beta-cyclodextrin20mg	Diclofenac 100mg	-0.02	-0.4	0.36	NS	True negative
	Herrera (2007)	VAS Pain	62	Unclear	4	Diclofenac CR 100mg	Diclofenac IR 50mg	Mean difference = 4.35	p=.334	-	NS	Unclear
	Herrera (2007)	WOMAC Pain	62	Unclear	4	Diclofenac CR 100mg	Diclofenac IR 50mg	Mean difference = 0.73	p>.05	-	NS	Unclear
	Chubick (1987)	Improved Afternoon weight bearing pain	173	Unclear	4	Sulindac 300-400mg QD	Sulindac 300-400mg BID	OR=1.73	0.76	3.92	NS	Unclear
	Chubick (1987)	Improved night pain	173	Unclear	4	Sulindac 300-400mg QD	Sulindac 300-400mg BID	OR=1.42	0.64	3.12	NS	Unclear
	Chubick (1987)	Improved tenderness	173	Unclear	4	Sulindac 300-400mg QD	Sulindac 300-400mg BID	OR=1.30	0.69	2.47	NS	Unclear

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Chubick (1987)	Improved afternoon weight bearing pain	173	Unclear	4	Sulindac 300-400mg QD	Sulindac 300-400mg BID	OR=1.73	0.76	3.92	NS	Unclear
	Schnitzer (2010)	WOMAC Pain	455	Yes	13	Naproxcinod 750mg	Naproxen	0.08	-0.1	0.27	NS	True negative
	Schnitzer (2010)	WOMAC Pain	466	Yes	13	Naproxcinod 375mg	Naproxen	0.12	-0.07	0.3	NS	True negative
	Schnitzer (2010)	VAS Pain during walking	375	Yes	13	Naproxcinod 750mg	Naproxen	-0.38	-0.59	-0.18	Naproxi nod	Not clinically important
	Schnitzer (2010)	VAS Pain during walking	386	Yes	13	Naproxcinod 375mg	Naproxen	-0.28	-0.48	-0.08	Naproxi nod	Not clinically important
	Schnitzer (2010)	VAS Pain at rest	375	Yes	13	Naproxcinod 750mg	Naproxen	-0.33	-0.54	-0.13	Naproxi nod	Not clinically important
	Schnitzer (2010)	VAS Pain at rest	386	Yes	13	Naproxcinod 375mg	Naproxen	-0.25	-0.45	-0.05	Naproxi nod	Not clinically important

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Chubick (1987)	Afternoon weight bearing pain	173	Unclear	4	Sulindac 300-400mg QD	Sulindac 300-400mg BID	OR=1.33	0.53	3.35	NS	Unclear
Stiffness	Herrera (2007)	WOMAC Stiffness	62	Unclear	4	Diclofenac CR 100mg	Diclofenac IR 50mg	Mean difference = 0.71	p>.05	-	NS	Unclear
	Karbowski (1991)	Morning stiffness	61	Unclear	6	Etodolac 300mg	Indomethacin 50mg	Mean difference = -1.6	p>.05	-	NS	Unclear
	Dick (1992)	Morning stiffness	116	Unclear	6	Etodolac 300mgx2	Piroxicam 20mg	Mean difference = -10.3	p>0.05	-	NS	Unclear
	Astorga (1991)	Morning stiffness	220	Unclear	4	Etodolac 300mg	Piroxicam 20mg	Mean difference = -2.6	p>0.05	-	NS	Unclear
	Astorga (1991)	Morning stiffness	220	Unclear	6	Etodolac 300mg	Piroxicam 20mg	Mean difference = -1.4	p>0.05	-	NS	Unclear

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Astorga (1991)	Morning stiffness	220	Unclear	8	Etodolac 300mg	Piroxicam 20mg	Mean difference = -2	p>0.05	-	NS	Unclear
	Astorga (1991)	Morning stiffness	220	Unclear	final follow-up	Etodolac 300mg	Piroxicam 20mg	Mean difference = -2.6	p>0.05	-	NS	Unclear
	Bellamy (1993)	WOMAC Stiffness	98	Unclear	12	Tenoxicam	Diclofenac	2.636	p>.05	-	NS	Unclear
	Ayral (2003)	WOMAC Stiffness	435	Yes	52	Tenidap 40mg	Tenidap 120mg	0.03	-0.16	0.22	NS	True negative
	Ayral (2003)	WOMAC Stiffness	438	Yes	52	Tenidap 40mg	Piroxicam 20	0.01	-0.18	0.2	NS	True negative
	Ayral (2003)	WOMAC Stiffness	429	Yes	52	Tenidap 120mg	Piroxicam 20	-0.02	-0.21	0.17	NS	True negative
WOMAC Total	Herrera (2007)	WOMAC Total	62	Unclear	4	Diclofenac CR 100mg	Diclofenac IR 50mg	Mean difference = 4.74	p=.334	-	NS	Unclear
	Ayral (2003)	WOMAC Total	415	Yes	52	Tenidap 40mg	Tenidap 120mg	0.06	-0.13	0.25	NS	True negative

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Ayral (2003)	WOMAC Total	418	Yes	52	Tenidap 40mg	Piroxicam 20	0.04	-0.15	0.23	NS	True negative
	Ayral (2003)	WOMAC Total	411	Yes	52	Tenidap 120mg	Piroxicam 20	-0.02	-0.21	0.17	NS	True negative
	Schnitzer (2010)	WOMAC total	375	yes	13	Naproxcinod 750mg	Naproxen	0.13	-0.08	0.33	NS	True negative
	Schnitzer (2010)	WOMAC total	385	yes	13	Naproxcinod 375mg	Naproxen	0.17	-0.03	0.37	NS	True negative
Global Assessment	Ayral (2003)	Patient Global Assessment	436	Unclear	52	Tenidap 40mg	Piroxicam 20mg	0.02	-0.17	0.21	NS	Moderate
	Ayral (2003)	Patient Global Assessment	427	Unclear	52	Tenidap 120mg	Piroxicam 20mg	-0.05	-0.24	0.14	NS	Moderate
	Ayral (2003)	Patient Global Assessment	431	Unclear	52	Tenidap 40mg	Tenidap 120mg	0.07	-0.12	0.26	NS	Moderate
	Ayral (2003)	Physician Global Assessment	440	Unclear	52	Tenidap 40mg	Piroxicam 20mg	0.01	-0.17	0.2	NS	Moderate
	Ayral (2003)	Physician Global Assessment	435	Unclear	52	Tenidap 120mg	Piroxicam 20mg	-0.04	-0.22	0.15	NS	Moderate

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Ayral (2003)	Physician Global Assessment	437	Unclear	52	Tenidap 40mg	Tenidap 120mg	0.05	-0.14	0.24	NS	Moderate
	Schnitzer (2010)	Patient Global Assessment of Disease	465	Unclear	13	Naproxen	Naproxcinod 375mg	-0.03	-0.21	0.16	NS	Moderate
	Schnitzer (2010)	Patient Global Assessment of Disease	454	Unclear	13	Naproxen	Naproxcinod 750mg	-0.02	-0.2	0.17	NS	Moderate
	Schnitzer (2005)	Patient Global Assessment of Disease	212	Unclear	6	Naproxcinod 125mg	Naproxcinod 375mg	OR=0.658	0.38	1.13	NS	Moderate
	Schnitzer (2005)	Patient Global Assessment of Disease	219	Yes	6	Naproxcinod 125mg	Naproxcinod 750mg	OR=0.471	0.28	0.81	Naproxcinod 750mg	Unclear
	Schnitzer (2005)	Patient Global Assessment of Disease	222	Yes	6	Naproxcinod 125mg	Naproxen 500mg	OR=0.540	0.32	0.92	Naproxen 500mg	Unclear
	Schnitzer (2005)	Patient Global Assessment of Disease	221	Unclear	6	Naproxcinod 375mg	Naproxcinod 750mg	OR=0.717	0.42	1.22	NS	Moderate

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Schnitzer (2005)	Patient Global Assessment of Disease	224	Unclear	6	Naproxcinod 375mg	Naproxen 500mg	OR=0.821	0.48	1.39	NS	Moderate
	Schnitzer (2005)	Patient Global Assessment of Disease	231	Unclear	6	Naproxcinod 750mg	Naproxen 500mg	OR=1.146	0.68	1.94	NS	Moderate
	Schnitzer (2010)	Patient Global Assessment of Disease Status	454	Unclear	13	Naproxcinod 750mg	Naproxen	0.06	-0.13	0.24	NS	True negative
	Schnitzer (2010)	Patient Global Assessment of Disease Status	465	Unclear	13	Naproxcinod 375mg	Naproxen	0.05	-0.13	0.23	NS	True negative
	Schnitzer (2005)	Patient Assessment of Treatment Response	212	Yes	6	Naproxcinod 125mg	Naproxcinod 375mg	OR=0.564	0.33	0.97	Naproxcinod 375mg	Unclear
	Schnitzer (2005)	Patient Assessment of Treatment Response	219	Yes	6	Naproxcinod 125mg	Naproxcinod 750mg	OR=0.420	0.24	0.72	Naproxcinod 750mg	Unclear

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Schnitzer (2005)	Patient Assessment of Treatment Response	221	Unclear	6	Naproxcinod 375mg	Naproxcinod 750mg	OR=0.744	0.44	1.27	NS	Moderate
	Schnitzer (2005)	Patient Assessment of Treatment Response	222	Yes	6	Naproxcinod 125mg	Naproxen 500mg	OR=0.360	0.21	0.62	Naproxen 500mg	Unclear
	Schnitzer (2005)	Patient Assessment of Treatment Response	224	Unclear	6	Naproxcinod 375mg	Naproxen 500mg	OR=0.639	0.37	1.1	NS	Moderate
	Schnitzer (2005)	Patient Assessment of Treatment Response	231	Unclear	6	Naproxcinod 750mg	Naproxen 500mg	OR=0.858	0.5	1.47	NS	Moderate
	Lohmander (2005)	Patient Assessment of Treatment Response	828	Yes	6	Naproxcinod	Naproxen	OR=1.042	0.77	1.42	NS	Low
Rescue Medicine	Schnitzer (2010)	Rescue acetaminophen	441	Unclear	13	Naproxcinod 750mg	Naproxen	-0.22	-0.4	-0.03	Naproxcinod	Unclear

Type	Study	Outcome	N	Sufficient Power	Week	Group 1	Group 2	SMD	LCI (or p value)	UCI	Favors	Clinical Importance
	Schnitzer (2010)	Rescue acetaminophen	451	Unclear	13	Naproxcinod 375mg	Naproxen	-0.28	-0.47	-0.09	Naproxi nod	Unclear

Table 159. Cox-2s Versus NSAIDs

	Study	Outcome	N	Power	Week	Cox-2	NSAID	ES	LCI	UCI	Favors	Clinical Importance
Function	Mckenna (2001)	WOMAC Function	398	Yes	6	Celecoxib 100mg	Diclofenac 100mg	0.14	-0.05	0.34	NS	True negative
Pain	Mckenna (2001)	WOMAC Pain	398	Yes	6	Celecoxib 100mg	Diclofenac 100mg	0.07	-0.12	0.27	NS	True negative
	Mckenna (2001)	VAS Pain	398	Yes	6	Celecoxib 100mg	Diclofenac 100mg	0.07	-0.13	0.26	NS	True negative
	Lücker (1994)	VAS Pain	186	Yes	4	Nimesulide 100mg	Etodolac	0.15	-0.14	0.43	NS	True negative
	Lücker (1994)	VAS Pain	180	Yes	8	Nimesulide 100mg	Etodolac	0.06	-0.23	0.36	NS	True negative
	Lücker (1994)	VAS Pain	167	Yes	12	Nimesulide 100mg	Etodolac	-0.08	-0.38	0.22	NS	True negative
	Kivits (2002)	VAS Pain	409	Yes	12	Valdecoxib 5mg	Naproxen 5mg	0.06	-0.13	0.25	NS	True negative
	Kivits (2002)	VAS Pain	409	Yes	6	Valdecoxib 5mg	Naproxen 5mg	0.07	-0.12	0.27	NS	True negative
	Kivits (2002)	VAS Pain	405	Yes	12	Valdecoxib 5mg	Naproxen 5mg	-0.04	-0.23	0.16	NS	True negative
	Kivits (2002)	VAS Pain	405	Yes	6	Valdecoxib 5mg	Naproxen 5mg	-0.02	-0.21	0.18	NS	True negative
	Kivits (2002)	VAS Pain	405	Yes	12	Valdecoxib 5mg	Naproxen 5mg	0.02	-0.18	0.21	NS	True negative
	Kivits (2002)	VAS Pain	405	Yes	6	Valdecoxib 5mg	Naproxen 5mg	0.04	-0.16	0.23	NS	True negative

	Study	Outcome	N	Power	Week	Cox-2	NSAID	ES	LCI	UCI	Favors	Clinical Importance
Stiffness	Mckenna (2001)	WOMAC Stiffness	398	Yes	6	Celecoxib 100mg	Diclofenac 100mg	0.17	-0.03	0.36	NS	True negative
	Kivits (2002)	WOMAC Stiffness	409	Yes	6	Valdecoxib 10mg	Naproxen 10mg	-0.01	-0.21	0.18	NS	True negative
	Kivits (2002)	WOMAC Stiffness	409	Yes	12	Valdecoxib 10mg	Naproxen 10mg	0.07	-0.12	0.27	NS	True negative
	Kivits (2002)	WOMAC Stiffness	405	Yes	12	Valdecoxib 20mg	Naproxen 20mg	0.05	-0.15	0.24	NS	True negative
	Kivits (2002)	WOMAC Stiffness	405	Yes	6	Valdecoxib 20mg	Naproxen 20mg	-0.02	-0.21	0.18	NS	True negative
	Kivits (2002)	WOMAC Stiffness	405	Yes	12	Valdecoxib 5mg	Naproxen 5mg	0.12	-0.08	0.31	NS	True negative
	Kivits (2002)	WOMAC Stiffness	405	Yes	6	Valdecoxib 5mg	Naproxen 5mg	0.09	-0.1	0.29	NS	True negative
WOMAC Total	Mckenna (2001)	WOMAC Total	398	Yes	6	Celecoxib 100mg	Diclofenac 100mg	0.14	-0.05	0.34	NS	True negative
	Kivits (2002)	WOMAC Total	409	Yes	12	Valdecoxib 10mg	Naproxen 10mg	0.04	-0.16	0.23	NS	True negative
	Kivits (2002)	WOMAC Total	409	Yes	6	Valdecoxib 10mg	Naproxen 10mg	0.01	-0.18	0.21	NS	True negative
	Kivits (2002)	WOMAC Total	405	Yes	6	Valdecoxib 20mg	Naproxen 20mg	-0.02	-0.21	0.18	NS	True negative
	Kivits (2002)	WOMAC Total	405	Yes	12	Valdecoxib 20mg	Naproxen 20mg	0.04	-0.15	0.24	NS	True negative
	Kivits (2002)	WOMAC Total	405	Yes	12	Valdecoxib 5mg	Naproxen 5mg	0.06	-0.13	0.26	NS	True negative

	Study	Outcome	N	Power	Week	Cox-2	NSAID	ES	LCI	UCI	Favors	Clinical Importance
	Kivits (2002)	WOMAC Total	405	Yes	6	Valdecoxib 5mg	Naproxen 5mg	0.08	-0.11	0.28	NS	True negative
Lequesne index	Lücker (1994)	Lequesne index	186	Unclear	4	Nimesulide 100mg	Etodolac	0.12	-0.17	0.41	NS	Unclear
	Lücker (1994)	Lequesne index	180	Unclear	8	Nimesulide 100mg	Etodolac	0.1	-0.19	0.4	NS	Unclear
	Lücker (1994)	Lequesne index	167	Unclear	12	Nimesulide 100mg	Etodolac	0	-0.31	0.3	NS	Unclear
Global Assessment	Mckenna (2001)	Patient Global Assessment	398	Unclear	6	Celecoxib	Diclofenac	-0.09	-0.29	0.11	NS	Unclear
	Kivits (2002)	Physician Global Assessment	409	Unclear	6	Valdecoxib 10mg	Naproxen	-0.05	-0.24	0.14	NS	Unclear
	Kivits (2002)	Physician Global Assessment	409	Unclear	12	Valdecoxib 10mg	Naproxen	-0.08	-0.28	0.11	NS	Unclear
	Kivits (2002)	Physician Global Assessment	405	Unclear	6	Valdecoxib 20mg	Naproxen	0.04	-0.15	0.24	NS	Unclear
	Kivits (2002)	Physician Global Assessment	405	Unclear	12	Valdecoxib 20mg	Naproxen	-0.02	-0.21	0.18	NS	Unclear
	Kivits (2002)	Physician Global Assessment	405	Unclear	6	Valdecoxib 5mg	Naproxen	0.01	-0.18	0.2	NS	Unclear

	Study	Outcome	N	Power	Week	Cox-2	NSAID	ES	LCI	UCI	Favors	Clinical Importance
	Kivits (2002)	Physician Global Assessment	405	Unclear	12	Valdecoxib 5mg	Naproxen	0	-0.19	0.19	NS	Unclear
	Mckenna (2001)	Physician Global Assessment	398	Yes	6	Celecoxib	Diclofenac (NSAID)	0.2	0	0.4	Diclofenac (NSAID)	Unclear
	Schnitzer (2005)	Patient Global Assessment of Disease responders	203	Yes	6	Rofecoxib 25mg	Naproxen 125mg	OR= 1.93	1.11	3.38	Rofecoxib 25mg	Unclear
	Schnitzer (2005)	Patient Global Assessment of Disease responders	205	Unclear	6	Rofecoxib 25mg	Naproxen 375mg	OR= 1.27	0.73	2.21	NS	Unclear
	Schnitzer (2005)	Patient Global Assessment of Disease responders	212	Unclear	6	Rofecoxib 25mg	Naproxen 750mg	OR= 0.91	0.52	1.58	NS	Unclear

	Study	Outcome	N	Power	Week	Cox-2	NSAID	ES	LCI	UCI	Favors	Clinical Importance
	Schnitzer (2005)	Patient Assessment of Treatment Response (good or excellent)	203	Yes	6	Rofecoxib 25mg	Naproxcinod 125mg	OR= 2.98	1.68	5.29	Rofecoxib 25mg	Unclear
	Schnitzer (2005)	Patient Assessment of Treatment Response (good or excellent)	205	Unclear	6	Rofecoxib 25mg	Naproxcinod 375mg	OR= 1.68	0.95	2.97	NS	Unclear
	Schnitzer (2005)	Patient Assessment of Treatment Response (good or excellent)	212	Unclear	6	Rofecoxib 25mg	Naproxcinod 750mg	OR= 1.25	0.71	2.2	NS	Unclear
	Kivitz (2004)	Patient Assessment of Treatment Response (good or excellent)	823	Yes	6	Rofecoxib 12.5mg	Nabumetone	OR= 1.37 1	1.04 2	1.80 3	Rofecoxib 12.5mg	Unclear

Table 160. Topical NSAIDs Versus Control

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors	Clinical Significance
Concomitant Cedecine	Bookman (2004)	Acetaminophen consumption	163	Unclear	4	Topical Diclofenac	Vehicle control	-0.23	-0.54	0.08	NS	Unclear
	Bookman (2004)	Acetaminophen consumption	168	Unclear	4	Topical Diclofenac	Placebo	-0.3	-0.61	0	NS	Unclear
	Barthel (2009)	Weeks with No rescue drug	491	Yes	12	Diclofenac sodium 1% gel in DMSO	DMSO vehicle	0.2	0.02	0.38	Diclofenac sodium 1% gel in DMSO	Unclear
	Bookman (2004)	Acetaminophen consumption	163	Unclear	4	Topical Diclofenac	Vehicle control	-0.23	-0.54	0.08	NS	Unclear
	Bookman (2004)	Acetaminophen consumption	168	Unclear	4	Topical Diclofenac	Placebo	-0.3	-0.61	0	NS	Unclear
	Barthel (2009)	Weeks with No rescue drug	491	Yes	12	Diclofenac sodium 1% gel in DMSO	DMSO vehicle	0.2	0.02	0.38	Diclofenac sodium 1% gel in DMSO	Unclear
Function	Roth (2004)	WOMAC Function	321	Yes	12	Topical Diclofenac	Vehicle control	-0.36	-0.58	-0.14	Topical Diclofenac	Possibly clinically significant
	Baer (2005)	WOMAC Function	212	Yes	6	Pennsaid (topical Diclofenac solution)	Vehicle control solution	-0.44	-0.71	-0.16	Pennsaid (topical Diclofenac solution)	Possibly clinically significant
	Bookman (2004)	WOMAC Function	168	Yes	4	Topical Diclofenac	Placebo	-0.37	-0.67	-0.06	Topical Diclofenac	Possibly clinically significant

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors	Clinical Significance
	Bookman (2004)	WOMAC Function	163	Yes	4	Topical Diclofenac	Vehicle control	-0.43	-0.74	-0.12	Topical Diclofenac	Possibly clinically significant
	Rother (2007)	WOMAC Function	270	Yes	6	Topical ketoprofen	Celecoxib	0.1	-0.14	0.33	NS	True negative
	Rother (2007)	WOMAC Function	265	Yes	6	Topical ketoprofen	Placebo	-0.21	-0.45	0.03	NS	Inconclusive
	Rother (2007)	WOMAC Function	259	Yes	6	Celecoxib	Placebo	-0.31	-0.56	-0.07	Celecoxib	Possibly clinically significant
	Bookman (2004)	WOMAC Function	168	Yes	4	Topical Diclofenac	Placebo	-0.37	-0.67	-0.06	Topical Diclofenac	Possibly clinically significant
	Bookman (2004)	WOMAC Function	163	Yes	4	Topical Diclofenac	Vehicle control	-0.43	-0.74	-0.12	Topical Diclofenac	Possibly clinically significant
Pain	Roth (2004)	WOMAC Pain	322	Yes	12	Topical Diclofenac	Vehicle control	-0.35	-0.57	-0.13	Topical Diclofenac	Possibly clinically significant
	Roth (2004)	WOMAC Pain on walking	322	Yes	12	Topical Diclofenac	Vehicle control	-0.28	-0.5	-0.07	Topical Diclofenac	Unclear
	Baer (2005)	WOMAC Pain	212	Yes	6	Pennsaid (topical Diclofenac solution)	Vehicle control solution	-0.41	-0.68	-0.13	Pennsaid (topical Diclofenac solution)	Possibly clinically significant

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors	Clinical Significance
	Baer (2005)	WOMAC Pain on walking	212	Yes	6	Pennsaid (topical Diclofenac solution)	Vehicle control solution	-0.35	-0.62	-0.08	Pennsaid (topical Diclofenac solution)	Unclear
	Ottillinger (2001)	VAS Pain	118	Yes	4	Eltenac gel 0.3%	Eltenac gel 0.1%	-0.11	-0.47	0.25	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	5	Eltenac gel 0.3%	Eltenac gel 0.1%	-0.15	-0.51	0.21	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	6	Eltenac gel 0.3%	Eltenac gel 0.1%	-0.1	-0.46	0.26	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	4	Eltenac gel 1%	Eltenac gel 0.3%	-0.18	-0.54	0.19	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	4	Eltenac gel 1%	Eltenac gel 0.1%	-0.29	-0.66	0.07	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	5	Eltenac gel 1%	Eltenac gel 0.3%	-0.12	-0.49	0.24	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	5	Eltenac gel 1%	Eltenac gel 0.1%	-0.28	-0.65	0.08	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	6	Eltenac gel 1%	Eltenac gel 0.3%	-0.1	-0.46	0.27	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	6	Eltenac gel 1%	Eltenac gel 0.1%	-0.2	-0.56	0.17	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	4	Eltenac gel 0.1%	Placebo gel	0.17	-0.19	0.53	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	5	Eltenac gel 0.1%	Placebo gel	0.15	-0.21	0.52	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	6	Eltenac gel 0.1%	Placebo gel	0.06	-0.3	0.42	NS	True negative

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors	Clinical Significance
	Ottillinger (2001)	VAS Pain	118	Yes	4	Eltenac gel 0.3%	Placebo gel	0.06	-0.3	0.42	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	5	Eltenac gel 0.3%	Placebo gel	0	-0.36	0.36	NS	True negative
	Ottillinger (2001)	VAS Pain	118	Yes	6	Eltenac gel 0.3%	Placebo gel	-0.04	-0.4	0.32	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	4	Eltenac gel 1%	Placebo gel	-0.13	-0.5	0.23	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	5	Eltenac gel 1%	Placebo gel	-0.12	-0.49	0.24	NS	True negative
	Ottillinger (2001)	VAS Pain	116	Yes	6	Eltenac gel 1%	Placebo gel	-0.13	-0.5	0.23	NS	True negative
	Bookman (2004)	WOMAC Pain	163	Yes	4	Topical Diclofenac	Vehicle control	-0.34	-0.65	-0.03	Topical Diclofenac	Possibly clinically significant
	Bookman (2004)	WOMAC Pain	168	Yes	4	Topical Diclofenac	Placebo	-0.37	-0.68	-0.07	Topical Diclofenac	Possibly clinically significant
	Bookman (2004)	WOMAC Pain on walking	163	Yes	4	Topical Diclofenac	Vehicle control	-0.47	-0.79	-0.16	Topical Diclofenac	Unclear
	Bookman (2004)	WOMAC Pain on walking	168	Yes	4	Topical Diclofenac	Placebo	-0.4	-0.7	-0.09	Topical Diclofenac	Unclear
	Rother (2007)	WOMAC Pain	270	Yes	6	Topical ketoprofen	Celecoxib	0.03	-0.21	0.27	NS	True negative
	Rother (2007)	WOMAC Pain	265	Yes	6	Topical ketoprofen	Placebo	-0.34	-0.58	-0.1	topical ketoprofen	Possibly clinically significant

Type	Study	Outcome	N	Power	Week	Group 1	Group 2	ES	LCI	UCI	Favors	Clinical Significance
	Rother (2007)	WOMAC Pain	259	Yes	6	Celecoxib	Placebo	-0.35	-0.6	-0.11	Celecoxib	Possibly clinically significant
	Bookman (2004)	WOMAC Pain	163	Yes	4	Topical Diclofenac	Vehicle control	-0.34	-0.65	-0.03	Topical Diclofenac	Possibly clinically significant
	Bookman (2004)	WOMAC Pain	168	Yes	4	Topical Diclofenac	Placebo	-0.37	-0.68	-0.07	Topical Diclofenac	Possibly clinically significant
	Bookman (2004)	WOMAC Pain on walking	163	Yes	4	Topical Diclofenac	Vehicle control	-0.47	-0.79	-0.16	Topical Diclofenac	
	Bookman (2004)	WOMAC Pain on walking	168	Yes	4	Topical Diclofenac	Placebo	-0.4	-0.7	-0.09	Topical Diclofenac	
Stiffness	Roth (2004)	WOMAC Stiffness	321	Yes	12	Topical Diclofenac	Vehicle control	-0.24	-0.46	-0.02	Topical Diclofenac	Possibly clinically significant
	Baer (2005)	WOMAC Stiffness	212	Yes	6	Pennsaid (topical Diclofenac solution)	Vehicle control solution	-0.44	-0.71	-0.16	Pennsaid (topical Diclofenac solution)	Possibly clinically significant
	Bookman (2004)	WOMAC Stiffness	168	Yes	4	Topical Diclofenac	Placebo	-0.42	-0.72	-0.11	Topical Diclofenac	Possibly clinically significant
	Bookman (2004)	WOMAC Stiffness	163	No	4	Topical Diclofenac	Vehicle control	-0.26	-0.56	0.05	NS	Inconclusive

Table 161. Interleukin Versus Control

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
Interleukin Versus Placebo	Pavelka (2007)	Paracetamol intake pills per day	165	Yes	4	Diacerein	Placebo	-0.15	-0.45	0.16	NS	Unclear
	Pavelka (2007)	Paracetamol intake pills per day	165	Yes	8	Diacerein	Placebo	-0.08	-0.39	0.22	NS	Unclear
	Pavelka (2007)	Paracetamol intake pills per day	165	Yes	12	Diacerein	Placebo	-0.08	-0.38	0.23	NS	Unclear
	Pavelka (2007)	Paracetamol intake pills per day	165	Yes	16	Diacerein	Placebo	-0.31	-0.62	0	Diacerein	Unclear
	Pavelka (2007)	Paracetamol intake pills per day	165	Yes	20	Diacerein	Placebo	-0.4	-0.71	-0.1	Diacerein	Unclear
	Pavelka (2007)	Paracetamol intake pills per day	165	Yes	24	Diacerein	Placebo	-0.41	-0.72	-0.1	Diacerein	Unclear
	Pavelka (2007)	WOMAC Function	165	No	8	Diacerein	Placebo	-0.22	-0.53	0.08	NS	Inconclusive
	Pavelka (2007)	WOMAC Function	165	Yes	16	Diacerein	Placebo	-0.4	-0.7	-0.09	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Function	165	Yes	20	Diacerein	Placebo	-0.54	-0.85	-0.23	Diacerein	Possibly clinically significant

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
	Pavelka (2007)	WOMAC Function	165	Yes	24	Diacerein	Placebo	-0.42	-0.73	-0.11	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Pain	165	No	8	Diacerein	Placebo	-0.21	-0.52	0.1	NS	Inconclusive
	Pavelka (2007)	WOMAC Pain	165	Yes	12	Diacerein	Placebo	-0.35	-0.66	-0.04	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Pain	165	Yes	16	Diacerein	Placebo	-0.4	-0.7	-0.09	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Pain	165	Yes	20	Diacerein	Placebo	-0.44	-0.75	-0.13	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Pain	165	Yes	24	Diacerein	Placebo	-0.39	-0.7	-0.08	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Stiffness	165	Yes	4	Diacerein	Placebo	-0.15	-0.46	0.15	NS	Inconclusive
	Pavelka (2007)	WOMAC Stiffness	165	Yes	8	Diacerein	Placebo	-0.18	-0.49	0.13	NS	Inconclusive
	Pavelka (2007)	WOMAC Stiffness	165	Yes	16	Diacerein	Placebo	-0.43	-0.74	-0.12	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Stiffness	165	Yes	20	Diacerein	Placebo	-0.65	-0.97	-0.34	Diacerein	Possibly clinically significant

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
	Pavelka (2007)	WOMAC Stiffness	165	Yes	24	Diacerein	Placebo	-0.43	-0.73	-0.12	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Total	165	Yes	4	Diacerein	Placebo	-0.22	-0.52	0.09	NS	Inconclusive
	Pavelka (2007)	WOMAC Total	165	No	8	Diacerein	Placebo	-0.22	-0.53	0.09	NS	Inconclusive
	Pavelka (2007)	WOMAC Total	165	Yes	16	Diacerein	Placebo	-0.41	-0.72	-0.1	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Total	165	Yes	20	Diacerein	Placebo	-0.55	-0.86	-0.24	Diacerein	Possibly clinically significant
	Pavelka (2007)	WOMAC Total	165	Yes	24	Diacerein	Placebo	-0.42	-0.73	-0.12	Diacerein	Possibly clinically significant
Interleukin Versus NSAID	Louthrenoo (2007)	Paracetamol intake pills per day	161	Yes	4	Diacerein	Piroxicam	0.19	-0.12	0.5	NS	Unclear
	Louthrenoo (2007)	Paracetamol intake pills per day	161	Yes	8	Diacerein	Piroxicam	0.2	-0.11	0.51	NS	Unclear
	Louthrenoo (2007)	Paracetamol intake pills per day	161	Yes	12	Diacerein	Piroxicam	0.3	-0.01	0.61	NS	Unclear
	Louthrenoo (2007)	Paracetamol intake pills per day	161	Yes	16	Diacerein	Piroxicam	0.31	0	0.62	Piroxicam	Unclear

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
	Louthrenoo (2007)	Paracetamol intake pills per day	161	Yes	20	Diacerein	Piroxicam	-0.42	-0.73	-0.11	Diacerein	Unclear
	Louthrenoo (2007)	Paracetamol intake pills per day	161	Yes	24	Diacerein	Piroxicam	-0.46	-0.77	-0.14	Diacerein	Unclear
	Louthrenoo (2007)	WOMAC Function	161	Yes	4	Diacerein	Piroxicam	0.33	0.02	0.64	Piroxicam	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Function	161	Yes	8	Diacerein	Piroxicam	0.23	-0.08	0.54	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Function	161	Yes	12	Diacerein	Piroxicam	0.14	-0.17	0.45	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Function	161	Yes	16	Diacerein	Piroxicam	0.13	-0.18	0.44	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Function	161	No	20	Diacerein	Piroxicam	-0.37	-0.68	-0.05	Diacerein	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Function	161	No	24	Diacerein	Piroxicam	-0.79	-1.11	-0.47	Diacerein	Clinically Significant
	Louthrenoo (2007)	SF-36 sum score	161	Yes	16	Diacerein	Piroxicam	-0.28	-0.59	0.03	NS	Unclear
	Louthrenoo (2007)	SF-36 sum score	161	Yes	24	Diacerein	Piroxicam	-0.11	-0.42	0.2	NS	Unclear
	Zheng (2006)	pain on walking	213	Yes	4	Diacerein	Diclofenac	0.08	-0.19	0.35	NS	True negative
	Zheng (2006)	Pain on walking	213	Yes	8	Diacerein	Diclofenac	0.06	-0.21	0.33	NS	True negative

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
	Zheng (2006)	Pain on walking	213	Yes	12	Diacerein	Diclofenac	0.07	-0.2	0.34	NS	True negative
	Zheng (2006)	Pain on walking	213	Yes	16	Diacerein	Diclofenac	-0.15	-0.42	0.12	NS	True negative
	Zheng (2006)	VAS Pain on walking improvement	213	Yes	12	Diacerein	Diclofenac	0.19	-0.08	0.46	NS	True negative
	Zheng (2006)	VAS Pain on walking improvement	213	Yes		Diacerein	Diclofenac	-0.29	-0.56	-0.02	Diacerein	Not clinically significant
	Louthrenoo (2007)	WOMAC Pain	161	Yes	4	Diacerein	Piroxicam	0.36	0.05	0.68	Piroxicam	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Pain	161	Yes	8	Diacerein	Piroxicam	0.2	-0.11	0.51	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Pain	161	Yes	12	Diacerein	Piroxicam	0.17	-0.14	0.48	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Pain	161	Yes	16	Diacerein	Piroxicam	0.18	-0.13	0.49	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Pain	161	Yes	20	Diacerein	Piroxicam	-0.49	-0.81	-0.18	Diacerein	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Pain	161	Yes	24	Diacerein	Piroxicam	-0.91	-1.24	-0.59	Diacerein	Clinically significant
	Louthrenoo (2007)	WOMAC Stiffness	161	Yes	4	Diacerein	Piroxicam	0.4	0.09	0.71	Piroxicam	Possibly clinically significant

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
	Louthrenoo (2007)	WOMAC Stiffness	161	Yes	8	Diacerein	Piroxicam	0.21	-0.1	0.52	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Stiffness	161	Yes	12	Diacerein	Piroxicam	0.17	-0.14	0.48	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Stiffness	161	Yes	16	Diacerein	Piroxicam	0.23	-0.08	0.54	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Stiffness	161	Yes	20	Diacerein	Piroxicam	-0.58	-0.9	-0.26	Diacerein	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Stiffness	161	Yes	24	Diacerein	Piroxicam	-0.53	-0.84	-0.22	Diacerein	Possibly clinically significant
	Zheng (2006)	WOMAC Total	213	Yes	4	Diacerein	Diclofenac	0.21	-0.06	0.48	NS	Inconclusive
	Zheng (2006)	WOMAC Total	213	Yes	8	Diacerein	Diclofenac	0.07	-0.2	0.34	NS	True negative
	Zheng (2006)	WOMAC Total	213	Yes	12	Diacerein	Diclofenac	-0.05	-0.32	0.22	NS	True negative
	Zheng (2006)	WOMAC Total	213	Yes	16	Diacerein	Diclofenac	-0.24	-0.51	0.03	NS	Inconclusive
	Zheng (2006)	WOMAC Total	213	Yes	12	Diacerein	Diclofenac	-0.16	-0.43	0.11	NS	Inconclusive
	Zheng (2006)	WOMAC Total	213	Yes		Diacerein	Diclofenac	-0.37	-0.65	-0.1	Diacerein	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Total	161	Yes	4	Diacerein	Piroxicam	0.35	0.04	0.67	Piroxicam	Possibly clinically significant

Comparison	Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
	Louthrenoo (2007)	WOMAC Total	161	Yes	8	Diacerein	Piroxicam	0.23	-0.08	0.54	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Total	161	Yes	12	Diacerein	Piroxicam	0.15	-0.16	0.46	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Total	161	Yes	16-Jan	Diacerein	Piroxicam	0.15	-0.16	0.46	NS	Inconclusive
	Louthrenoo (2007)	WOMAC Total	161	Yes	20	Diacerein	Piroxicam	-0.43	-0.74	-0.11	Diacerein	Possibly clinically significant
	Louthrenoo (2007)	WOMAC Total	161	Yes	24	Diacerein	Piroxicam	-0.82	-1.15	-0.5	Diacerein	Clinically significant

Table 162. Acetaminophen Versus Control

Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
Micelli (2004)	VAS Pain	774	Unclear	6	Acetaminophen	Placebo	Mean Difference=.8	-2.8	4.44	NS	Inconclusive
Bradely (1991)	HAQ Disability	121	Unclear	4	Acetaminophen	Ibuprofen	0	-0.36	0.36	NS	Unclear
Bradely (1991)	HAQ Disability	121	Unclear	4	Acetaminophen	Ibuprofen	-0.07	-0.43	0.29	NS	Unclear
Bradely (1991)	Health Assessment Questionnaire	121	Unclear	4	Acetaminophen	Ibuprofen	0.04	-0.32	0.39	NS	Unclear
Bradely (1991)	Health Assessment Questionnaire	121	Unclear	4	Acetaminophen	Ibuprofen	-0.02	-0.38	0.33	NS	Unclear
Bradely (1991)	Walk time (sec) improvement	121	Unclear	4	Acetaminophen	Ibuprofen	0	-0.36	0.36	NS	Unclear
Bradely (1991)	Walk time (sec)	121	Unclear	4	Acetaminophen	Ibuprofen	0.07	-0.28	0.43	NS	Unclear
Gualda (2007)	VAS Pain	168	Yes	6	Paracetamol	Aceclofenac	0.32	0.02	0.63	Aceclofenac	Unclear
Gualda (2007)	Lequesne index	168	Yes	6	Paracetamol	Aceclofenac	0.45	0.14	0.75	Aceclofenac	Unclear
Gualda (2007)	Patient Global Assessment	168	Yes	6	Paracetamol 1000mg	Aceclofenac 100mg	0.364933	0.059852	0.670014	Aceclofenac 100mg	Not Clinically Significant

Gualda (2007)	Physician Global Assessment	168	Yes	6	Paracetamol	Aceclofenac	0.304891	0.000583	0.6092	Aceclofenac	Unclear
Schnitzer (2009)	Patient Assessment of Treatment Response	203	Yes	4	Acetaminophen ER	Rofecoxib 25mg	0.368	0.231	0.505	Rofecoxib 25mg	Unclear
Schnitzer (2005)	Patient Assessment of Treatment Response	792	Yes	6	Acetaminophen 4000mg	Celecoxib 200mg	OR=0.663	0.492	0.893	Celecoxib 200mg	Unclear
Schnitzer (2005)	Patient Assessment of Treatment Response	528	Yes	6	Acetaminophen 4000mg	Rofecoxib 12.5mg	OR=0.697	0.494	0.984	Rofecoxib 12.5mg	Unclear
Schnitzer (2005)	Patient Assessment of Treatment Response	796	Yes	6	Acetaminophen 4000mg	Rofecoxib 25mg	OR=0.548	0.407	0.739	Rofecoxib 25mg	Unclear
Schnitzer (2009)	Physician Assessment of Treatment Response	211	Yes	4	Acetaminophen 1300mg	Rofecoxib 12.5mg	-0.18	-0.312	-0.045	Acetaminophen 1300mg	Unclear
Schnitzer (2009)	Physician Assessment of Treatment Response	203	Yes	4	Acetaminophen 1300mg	Rofecoxib 25mg	-0.354	-0.49	-0.21	Acetaminophen 1300mg	Unclear

Table 163. Tramadol Versus Control

Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
Schnitzer (1999)	Minimum effective Naproxen dose: Naproxen responder subgroup	90	Unclear	8	Tramadol	Placebo	Mean difference=18.6 (p=.021)	-	-	Tramadol	Unclear
Schnitzer (1999)	Minimum effective Naproxen dose: Naproxen non-responder subgroup	147	Unclear	8	Tramadol	Placebo	Mean difference=23 (p=.706)	-	-	NS	Unclear
Fleischmann (2001)	WOMAC Function	129	Yes	13	Tramadol	Placebo	-0.33277	-0.68044	0.014912	NS	inconclusive
Babul (2004)	WOMAC Function	246	Yes	12	Tramadol ER	Placebo	Mean difference=-9.916 (p<.001)	-	-	Tramadol	Unclear
Babul (2004)	Patients' Global	246	Yes	12	Tramadol ER	Placebo	Mean difference=-14.8 (p<.001)	-	-	Tramadol	Unclear

Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
Fishman (2007)	WOMAC Pain, percent improvement from baseline	322	Unclear	12	Tramadol Contramid	Placebo	0.179827	-0.05729	0.416943	NS	Unclear
Fishman (2007)	WOMAC Pain, percent improvement from baseline	330	Unclear	12	Tramadol Contramid	Placebo	0.219965	-0.01115	0.451077	NS	Unclear
Fishman (2007)	WOMAC Pain, percent improvement from baseline	327	Yes	12	Tramadol Contramid	Placebo	0.298874	0.065005	0.532742	Tramadol	Unclear
Fishman (2007)	WOMAC Pain, percent improvement from baseline	206	Unclear	12	Tramadol Contramid 100mg	Tramadol Contramid 200mg	-0.02477	-0.2981	0.248559	NS	Unclear
Fishman (2007)	WOMAC Pain, percent improvement from baseline	203	Unclear	12	Tramadol Contramid 100mg	Tramadol Contramid 300mg	-0.09695	-0.37232	0.178426	NS	Unclear

Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
Fishman (2007)	WOMAC Pain, percent improvement from baseline	211	Unclear	12	Tramadol Contramid 200mg	Tramadol Contramid 300mg	-0.07361	-0.34359	0.196374	NS	Unclear
Burch (2007)	Improvement in pain intensity numerical rating scale	589	Yes	12	Tramadol Contramid OAD	Placebo	-0.35679	-0.5294	-0.18419	Tramadol	Unclear
Fleischmann (2001)	WOMAC Pain	129	Yes	13	Tramadol	Placebo	-0.43138	-0.78072	-0.08204	Tramadol	Possibly clinically significant
Babul (2004)	VAS	246	Yes	12	Tramadol ER	Placebo	Mean difference=-15.3 (p<.001)	-	-	Tramadol	Unclear
Babul (2004)	WOMAC Pain	246	Yes	12	Tramadol ER	Placebo	Mean difference=-2.76 (p<.001)	-	-	Tramadol	Unclear
Fleischmann (2001)	WOMAC Stiffness	129	Yes	13	Tramadol	Placebo	-0.358	-0.71	-0.01	Tramadol	Possibly clinically significant
Babul (2004)	WOMAC Stiffness	246	Yes	12	Tramadol ER	Placebo	Mean difference=-1.204 (p<.001)	-	-	Tramadol	Unclear
Beaulieu (2008)	WOMAC Pain	97	No	6	Tramadol	Diclofenac	.067	-.33	.47	NS	Inconclusive

Study	Outcome	N	Power	Week	Group 1	Group 2	Effect Size	LCL	UCL	Favors	Clinical Importance
Beaulieu (2008)	WOMAC Function	97	No	6	Tramadol	Diclofenac	.061	-.34	.46	NS	Inconclusive
Beaulieu (2008)	WOMAC Stiffness	97	No	6	Tramadol	Diclofenac	.01	-.39	.41	NS	Inconclusive

Table 164. Active Treatments Versus Placebo: Patient and Physician Global Assessments

	Study	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Strength of Evidence
Patient Global Assessment	Williams (2000)	453	Yes	6	Celecoxib 200mg	Placebo	-0.33159	-0.51707	-0.14611	Celecoxib 200mg	Moderate
	Fleischmann (2004)	694	Yes	13	Lumiracoxib 400mg	Placebo	-0.34539	-0.50432	-0.18646	Lumiracoxib 400mg	Low
	Fleischmann (2004)	693	Yes	13	Lumiracoxib 200mg	Placebo	-0.32586	-0.48473	-0.16699	Lumiracoxib 200mg	Low
	Mckenna (2001)	399	Yes	6	Celecoxib	Placebo	-0.4335	-0.63206	-0.23495	Celecoxib	Moderate
	Mckenna (2001)	399	Yes	6	Diclofenac	Placebo	-0.52021	-0.71977	-0.32064	Diclofenac	Moderate
	Williams (2000)	462	Yes	6	Celecoxib 100mg	Placebo	-0.32841	-0.51202	-0.1448	Celecoxib 100mg	Moderate
	Williams (2001)	484	Yes	6	Celecoxib 100mg	Placebo	-3.06211	-3.32529	-2.79893	Celecoxib 100mg	Moderate

	Study	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Strength of Evidence
	Williams (2001)	474	Yes	6	Celecoxib 200mg	Placebo	-6.11409	-6.54443	-5.68376	Celecoxib 200mg	Moderate
	Roth(2004)	320	Yes	12	Topical Diclofenac	Placebo	-0.33255	-0.55321	-0.11188	Topical Diclofenac	High
	Gibofsky (2003)	285	Yes	6	Celecoxib 200mg	Placebo	OR=2.50	1.47	4.26	Celecoxib 200mg	Moderate
	Gibofsky (2003)	286	Yes	6	Rofecoxib 25mg	Placebo	OR=2.04	1.20	3.49	Rofecoxib 25mg	Moderate
Physician Global Assessment	Fleischmann (2006)	675	Yes	13	Celecoxib (Cox-2)	Placebo	-0.25204	-0.41161	-0.09247	Celecoxib (Cox-2)	Low
	Fleischmann (2006)	693	Yes	13	Lumiracoxib 200mg	Placebo	-0.35846	-0.51753	-0.1994	Lumiracoxib 200mg	Low
	Fleischmann (2006)	694	Yes	13	Lumiracoxib 400mg	Placebo	-0.34115	-0.50005	-0.18224	Lumiracoxib 400mg	Low
	Kivits (2002)	410	Yes	6	Valdecoxib 10mg (Cox-2)	Placebo	-0.2834	-0.47797	-0.08883	Valdecoxib 10mg (Cox-2)	Moderate
	Kivits (2002)	410	Yes	12	Valdecoxib 10mg (Cox-2)	Placebo	-0.28799	-0.48259	-0.09338	Valdecoxib 10mg (Cox-2)	Moderate
	Kivits (2002)	406	Unclear	6	Valdecoxib 20mg (Cox-2)	Placebo	-0.19324	-0.38825	0.001769	NS	Moderate
	Kivits (2002)	406	Yes	12	Valdecoxib 20mg (Cox-2)	Placebo	-0.22194	-0.4171	-0.02679	Valdecoxib 20mg (Cox-2)	Moderate
	Kivits (2002)	406	Yes	6	Valdecoxib 5mg (Cox-2)	Placebo	-0.22375	-0.41892	-0.02859	Valdecoxib 5mg (Cox-2)	Moderate
	Kivits (2002)	406	Yes	12	Valdecoxib 5mg (Cox-2)	Placebo	-0.19912	-0.39416	-0.00408	Valdecoxib 5mg (Cox-2)	Moderate
	Kivits (2002)	409	Yes	6	Naproxen	Placebo	-0.23307	-0.42757	-0.03858	Naproxen	Moderate

	Study	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Strength of Evidence
					(NSAID)					(NSAID)	
	Kivits (2002)	409	Yes	12	Naproxen (NSAID)	Placebo	-0.20185	-0.39618	-0.00753	Naproxen (NSAID)	Moderate
	Mckenna (2001)	399	Yes	6	Celecoxib (Cox-2)	Placebo	-0.3884	-0.5865	-0.19029	Celecoxib (Cox-2)	Moderate
	Mckenna (2001)	399	Yes	6	Diclofenac (NSAID)	Placebo	-0.55943	-0.75951	-0.35935	Diclofenac (NSAID)	Moderate
	Williams (2001)	484	Yes	6	Celecoxib 100mg	Placebo	-4.99222	-5.35479	-4.62964	Celecoxib 100mg	Moderate
	Williams (2001)	474	Yes	6	Celecoxib 200mg	Placebo	-6.65607	-7.1181	-6.19404	Celecoxib 200mg	Moderate
	Gibofsky (2003)	285	yes	6	Celecoxib 200mg	Placebo	OR=1.99	1.19	3.33	Celecoxib 200mg	Moderate
	Gibofsky (2003)	286	Unclear	6	Rofecoxib 25mg	Placebo	OR=1.59	0.95	2.66	NS	Moderate
Patient Global Assessment of Disease: Versus Placebo	Lehmann (2005)	844	Yes	13	Celecoxib	Placebo	-0.1617	-0.29685	-0.02655	Celecoxib	Low
	Lehmann (2005)	844	Yes	13	Lumiracoxib	Placebo	-0.25402	-0.3895	-0.11855	Lumiracoxib	Low
	Schnitzer (2010)	461	Yes	13	Naproxcinod 375mg	Placebo	-0.41661	-0.60131	-0.2319	Naproxcinod 375mg	Moderate
	Schnitzer (2010)	450	Yes	13	Naproxcinod 750mg	Placebo	-0.48149	-0.66899	-0.294	Naproxcinod 750mg	Moderate
	Schnitzer (2010)	446	Unclear	13	Naproxen	Placebo	-0.07352	-0.25921	0.11216	NS	Moderate

	Study	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Strength of Evidence
	Tannenbaum (2004)	724	Yes	13	Celecoxib 200mg	Placebo	-0.25907	-0.41391	-0.10424	Celecoxib 200mg	Moderate
	Tannenbaum (2004)	730	Yes	13	Lumiracoxib 200mg	Placebo	-0.28128	-0.43589	-0.12666	Lumiracoxib 200mg	Moderate
	Tannenbaum (2004)	734	Yes	13	Lumiracoxib 400mg	Placebo	-0.33077	-0.48544	-0.17611	Lumiracoxib 400mg	Moderate
	Ehrich (1999)	145	Yes	6	Rofecoxib 125mg	Placebo	-1.21037	-1.56523	-0.85551	Rofecoxib 125mg	Moderate
	Ehrich (1999)	145	Yes	6	Rofecoxib 25mg	Placebo	-1.03651	-1.38379	-0.68923	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	209	Unclear	6	Naproxcinod 125mg	Placebo	OR=1.42	0.81	2.48	NS	Moderate
	Schnitzer (2005)	211	Yes	6	Naproxcinod 375mg	Placebo	OR=2.15	1.24	3.75	Naproxcinod 375mg	Moderate
	Schnitzer (2005)	218	Yes	6	Naproxcinod 750mg	Placebo	OR=3.01	1.73	5.22	Naproxcinod 750mg	Moderate
	Schnitzer (2005)	202	Yes	6	Rofecoxib 25mg	Placebo	OR=2.74	1.55	4.85	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	221	Yes	6	Naproxen 500mg	Placebo	OR=2.62	1.52	4.53	Naproxen 500mg	Moderate
Physician Global Assessment of Disease: Versus	Ehrich (1999)	145	Yes	6	Rofecoxib 125mg	Placebo	-1.24218	-1.59853	-0.88583	Rofecoxib 125mg	Moderate
	Ehrich (1999)	145	Yes	6	Rofecoxib 25mg	Placebo	-1.04206	-1.38957	-0.69455	Rofecoxib 25mg	Moderate
	Lehmann	844	Yes	13	Celecoxib	Placebo	-0.22744	-0.36281	-0.09208	Celecoxib	Low

	Study	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Strength of Evidence
Placebo	(2005)				200mg					200mg	
	Lehmann (2005)	844	Yes	13	Lumiracoxib 100mg	Placebo	-0.26683	-0.40236	-0.1313	Lumiracoxib 100mg	Low
	Tannenbaum	724	Yes	13	Celecoxib 200mg	Placebo	-0.19281	-0.34739	-0.03823	Celecoxib 200mg	Moderate
	Tannenbaum	730	Yes	13	Lumiracoxib 200mg	Placebo	-0.21671	-0.37105	-0.06237	Lumiracoxib 200mg	Moderate
	Tannenbaum	734	Yes	13	Lumiracoxib 400mg	Placebo	-0.24974	-0.404	-0.09548	Lumiracoxib 400mg	Moderate
Patient Global Assessment of Response to Treatment: Versus Placebo	Ehrich (1999)	145	Yes	6	Rofecoxib 125mg	Placebo	-1.4568	-1.82405	-1.08955	Rofecoxib 125mg	Moderate
	Ehrich (1999)	145	Yes	6	Rofecoxib 25mg	Placebo	-1.21549	-1.57058	-0.86039	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	209	Unclear	6	Naproxcinod 125mg	Placebo	OR= 1.49218	0.846163	2.631409	NS	Moderate
	Schnitzer (2005)	211	Yes	6	Naproxcinod 375mg	Placebo	OR= 2.644571	1.507841	4.638257	Naproxcinod 375mg	Moderate
	Schnitzer (2005)	218	Yes	6	Naproxcinod 750mg	Placebo	OR= 3.552502	2.02858	6.221234	Naproxcinod 750mg	Moderate
	Schnitzer (2005)	202	Yes	6	Rofecoxib 25mg	Placebo	OR= 4.4375	2.458447	8.009691	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	221	Yes	6	Naproxen 500mg	Placebo	OR= 4.141667	2.359783	7.269059	Naproxen 500mg	Moderate
	Lohmander (2005)	532	Yes	6	Naproxcinod	Placebo	OR= 3.281416	2.128709	5.05832	Naproxcinod	Low

	Study	N	Sufficient Power	Week	Group 1	Group 2	Effect Size	Lower CI	Upper CI	Favors (NS=Not Significant)	Strength of Evidence
	Lohmander (2005)	516	Yes	6	Naproxen	Placebo	OR= 3.15	2.041247	4.860999	Naproxen	Low
	Kivitz (2004)	625	Yes	6	Rofecoxib 12.5mg	Placebo	OR= 3.370968	2.346792	4.842109	Rofecoxib 12.5mg	High
	Kivitz (2004)	614	Yes	6	Nabumetone	Placebo	OR= 2.459423	1.710647	3.535951	Nabumetone	High
	Gibofsky (2003)	285	Yes	6	Celecoxib 200mg	Placebo	OR=1.99	1.19	3.33	Celecoxib 200mg	Moderate
	Gibofsky (2003)	286	Unclear	6	Rofecoxib 25mg	Placebo	OR=1.59	0.95	2.66	NS	Moderate
Physician Global Assessment of Response to Treatment: Versus Placebo	Ehrich (1999)	145	Yes	6	Rofecoxib 125mg	Placebo	-1.20414	-1.55871	-0.84957	Rofecoxib 125mg	Moderate
	Ehrich (1999)	145	Yes	6	Rofecoxib 25mg	Placebo	-1.09595	-1.4457	-0.74619	Rofecoxib 25mg	Moderate

Table 165. Active Treatment Comparison: Patient and Physician Global Assessments

Outcome	Study	N	Sufficient Power	Week	Group 1	Group 2	Standardized Mean Difference	Lower Confidence	Upper Confidence	Favors (NS=Not Significant)	Strength of Evidence

							ce	Interval	Interval		
Patient Global Assessment	Ayral (2003)	436	Unclear	52	Tenidap 40mg	Piroxicam 20mg	0.01802 6	-0.16972	0.205768	NS	Moderate
	Ayral (2003)	427	Unclear	52	Tenidap 120mg	Piroxicam 20mg	-0.05034	-0.24009	0.139398	NS	Moderate
	Ayral (2003)	431	Unclear	52	Tenidap 40mg	Tenidap 120mg	0.06677 3	-0.12214	0.255683	NS	Moderate
	Gualda (2007)	168	Yes	6	Paracetamol 1000mg	Aceclofe nac 100mg	0.36493 3	0.05985 2	0.670014	Aceclofenac 100mg	High
	Williams (2000)	453	Unclear	6	Celecoxib 200mg	Celecoxib 100mg	0	-0.18421	0.184211	NS	Moderate
	Fleischmann (2004)	906	Yes	13	Lumiracoxib 200mg	Celecoxib 200mg	-0.03012	-0.16038	0.100147	NS	Low
	Fleischmann (2004)	907	Yes	13	Lumiracoxib 400mg	Celecoxib 200mg	-0.04916	-0.17937	0.081048	NS	Low
	Williams (2000)	472	Yes	6	Celecoxib 100	Celecoxib 200mg	3.32801 2	3.04869 3	3.607332	Celecoxib 200mg	Moderate
	Mckenna (2001)	398	Unclear	6	Celecoxib	Diclofena c	-0.09074	-0.28733	0.105854	NS	Moderate

	Fleischmann (2004)	925	Yes	13	Lumiracoxib 200mg	Lumiracoxib 400mg	-1.79404	-1.94676	-1.64132	Lumiracoxib 200mg	Low
	Gibofsky (2003)	379	Unclear	6	Celecoxib 200mg	Rofecoxib 25mg	OR=1.23	0.816	1.833	NS	Moderate
Physician Global Assessment	Ayral (2003)	440	Unclear	52	Tenidap 40mg	Piroxicam 20mg	0.01343	-0.17345	0.200309	NS	Moderate
	Ayral (2003)	435	Unclear	52	Tenidap 120mg	Piroxicam 20mg	-0.03605	-0.22402	0.151914	NS	Moderate
	Ayral (2003)	437	Unclear	52	Tenidap 40mg	Tenidap 120mg	0.049571	-0.13799	0.237128	NS	Moderate
	Fleischmann (2006)	906	Yes	13	Lumiracoxib 200mg	Celecoxib 200mg	-0.11041	-0.24077	0.019947	NS	Low
	Fleischmann (2006)	907	Yes	13	Lumiracoxib 400mg	Celecoxib 200mg	-0.09055	-0.22081	0.039704	NS	Low
	Fleischmann (2006)	925	Yes	13	Lumiracoxib 200mg	Lumiracoxib 400mg	-0.02043	-0.14932	0.108461	NS	Low
	Gualda (2007)	168	Yes	6	Paracetamol	Aceclofenac	0.304891	0.000583	0.6092	Aceclofenac	High
	Kivits (2002)	409	Unclear	6	Valdecoxib 10mg (Cox-2)	Naproxen (NSAID)	-0.05067	-0.24453	0.143191	NS	Moderate
	Kivits (2002)	409	Unclear	12	Valdecoxib 10mg (Cox-2)	Naproxen	-0.08491	-0.27883	0.109002	NS	Moderate

					2)	(NSAID)					
	Kivits (2002)	405	Unclear	6	Valdecoxib 20mg	Naproxen	0.04073 3	-0.15408	0.235542	NS	Moderate
	Kivits (2002)	405	Unclear	12	Valdecoxib 20mg	Naproxen	-0.01896	-0.21375	0.175831	NS	Moderate
	Kivits (2002)	405	Unclear	6	Valdecoxib 5mg	Naproxen	0.01018 3	-0.18461	0.204973	NS	Moderate
	Kivits (2002)	405	Unclear	12	Valdecoxib 5mg	Naproxen	0	-0.19479	0.194788	NS	Moderate
	Mckenna (2001)	398	Yes	6	Celecoxib (Cox-2)	Diclofena c (NSAID)	0.20041 9	0.00343 4	0.397405	Diclofenac (NSAID)	Moderate
	Williams (2001)	472	Yes	6	Celecoxib 100mg	Celecoxib 200mg	1.66400 8	1.45440 9	1.873608	Celecoxib 200mg	Moderate
	Gibofsky (2003)	379	Unclear	6	Celecoxib 200mg	Rofecoxib 25mg	OR=1.2 49	0.833	1.872	NS	Moderate
Patient Global Assessment of Disease	Lehmann (2005)	844	Yes	13	Lumiracoxib	Celecoxib	-0.09042	-0.22542	0.044579	NS	Low
	Gottesdiener (2002)	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.01121	-0.27313	0.250699	NS	High
	Schnitzer (2010)	465	Unclear	13	Naproxen	Naproxcin od 375mg	-0.02577	-0.20765	0.156116	NS	Moderate

	Schnitzer (2010)	454	Unclear	13	Naproxen	Naproxin od 750mg	-0.01771	-0.2017	0.166269	NS	Moderate
	Gottesdiener (2002)	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	-0.0072	-0.26513	0.250735	NS	High
	Gottesdiener (2002)	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.08938 4	-0.17626	0.355026	NS	High
	Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.36156 5	0.10032 3	0.622807	Etoricoxib 60mg	High
	Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.27012 9	0.00983 3	0.530426	Etoricoxib 90mg	High
	Gottesdiener (2002)	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.0965	-0.17079	0.363787	NS	High
	Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.36751 2	0.10452 2	0.630503	Etoricoxib 60mg	High
	Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.27648 2	0.01445 7	0.538506	Etoricoxib 90mg	High
	Gottesdiener (2002)	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.28355 9	0.01393 8	0.55318	Etoricoxib 60mg	High
	Gottesdiener (2002)	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.18860 2	-0.08026	0.457461	NS	High
	Gottesdiener	224	Unclear	6	Etoricoxib	Etoricoxib	-0.09502	-0.35709	0.167037	NS	High

	(2002)				60mg	90mg					
	Schnitzer (2005)	212	Unclear	6	Naproxcinod 125mg	Naproxcin od 375mg	OR=0.658	0.383	1.131	NS	Moderate
	Schnitzer (2005)	219	Yes	6	Naproxcinod 125mg	Naproxcin od 750mg	OR=0.471	0.275	0.809	Naproxcinod 750mg	Moderate
	Schnitzer (2005)	203	Yes	6	Naproxcinod 125mg	Rofecoxib 25mg	OR=0.517	0.296	0.904	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	222	Yes	6	Naproxcinod 125mg	Naproxen 500mg	OR=0.540	0.317	0.921	Naproxen 500mg	Moderate
	Schnitzer (2005)	221	Unclear	6	Naproxcinod 375mg	Naproxcin od 750mg	OR=0.717	0.420	1.224	NS	Moderate
	Schnitzer (2005)	205	Unclear	6	Naproxcinod 375mg	Rofecoxib 25mg	OR=0.786	0.452	1.368	NS	Moderate
	Schnitzer (2005)	224	Unclear	6	Naproxcinod 375mg	Naproxen 500mg	OR=0.821	0.484	1.393	NS	Moderate
	Schnitzer (2005)	212	Unclear	6	Naproxcinod 750mg	Rofecoxib 25mg	OR=1.097	0.632	1.905	NS	Moderate
	Schnitzer (2005)	231	Unclear	6	Naproxcinod 750mg	Naproxen 500mg	OR=1.146	0.677	1.941	NS	Moderate
Physician Global Assessment of Disease	Gottesdiener	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	-0.0072	-0.26513	0.250735	NS	High
	Gottesdiener	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.089384	-0.17626	0.355026	NS	High
	Gottesdiener	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.0965	-0.17079	0.363787	NS	High
	Gottesdiener	229	Yes	6	Etoricoxib	Etoricoxib	0.36156	0.10032	0.622807	Etoricoxib	High

	(2002)				5mg	60mg	5	3		60mg	
	Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.367512	0.104522	0.630503	Etoricoxib 60mg	High
	Gottesdiener (2002)	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.283559	0.013938	0.55318	Etoricoxib 60mg	High
	Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.270129	0.009833	0.530426	Etoricoxib 90mg	High
	Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.276482	0.014457	0.538506	Etoricoxib 90mg	High
	Gottesdiener (2002)	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.188602	-0.08026	0.457461	NS	High
	Gottesdiener (2002)	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.09502	-0.35709	0.167037	NS	High
	Lehmann (2005)	844	Unclear	13	Lumiracoxib 100mg	Celecoxib 200mg	-0.0413	-0.17625	0.093641	NS	Low
Patient Assessment of Treatment Response	Schnitzer (2009)	203	Yes	4	Acetaminophen ER	Rofecoxib 25mg	0.368	0.231	0.505	Rofecoxib 25mg	Moderate
	Schnitzer (2009)	209	Unclear	4	Rofecoxib 12.5mg	Rofecoxib 25mg	0.187256	-0.08475	0.459259	NS	Moderate
	Gottesdiener (2002)	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	0.036058	-0.2219	0.294014	NS	High

Gottesdiener (2002)	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.09177 6	-0.17387	0.357425	NS	High
Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.42249 9	0.16047 7	0.68452	Etoricoxib 60mg	High
Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.31989 2	0.05911 4	0.58067	Etoricoxib 90mg	High
Gottesdiener (2002)	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.05496 9	-0.21221	0.32215	NS	High
Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.38558 6	0.12237 2	0.648801	Etoricoxib 60mg	High
Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.28316 5	0.02107 9	0.545251	Etoricoxib 90mg	High
Gottesdiener (2002)	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.33758 2	0.06739 3	0.607771	Etoricoxib 60mg	High
Gottesdiener (2002)	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.23323 9	-0.03594	0.502418	NS	High
Gottesdiener (2002)	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.10288	-0.36497	0.159209	NS	High
Schnitzer (2005)	212	Yes	6	Naproxcinod 125mg	Naproxcinod 375mg	OR=0.5 64	0.327	0.973	Naproxcinod 375mg	Moderate
Schnitzer (2005)	219	Yes	6	Naproxcinod 125mg	Naproxcinod 750mg	OR=0.4 20	0.244	0.723	Naproxcinod 750mg	Moderate

	Schnitzer (2005)	221	Unclear	6	Naproxcinod 375mg	Naproxcinod 750mg	OR=0.744	0.435	1.274	NS	Moderate
	Schnitzer (2005)	222	Yes	6	Naproxcinod 125mg	Naproxen 500mg	OR=0.360	0.209	0.621	Naproxen 500mg	Moderate
	Schnitzer (2005)	224	Unclear	6	Naproxcinod 375mg	Naproxen 500mg	OR=0.639	0.372	1.095	NS	Moderate
	Schnitzer (2005)	231	Unclear	6	Naproxcinod 750mg	Naproxen 500mg	OR=0.858	0.501	1.469	NS	Moderate
	Schnitzer (2005)	203	Yes	6	Naproxcinod 125mg	Rofecoxib 25mg	OR=0.336	0.189	0.597	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	205	Unclear	6	Naproxcinod 375mg	Rofecoxib 25mg	OR=0.596	0.337	1.052	NS	Moderate
	Schnitzer (2005)	212	Unclear	6	Naproxcinod 750mg	Rofecoxib 25mg	OR=0.801	0.454	1.412	NS	Moderate
	Schnitzer (2005)	782	Unclear	6	Celecoxib 200mg	Rofecoxib 12.5mg	OR=1.051	0.780	1.416	NS	Moderate
	Schnitzer (2005)	1050	Unclear	6	Celecoxib 200mg	Rofecoxib 25mg	OR=0.827	0.649	1.054	NS	Moderate
	Schnitzer (2005)	792	Yes	6	Acetaminophen 4000mg	Celecoxib 200mg	OR=0.663	0.492	0.893	Celecoxib 200mg	Moderate
	Schnitzer (2005)	528	Yes	6	Acetaminophen 4000mg	Rofecoxib 12.5mg	OR=0.697	0.494	0.984	Rofecoxib 12.5mg	Moderate
	Schnitzer (2005)	796	Yes	6	Acetaminophen 4000mg	Rofecoxib 25mg	OR=0.548	0.407	0.739	Rofecoxib 25mg	Moderate
	Schnitzer (2005)	786	Unclear	6	Rofecoxib 12.5mg	Rofecoxib 25mg	OR=0.786	0.584	1.059	NS	Moderate
	Lohmander (2005)	828	Yes	6	Naproxcinod	Naproxen	OR=1.042	0.767	1.415	NS	Low
	Kivitz (2004)	823	Yes	6	Rofecoxib 12.5mg	Nabumetone	OR=1.371	1.042	1.803	Rofecoxib 12.5mg	High

	McIlwain (1989)	65	Unclear	12	Orgotein 8x3	Orgotein 16x2	OR=0.783	0.272	2.253	NS	Moderate
	Gottesdiener (2002)	231	Unclear	6	Etoricoxib 5mg	Etoricoxib 10mg	0.03794	-0.22002	0.295898	NS	High
Physician Assessment of Treatment Response	Gottesdiener (2002)	219	Unclear	6	Etoricoxib 5mg	Etoricoxib 30mg	0.090097	-0.17555	0.355741	NS	High
	Gottesdiener (2002)	216	Unclear	6	Etoricoxib 10mg	Etoricoxib 30mg	0.051369	-0.21581	0.318544	NS	High
	Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 60mg	0.36834	0.107018	0.629663	Etoricoxib 60mg	High
	Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 60mg	0.329494	0.066939	0.592048	Etoricoxib 60mg	High
	Gottesdiener (2002)	214	Yes	6	Etoricoxib 30mg	Etoricoxib 60mg	0.283925	0.014301	0.55355	Etoricoxib 60mg	High
	Gottesdiener (2002)	229	Yes	6	Etoricoxib 5mg	Etoricoxib 90mg	0.311184	0.050496	0.571872	Etoricoxib 90mg	High
	Gottesdiener (2002)	226	Yes	6	Etoricoxib 10mg	Etoricoxib 90mg	0.272466	0.010478	0.534454	Etoricoxib 90mg	High
	Gottesdiener (2002)	214	Unclear	6	Etoricoxib 30mg	Etoricoxib 90mg	0.22585	-0.04327	0.494971	NS	High
	Gottesdiener (2002)	224	Unclear	6	Etoricoxib 60mg	Etoricoxib 90mg	-0.05728	-0.31925	0.204684	NS	High

	Schnitzer (2009)	211	Yes	4	Acetaminop hen 1300mg	Rofecoxib 12.5mg	-0.18	-0.312	-0.045	Acetaminop hen 1300mg	Moderate
	Schnitzer (2009)	203	Yes	4	Acetaminop hen 1300mg	Rofecoxib 25mg	-0.354	-0.49	-0.21	Acetaminop hen 1300mg	Moderate
	Schnitzer (2009)	208	Unclear	4	Rofecoxib 12.5mg	Rofecoxib 25mg	0.17352 3	-0.099	0.446042	NS	Moderate

Figure 47. Network Meta-Analysis: Analgesics Versus Placebo (Pain)

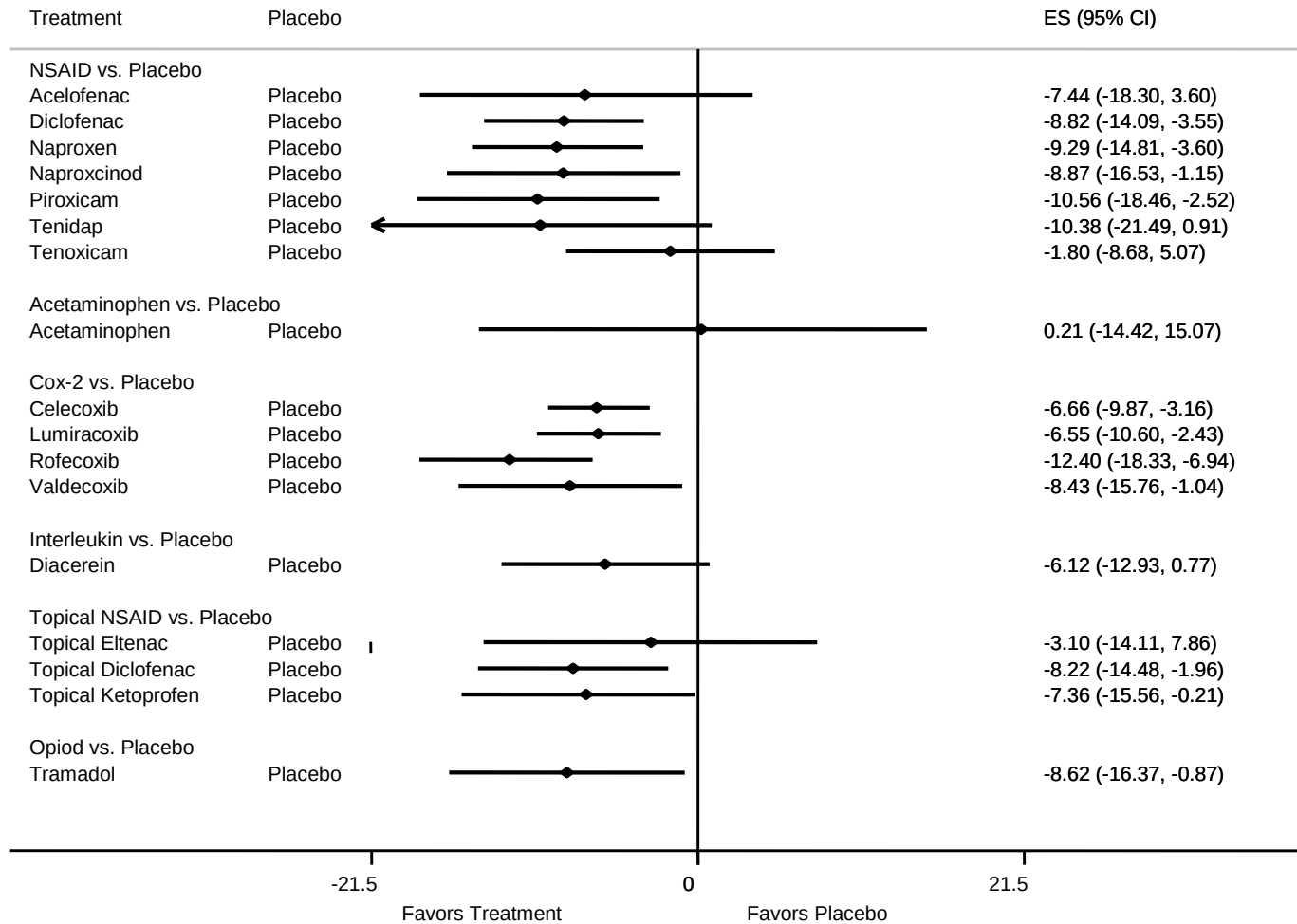


Figure 48. Network Meta-Analysis: Cox-2 Versus NSAIDs (Pain)

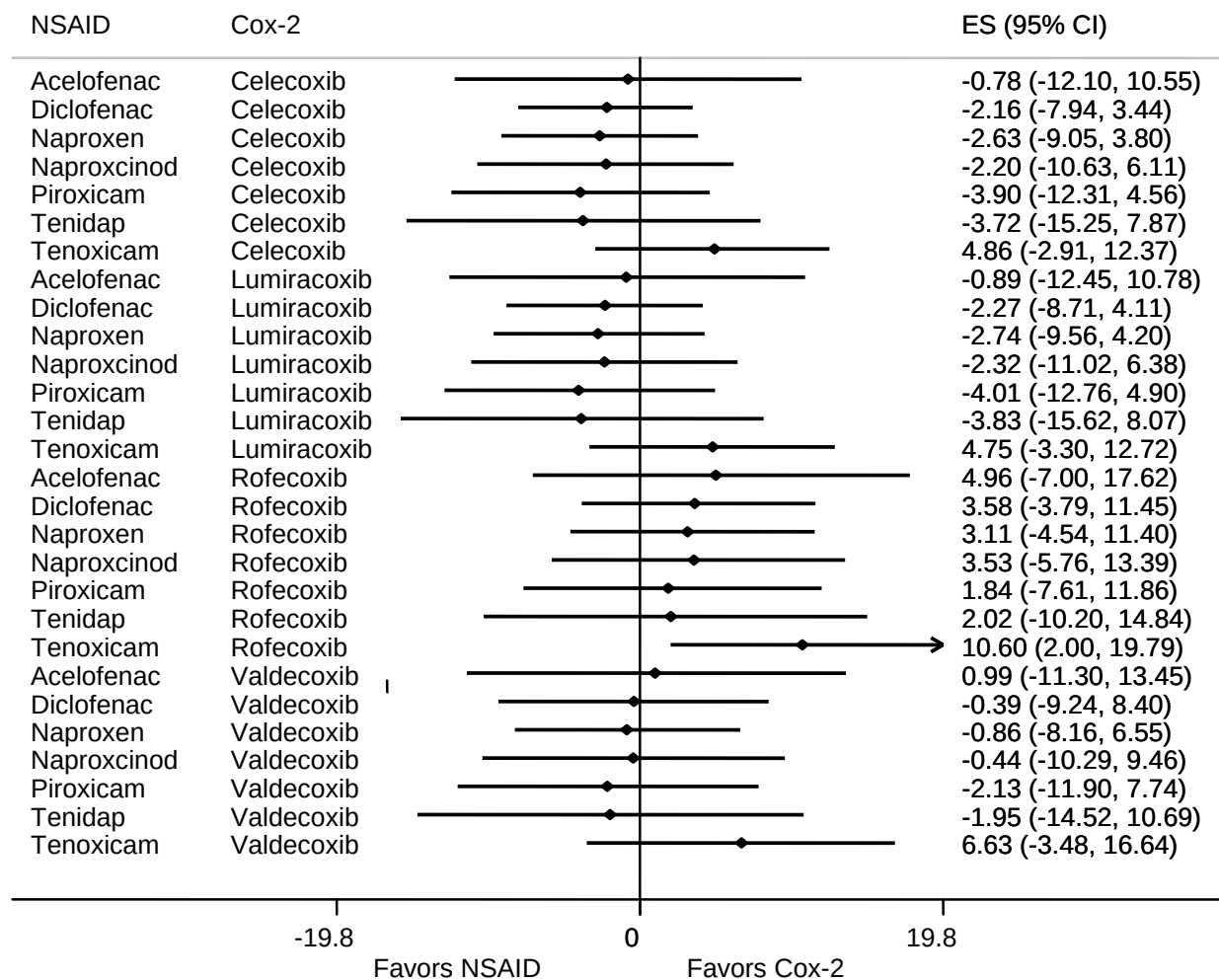


Figure 49. Network Meta-Analysis: Cox-2 Versus Cox-2 (Pain)

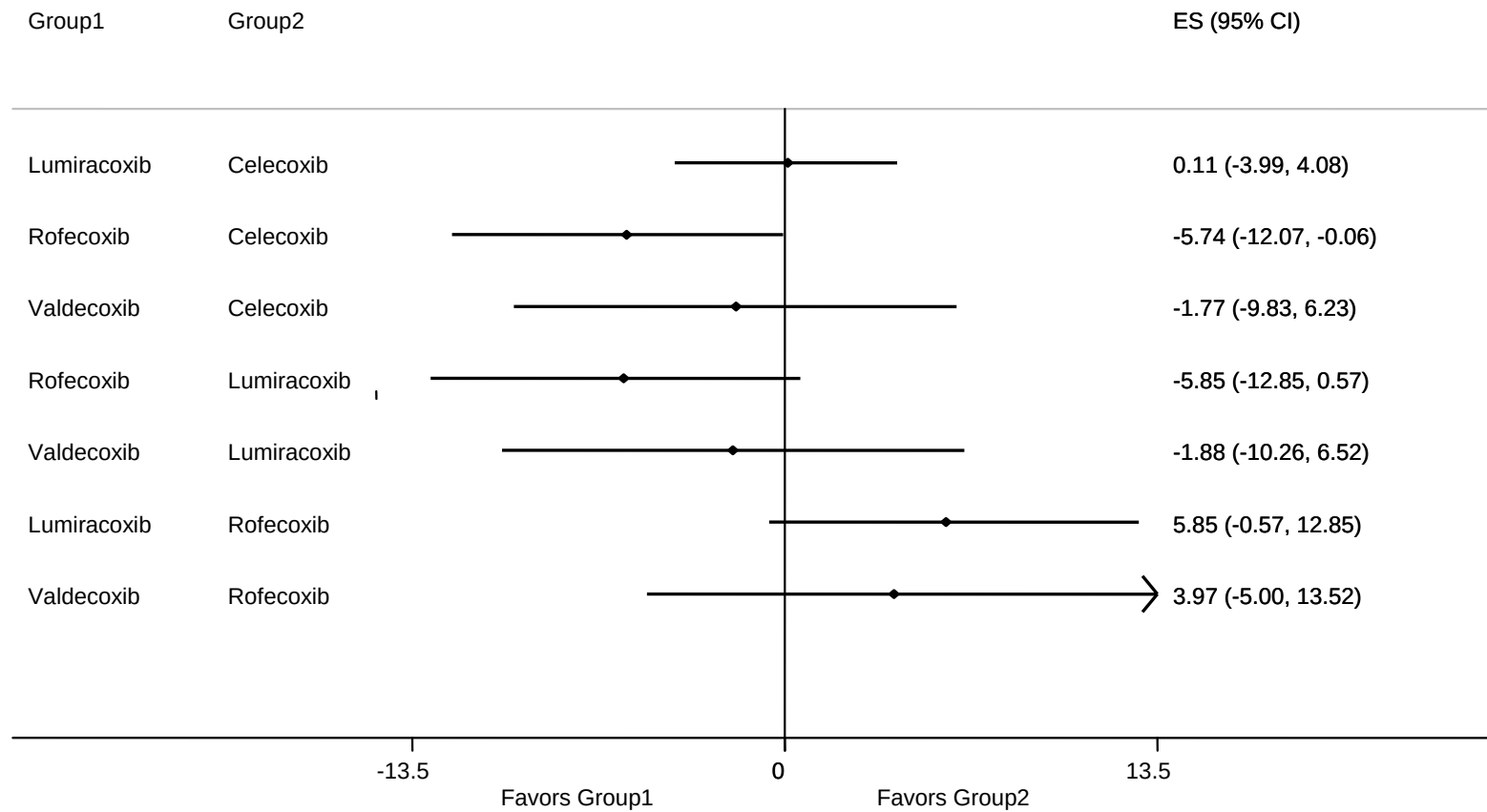


Figure 50. Network Meta-Analysis: NSAID Versus NSAID (Pain)

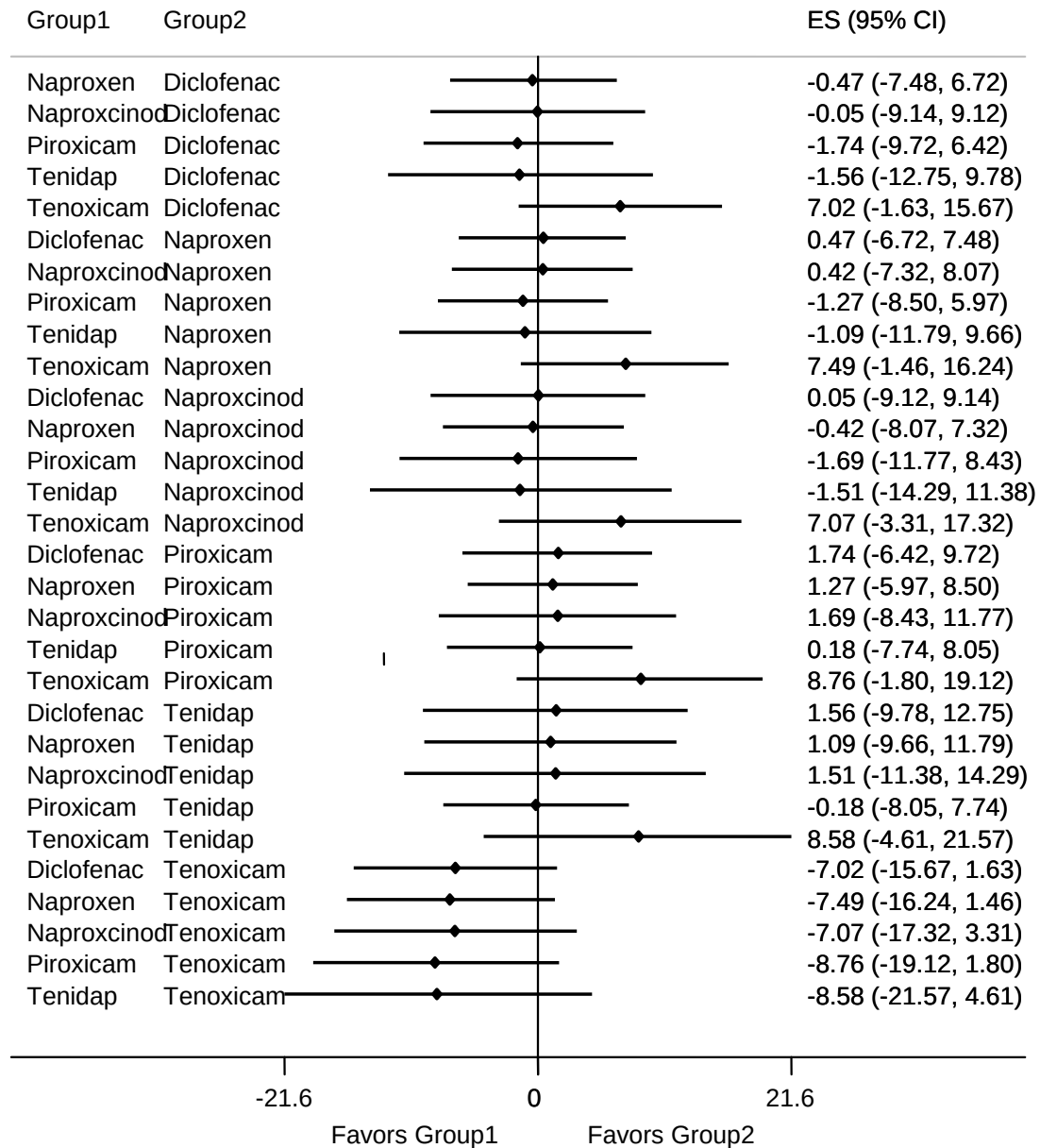


Figure 51. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (Pain)

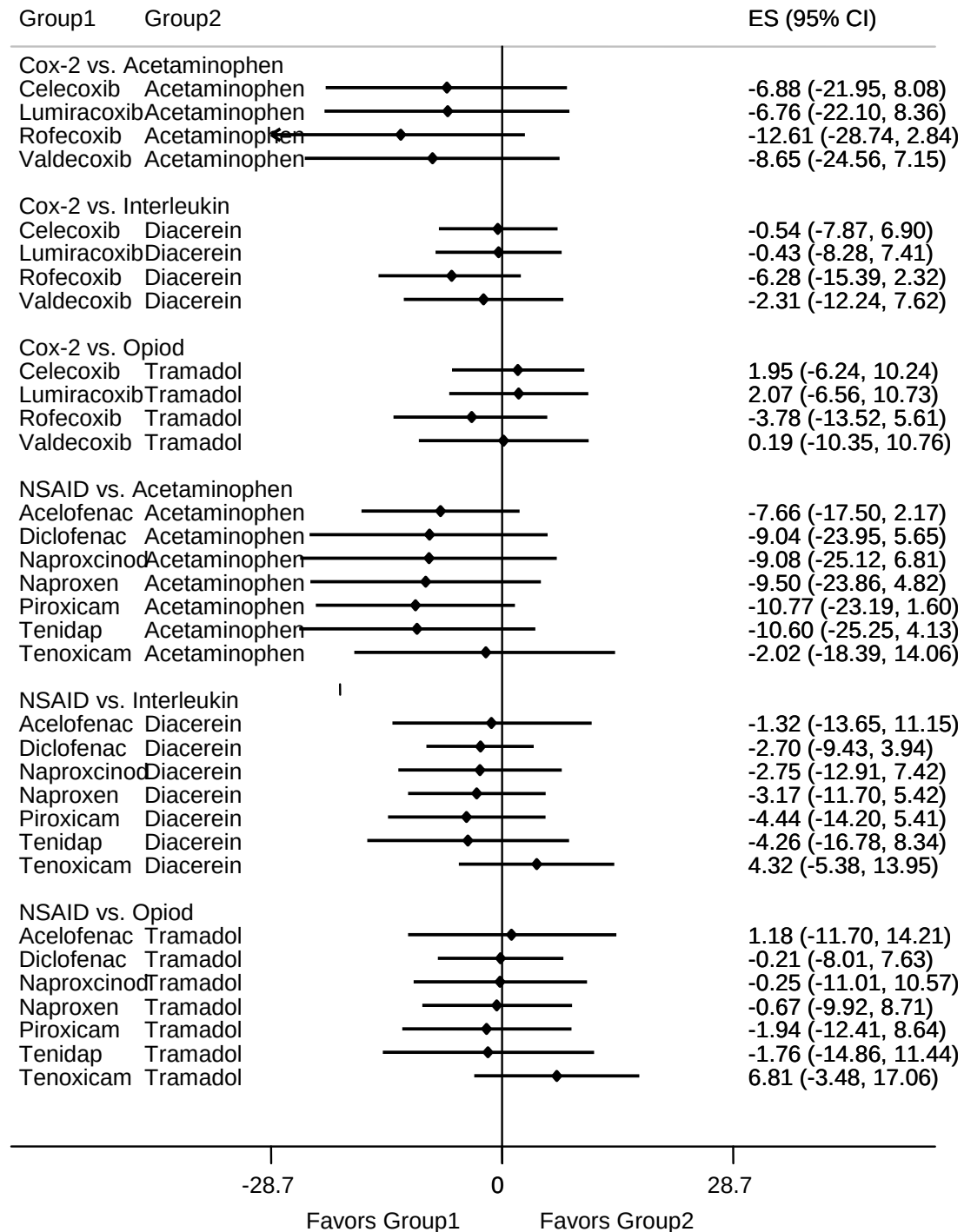


Figure 52. Network Meta-Analysis: Topical NSAIDS Versus Oral Analgesics (Pain)

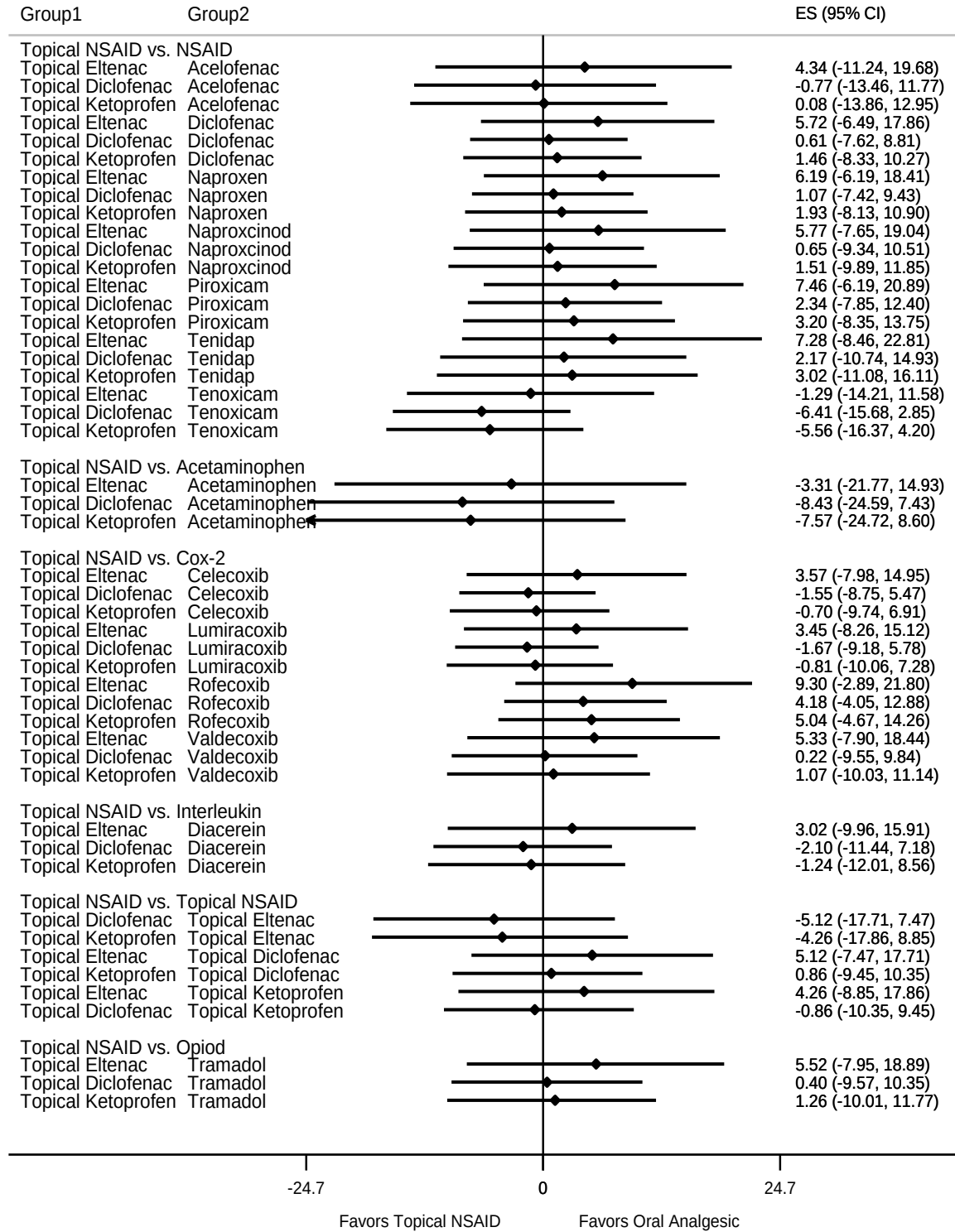
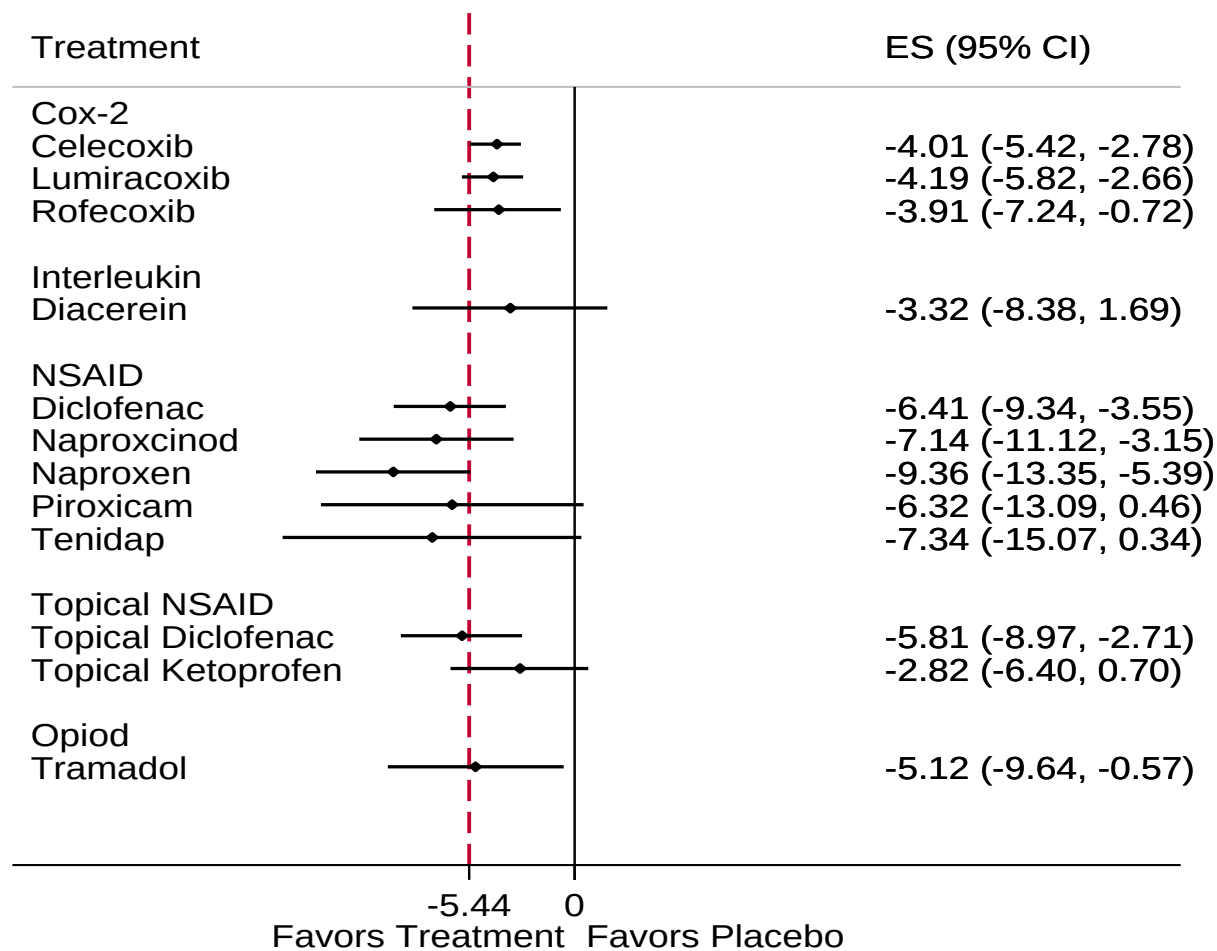
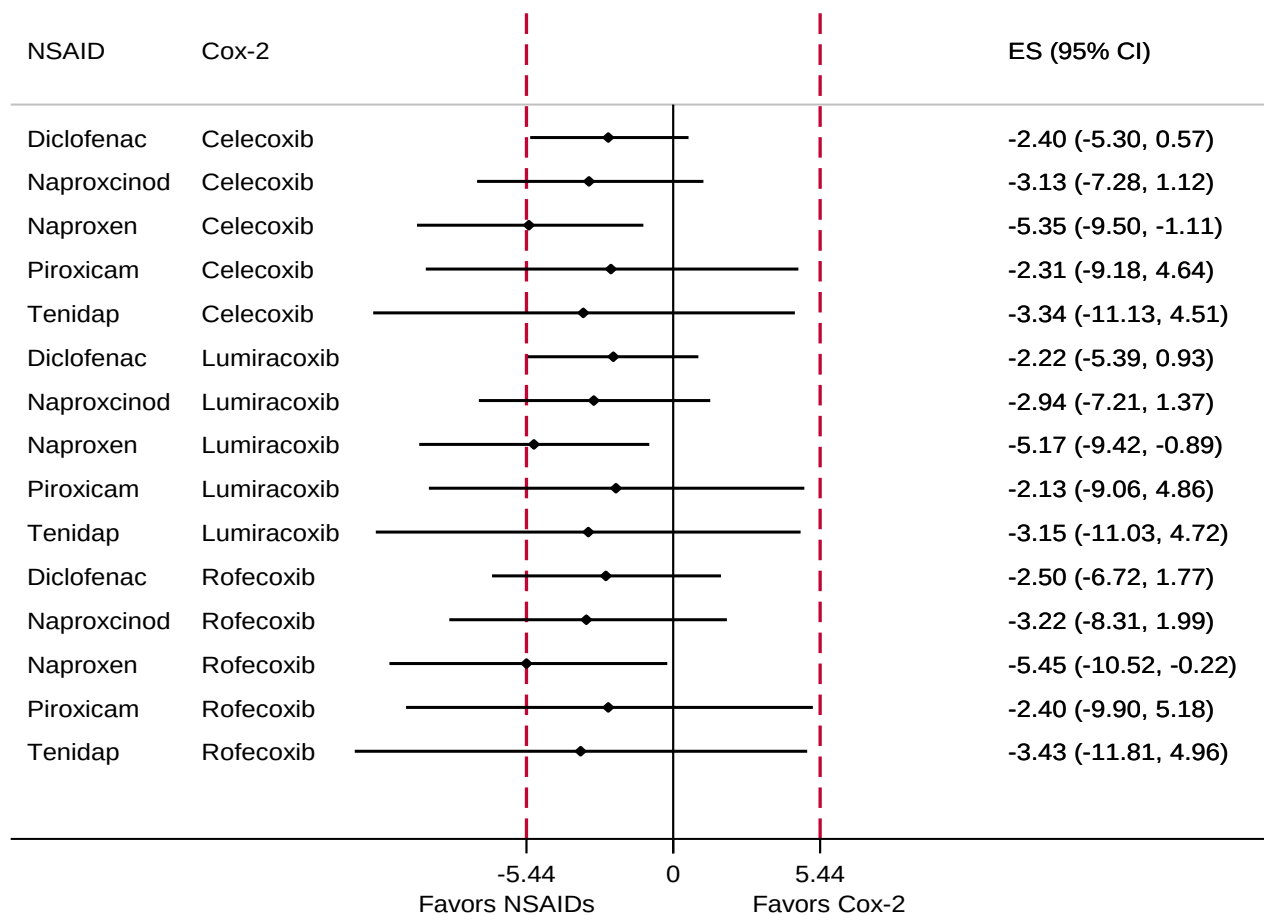


Figure 53. Network Meta-Analysis: Analgesics Versus Placebo (WOMAC Function)



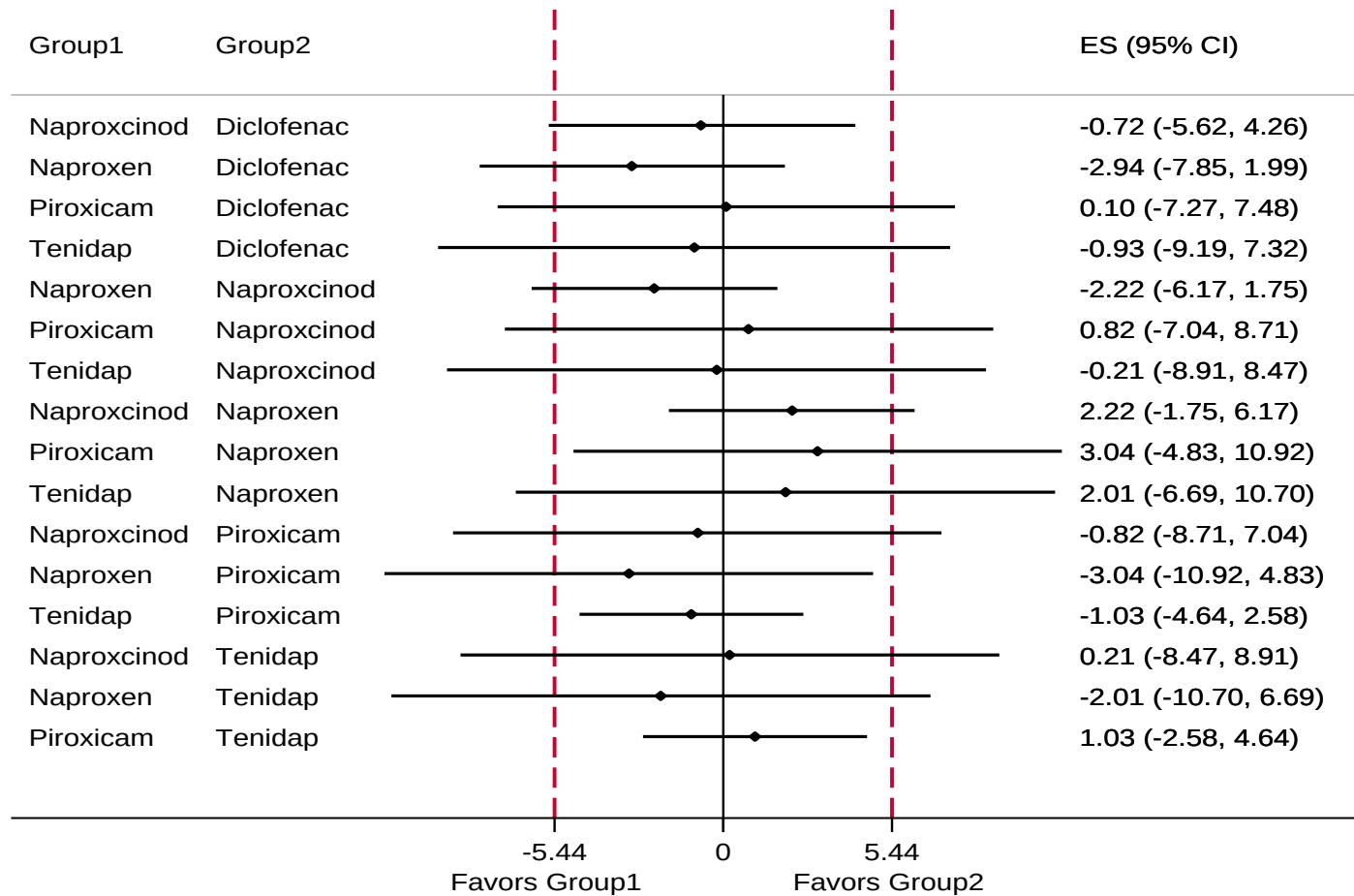
The red line indicates the MCII

Figure 54. Network Meta-Analysis: Cox-2 Versus NSAIDs (WOMAC Function)



The red line indicates the MCII

Figure 55. Network Meta-Analysis: NSAID Versus NSAID (WOMAC Function)



The red line indicates the MCII

Figure 56. Network Meta-Analysis: Cox-2 Versus Cox-2 (WOMAC Function)

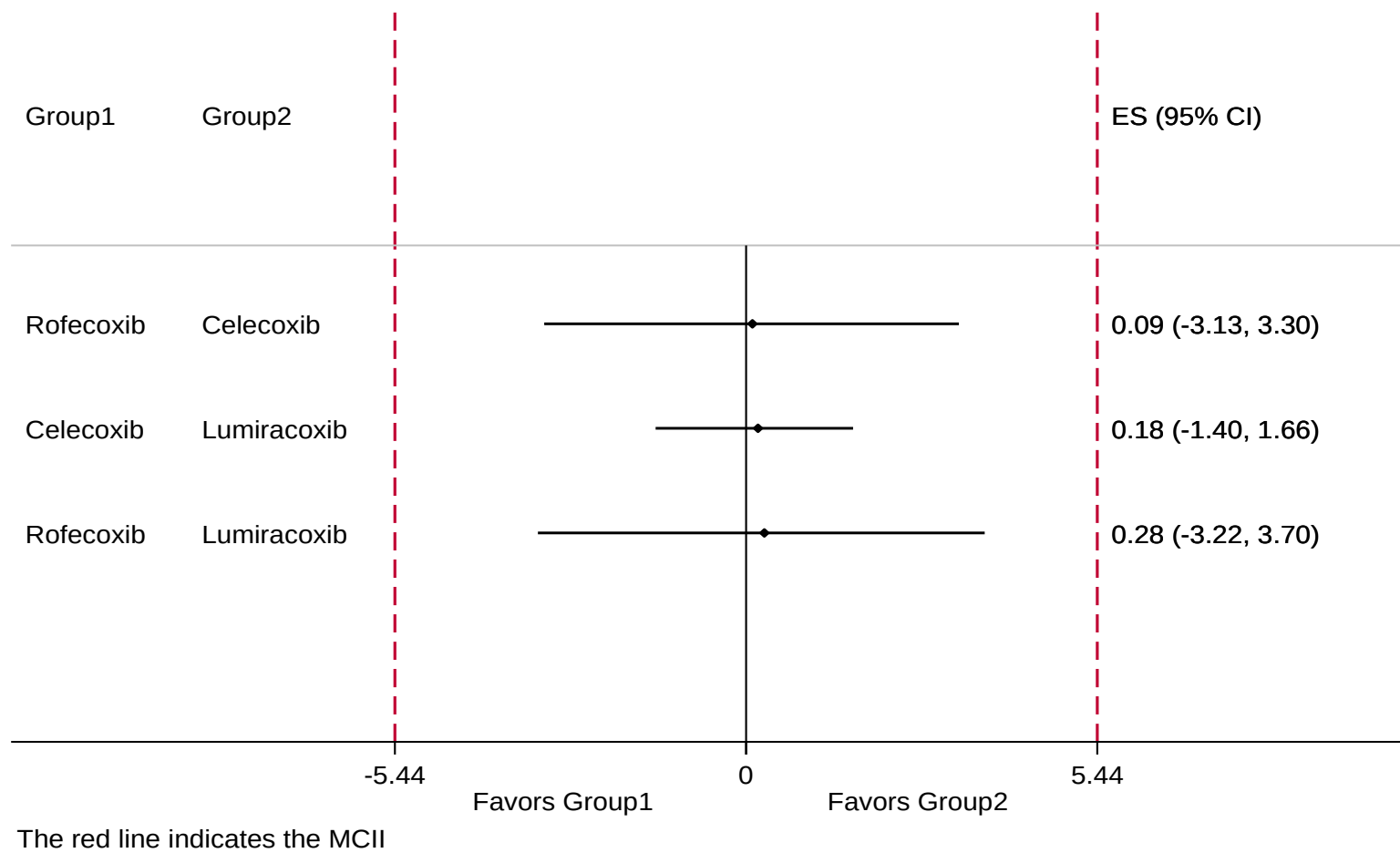
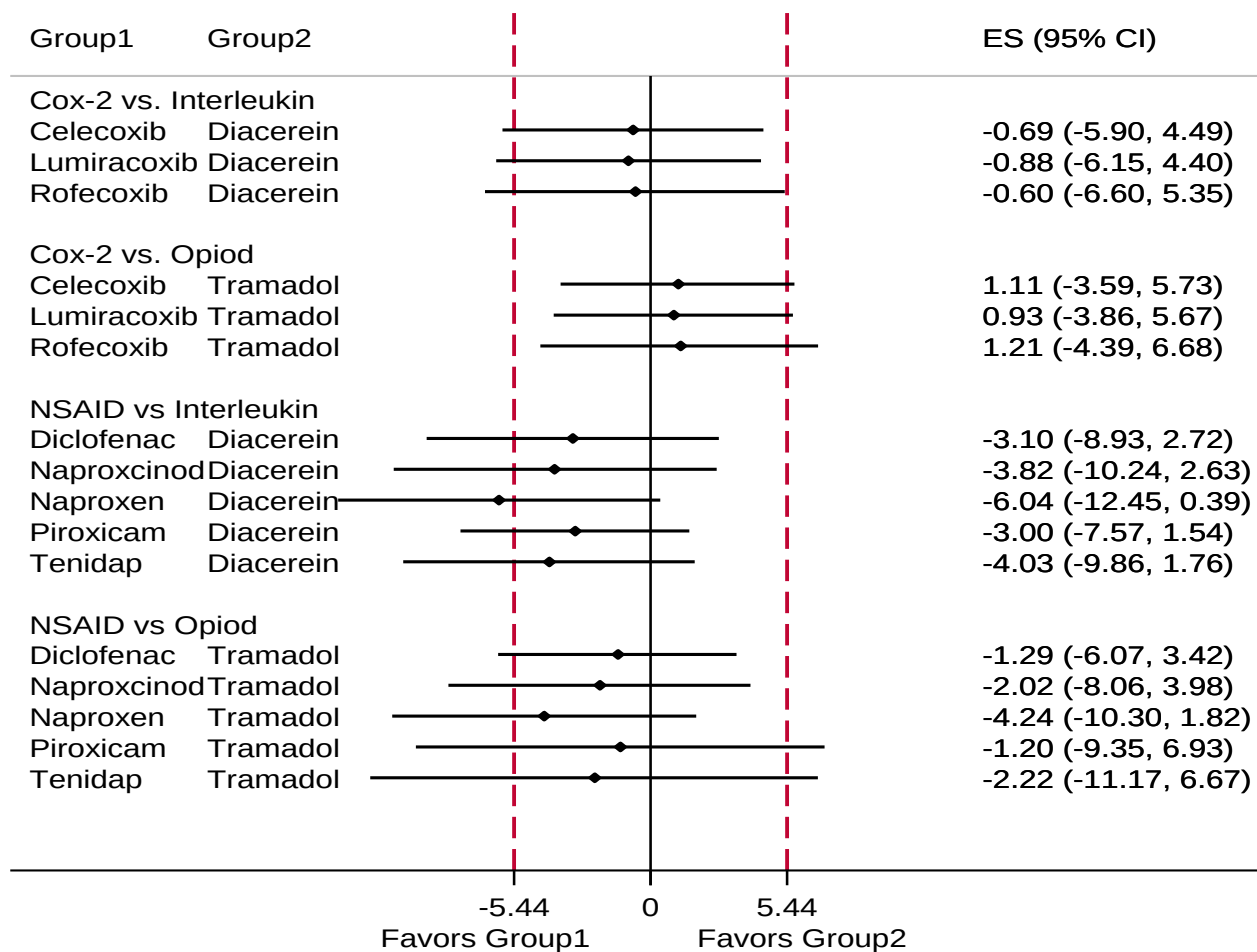
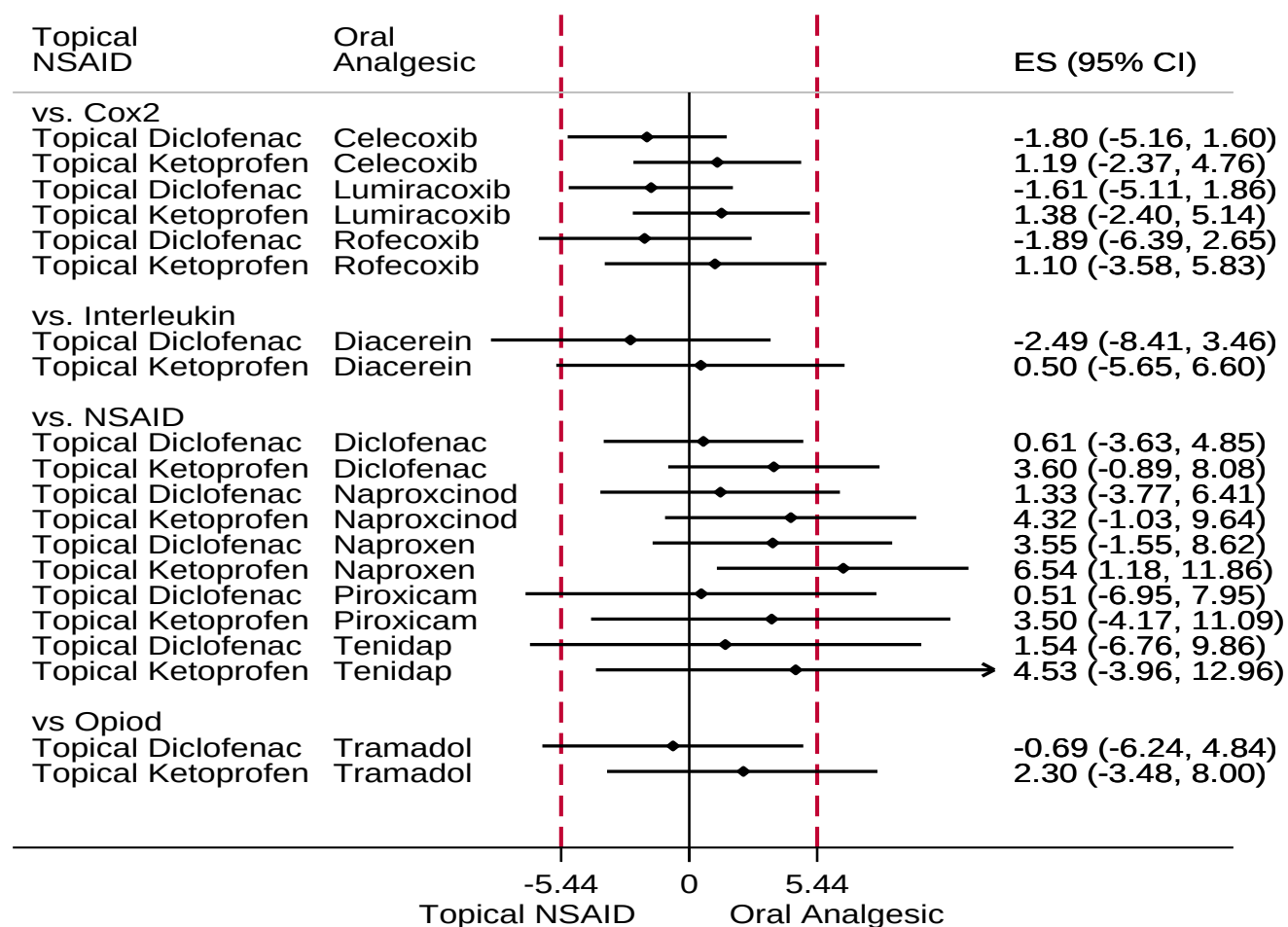


Figure 57. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (WOMAC Function)



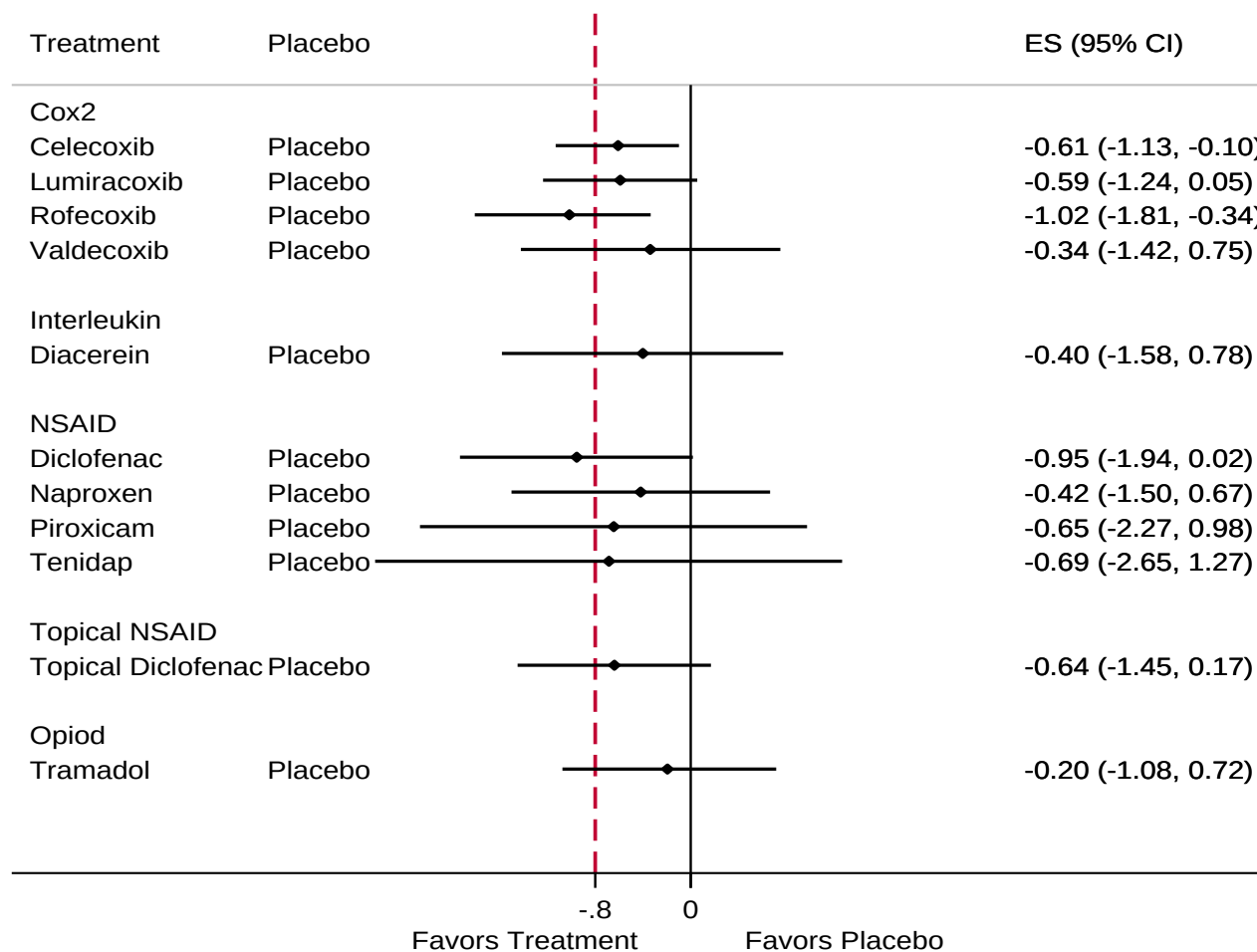
The red line indicates the MCII

Figure 58. Network Meta-Analysis: Topical NSAIDs Versus Other Analgesics (WOMAC Function)



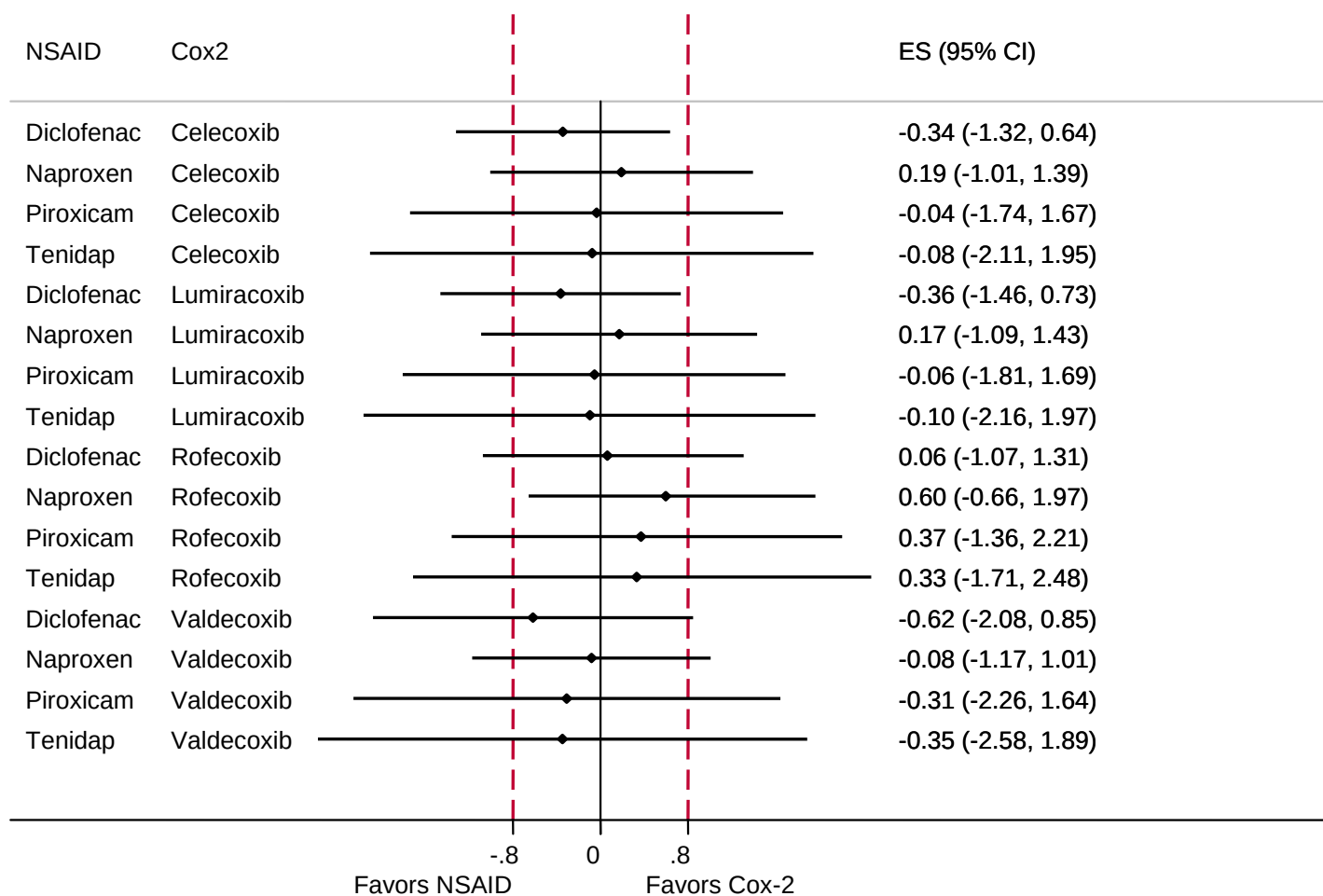
The red line indicates the MCII

Figure 59. Network Meta-Analysis: Analgesics Versus Placebo (WOMAC Stiffness)



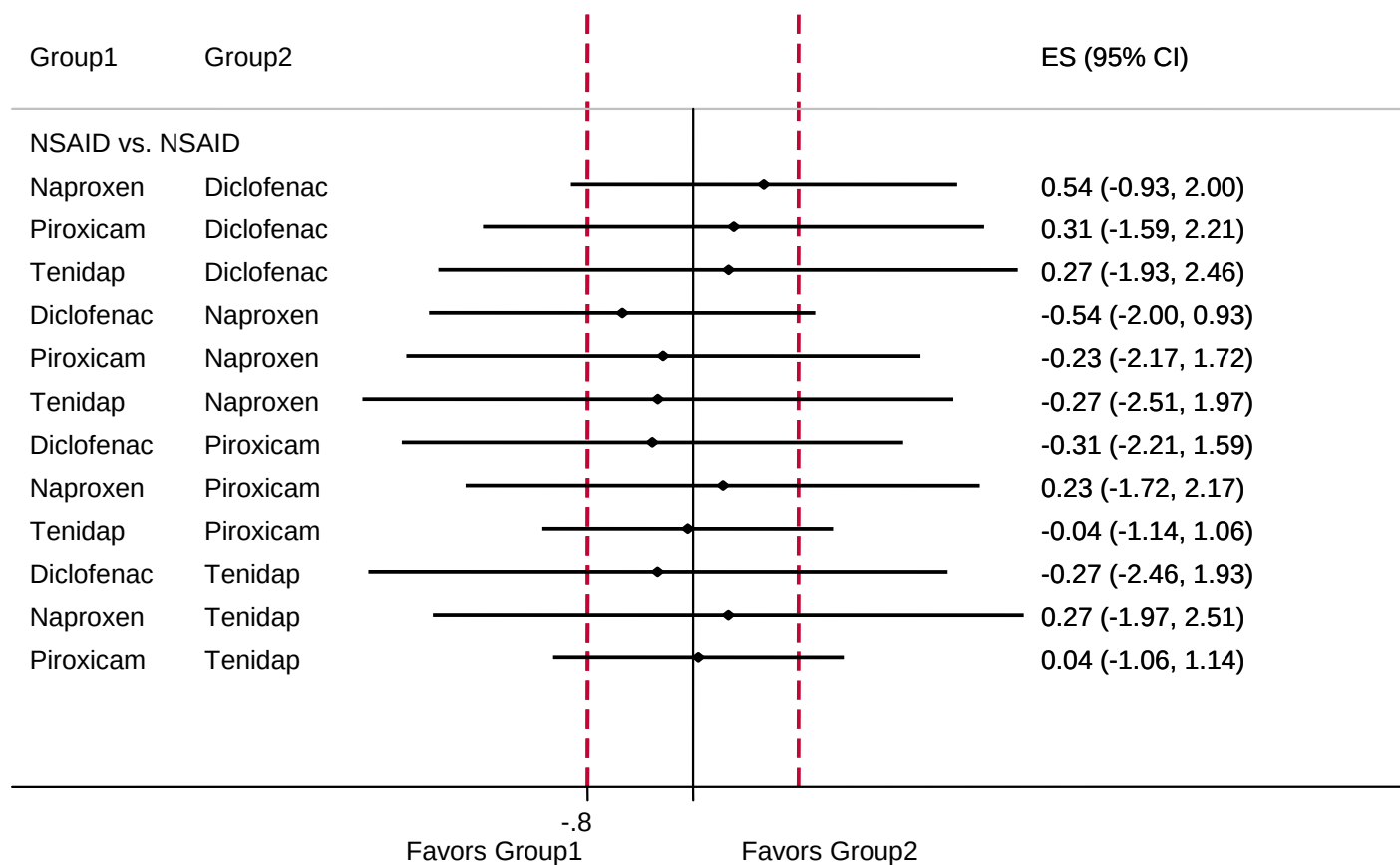
The red line indicates the MCII

Figure 60. Network Meta-Analysis: Cox-2 Versus NSAIDs (WOMAC Stiffness)



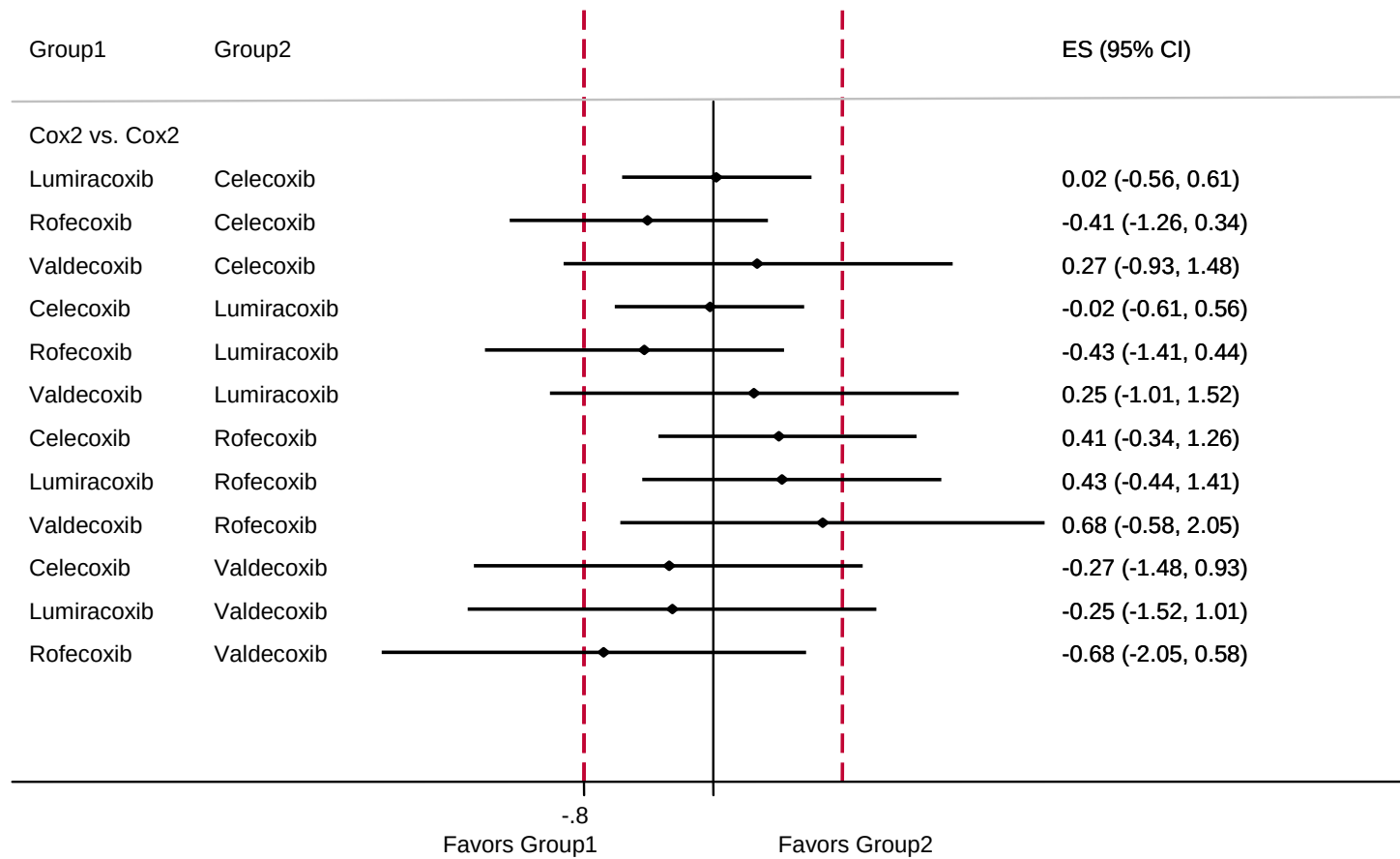
The red line indicates the MCII

Figure 61. Network Meta-Analysis: NSAIDS Versus NSAIDS (WOMAC Stiffness)



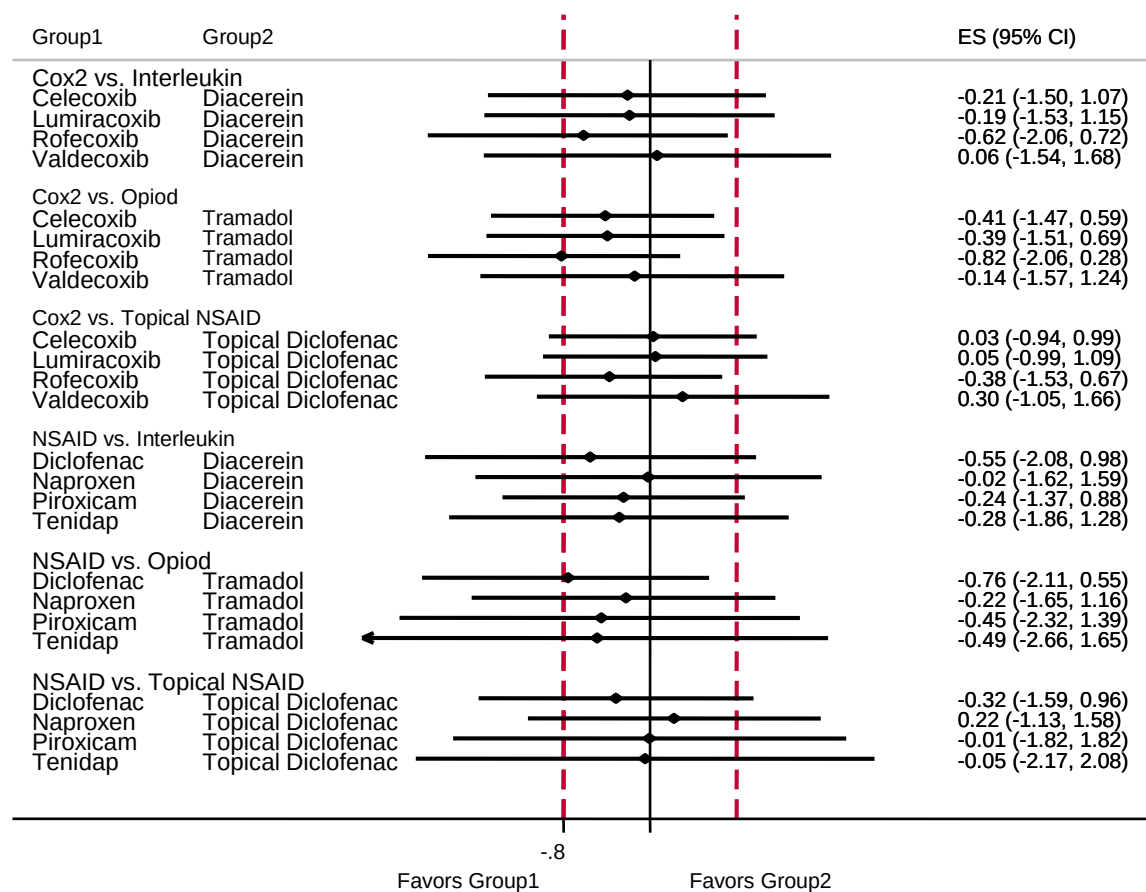
The red line indicates the MCII

Figure 62. Network Meta-Analysis: Cox-2 Versus Cox-2 (WOMAC Stiffness)



The red line indicates the MCII

Figure 63. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (WOMAC Stiffness)



The red line indicates the MCII

Figure 64. Network Meta-Analysis: Analgesics Versus Placebo (WOMAC Total)

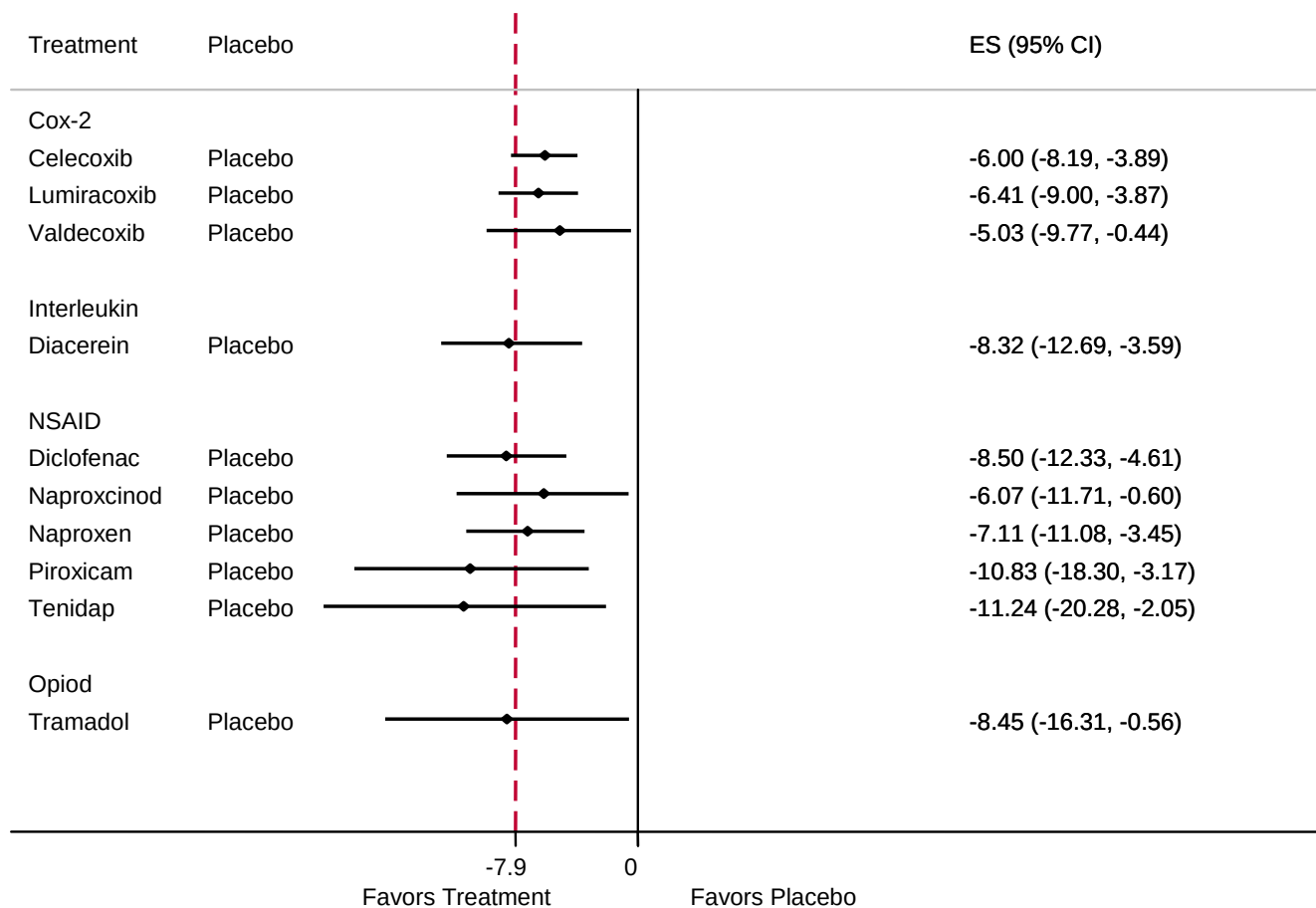
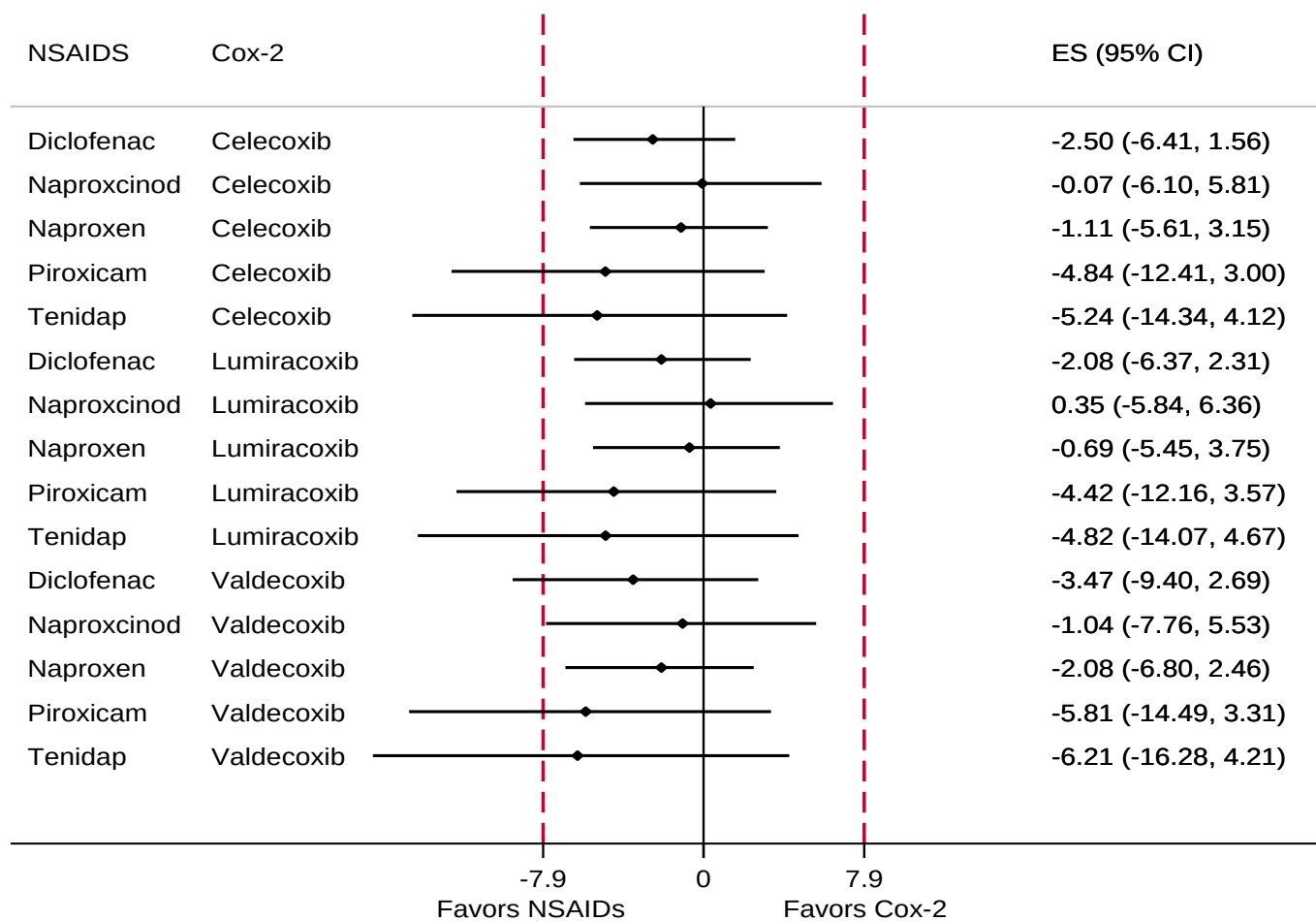


Figure 65. Network Meta-Analysis: NSAIDS Versus Cox-2 (WOMAC Total)



The red line indicates the MCII

Figure 66. Network Meta-Analysis: NSAIDS Versus NSAIDS (WOMAC Total)

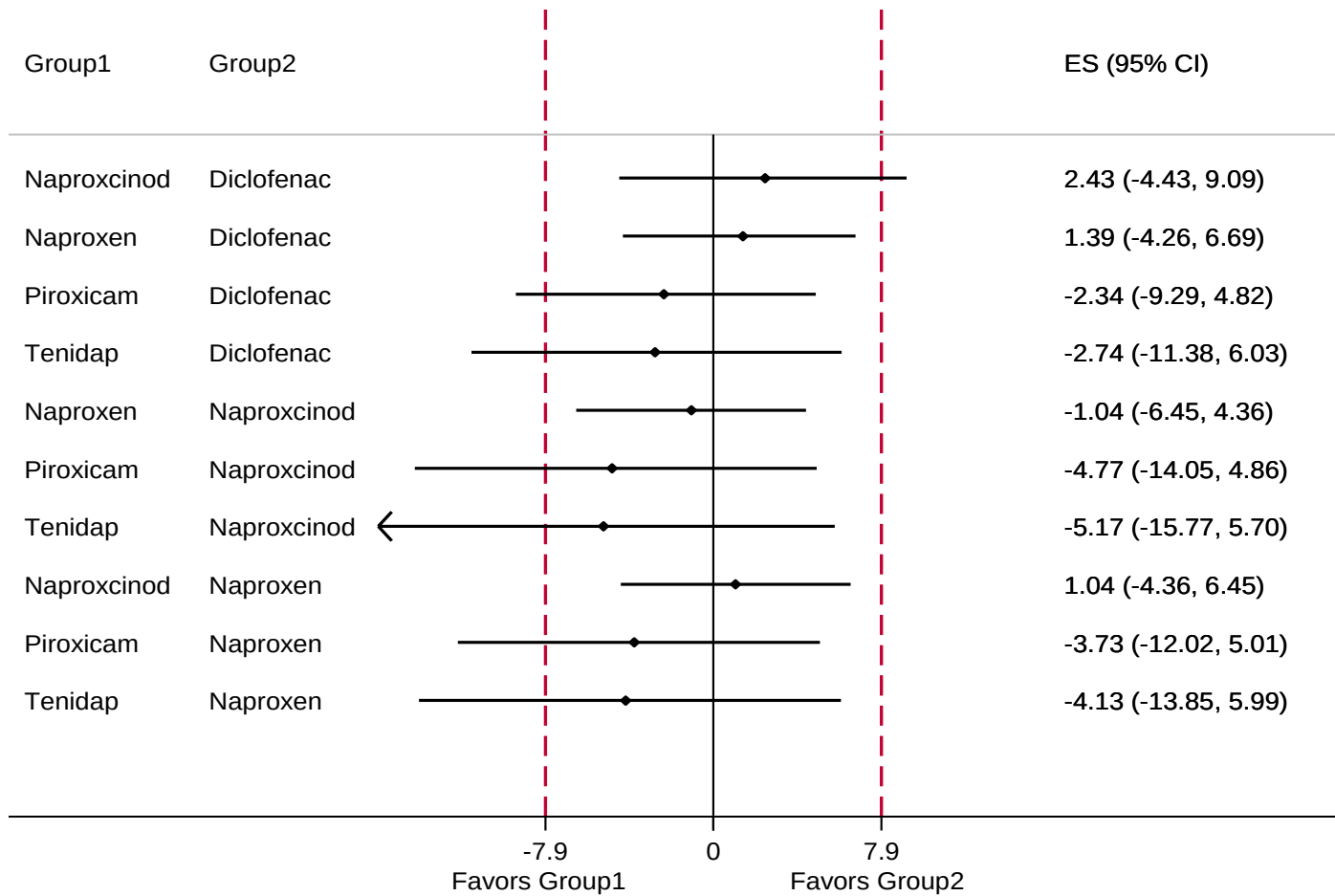


Figure 67. Network Meta-Analysis: Cox-2 Versus Cox-2 (WOMAC Total)

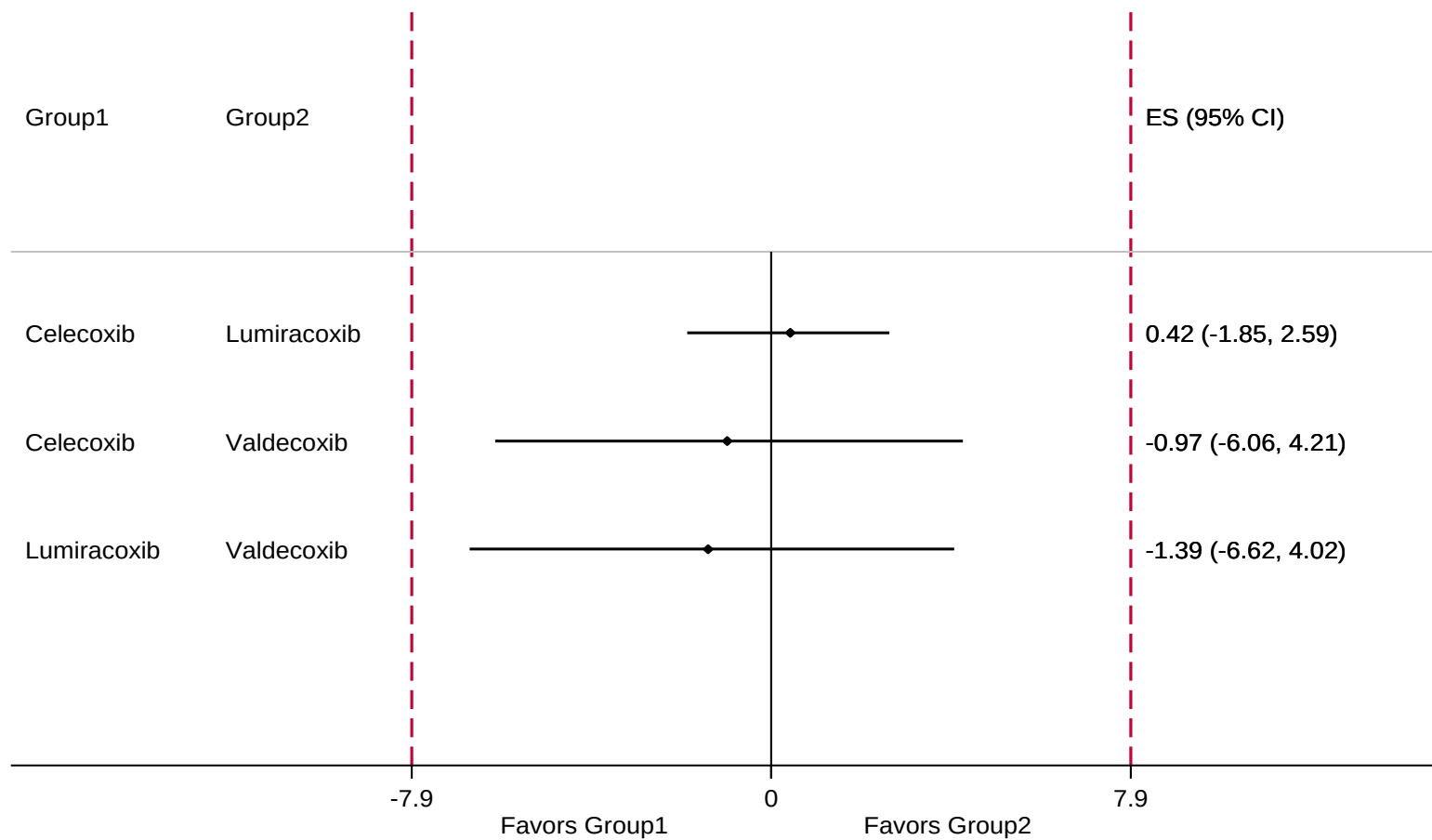
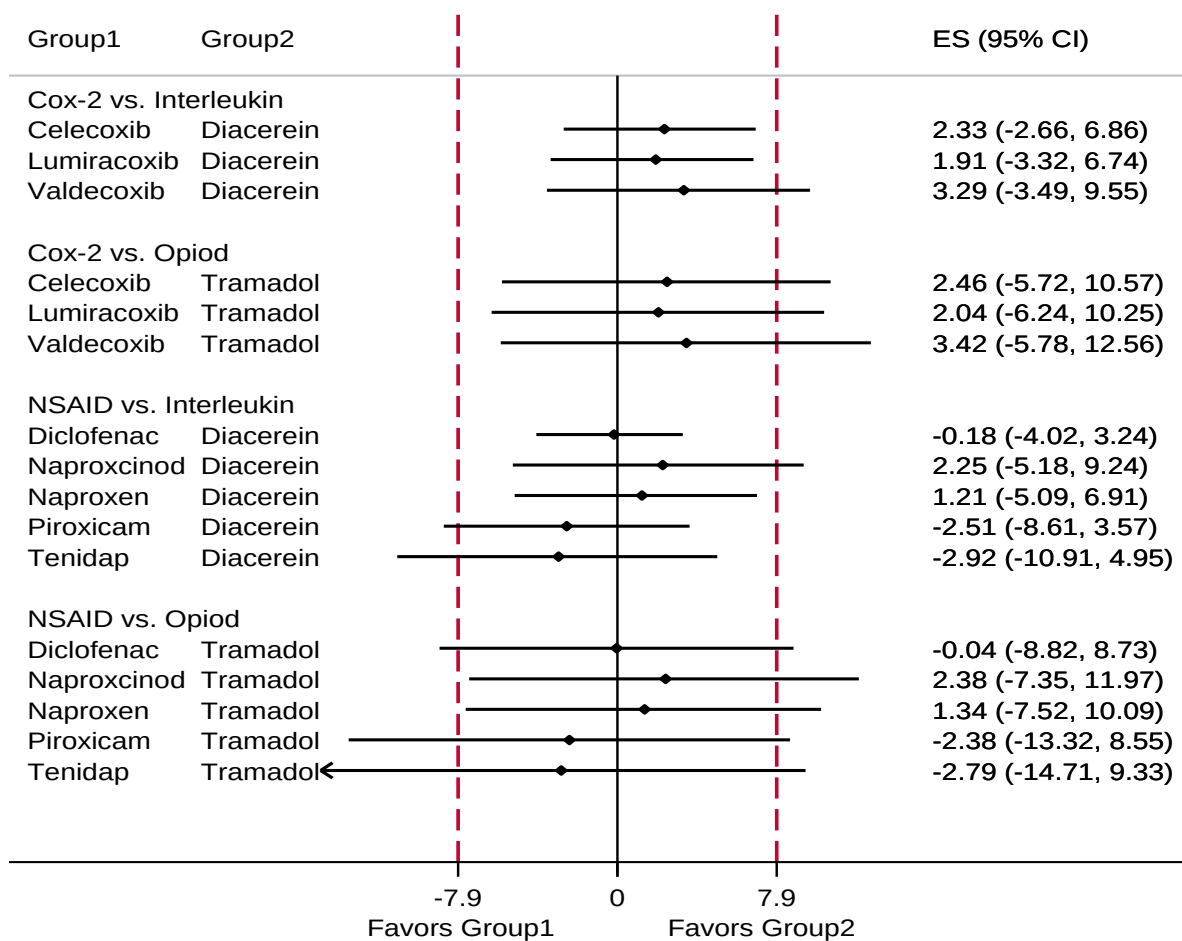
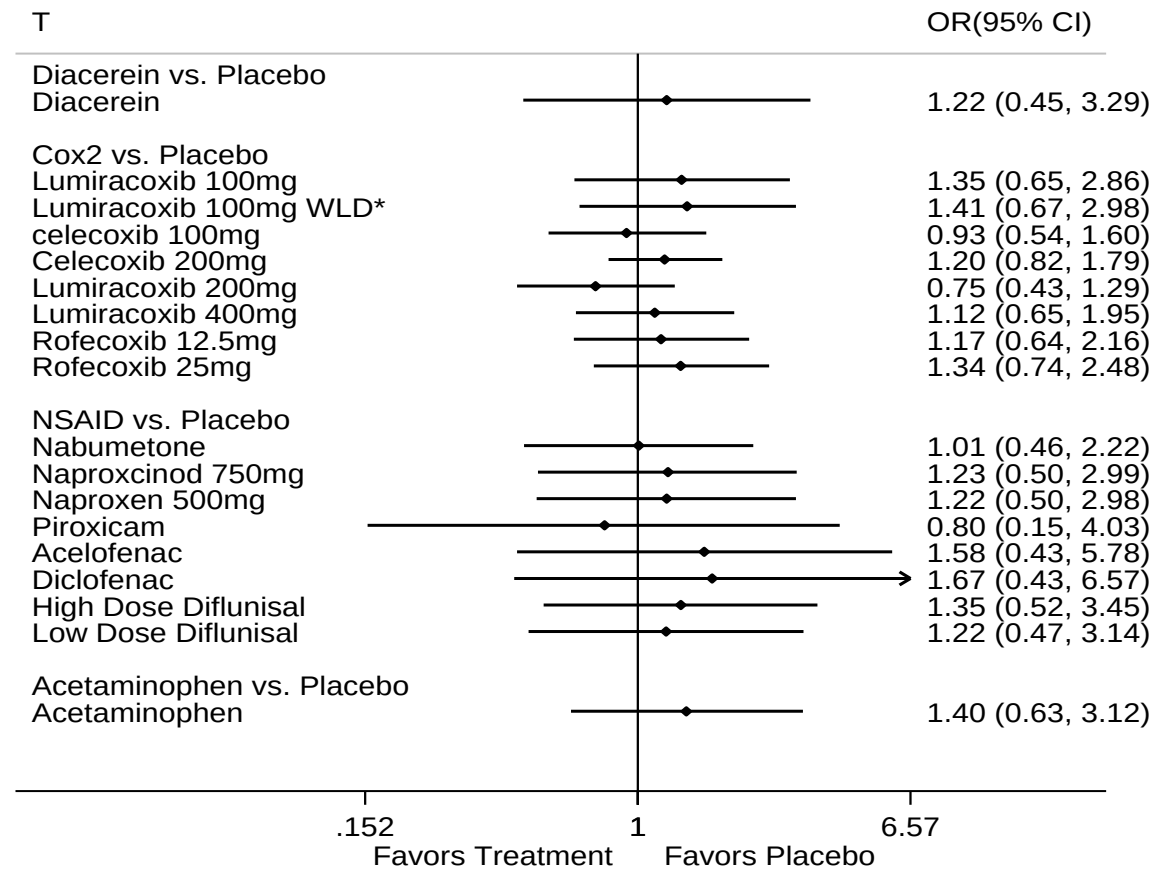


Figure 68. Network Meta-Analysis: Cox-2 and NSAIDS Versus Other Analgesics (WOMAC Total)



The red line indicates the MCII

Figure 69. Network Meta-Analysis: Analgesics Versus Placebo (Adverse Events)



WLD=With Loading Dose

Figure 70. Network Meta-Analysis: Cox-2 Versus Cox-2 (Adverse Events)

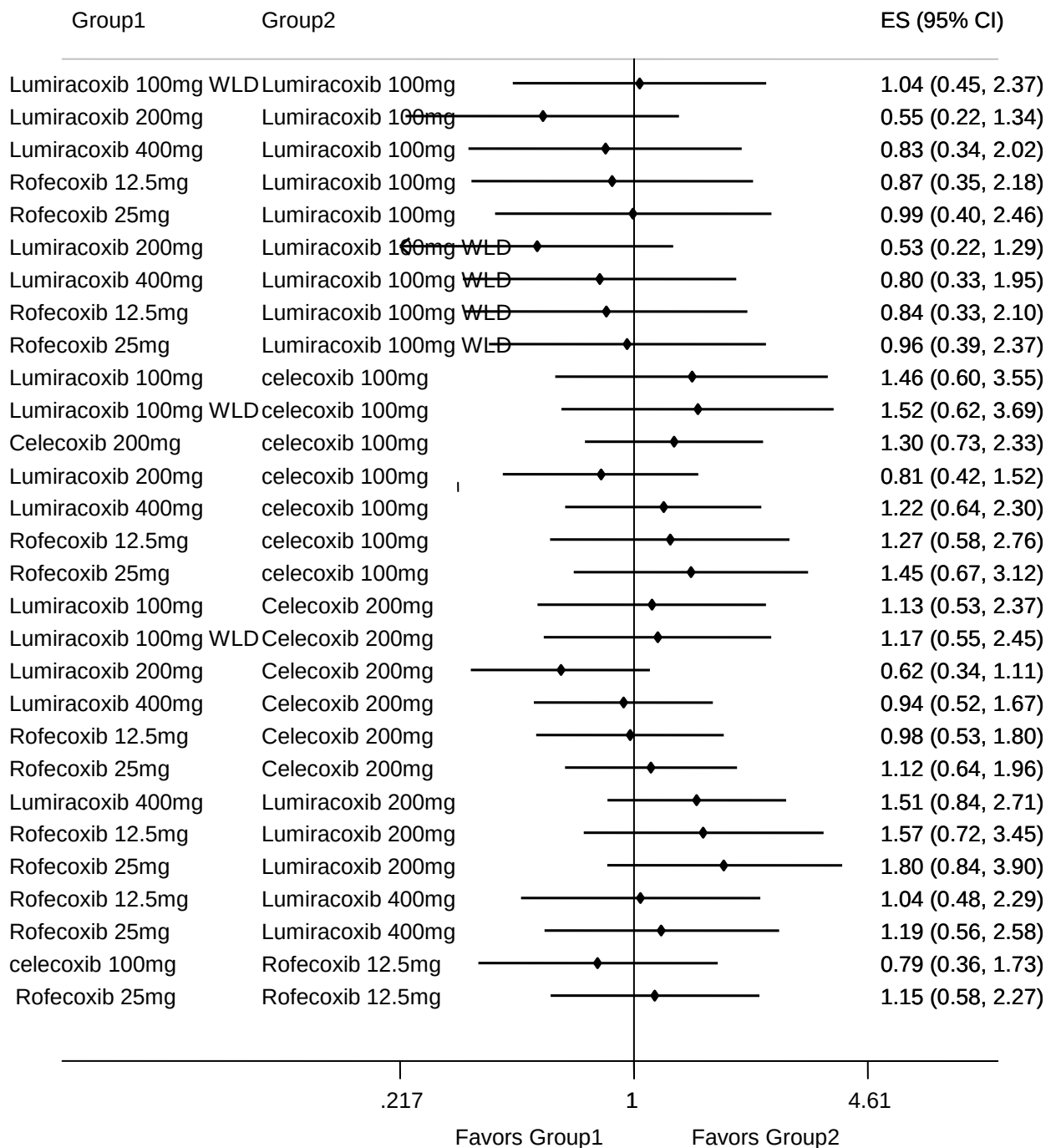


Figure 71. Network Meta-Analysis: NSAID Versus NSAID (Adverse Events)

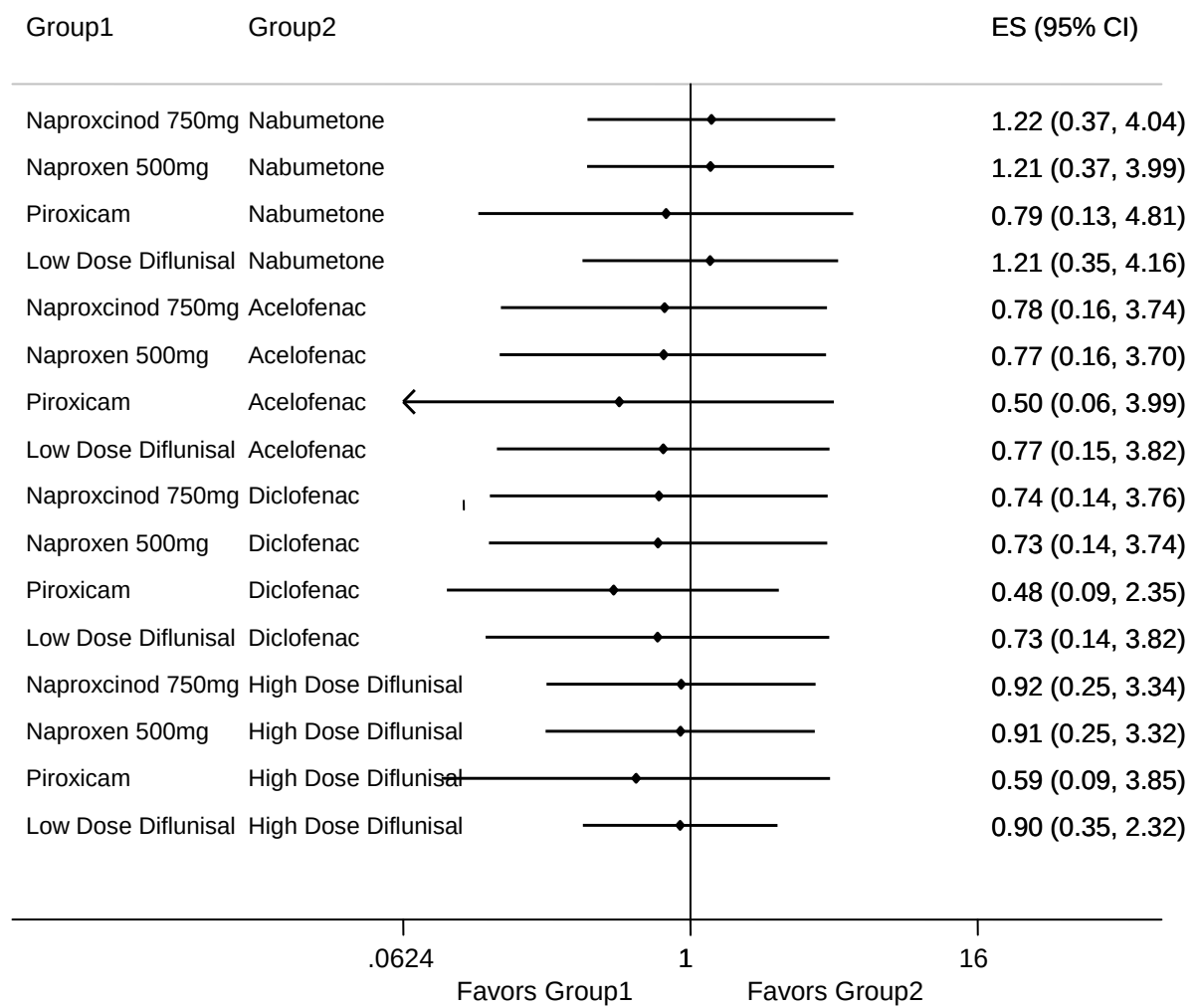
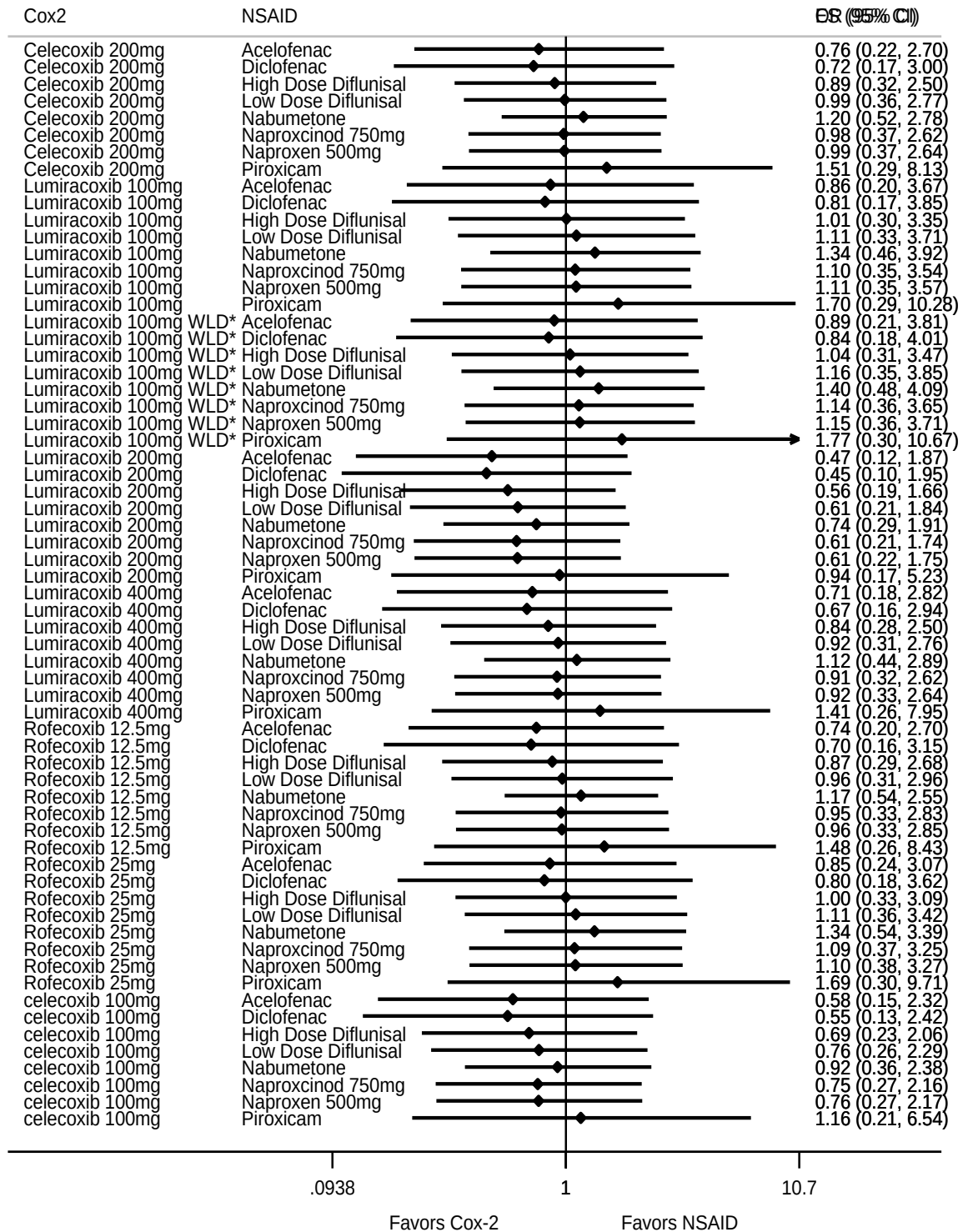


Figure 72. Network Meta-Analysis: Cox-2 Versus NSAID (Adverse Events)



*WLD= With Loading Dose

Figure 73. Network Meta-Analysis: Acetaminophen Versus Cox-2 and NSAIDS (Adverse Events)

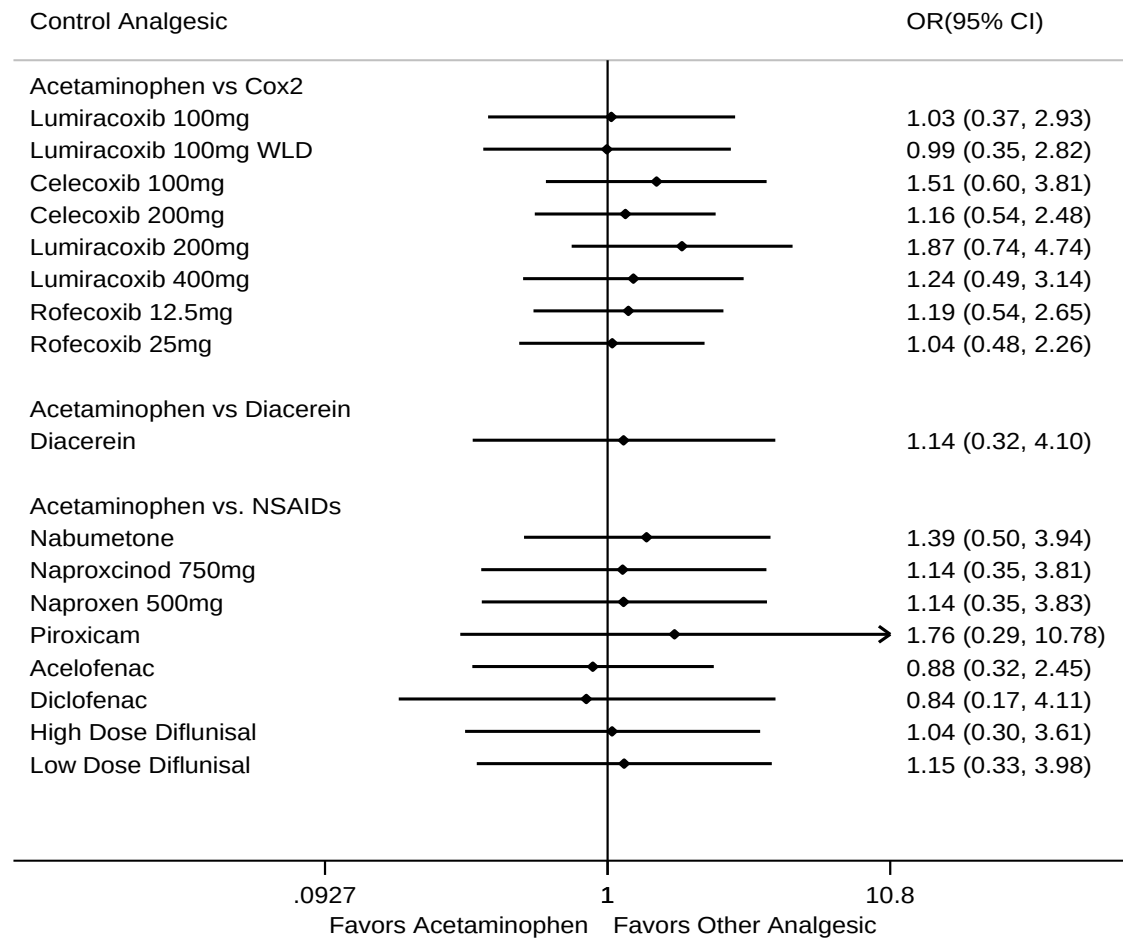
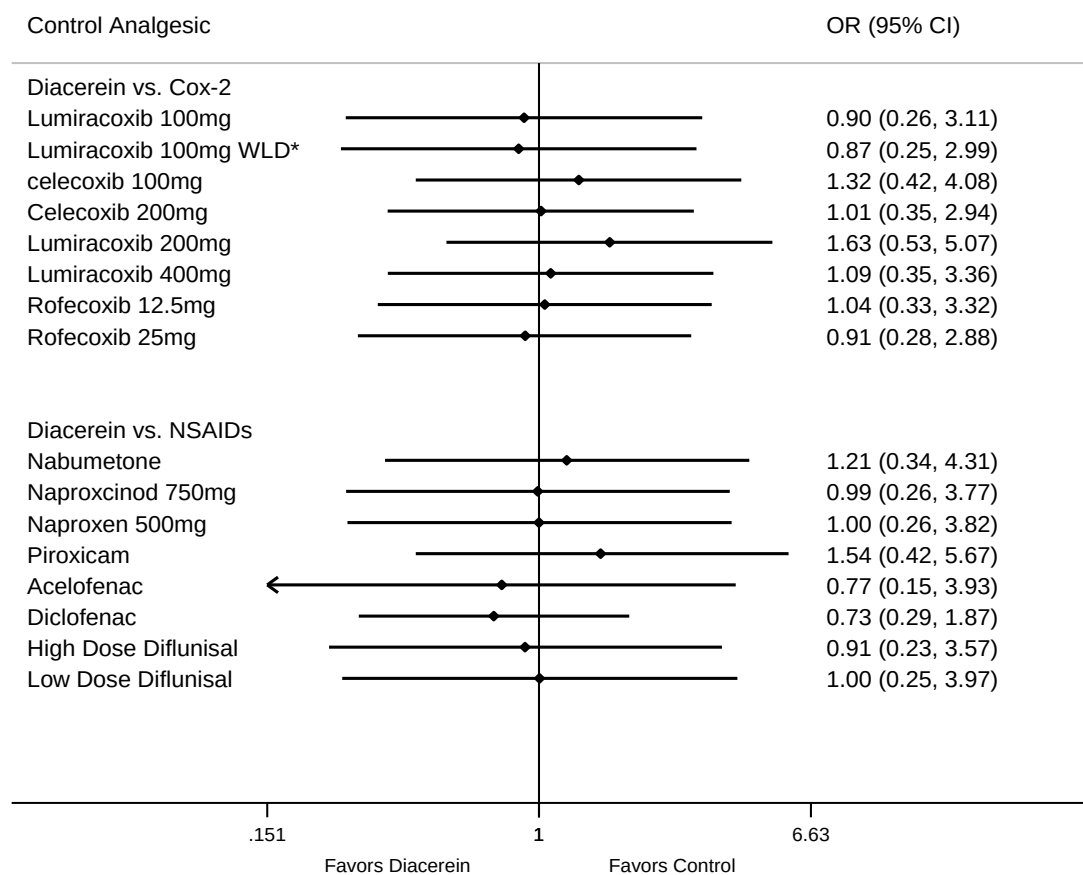


Figure 74. Network Meta-Analysis: Diacerein (Interleukin) Versus Cox-2 Inhibitors and NSAIDs (Adverse Events)



*WLD = With Loading Dose

**Figure 75. Network Meta-Analysis: Gastrointestinal Cox-2 Versus NSAIDS
(Adverse Events)**

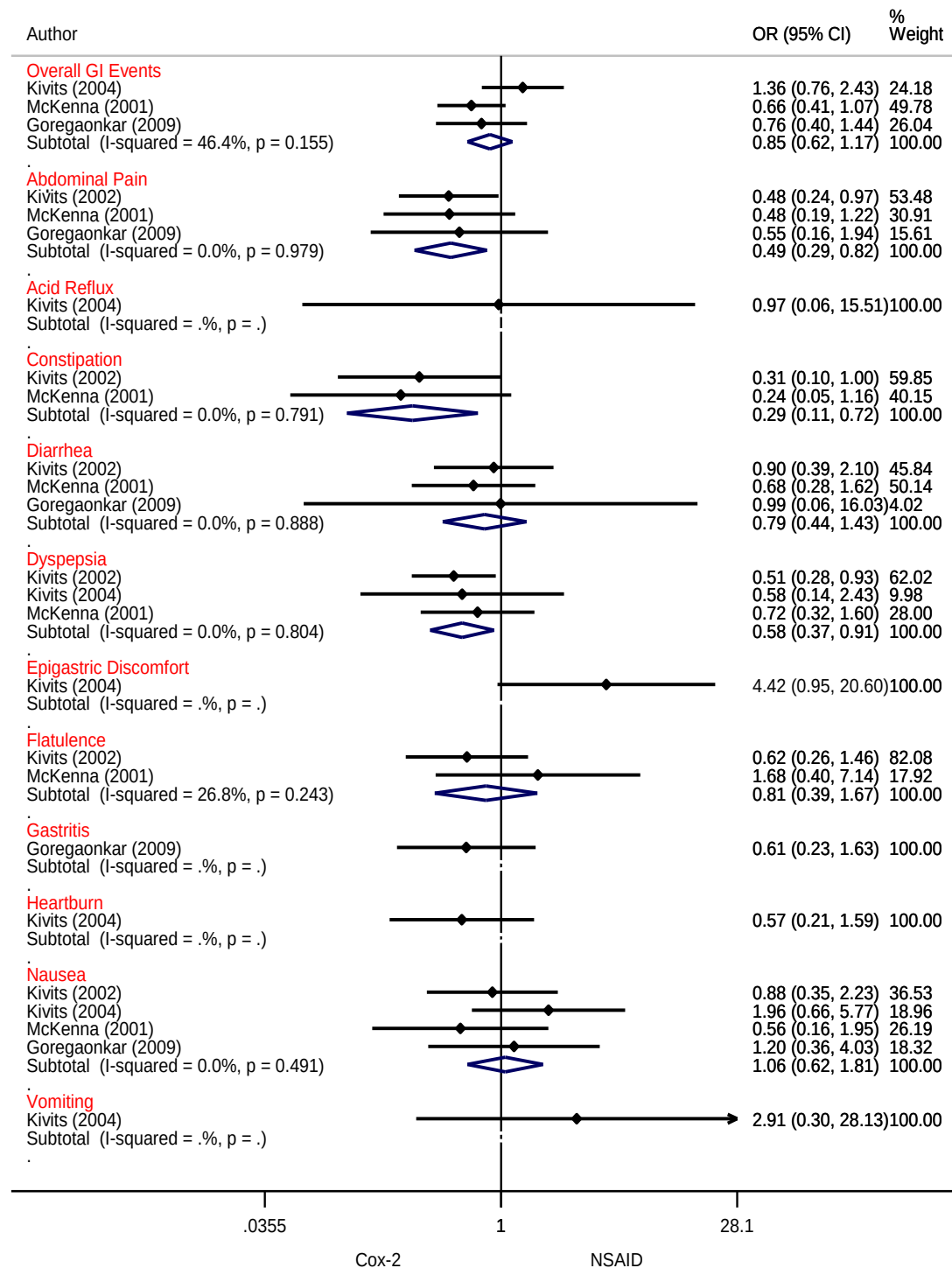


Figure 76. Network Meta-Analysis: Cox-2 Versus NSAID Non-Gastrointestinal (Adverse Events)

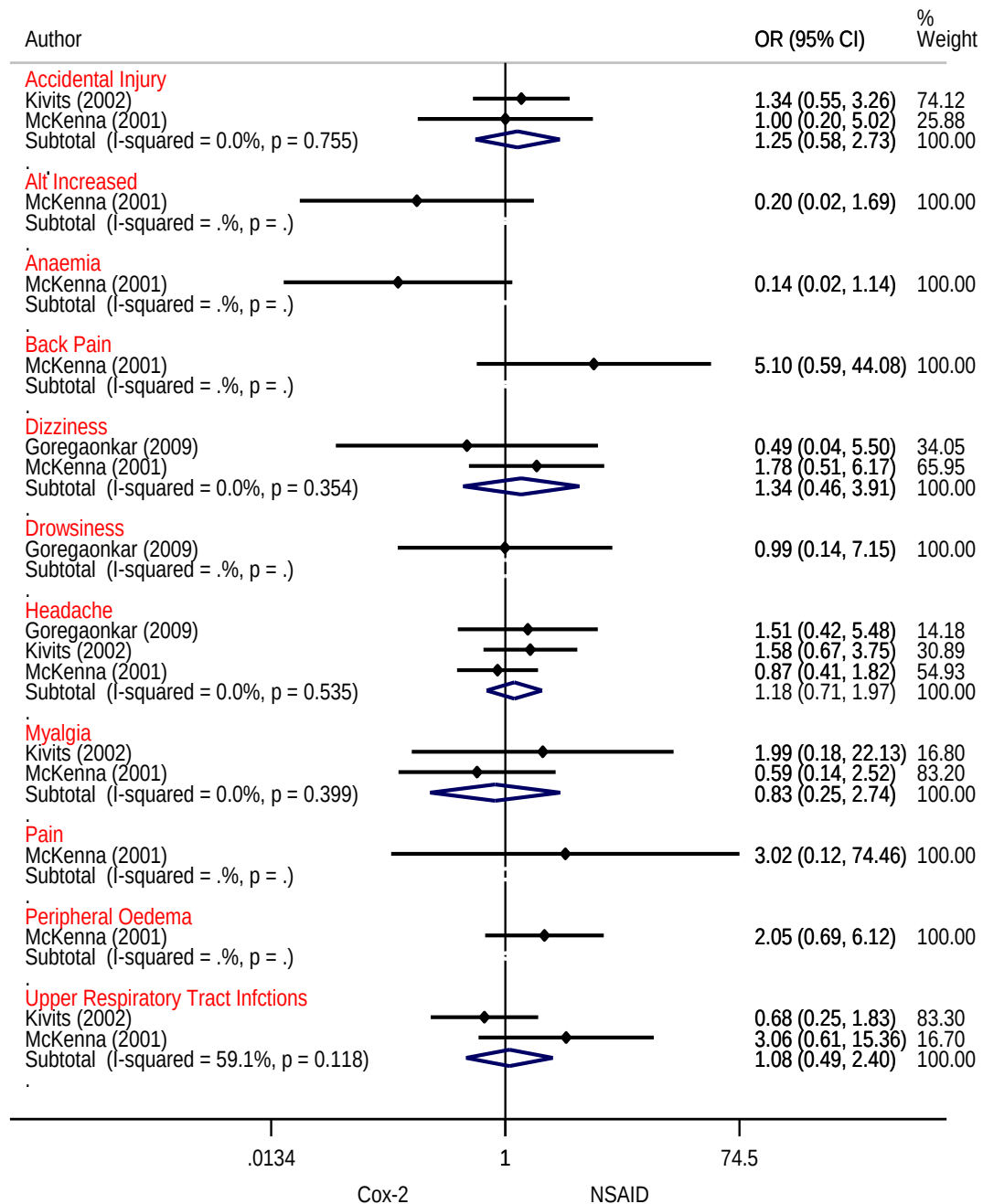


Figure 77. Network Meta-Analysis: Acetaminophen Versus Celecoxib (Adverse Events)

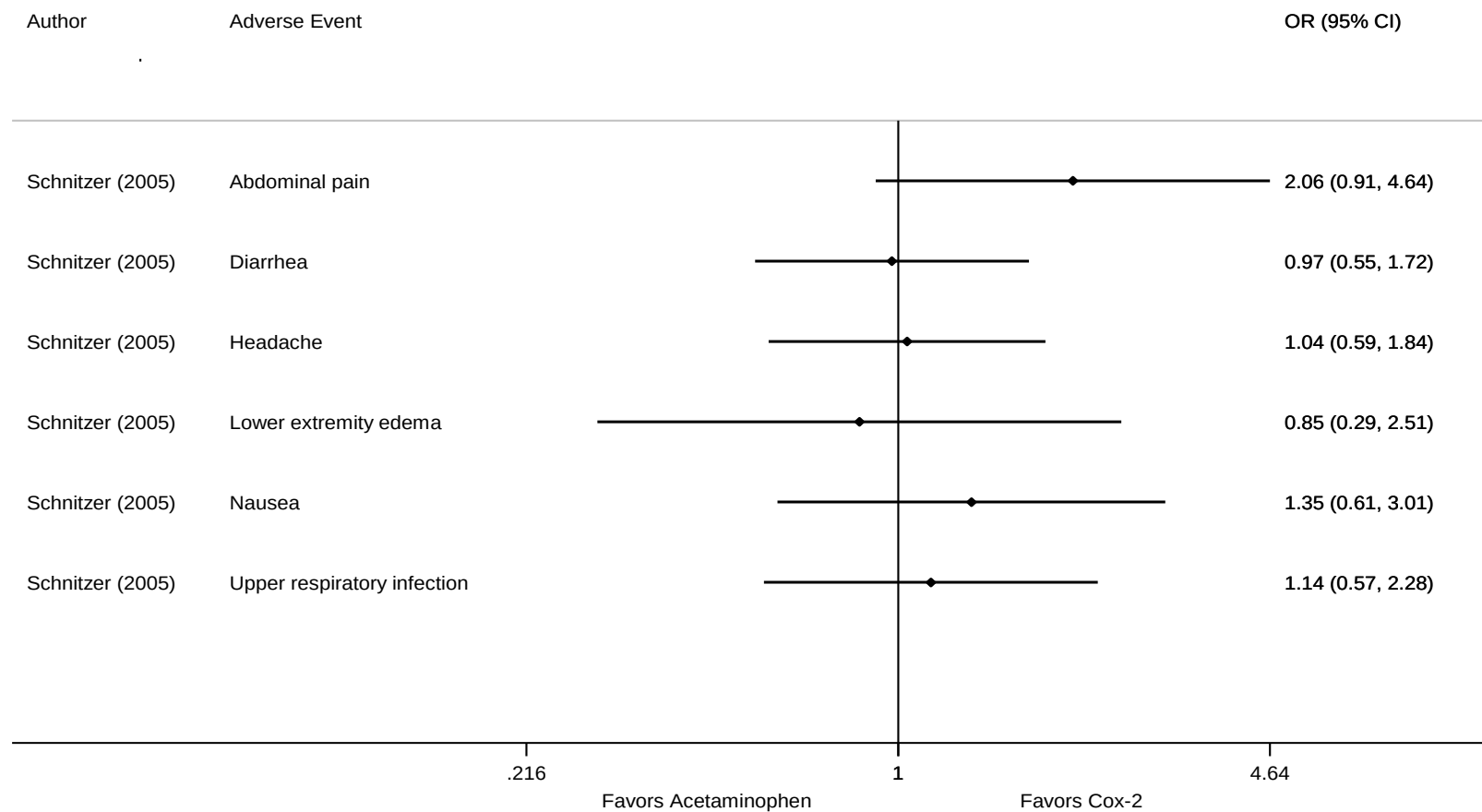


Figure 78. Network Meta-Analysis: Acetaminophen Versus Rofecoxib 12.5 mg (Adverse Events)

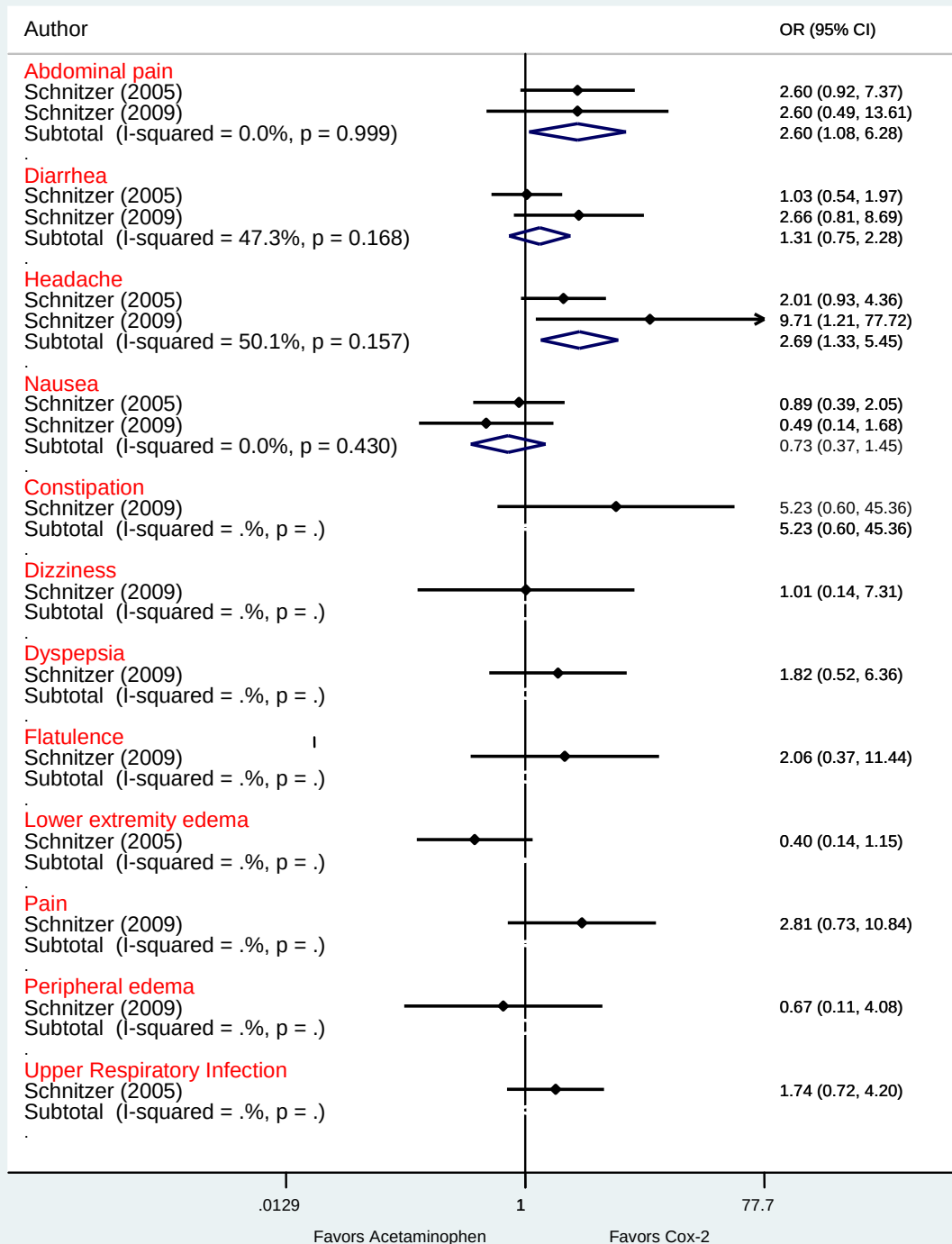


**Figure 79. Network Meta-Analysis: Acetaminophen Versus Rofecoxib 25mg
(Adverse Events)**

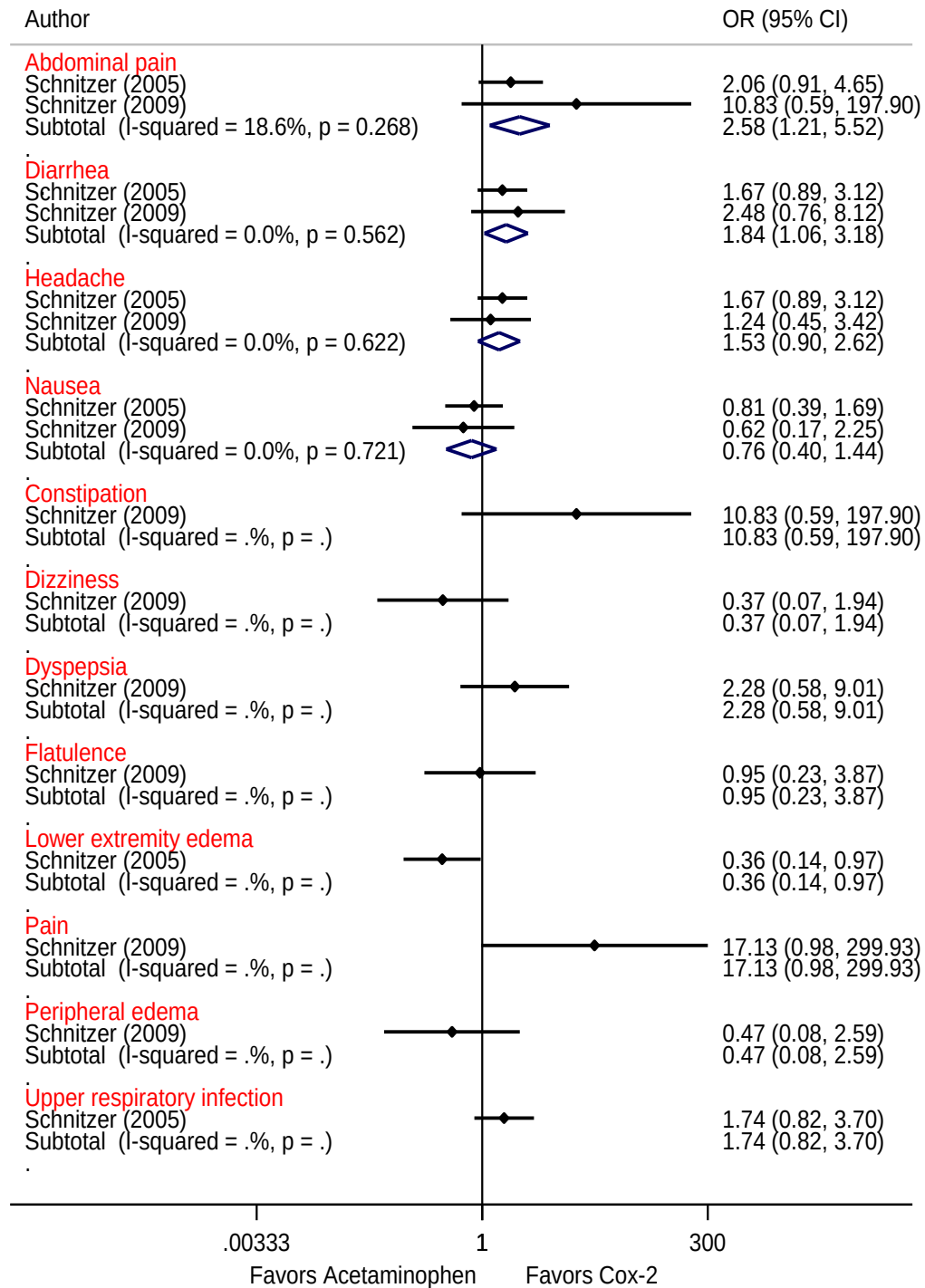
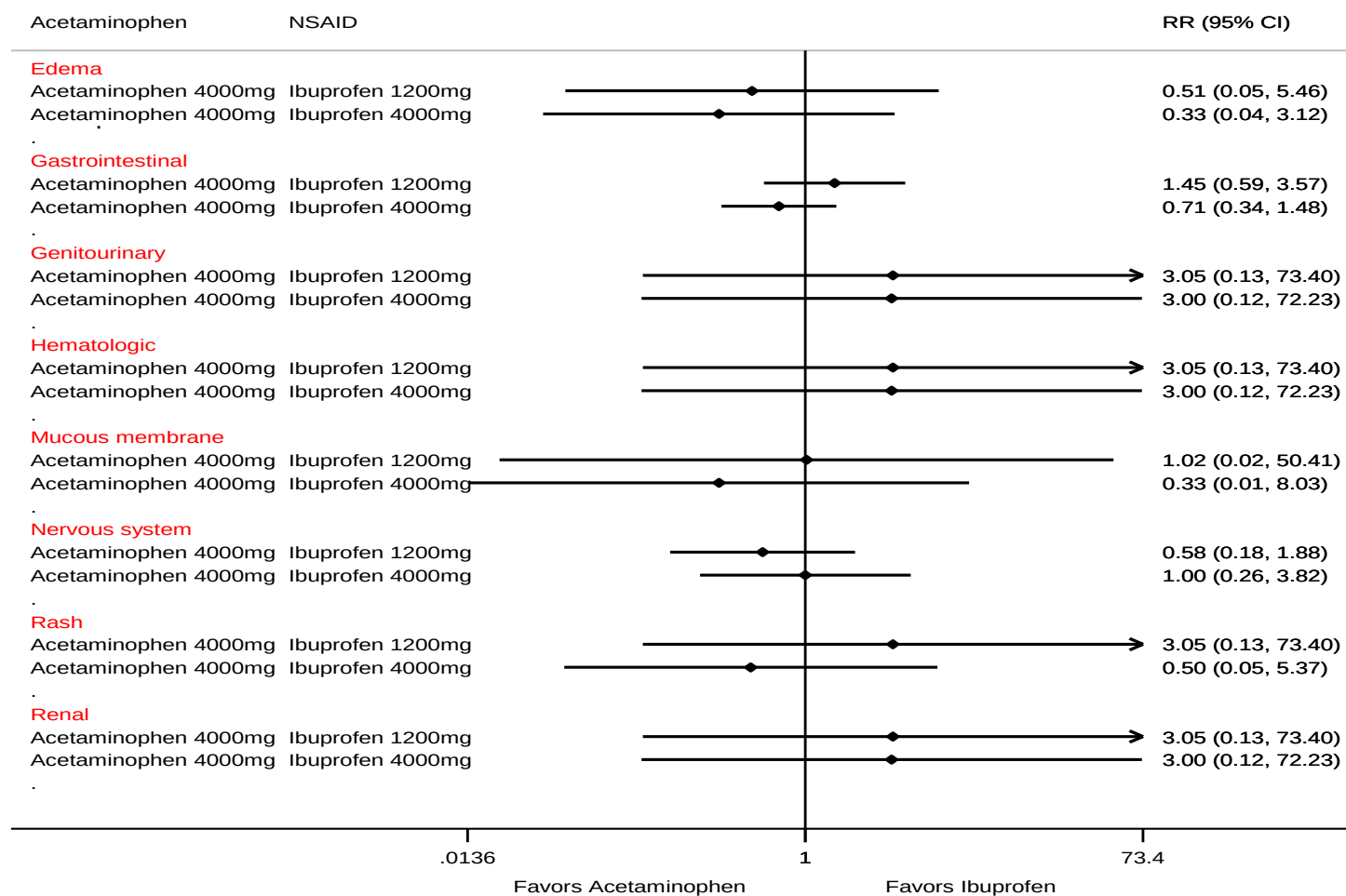


Figure 80. Network Meta-Analysis: Acetaminophen Versus Ibuprofen-Adverse Events (Bradley 1991)



RECOMMENDATION 8

We are unable to recommend for or against the use of intraarticular (IA) corticosteroids for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

Our search found only four placebo comparison studies that met criteria and evaluated pain relief for a minimum treatment period of four weeks.¹⁰²⁻¹⁰⁵ One study found IA corticosteroids to be superior to placebo on WOMAC total subscale scores at four weeks.¹⁰² However, another study found IA corticosteroid injections inferior to hyaluronic acid injections¹⁰⁶ and a third study found IA corticosteroids inferior to needle lavage (tidal irrigation).¹⁰⁷ Since the evidence in the guideline did not support the use of hyaluronic acid or needle lavage, the work group interpreted the evidence to be inconclusive as to the benefit of IA corticosteroids.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 166-Table168](#), [Table 169-Table 171](#)

There were four moderate quality studies that compared intraarticular (IA) corticosteroids to placebo. None were flawed in the hypothesis, blinding, treatment integrity or measurement domains. All four studies were flawed in the group assignment domain, and three studies were flawed in the group comparability and investigator bias domains.

One additional moderate quality study compared IA corticosteroids to Hylan G-F 20 injections based on 10 outcomes.¹⁰⁶ None were flawed in the hypothesis, blinding, treatment integrity or measurement domains. They were all flawed in the group assignment, group comparability and investigator bias domains.

Another moderate quality study compared corticosteroids to tidal irrigation.¹⁰⁷ There was uncertainty about the comparability of the groups at baseline. Also, there was potential for investigator bias in the study.

APPLICABILITY

Relevant Tables: [Table 166-Table168](#), [Table 169-Table 171](#)

In all but one included studies, the participants may not have been representative of those seen in clinical practice. Also, it was unclear if any of the studies administered treatment similarly provided in clinical settings. Compliance and adherence for all included studies were similar to what is seen in clinical practice. Finally, all but one study included all enrolled patients in the final analysis.

FINAL STRENGTH OF EVIDENCE

Four out of five studies comparing IA corticosteroids to placebo had moderate quality and moderate applicability resulting in a moderate strength of evidence rating. One study had high quality and moderate applicability so its strength of evidence was high.

Table 166. Quality and Applicability Summary: IA Corticosteroids Versus Placebo

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Chao (2010)	WOMAC Pain	4 weeks	Moderate	Moderate	Moderate
Chao (2010)	WOMAC Total	4 weeks	Moderate	Moderate	Moderate
Gaffney (1995)	VAS Pain	6 weeks	Moderate	Moderate	Moderate
Gaffney (1995)	Health Assessment Questionnaire	6 weeks	Moderate	Moderate	Moderate
Gaffney (1995)	Walk Distance (1 minute)	6 weeks	Moderate	Moderate	Moderate
Raynauld (2003)	VAS Patient Pain Assessment at Night	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	VAS Patient Pain at Night	2 years	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Pain	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Pain	2 years	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Function	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Function	2 years	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Raynauld (2003)	50-foot walking time (seconds)	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	50-foot walking time (seconds)	2 years	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Stiffness	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Stiffness	2 years	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Total	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	WOMAC Total	2 years	Moderate	Moderate	Moderate
Raynauld (2003)	Physician Global Assessment	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	Patient Global Assessment	1 year	Moderate	Moderate	Moderate
Raynauld (2003)	Physician Global Assessment	2 years	Moderate	Moderate	Moderate
Raynauld (2003)	Patient Global Assessment	3 years	High	Moderate	High
Smith (2003)	OARSI Responders	4 weeks	High	Moderate	High
Smith (2003)	OARSI Responders	8 weeks	High	Moderate	High
Smith (2003)	OARSI Responders	12 weeks	High	Moderate	High
Smith (2003)	OARSI Responders	24 weeks	High	Moderate	High

Table 167. Quality and Applicability Summary: IA Corticosteroids Versus Hyaluronic Acid

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Carbon (2004)	WOMAC Pain on walking	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Pain on walking	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC total	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC total	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Function	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Function	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	Patient overall assessment (VAS)	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	Patient Global Assessment	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	Physician Global Assessment	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	Physician Global Assessment	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Pain on walking	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Pain on walking	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC total	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC total	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Function	12 weeks	Moderate	Moderate	Moderate
Carbon (2004)	WOMAC Function	26 weeks	Moderate	Moderate	Moderate
Carbon (2004)	Patient overall assessment (VAS)	12 weeks	Moderate	Moderate	Moderate

Table 168. Quality and Applicability Summary: IA Corticosteroids Versus Needle Lavage

Arden (2008)	WOMAC pain	4	Moderate	Moderate	Moderate
Arden (2008)	WOMAC pain	12	Moderate	Moderate	Moderate
	WOMAC Total				
Arden (2008)	function	12	Moderate	Moderate	Moderate
	WOMAC Total				
Arden (2008)	stiffness	12	Moderate	Moderate	Moderate
Arden (2008)	WOMAC pain	26	Moderate	Moderate	Moderate
	WOMAC Total				
Arden (2008)	function	26	Moderate	Moderate	Moderate
	WOMAC Total				
Arden (2008)	stiffness	26	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Figure 81-Figure 82](#), [Table 172-Table 174](#)

There were seven studies included in this recommendation. None provided enough information to determine whether or not the patient population had acute or chronic osteoarthritis of the knee. However, the average symptom duration was several years for six of the studies (the seventh study did not provide average symptom duration), so a majority of the patient population was likely suffering from chronic osteoarthritis. Also, excluding Raynauld et al., all studies included patients with a full range of osteoarthritis severity levels.

Five studies with 19 outcomes compared IA corticosteroid injections to the placebo assignment. Four of the outcomes were statistically significant in favor of the treatment. Pain and function were the two critical outcomes. There were five pain outcomes and one self reported functional outcome.

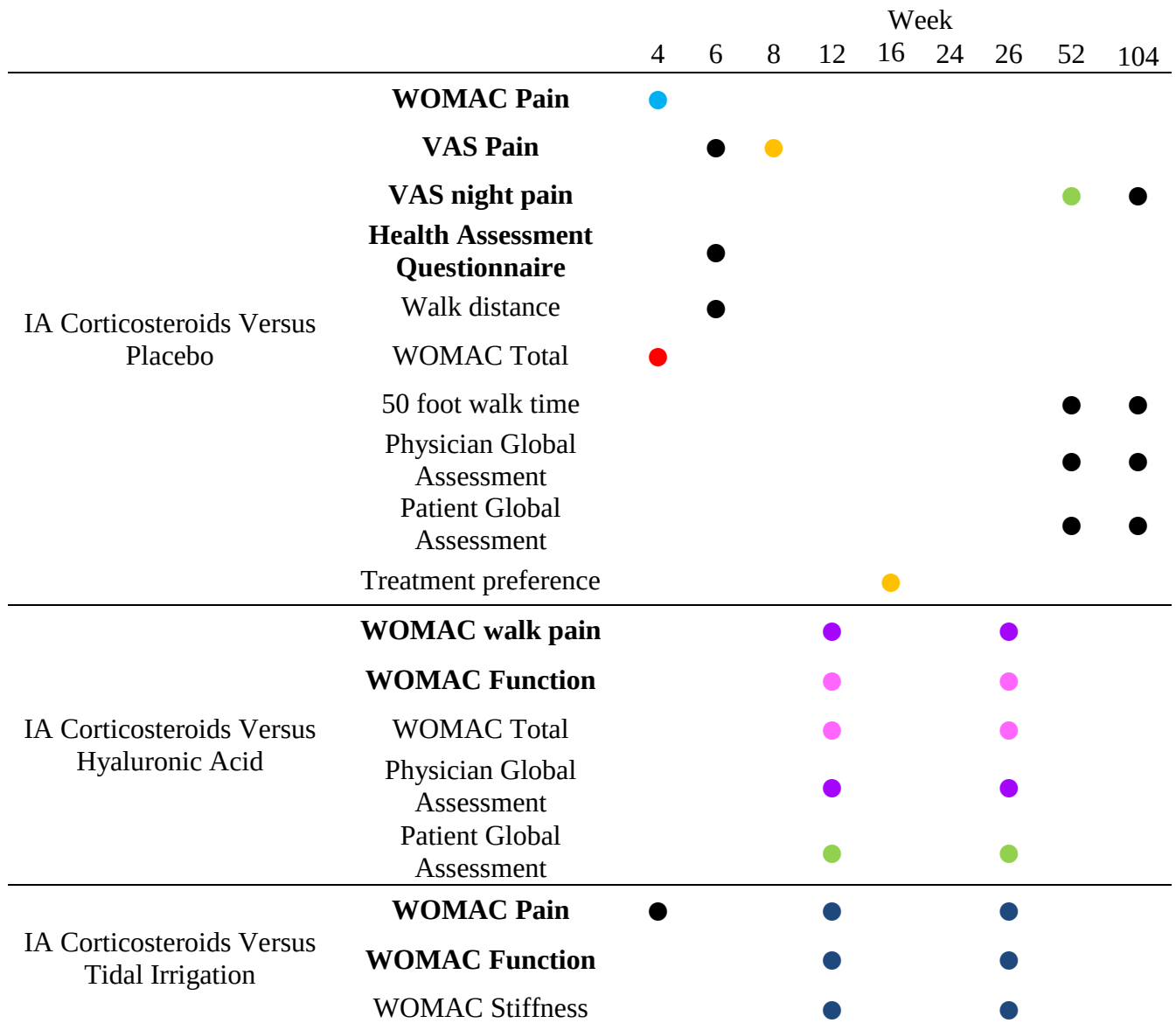
Of the five pain outcomes, three were statistically significant in favor of IA corticosteroids. However, one of them was not clinically important. The one other outcome, WOMAC Pain (Raynauld et al.¹⁰⁴) was underpowered. The findings were included in a meta-analysis comparing pain in the corticosteroid and placebo groups. Chao et al.¹⁰² and Raynauld et al.¹⁰⁴ used the visual analogue versions of WOMAC Pain, and Gaffney et al.¹⁰³ used the traditional VAS pain scale (both were 100mm long). Results showed that the treatment group had a lower weighted mean of 8.8mm on the VAS scale, which was statistically significant. Since WOMAC pain and VAS pain were combined, the clinical importance of IA corticosteroids could not be determined.

There were four functional outcomes included. One was the Health Assessment Questionnaire (HAQ) and the other three were functional task outcomes. Since the HAQ is a self reported measure of function, it was a critical outcome. All four functional outcomes were not statistically significant.

Carborn et al.¹⁰⁶ compared IA corticosteroids to Hylan G-F 20 at 12 and 26 weeks. Ten of 10 outcomes were statistically significant in favor of hyaluronic acid. WOMAC walking pain and WOMAC function were the critical outcomes presented in this study. (See [Figure 81](#) for the results summary.)

Arden et al.¹⁰⁷ compared IA corticosteroids to tidal irrigation. Clinically significant results were found in favor of corticosteroids for six of 7 outcomes of which WOMAC function and pain were the critical variables. Four of five critical outcomes were significant in favor of the IA corticosteroid group (see [Figure 81](#)).

Figure 81. Results Summary: IA Corticosteroids



Key 1 ●=Not Significant; ●=Not Clinically Significant ●=Statistically Significant; ●=Possibly Clinically Significant; ●=Clinically Significant. ●=Favors HA; ●= Possibly Clinically Significant in Favor of HA. ●= Possibly Clinically Significant in Favor of Tidal Irrigation. Bold lettering indicates a critical outcome.

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 169. Quality and Applicability: IA Corticosteroids Versus Placebo

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Jones (1996)	15% improvement in VAS Pain	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Jones (1996)	Treatment preference	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chao (2010)	WOMAC Pain	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Chao (2010)	WOMAC Total	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Gaffney (1995)	VAS Pain	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Gaffney (1995)	Health Assessment Questionnaire	●	◐	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Gaffney (1995)	Walk Distance (1 minute)	●	◐	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Raynauld (2003)	VAS Patient Pain Assessment at Night Week 52	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	VAS Patient Pain at Night 104 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Pain Week 52	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Pain 104 weeks	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Function Week 52	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Raynauld (2003)	WOMAC Function 104 weeks	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	50-foot walking time (seconds) Week 52	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	50-foot walking time (seconds) 104 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Stiffness Week 52	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Stiffness 104 weeks	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Total Week 52	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	WOMAC Total 104 weeks	●	○	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Raynauld (2003)	Physician Global Assessment Week 52	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	Patient Global Assessment 52 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	Physician Global Assessment 104 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Raynauld (2003)	Patient Global Assessment 104 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Chao (2010)	WOMAC Pain	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate

Table 170. Quality and Applicability: IA Corticosteroids Versus Hyaluronic Acid

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Caborn (2004)	WOMAC Pain on walking week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Pain on walking week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Total week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Total week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Function week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Function week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	Patient Overall Assessment (VAS)	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
	week 12														
Caborn (2004)	Patient Global Assessment week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	Physician Global Assessment week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	Physician Global Assessment week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Pain on walking week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Pain on walking week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Total week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Total week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Caborn (2004)	WOMAC Function week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	WOMAC Function week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Caborn (2004)	Patient overall assessment (VAS) week 12	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

Table 171. Quality and Applicability: Needle Lavage Versus IA Corticosteroids

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Week</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Arden (2008)	WOMAC Pain	4	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Pain	12	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Function	12	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Stiffness	12	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Pain	26	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Function	26	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Stiffness	26	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate

FINDINGS

Table 172. IA Corticosteroids Versus Placebo

Type	Study	Outcome	N	Power	Week	Avg. Disease Length (Years)	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pain	Gaffney (1995)	VAS Pain	84	Yes	6	6.9	Ledinger-Ham Scale 0 to 3	Triamcinolone	Placebo	-0.27 (-0.70, 0.16)	No	True negative	Moderate
	Raynauld (2003)	VAS Patient Pain Assessment at Night	66	Yes	52	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	-0.66 (-1.16, -0.17)	Favors IA Corticosteroids	Not clinically Important	Moderate
	Raynauld (2003)	VAS Patient Pain at Night	66	Yes	104	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	-0.08 (-0.56, 0.40)	No	True negative	Moderate

Type	Study	Outcome	N	Power	Week	Avg. Disease Length (Years)	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Chao (2010)	WOMAC Pain	67	Yes	4	14	Altman All Grades	Corticosteroid injections	Placebo	-0.87 (-1.37, -0.36)	Favors IA Corticosteroids	Possibly clinically significant	Moderate
	Jones (1996)	15% improvement in VAS Pain	59 (Crossover Study)	Yes	8	NR	NR	Corticosteroid injections	Placebo	OR=5.02 (2.09, 12.03)	Favors IA corticosteroids	N/A	Moderate
Function	Gaffney (1995)	Health Assessment Questionnaire	84	Unclear	6	6.9	Ledingham Scale 0 to 3	Triamcinolone	Placebo	0.30 (-0.13, 0.73)	No	N/A	Moderate
	Gaffney (1995)	Walk Distance (1 minute)	84	Unclear	6	6.9	Ledingham Scale 0 to 3	Triamcinolone	Placebo	-0.05 (-0.48, 0.37)	No	N/A	Moderate

Type	Study	Outcome	N	Power	Week	Avg. Disease Length (Years)	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Raynauld (2003)	50-foot walking time (seconds)	66	Unclear	52	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	-0.06 (-0.55, 0.42)	No	N/A	Moderate
	Raynauld (2003)	50-foot walking time (seconds)	66	Unclear	104	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	-0.14 (-0.62, 0.34)	No	N/A	Moderate
WOMAC Total	Chao (2010)	WOMAC Total	61	Yes	4	14	Altman All Grades	Corticosteroid injections	Placebo	-0.96 (-1.49, -0.43)	Favors IA Corticosteroids	Clinically significant	Moderate
Global Assessment	Raynauld (2003)	Physician Global Assessment	66	Unclear	52	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	0.18 (-0.30, 0.66)	No	N/A	Moderate
	Raynauld (2003)	Patient Global Assessment	66	Yes	52	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	0.01 (-0.47, 0.49)	No	True negative	Moderate

Type	Study	Outcome	N	Power	Week	Avg. Disease Length (Years)	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
	Raynauld (2003)	Physician Global Assessment	66	Unclear	104	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	0.01 (-0.47, 0.49)	No	N/A	Moderate
	Raynauld (2003)	Patient Global Assessment	66	Yes	104	9.25	K-L 2 to 3	Corticosteroid injections	Placebo	-0.02 (-0.50, 0.46)	No	True negative	Moderate
Preferred Treatment	Jones (1996)	Preferred Treatment	59 (Cross-over Study)	Yes	16	NR	NR	Corticosteroid injections	Placebo	OR=3.33 (1.51, 7.31)	Favors IA corticosteroids	N/A	Moderate

Table 173. IA Corticosteroids Versus Hyaluronic Acid (Caborn et al., 2004)

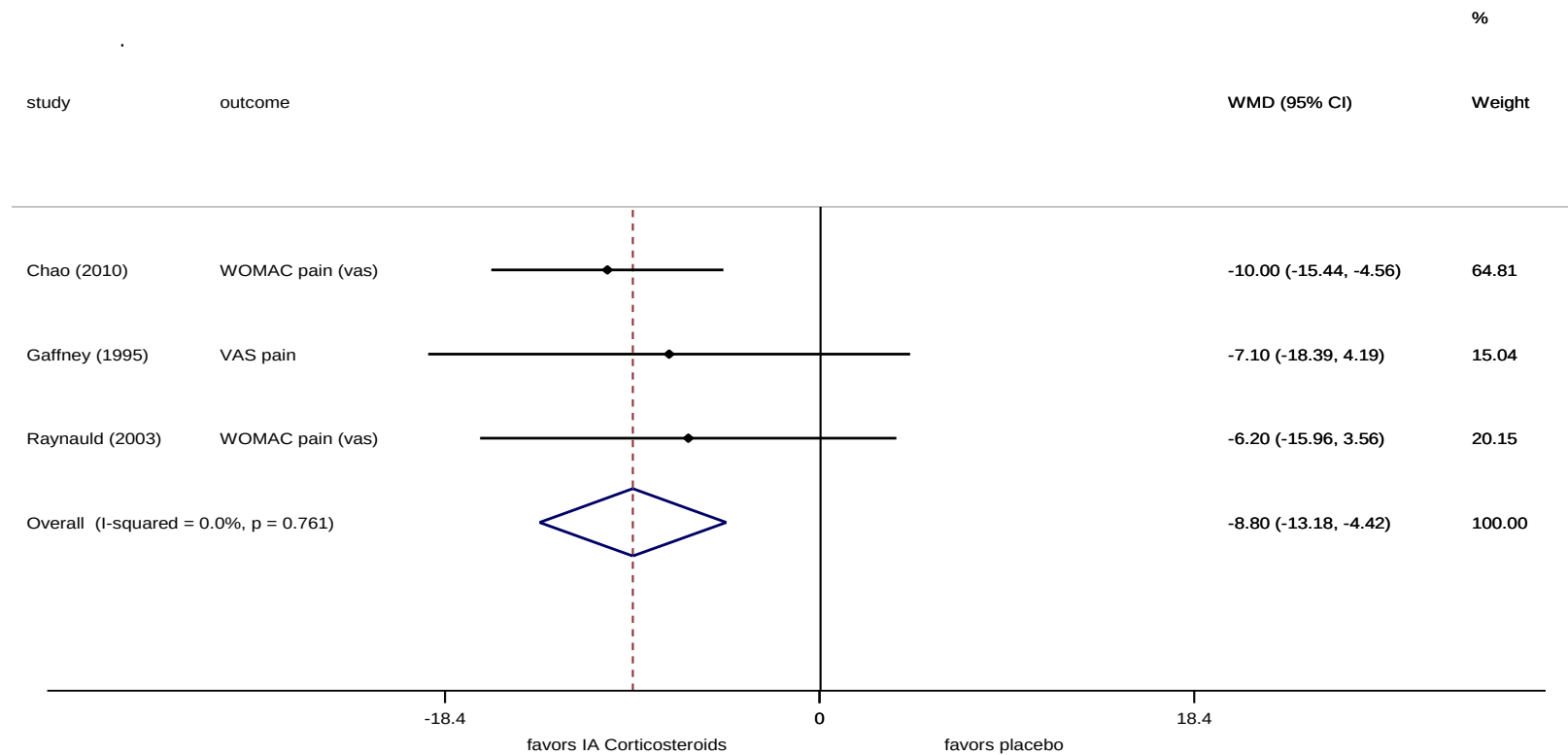
Outcome	N	Sufficient Power	Week	Symptom Duration	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
WOMAC Pain on walking	215	Yes	12	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.38 (0.11, 0.65)	Favors HA	Unclear	Moderate
WOMAC Pain on walking	215	Yes	26	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.29 (0.02, 0.56)	Favors HA	Unclear	Moderate
WOMAC Total	215	Yes	12	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.47 (0.2, 0.74)	Favors HA	Possibly clinically significant	Moderate
WOMAC Total	215	Yes	26	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.44 (0.17, 0.71)	Favors HA	Possibly clinically significant	Moderate
WOMAC Function	215	Yes	12	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.46 (0.19, 0.73)	Favors HA	Possibly clinically significant	Moderate
WOMAC Function	215	yes	26	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.44 (0.17, 0.71)	Favors HA	Possibly clinically significant	Moderate

Outcome	N	Sufficient Power	Week	Symptom Duration	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Patient Global Assessment	215	Yes	12	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.57 (0.3, 0.84)	Favors HA	Not clinically significant	Moderate
Patient Global Assessment	215	Yes	26	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.59 (0.32, 0.86)	Favors HA	Not clinically significant	Moderate
Physician Global Assessment	215	Yes	12	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.29 (0.02, 0.56)	Favors HA	N/A	Moderate
Physician Global Assessment	215	Yes	26	Minimum of 2 months	NR	IA Corticosteroid	Hylan GF-20	0.47 (0.2, 0.75)	Favors HA	N/A	Moderate

Table 174. Needle Lavage Versus Corticosteroids

Study	Outcome	N	Sufficient Power	Week	Avg. Disease Duration (years)	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Arden (2008)	WOMAC Pain	146	Yes	4	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.24(-0.09, 0.56)	No	Inconclusive	Moderate
Arden (2008)	WOMAC Pain	146	Yes	12	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.35(0.02, 0.67)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total function	145	Yes	12	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.34(0.01, 0.66)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total stiffness	138	Yes	12	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.4(0.06, 0.74)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC pain	146	Yes	26	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.52(0.19, 0.85)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total function	145	Yes	26	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.44(0.11, 0.77)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total stiffness	138	Yes	26	4.75	K-L 1-4	Needle Lavage	IA Corticosteroid	0.45(0.11, 0.79)	Favors Needle Lavage	Possibly clinically significant	Moderate

Figure 82. Network Meta-Analysis: IA Corticosteroids Versus Placebo (Pain)



RECOMMENDATION 9

We cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RATIONALE

Fourteen studies (three high-strength studies and 11 moderate-strength studies) assessed intraarticular hyaluronic acid (HA) injections. A comparison of the patients in these studies and the ones validating the MCIIIs we used to judge clinical significance revealed that they were demographically comparable for WOMAC and VAS pain as well as WOMAC function on the basis of age, baseline pain scores, BMI, weight and gender. Meta-analysis in meaningfully important difference (MID) units showed that the over effect was less than 0.5 MID units, indicating a low likelihood that an appreciable number of patients achieved clinically important benefits in the outcomes ([Guyatt et al.](#)). Although meta-analyses of WOMAC pain, function, and stiffness subscales scores all found statistically significant treatment effects, none of the improvements met the minimum clinically important improvement thresholds. When we differentiated high- versus low- molecular weight viscosupplementation, our analyses did show that most of the statistically significant outcomes were associated with high-molecular cross linked hyaluronic acid but when compared to mid-range molecular weight, statistical significance was not maintained. Treatment comparisons between any weights higher than 750 kDa were not significantly different. The strength of this recommendation was based on lack of efficacy, not on potential harm.

The 2008 edition of this guideline where the benefits of viscosupplementation were found to be inconclusive rather than non-affirming used a systematic review from AHRQ that compared Hylan G-F 20 to placebo. Although there was a statistically significant treatment effect associated with the high molecular weight, different pain measurement outcomes (WOMAC and VAS pain) were combined so clinical significance could not be determined. Also, the work group found evidence of publication bias (publicizing of primarily favorable studies). We excluded the AHRQ systematic review because the selection criteria did not match ours. The primary difference was that in the current edition of the guideline clinical efficacy beyond a 4-week treatment period was required for studies to be included. This 2nd edition was based on meta-analyses that combined like measurement instruments, which made it possible to determine that the overall effect of hyaluronic acid did not provide minimum clinically important improvement to patients. Additionally, the AHRQ review included trials of varying research-design quality due in part to variations in sample sizes. In AAOS clinical practice guidelines, evidence of lower strength is excluded when there are at least two higher strength studies evaluating an outcome, and we excluded many of the lower strength studies included in the AHRQ review since they did not meet our selection criterion of at

least 30 patients in each treatment group. Noted in the AHRQ review was that “There is evidence consistent with potential publication bias. Pooled results from small trials (<100 patients) showed effects up to twice those of larger trials consistent with selective publication of underpowered positive trials” (page 64).” Future research using clinically relevant outcomes, sub-group analyses, and controls for bias are needed.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 175-Table176](#), [Table 177-Table 178](#)

There were 94 outcomes from 14 studies that compared intraarticular hyaluronic acid (HA) injections to control treatments. Twelve compared HA to placebo; one compared the treatment to conventional care, and one compared 25mg sodium hyaluron to .25mg hyaluron. All studies were of moderate quality except Lundsgaard et al.,¹⁰⁸ Huang et al.¹⁰⁹ and Puhl et al.,¹¹⁰ which were rated as high quality.

All included studies were prospective and had no problems with the way the outcomes were measured. Every one, except the studies by Lundsgaard et al.,¹⁰⁸ and Puhl et al.,¹¹⁰ was flawed in the group assignment domain. Ten out of 14 studies had potential group comparability flaws. Investigator bias was problematic in 12 out of 14 studies. Also, excluding Day et al.,¹¹¹ every study was not flawed in the treatment integrity domain and all but one study was sufficiently blinded.

There were seven studies with 43 outcomes that compared high versus low molecular weight HA. Four of seven studies were of moderate quality. Juni et al.¹¹² and Maheu et al.¹¹³ were high quality studies, and Lee et al.¹¹⁴ was a low quality study.

None of the molecular weight HA studies were flawed in the prospective hypothesis, blinding or measurement domains. Excluding the articles by Juni et al.¹¹² and Maheu et al.,¹¹³ all studies were flawed in the group assignment domain. Three of seven studies were not flawed in group comparability. Juni et al.¹¹² and Raman et al.¹¹⁵ were the only studies with limited potential for investigator bias. The Raman et al.¹¹⁵ and Lee et al.¹¹⁴ studies were flawed in the treatment integrity domain.

APPLICABILITY

Relevant Tables: [Table 175-Table176](#), [Table 177-Table 178](#)

For all studies that compared HA to a control group, there was uncertainty if the treatments were applied in a manner reflecting clinical practice. In all but two studies, there was uncertainty about whether the patients were representative of the typical patient population. Karlsson et al.¹¹⁶ were the only researchers who did not include all enrolled patients in the final analysis. No unusual steps were taken by investigators in any of the studies to ensure a level of patient compliance beyond what is typically found in clinical settings.

Five out of seven molecular weight studies had participants that may not have been representative of the general osteoarthritis of the knee population. Each molecular weight study was flawed since the intervention was not applied in a similar manner to clinical practice. Only the Karlsson et al.¹¹⁶ molecular weight study did not include all patients in the final analysis. Finally, compliance and adherence were similar to typical clinical practice in every study.

FINAL STRENGTH OF EVIDENCE

Thirteen out of 18 studies were rated as having moderate strength of evidence. Four studies were rated as having high evidence strength, and one low strength. Due to the moderate applicability ratings for all outcomes, every strength of evidence rating was the same as the quality ratings.

Table 175. Quality and Applicability Summary: Hyaluronic Acid Versus Control

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Altman (2004)	WOMAC Pain	6 weeks	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Pain	3 months	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Pain	6 months	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Function	6 weeks	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Function	3 months	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Function	6 months	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Stiffness	6 weeks	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Stiffness	3 months	Moderate	Moderate	Moderate
Altman (2004)	WOMAC Stiffness	6 months	Moderate	Moderate	Moderate
Altman (2009)	Change in 50 foot walk pain score	6 months	Moderate	Moderate	Moderate
Altman (2009)	SF-36 physical Function	6 months	Moderate	Moderate	Moderate
Altman (2009)	WOMAC Function	6 months	Moderate	Moderate	Moderate
Altman (2009)	WOMAC Pain	6 months	Moderate	Moderate	Moderate
Altman (2009)	WOMAC Stiffness	6 months	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Day (2004)	WOMAC Function	18 weeks	Moderate	Moderate	Moderate
Day (2004)	WOMAC Pain	18 weeks	Moderate	Moderate	Moderate
Huang (2011)	VAS pain on walking change from W0 to W5	5 weeks	High	Moderate	High
Huang (2011)	VAS pain on walking change from W0 to W13	12 weeks	High	Moderate	High
Huang (2011)	VAS pain on walking change from W0 to W25	25 weeks	High	Moderate	High
Huang (2011)	WOMAC Pain	25 weeks	High	Moderate	High
Huang (2011)	WOMAC Stiffness	25 weeks	High	Moderate	High
Huang (2011)	WOMAC Function	25 weeks	High	Moderate	High
Day (2004)	WOMAC Stiffness	18 weeks	Moderate	Moderate	Moderate
Jorgenson (2010)	Lequesne index difference between groups	13 weeks	Moderate	Moderate	Moderate
Jorgenson (2010)	Lequesne index difference between groups	6 months	Moderate	Moderate	Moderate
Jorgenson (2010)	Lequesne index difference between groups s	1 year	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Jorgenson (2010)	VAS Pain difference between groups	13 weeks	Moderate	Moderate	Moderate
Jorgenson (2010)	VAS Pain difference between groups	52 weeks	Moderate	Moderate	Moderate
Jorgenson (2010)	VAS Pain difference between groups 26 weeks	6 months	Moderate	Moderate	Moderate
Kahan (2003)	Change in Pain on Walking	9 months	Moderate	Moderate	Moderate
Kahan (2003)	Lequesne index	9 months	Moderate	Moderate	Moderate
Kahan (2003)	WOMAC Pain	9 months	Moderate	Moderate	Moderate
Kahan (2003)	WOMAC Stiffness	9 months	Moderate	Moderate	Moderate
Kahan (2003)	WOMAC Total	9 months	Moderate	Moderate	Moderate
Kahan (2003)	WOMAC Function	9 months	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 12 (high molecular weight)	12 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 12 (low molecular weight)	12 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 20 (high molecular weight)	20 weeks	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Karlsson (2002)	VAS weight bearing pain week 20 (low molecular weight)	20 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 26	6 months	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 26	6 months	Moderate	Moderate	Moderate
Karlsson (2002)	Lequesne index week 20 (High Molecular Weight)	20 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	Lequesne index week 20 (low molecular weight)	20 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	Lequesne index week 26 (High Molecular Weight)	26 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	Lequesne index week 26 (low molecular weight)	6 months	Moderate	Moderate	Moderate
Lohmander (1996)	Lequesne index	6 months	Moderate	Moderate	Moderate
Lundsgaard (2008)	KOOS Activities	6 months	High	Moderate	High
Lundsgaard (2008)	KOOS Pain	6 months	High	Moderate	High
Lundsgaard (2008)	KOOS Sports	6 months	High	Moderate	High
Lundsgaard (2008)	VAS Pain at movement	6 months	High	Moderate	High
Lundsgaard (2008)	VAS Pain at night	6 months	High	Moderate	High

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Lundsgaard (2008)	VAS Pain at rest	6 months	High	Moderate	High
Navarro-Sarabia (2011)	OARSI Responders last follow-up	40 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	OARSI Responders	7 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	OARSI Responders	14 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	OARSI Responders	21 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	OARSI Responders	27 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	OARSI Responders	34 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	Pain or function reduction 50%	40 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	Overall pain reduction 20%	40 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	Function improvement 20%	40 months	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Navarro-Sarabia (2011)	Patient Global Assessment reduction 20% (10 mm), n (%)	40 months	Moderate	Moderate	Moderate
Navarro-Sarabia (2011)	Mean consumption of Paracetamol mg/day	40 months	Moderate	Moderate	Moderate
Petrella (2006)	Change in VAS stepping Pain 13 weeks	13 weeks	Moderate	Moderate	Moderate
Petrella (2006)	Change in VAS stepping Pain 6 weeks	6 weeks	Moderate	Moderate	Moderate
Petrella (2006)	Change in VAS Walking Pain	6 weeks	Moderate	Moderate	Moderate
Petrella (2006)	Change in VAS Walking Pain	13 weeks	Moderate	Moderate	Moderate
Petrella (2006)	SF-36 Physical 13 weeks	13 weeks	Moderate	Moderate	Moderate
Petrella (2006)	SF-36 Physical Function 6 weeks	6 weeks	Moderate	Moderate	Moderate
Petrella (2006)	WOMAC Function	13 weeks	Moderate	Moderate	Moderate
Petrella (2006)	WOMAC Pain	13 weeks	Moderate	Moderate	Moderate
Petrella (2006)	WOMAC Stiffness	13 weeks	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Wobig (1998)	Evaluator assessment of VAS night pain-number symptom free	26 weeks	Moderate	Moderate	Moderate
Wobig (1998)	Evaluator assessment of weight bearing pain	26 weeks	Moderate	Moderate	Moderate
Wobig (1998)	Evaluator VAS assessment of night pain-number symptom free	12 weeks	Moderate	Moderate	Moderate
Wobig (1998)	Evaluator VAS Assessment of Weight bearing pain-number symptom free	12 weeks	Moderate	Moderate	Moderate
Wobig (1998)	Patient VAS Assessment of night pain-number symptom free	12weeks	Moderate	Moderate	Moderate
Wobig (1998)	Patient VAS assessment of pain during most painful knee movement-number symptom free	12 weeks	Moderate	Moderate	Moderate
Wobig (1998)	Patient VAS Assessment of Weight bearing pain-number symptom free	12 weeks	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Wobig (1998)	Evaluator Assessment of Loss of Activities (symptom free)	12 weeks	Moderate	Moderate	Moderate
Wobig (1998)	Evaluator Assessment of Loss of Activities (symptom free)	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	WOMAC Pain	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	WOMAC Function	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	OARSI Responders	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Any treatment-emergent target knee AE	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Any treatment and/or procedure-related target knee AE	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Arthralgia	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Joint effusion	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Arthropathy	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Injection site pain	26 weeks	Moderate	Moderate	Moderate
Chevalier (2010)	Any treatment-related target knee AE	26 weeks	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Chevalier (2010)	Any procedure-related target knee AE	26 weeks	Moderate	Moderate	Moderate
Puhl (1993)	Lequesne index week 10	10 weeks	High	Moderate	High
Puhl (1993)	Lequesne index week 14	14 weeks	High	Moderate	High

Table 176. Quality and Applicability Summary: High Versus Low Molecular Weight Hyaluronic Acid

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Juni (2007)	WOMAC Function	6 months	High	Moderate	High
Juni (2007)	WOMAC Pain	12 weeks	High	Moderate	High
Juni (2007)	WOMAC Pain	6 months	High	Moderate	High
Juni (2007)	WOMAC Stiffness	6 months	High	Moderate	High
Juni (2007)	WOMAC Total	6 months	High	Moderate	High
Karlsson (2002)	Lequesne index week 20	20 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	Lequesne index week 26	6 months	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain	12 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 20	20 weeks	Moderate	Moderate	Moderate
Karlsson (2002)	VAS weight bearing pain week 26	6 months	Moderate	Moderate	Moderate
Lee (2006)	VAS weight bearing pain	12 weeks	Low	Moderate	Low

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Maheu (2011)	LFI score	24	Moderate	Moderate	Moderate
Maheu (2011)	Global pain	24	Moderate	Moderate	Moderate
Maheu (2011)	Investigator's assessment	24	Moderate	Moderate	Moderate
Maheu (2011)	SF-12 Physical component	24	Moderate	Moderate	Moderate
Maheu (2011)	SF-12 Mental component	24	Moderate	Moderate	Moderate
Maheu (2011)	OARSI OMERACT Responders	24	Moderate	Moderate	Moderate
Maheu (2011)	OARSI OMERACT Responders	24	Moderate	Moderate	Moderate
Maheu (2011)	Rescue medication: Patients who did NOT take Paracetamol during the study period	24	Moderate	Moderate	Moderate
Maheu (2011)	Rescue medication: Patients who did NOT	24	Moderate	Moderate	Moderate
Maheu (2011)	Patients with one or more AE	24	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Maheu (2011)	Patients with treatment emergent AE	24	Moderate	Moderate	Moderate
Maheu (2011)	Patients with serious AE	24	Moderate	Moderate	Moderate
Pavelka (2011)	WOMAC Pain	26	Moderate	Moderate	Moderate
Pavelka (2011)	WOMAC Pain	4	Moderate	Moderate	Moderate
Pavelka (2011)	WOMAC Pain	12	Moderate	Moderate	Moderate
Pavelka (2011)	WOMAC Function	26	Moderate	Moderate	Moderate
Pavelka (2011)	WOMAC Stiffness	26	Moderate	Moderate	Moderate
Pavelka (2011)	WOMAC Total	26	Moderate	Moderate	Moderate
Pavelka (2011)	Lequesne index	4	Moderate	Moderate	Moderate
Pavelka (2011)	Lequesne index	12	Moderate	Moderate	Moderate
Pavelka (2011)	Lequesne index	26	Moderate	Moderate	Moderate
Pavelka (2011)	Percent using rescue medication	4 weeks	Moderate	Moderate	Moderate
Pavelka (2011)	Percent using rescue medication	4 to 12 weeks	Moderate	Moderate	Moderate
Pavelka (2011)	Percent using rescue medication	12-26 weeks	Moderate	Moderate	Moderate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Pavelka (2011)	Percent using rescue medication	Baseline to 26 weeks	Moderate	Moderate	Moderate
Raman (2008)	WOMAC Pain	6 weeks	Moderate	Moderate	Moderate
Raman (2008)	WOMAC Pain	13 weeks	Moderate	Moderate	Moderate
Raman (2008)	WOMAC Pain	6 months	Moderate	Moderate	Moderate
Raman (2008)	WOMAC Pain	1 year	Moderate	Moderate	Moderate
Wobig (1999)	Evaluator VAS overall condition improvement	12 weeks	Moderate	Moderate	Moderate
Wobig (1999)	Patient VAS improvement in most painful knee	12 weeks	Moderate	Moderate	Moderate
Wobig (1999)	VAS Pain	12 weeks	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Figure 83-Figure 91](#), [Table 179-Table189](#)

Out of 37 total pain outcomes comparing HA to placebo, twelve were statistically improved in the treatment group. [Figure 88](#) shows the pooled weighted mean differences between HA and placebo for WOMAC pain. The meta-analysis excludes the studies by Kahan et al.¹¹⁷ and Altman et al.¹¹⁸ because they were both significant causes of heterogeneity in the model. Kahan et al.¹¹⁷ did not blind the patients or investigators. The lack of blinding caused a much larger treatment effect than was found in the other studies, which is where the heterogeneity originated. The Altman et al.¹¹⁸ study enrolled significantly more women in the placebo group than in the treatment group. The authors note that the statistically insignificant results of the primary analysis may have been confounded by the inclusion of patients whose osteoarthritis was not confined to the knee. When they analyzed a subgroup of patients with osteoarthritis localized to the knee, they found that responder rates (40% reduction in WOMAC pain with a minimum improvement of five points) were significantly higher in the treatment group

When the Kahan et al.¹¹⁷ and Altman et al.¹¹⁸ studies were removed from the analysis, the HA group reported significantly lower pain scores than the control group. This difference was not clinically significant since the lower bound of the confidence interval was higher than the MCII ([Figure 88](#)).

[Figure 89](#) shows the meta-analysis results for pain on weight bearing/movement. Each outcome was measured by the Visual Analogue Scale. Again the results were statistically significant but not clinically important.

Seven of 16 function outcomes were statistically significant in favor of HA over the control treatments. [Figure 90](#) contains the results for a meta-analysis of the difference in function scores between the HA and placebo groups. Each study used WOMAC function (scaled to 100mm VAS) as an outcome. Altman et al.¹¹⁸ and Kahan et al.¹¹⁷ were again excluded from the analysis to reduce the heterogeneity to an acceptable level. The final results indicate that HA did produce statistically significant improvement in function but the effect was not clinically important.

One of eight WOMAC stiffness outcomes was statistically significant in favor of HA over the control assignment. Results of the meta-analysis for this outcome can be found in [Figure 91](#). Again, Altman et al.¹¹⁸ and Kahan et al.¹¹⁷ were excluded. The results showed that WOMAC stiffness scores were significantly lower in patients receiving HA than those in the control group but the difference was not clinically important.

Kahan et al.¹¹⁷ compared WOMAC total scores between treatment and control groups. They found that patients who received HA plus conventional treatment reported significantly better scores than those who received only usual care and the difference was clinically important.

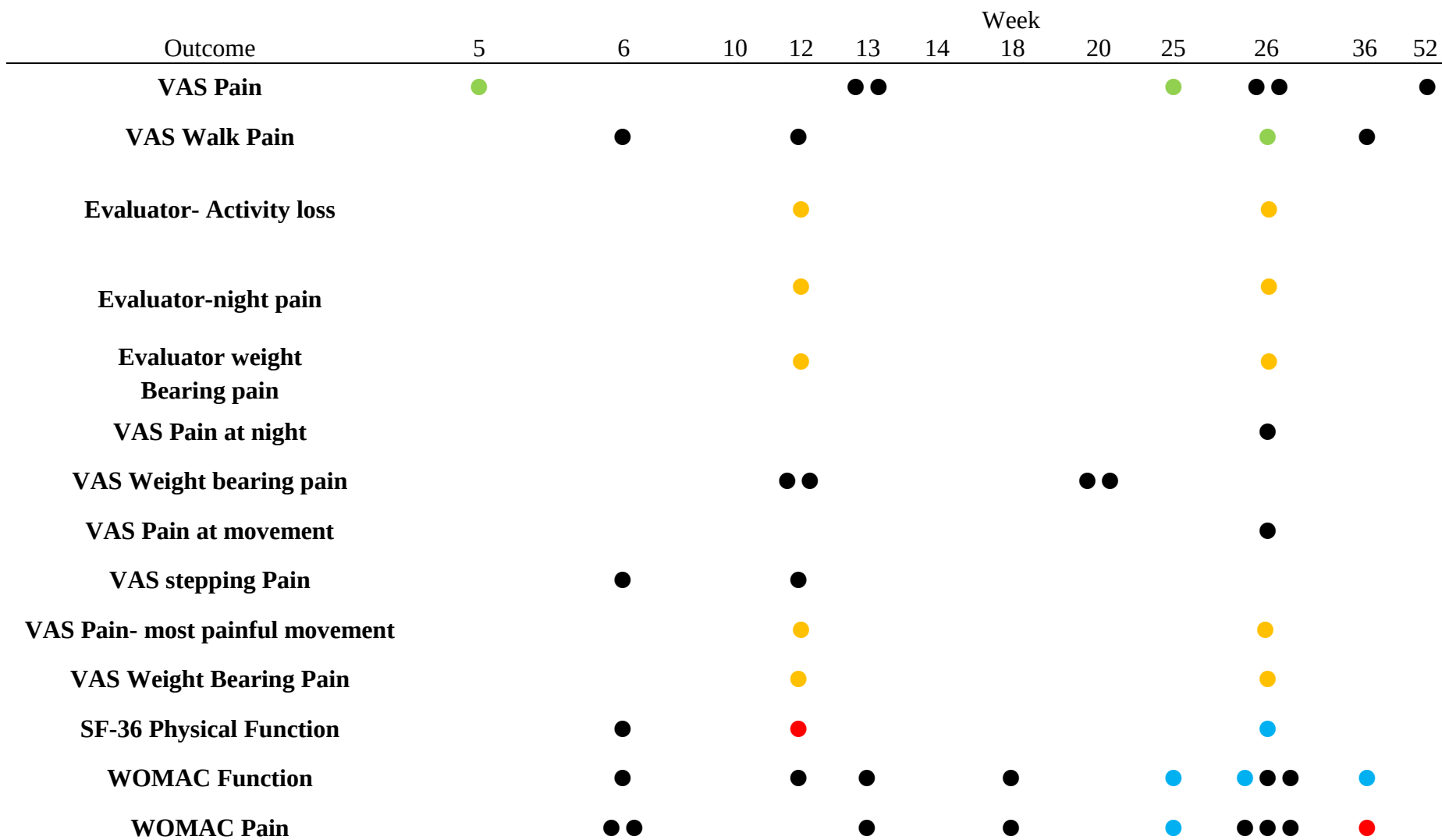
There were nine Lequesne index outcomes comparing HA and control treatments. Only one was statistically significant in favor of HA.

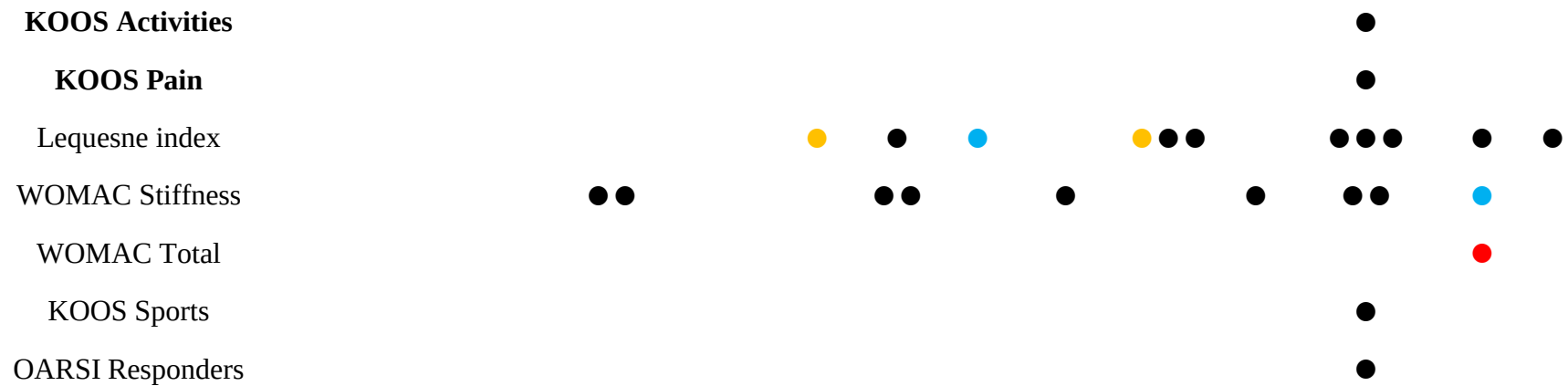
There was evidence to suggest that high molecular weight HAs were more effective than those with lower weights. Eight of 12 pain outcomes significantly favored Hylan G-F 20 (6 million Da) over placebo assignment. Nine of the 12 statistically significant placebo-compared pain outcomes were of HAs of at least 2.4 million Daltons.

Five of six placebo-compared functional outcomes that compared HA of at least 2.4 million Daltons to placebo were statistically significant in favor of the treatment group. Also, high molecular weight HA accounted for five of the seven significant pain outcomes. Out of eight WOMAC stiffness outcomes, the only one that was statistically significant compared to placebo was for Hylan G-F 20 (6 million Da).

Six of seven pain outcomes were statistically significant in favor of Hylan G-F 20 over HAs with a molecular weight of .5 to .75 Daltons. These treatments represented the highest and lowest molecular weight HAs, and the results suggested statistically and possibly clinically important differences in favor of Hylan G-F 20. Three outcomes were possibly clinically important, and the other three were indeterminable. There were not any statistically significant differences between high and medium molecular weight HAs, or between the medium and low molecular weights.

Figure 83. Results Summary: Intraarticular Hyaluronic Acid Versus Control





Key: ●=Not Significant; ●=Statistically Significant; ●=Possibly Clinically Significant; ●=Clinically Significant.
 (Bold lettering indicates a critical outcome.)

Figure 84. Results Summary: High Versus Low Molecular Weight Hyaluronic Acid

		Weeks							
Molecular Weight Comparison	Outcome	4	6	12	13	20	24	26	52
Comparison 1: 6 million Da versus 1-2.9 million Da	WOMAC pain			●				●	
	WOMAC function								
	WOMAC stiffness								
	WOMAC total								
Comparison 2: 6 million Da versus 2.2-2.7 million Da	Lequesne index							●	
	Global pain							●	
	Investigator's assessment							●	
	SF12 : Physical component							●	
	SF12 : Mental component							●	
	OARSI OMERACT Responder			●				●	
	Rescue medication use							●	
	patients with one or more AE							●	
	patients with treatment emergent AE							●	
	Patients with serious AE							●	
Comparison 3: 6 million Da versus 800kda-1200kda	WOMAC pain	●		●				●	
	WOMAC function							●	
	WOMAC stiffness							●	
	WOMAC total							●	
	Lequesne index	●		●				●	
	rescue medication use	●		●				●	
	Patients with treatment related adverse events							●	
	Patients with severe adverse events							●	
Comparison 4: 7 million Da versus 1 million Da	VAS Weight bearing pain			●		●		●	

Molecular Weight Comparison	Outcome	Weeks							
		4	6	12	13	20	24	26	52
Comparison 5: All molecular weights >.75kDa versus .5-.75 kDa	WOMAC pain		●		●			●	●
	VAS pain							●	
	ICOAP-total pain							●	
	ICOAP-constant pain							●	
	ICOAP-intermittent pain							●	
	significant pain improvement							●	
	VAS Weight bearing pain			●					
	evaluator assessment			●					
	patient assessment			●					
	WOMAC function							●	
	WOMAC total							●	
	lequesne index							●	
	adverse events			●					
	treatment related Adverse events								●

Key: ●=Not Significant; ●=Statistically Significant in Favor of High Molecular Weight: ●=Possibly Clinically Significant in Favor of High Molecular Weight Hyaluronic Acid

EVIDENCE TABLES AND FIGURES

QUALITY AND APPLICABILITY

Table 177. Quality and Applicability: Hyaluronic Acid Versus Control

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Heybeli (2008)	WOMAC Pain	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Heybeli (2008)	WOMAC Function	●	●	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Lundsgaard (2008)	KOOS Pain	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Altman (2009)	Change in 50 foot walk pain score	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2009)	WOMAC Pain	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Altman (2009)	SF-36 Physical Function	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2009)	WOMAC Function	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2009)	WOMAC Stiffness	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Pain 6 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Pain 13 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Pain 26 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Altman (2004)	WOMAC Function 6 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Function 13 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Function 36 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Stiffness 6 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Stiffness 13 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Altman (2004)	WOMAC Stiffness 26 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Day (2004)	WOMAC Pain	●	●	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate
Day (2004)	WOMAC Function	●	●	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate
Day (2004)	WOMAC Stiffness	●	●	○	●	○	○	●	○	Moderate	○	○	●	●	Moderate
Jorgenson (2010)	VAS Pain difference between groups 13 weeks	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jorgenson (2010)	VAS Pain difference between groups 26 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jorgenson (2010)	VAS Pain difference between groups 52 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Jorgenson (2010)	Lequesne index difference between groups 13 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jorgenson (2010)	Lequesne index difference between groups 26 weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Jorgenson (2010)	Lequesne index difference between groups 52weeks	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kahan (2003)	Change in Pain on Walking	●	●	○	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Kahan (2003)	WOMAC Pain	●	●	○	○	●	●	●	○	Moderate	●	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Kahan (2003)	WOMAC Stiffness	●	●	○	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Kahan (2003)	WOMAC Total	●	●	○	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Kahan (2003)	Lequesne index	●	●	○	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Kahan (2003)	WOMAC Function	●	●	○	○	●	●	●	○	Moderate	●	○	●	●	Moderate
Karlsson (2002)	VAS weight bearing pain week 12 (high molecular weight)	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	VAS weight bearing pain week 12 (low molecular weight)	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson	VAS weight bearing pain week 20 (high	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
(2002)	molecular weight)														
Karlsson (2002)	VAS weight bearing pain week 20 (low molecular weight)	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	VAS weight bearing pain week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	VAS weight bearing pain week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	Lequesne index week 20 (High Molecular Weight)	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	Lequesne index week 20 (low molecular	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
	weight)														
Karlsson (2002)	Lequesne index week 26 (High Molecular Weight)	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	Lequesne index week 26 (low molecular weight)	●	◐	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Lohmander (1996)	Lequesne index	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Lundsgaard (2008)	VAS Pain at movement	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Lundsgaard (2008)	VAS Pain at rest	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Lundsgaard (2008)	VAS Pain at night	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Lundsgaard (2008)	KOOS Activities	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Lundsgaard (2008)	KOOS Sports	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Petrella (2006)	Change in VAS Walking Pain 6 weeks	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	Change in VAS Walking Pain 13 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	Change in VAS stepping Pain 6 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Petrella (2006)	Change in VAS stepping Pain 13 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	SF-36 Physical Function 6 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	SF-36 Physical 13 weeks	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	WOMAC Function	●	○	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	WOMAC Stiffness	●	○	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Petrella (2006)	WOMAC Pain	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Wobig (1998)	Patient VAS Assessment of Weight bearing pain-number symptom free	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1998)	Patient VAS Assessment of night pain- number symptom free	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1998)	Patient VAS assessment of pain during most painful knee movement-number symptom free	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1998)	Evaluator VAS Assessment of Weight	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
	bearing pain-number symptom free														
Wobig (1998)	Evaluator VAS assessment of night pain-number symptom free	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1998)	Evaluator assessment of weight bearing pain	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1998)	Evaluator assessment of VAS night pain-number symptom free	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1998)	Evaluator Assessment of Loss of Activities (symptom free)	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Wobig (1998)	Evaluator Assessment of Loss of Activities (symptom free)	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Navarro-Sarabia (2011)	OARSI Responders last follow-up, 40 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	OARSI Responders 7 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	OARSI Responders 14 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia	OARSI Responders 21 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
(2011)															
Navarro-Sarabia (2011)	OARSI Responders 27 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	OARSI Responders 34 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	Pain or function reduction 50%	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	Overall pain reduction 20%	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Navarro-Sarabia (2011)	Function improvement 20%	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	Patient Global Assessment reduction 20% (10 mm), n (%)	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Navarro-Sarabia (2011)	Mean consumption of Paracetamol mg/day	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Huang (2011)	VAS Pain on walking Change from W0 to W5	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Huang (2011)	VAS Pain on walking Change from W0 to W13	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Huang (2011)	VAS Pain on walking Change from W0 to W25	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Huang (2011)	WOMAC Pain	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Huang (2011)	WOMAC Stiffness	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Huang (2011)	WOMAC Function	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Chevalier (2010)	WOMAC Pain	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	WOMAC Function	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	OARSI Responders	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Any treatment-emergent target knee AE	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Chevalier (2010)	Any treatment and/or procedure-related target knee AE	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Arthralgia	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Joint effusion	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Arthropathy	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Injection site pain	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Any treatment-related target knee AE	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Chevalier (2010)	Any procedure-related target knee AE	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Puhl (1993)	Lequesne index week 10	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Puhl (1993)	Lequesne index week 14	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate

Table 178. Quality and Applicability: High Versus Low Molecular Weight Hyaluronic Acid

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Karlsson (2002)	VAS weight bearing pain	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Juni (2007)	WOMAC Pain	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Juni (2007)	WOMAC Pain	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Berenbaum (2012)	WOMAC Pain	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	WOMAC Function	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	WOMAC Stiffness	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	WOMAC Total	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate

Berenbaum (2012)	VAS Pain	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	Lequesne index	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	ICOAP-total pain	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	ICOAP-constant pain	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Berenbaum (2012)	ICOAP-Intermittent pain	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Juni (2007)	WOMAC Function between groups difference	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Juni (2007)	WOMAC Stiffness	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Juni (2007)	WOMAC Total	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Karlsson (2002)	VAS weight bearing pain week 20	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	VAS weight bearing pain week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	Lequesne index week 20	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate
Karlsson (2002)	Lequesne index week 26	●	●	○	●	○	●	●	○	Moderate	○	○	●	○	Moderate

Lee (2006)	VAS weight bearing pain	●	●	○	●	○	○	●	○	Low	○	○	●	●	Moderate
Raman (2008)	WOMAC Pain	●	●	○	●	○	○	●	●	Moderate	●	○	●	●	Moderate
Raman (2008)	WOMAC Pain	●	●	○	●	○	○	●	●	Moderate	●	○	●	●	Moderate
Raman (2008)	WOMAC Pain	●	●	○	●	○	○	●	●	Moderate	●	○	●	●	Moderate
Raman (2008)	WOMAC Pain	●	●	○	●	○	○	●	●	Moderate	●	○	●	●	Moderate
Wobig (1999)	VAS Pain	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1999)	Evaluator VAS overall condition improvement	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Wobig (1999)	Patient VAS improvement in most painful knee	●	●	○	●	○	●	●	○	Moderate	●	○	●	●	Moderate
Maheu (2011)	LFI Score (change Baseline - W24)	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	Global pain (change Baseline - W24)	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

Maheu (2011)	Investigator's assessment (change Baseline - W24)	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	SF-12 Physical component (change Baseline - W24)	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	SF-12 Mental component (change Baseline - W24)	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	OARSI OMERACT Responders rate at W 12	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	OARSI OMERACT Responders rate at W24	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	Rescue medication: Patients who did NOT take Paracetamol during the study period	●	●	●	●	●	●	●	○	High	○	○	●	●	Moderate

Maheu (2011)	Rescue medication: Patients who did NOT	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	Patients with one or more AE	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	Patients with treatment emergent AE	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Maheu (2011)	Patients with serious AE	●	◐	●	●	●	●	●	○	High	○	○	●	●	Moderate
Pavelka (2011)	WOMAC Pain week 26	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	WOMAC Pain week 4	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	WOMAC Pain week 12	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	WOMAC Function week 26	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	WOMAC Stiffness week 26	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	WOMAC Total week 26	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	Lequesne index week 4	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	Lequesne index week 12	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

Pavelka (2011)	Lequesne index week 26	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	Percent using Rescue medication 4 weeks	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	Percent using Rescue medication 4 to 12 weeks	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	Percent using Rescue medication 12-26 weeks	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Pavelka (2011)	Percent using Rescue medication baseline to 26 weeks	●	◐	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate

FINDINGS

Table 179. Hyaluronic Acid Versus Control: Pain

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance
Huang (2011)	VAS Pain	198	Yes	5	K-L 2-3	5	500- 730kda	Hyalgan	Placebo	-0.31 (-0.59, - 0.03)	Favors HA	Not clinically significant
Huang (2011)	VAS Pain	198	Yes	13	K-L 2-3	5	500- 730kda	Hyalgan	Placebo	-0.20 (-0.48, - 0.08)	No	True negative
Huang (2011)	VAS Pain	198	Yes	25	K-L 2-3	5	500- 730kda	Hyalgan	Placebo	-0.47 (-0.75, - 0.19)	Favors HA	Not clinically significant
Huang (2011)	WOMAC Pain	198	Yes	25	K-L 2-3	5	500- 730kda	Hyalgan	Placebo	-0.40 (-0.68, - 0.12)	Favors HA	Possibly clinically important
Karlsson (2002)	VAS weight bearing pain	133	Yes	12	Ahlback 1-2	3	10 ⁶ Da	HA (Artzal)	Placebo	-.10(-.44, .24)	No	N/A
Karlsson (2002)	VAS weight bearing pain	133	Yes	20	Ahlback 1-2	3	10 ⁶ Da	HA (Artzal)	Placebo	-.27(-.62, .07)	No	N/A

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance
Karlsson (2002)	VAS weight bearing pain	133	Yes	26	Ahlback 1-2	3	10 ⁶ Da	HA (Artzal)	Placebo	.03(-.31, .37)	No	N/A
Day (2004)	WOMAC Pain	116	Yes	18	NR	5	6.2- 11.7 x 10 ⁵ Da	HA	Placebo	-.24(-.49, .01)	No	True negative
Heybeli (2008)	WOMAC Pain	67	Yes	26	K-L 2-3	3	1-2.9 million Da	HA	Placebo	-0.20 (-0.68, 0.28)	No	Inconclusi
Altman (2009)	Change in 50 foot walk pain score	586	Yes	26	K-L 2-3	3	2.4-3.6 Million Daltons	HA	Placebo	-0.23 (-0.40, - 0.07)	Favors HA	Not clinically significan
Altman (2009)	WOMAC Pain	586	Yes	26	K-L 2-3	3	2.4-3.6 Million Daltons	HA	Placebo	-0.11 (-0.27, 0.05)	No	True negative

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importan
Wobig (1998)	Patient VAS Assessment of Weight bearing pain- number symptom free	117	yes	12	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=9.69(3.763 24.960)	Favors HA	N/A
Wobig (1998)	Patient VAS Assessment of night pain- number symptom free	117	yes	12	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=4.11 (1.76, 9.63)	Favors HA	N/A

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importan
Wobig (1998)	Patient VAS assessment of pain during most painful knee movement- number symptom free	117	Yes	12	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=9.61(3.86, 23.95)	Favors HA	N/A
Wobig (1998)	Evaluator VAS Assessment of Weight bearing pain- number symptom free	117	Yes	12	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=9.90(3.45, 28.37)	Favors HA	N/A

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance
Wobig (1998)	Evaluator VAS assessment of night pain- number symptom free	117	Yes	12	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=4.74(2.12, 10.59)	Favors HA	N/A
Wobig (1998)	Evaluator assessment of weight bearing pain	117	Yes	26	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=4.09(1.64, 10.21)	Favors HA	N/A
Wobig (1998)	Evaluator assessment of VAS night pain- number symptom free	117	Yes	26	Larsen Grade 1-4	3	6 million Daltons	Hylan G-F 20	Placebo	OR=2.88(1.34, 6.16)	Favors HA	N/A
Chevalier (2010)	WOMAC Pain	253	Yes	26	NR	NR	6 million Da	Hylan G-F 20	Placebo	-.225(-.473, .022)	No	Inconclusi

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance
Kahan (2003)	WOMAC Pain	497	Yes	36	K-L 1-4	3	6 million Da	Hylan G-F 20	Usual care	-.60(-.77, -.42)	Favors HA	Clinically significant
Karlsson (2002)	VAS weight bearing pain	134	Yes	12	Ahlback 1-2	3	7 million Da	Hylan G-F 20	Placebo	-.10(-.45, .24)	No	N/A
Karlsson (2002)	VAS weight bearing pain	134	Yes	20	Ahlback 1-2	3	7 million Da	HA (synvisc)	Placebo	-.07(-.42, .27)	No	N/A
Karlsson (2002)	VAS weight bearing pain	134	Yes	26	Ahlback 1-2	3	7 million Da	HA (synvisc)	Placebo	.016(-.018, .50)	No	N/A
Lundsgaard (2008)	KOOS Pain	162	Unclear	26	K-L 1-4	4	NR	HA	Placebo	.01(-.29, .31)	No	N/A
Petrella (2006)	Change in VAS Walking Pain	106	Unclear	6	NR	6	NR	HA	Placebo	0.00 (-0.38, 0.38)	No	N/A

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance
Petrella (2006)	Change in VAS Walking Pain	106	Yes	12	NR	6	NR	HA	Placebo	-0.07 (-0.31, 0.45)	No	N/A
Petrella (2006)	Change in VAS stepping Pain	106	Yes	6	NR	6	NR	HA	Placebo	0.04 (-0.42, 0.34)	No	N/A
Petrella (2006)	Change in VAS stepping Pain	106	Yes	12	NR	6	NR	HA	Placebo	-0.06 (-0.32, 0.45)	No	N/A
Lundsgaard (2008)	VAS Pain at movement	162	Yes	26	K-L 1-4	4	NR	HA	Placebo	.06(-.24, .36)	No	N/A
Lundsgaard (2008)	VAS Pain at rest	162	Yes	26	K-L 1-4	4	NR	HA	Placebo	-.02(-.33, .28)	No	N/A
Lundsgaard (2008)	VAS Pain at night	162	Yes	26	K-L 1-4	4	NR	HA	Placebo	-.08(-.39, .22)	No	N/A
Petrella (2006)	WOMAC Pain	106	Yes	6	NR	6	NR	HA	Placebo	.01(-.37, .39)	No	Negative
Altman (2004)	WOMAC Pain	346	Yes	6	NR	NR	NR	HA	Placebo	0.06 (-0.15, 0.27)	No	True negative

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance
Altman (2004)	WOMAC Pain	346	Yes	13	NR	NR	NR	HA	Placebo	0.14 (-0.08, 0.35)	No	True negative
Altman (2004)	WOMAC Pain	346	Yes	26	NR	NR	NR	HA	Placebo	0.10 (-0.12, 0.31)	No	True negative
Jorgensen (2010)	VAS Pain difference between groups	298	Yes	13	NR	5	NR	Sodium Hyaluronate	Placebo	Raw mean difference= 0.07(-.33, .46)	No	N/A
Jorgensen (2010)	VAS Pain difference between groups	298	Unclear	26	NR	5	NR	Sodium Hyaluronate	Placebo	Raw mean difference= 0.05(-.47, .58)	No	N/A
Jorgensen (2010)	VAS Pain difference between groups	298	Unclear	52	NR	5	NR	Sodium Hyaluronate	Placebo	Raw mean difference= 0.22(-.71, 1.14)	No	N/A

Table 180. High Versus Low Molecular Weight: Pain

Study	Outcome	N	Power ed	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Karlsson (2002)	VAS weight bearing pain	15 3	Yes	12	Ahlback 1-2	3	High Molecular Weight HA (7x10 ⁶ Da)	Low Molecular Weight HA (10 ⁶ Da)	.00(-.32, .32)	No	True negative	Moderate
Karlsson (2002)	VAS weight bearing pain	15 3	Yes	20	Ahlback 1-2	3	High Molecular Weight HA (7x10 ⁶ Da)	Low Molecular Weight HA (10 ⁶ Da)	-.22(-.53, .10)	No	True negative	Moderate

Study	Outcome	N	Power ed	Week	Sever- ity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Karlsson (2002)	VAS weight bearing pain	15 3	Yes	26	Ahlba ck 1-2	3	High Molecul ar Weight HA (7x10 ⁶ Da)	Low Molecula r Weight HA (10 ⁶ Da)	-.13(-.45, .19)	No	True negative	Moderate
Juni (2007)	WOMAC Pain	65 7	Yes	12	K-L 2+	3	High Molecul ar Weight HA (6 million Da)	Medium or Low Molecula r Weight HA	Mean Differenc e= .1(-.3, .4)	No	N/A	High

Study	Outcome	N	Power ed	Week	Severity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Juni (2007)	WOMAC Pain	65 7	Yes	26	K-L 2+	3	High Molecul ar Weight HA (6 million Da)	Medium or Low Molecula r Weight HA	Mean Differenc e= .0 (-.3.,2)	No	N/A	High
Berenbaum (2012)	VAS Pain	42 6	Yes	26	K-L 2- 3	3	Medium MW HA (800- 1500kDa)	Low MW HA (500-700 kDa)	-.26(-.45, -.07)	Favors MMW	Not clinically important	Moderate
Berenbaum (2012)	ICOAP- total pain	42 6	Unclear	26	K-L 2- 3	3	Medium MW HA (800- 1500kDa)	Low MW HA (500-700 kDa)	-0.15 (- 0.34, 0.04)	No	Unclear	Moderate

Study	Outcome	N	Power ed	Week	Sever- ity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Berenbaum (2012)	ICOAP – constant pain	42 6	Yes	26	K-L 2- 3	3	Medium MW HA (800- 1500kD a)	Low MW HA (500-700 kDa)	-0.20 (- 0.39, -0.01)	Favors MMW	Unclear	Moderate
Berenbaum (2012)	ICOAP – intermitt ent pain	42 6	Unclear	26	K-L 2- 3	3	Medium MW HA (800- 1500kD a)	Low MW HA (500-700 kDa)	-0.09 (- 0.28, 0.10)	No	Unclear	Moderate
Berenbaum (2012)	Pain MCII	42 6	Yes	26	K-L 2- 3	3	Medium MW HA (800- 1500kD a)	Low MW HA (500-700 kDa)	OR= 1.70 (1.14, 2.55)	Favors MMW	Unclear	Moderate
Lee (2006)	VAS weight bearing pain	78	Yes	12	K-L 1-3	5	High Molecul ar weight (3000 kDa)	Low molecular weight (750kD)	-.22(-.70, .26)	No	Not clinically important	Low

Study	Outcome	N	Power ed	Week	Sever- ity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Raman (2008)	WOMAC Pain	39 2	Yes	6	60% with K-L 3	3	Hylan G-F 20 (6 million Daltons)	Sodium Hyaluron ate (.5 to .73 million Daltons)	Raw score mean difference = 1.8 (p>.05)	No	N/A	Moderate
Raman (2008)	WOMAC Pain	39 2	Yes	13	60% with K-L 3	3	Hylan G-F 20 (6 million Daltons)	Sodium Hyaluron ate (.5 to .73 million Daltons)	Mean difference =-2.1 (.33, 3.87)	Favors High Molecul ar Weight (HMW)	Possibly clinically significan t	Moderate
Raman (2008)	WOMAC Pain	39 2	Yes	26	60% with K-L 3	3	Hylan G-F 20 (6 million Daltons)	Sodium Hyaluron ate (.5 to .73 million Daltons)	Mean difference =-3.2(.77,5.63)	Favors HMW	Possibly clinically significan t	Moderate

Study	Outcome	N	Power ed	Week	Sever- ity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Raman (2008)	WOMAC Pain	39 2	Yes	52	60% with K-L 3	3	Hylan G-F 20 (6 million Daltons)	Sodium Hyaluron ate (.5 to .73 million Daltons)	Mean difference =-2.7 (.75,4.65)	Favors HMW	Possibly clinically significan t	Moderate
Wobig (1999)	VAS Pain	73	Yes	12	Larsen Grade 1-4	3	Hylan G-F 20 (6 million Daltons)	Low MW Hyaluroni c Acid (.75 – million)	Mean difference =16 (p<.05)	Favors HMW	N/A	Moderate
Wobig (1999)	Evaluator VAS overall condition improvement	73	Yes	12	Larsen Grade 1-4	3	Hylan G-F 20 (6 million Daltons)	Low MW Hyaluroni c Acid (.75 – million)	Mean difference =14 (p<.05)	Favors HMW	N/A	Moderate

Study	Outcome	N	Power ed	Week	Severity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Wobig (1999)	Patient VAS improvement in most painful knee	73	Yes	12	Larsen Grade 1-4	3	Hylan G-F 20 (6 million Daltons)	Low MW Hyaluronic Acid (.75 – million)	Mean difference =16 (p<.05)	Favors HMW	N/A	Moderate
Maheu (2011)	Global pain (change Baseline - W24)	23 6	yes	24	K-L 2- 3	3	Structov ial (2.2- 2.7 mda)	synsivic (6 million daltons)	SMD=0.0 7 (-0.19, 0.32)	no	true negative	
Pavelka (2011)	WOMAC pain	38 0	unclear	26	K-L 2- 3	3	synvisc (6 million da)	Sinovial (800kda- 1200kda)	mean difference = 0.0 (95% CI - 4.7 to 4.8)	no	true negative	

Study	Outcome	N	Power ed	Week	Severity	# Of Injectio ns	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differenc e When Indicated)	Sig	Clinical Importa nce	Strengt h of Eviden ce
Pavelka (2011)	WOMAC pain	38 0	unclear	4	K-L 2- 3	3	synvisc (6 million da)	Sinovial (800kda- 1200kda)	mean difference = 1.3 (95%CI - 2.6 to 5.3)	no	true negative	
Pavelka (2011)	WOMAC pain	38 0	unclear	12	K-L 2- 3	3	synvisc (6 million da)	Sinovial (800kda- 1200kda)	mean difference = 1.6(- 2.8 to 6.0)	no	true negative	

Table 181. Hyaluronic Acid Versus Control: Function

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of evidence
Huang (2011)	WOMAC Function	198	Yes	25	K-L 2-3	5	500-730k Da	Hyalgan	Placebo	-0.41 (-0.70, -0.13)	Favors HA	Possibly clinically important	High
Day (2004)	WOMAC Function	240	Yes	18	NR	5	6.2-11.7 x 10 ⁵ Da	Sodium HA	Placebo	-.22(-.48, .03)	No	Inconclusive	Moderate
Heybeli (2008)	WOMAC Function	67	Yes	26	K-L 2-3	3	1-2.9 million Da	HA	Placebo	-0.28 (-0.76, 0.20)	No	Inconclusive	Moderate
Altman (2009)	SF-36 physical Function	586	Yes	26	K-L 2-3	3	2.4-3.6 Million Da	HA	Placebo	.17(.07, .33)	Favors HA	Possibly clinically important	Moderate

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of evidence
Altman (2009)	WOMAC Function	586	Yes	26	K-L 2-3	3	2.4-3.6 Million Da	HA	Placebo	-.19(-.36, -.03)	Favors HA	Possibly Clinically significant	Moderate
Chevalier (2010)	WOMAC Function	253	Yes	26	NR	NR	6 million Da	Hylan G-F 20	Placebo	-.044 (-.291, .202)	No	Inconclusive	Moderate
Wobig (1998)	Evaluator Assessment of Loss of Activities (symptom free)	117	Yes	12	Larsen Grade 1-4	3	6 million Da	HA	Placebo	OR=7.39 (3.13, 17.48)	Favors HA	N/A	Moderate

Study	Outcome	N	Powered	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of evidence
Wobig (1998)	Evaluator Assessment of Loss of Activities (symptom free)	117	Yes	26	Larsen Grade 1-4	3	6 million Da	HA	Placebo	OR=4.07(1.86, 8.86)	Favors HA	N/A	Moderate
Kahan (2003)	WOMAC Function	506	Yes	36	K-L 1-4	3	6 million Da	HA	Conventional Treatment	-.57(-.75, -.39)	Favors HA	Clinically significant	Moderate
Altman (2004)	WOMAC Function	346	Yes	6	NR	NR	NR	HA injection	Placebo	0.08 (-0.13, 0.29)	No	True negative	Moderate
Altman (2004)	WOMAC Function	346	Yes	13	NR	NR	NR	HA injection	Placebo	0.14 (-0.07, 0.35)	No	True negative	Moderate
Altman (2004)	WOMAC Function	346	Yes	26	NR	NR	NR	HA injection	Placebo	0.12 (-0.09, 0.34)	No	True negative	Moderate

Study	Outcome	N	Power ed	Week	Severity	# Of Injecti ons	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of evidence
Lundsgaard (2008)	KOOS Activities	16 7	Unclear	26	K-L 1-4	4	NR	HA injection	Placebo	-.01(- .31,.29)	No	N/A	High
Lundsgaard (2008)	KOOS Sports	16 7	Unclear	26	K-L 1-4	4	NR	HA injection	Placebo	.11(-.20, .41)	No	N/A	High
Petrella (2006)	SF-36 Physical Function	10 6	Yes	6	NR	6	NR	HA injection	Placebo	0.08 (- 0.30, 0.46)	No	Inconclusive	Moderate
Petrella (2006)	SF-36 Physical	10 6	Yes	12	NR	6	NR	HA injection	Placebo	0.65 (0.26, 1.04)	Favors HA injections	Clinically important	Moderate
Petrella (2006)	WOMAC Function	10 6	No	12	NR	6	NR	HA injection	Placebo	.02(-.36, .40)	No	Inconclusive	Moderate

Table 182. High Versus Low Molecular Weight: WOMAC Function

Outcome	N	Power	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Juni (2007)	657	Unclear	26	K-L 2+	3	High Molecular Weight HA (6 million Da)	Medium or Low Molecular Weight HA	Mean Difference =.1(-.2, .4)	No	True negative	High
Berenbaum (2012)	426	Yes	26	K-L 2-3	3	Medium MW HA (800- 1500kDa)	Low MW HA (500-700 kDa)	-.32 (-.52, -.13)	Favor s MM W	Possibly clinically significant	Moderate
Maheu (2011)	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	SMD=0.17 (-0.09, 0.42)	no	n/a	high
Maheu (2011)	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	SMD=- 0.02 (-0.28, 0.23)	no	n/a	high
Pavelka (2011)	380	unclear	26	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda- 1200kda)	mean difference = 0.2 p>.05	no	n/a	moderate

Table 183. Hyaluronic Acid Versus Control: WOMAC Stiffness

Study	Outcome	N	Power	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differen ce When Indicate d)	Sig	Clinical Importance	Strength of Evidence
Altman (2004)	WOMAC Stiffness	346	yes	6	NR	NR	NR	HA injections	Placebo	0.09 (- 0.12, 0.30)	No	True negative	Moderate
Altman (2004)	WOMAC Stiffness	346	yes	13	NR	NR	NR	HA injections	Placebo	0.18 (- 0.03, 0.39)	No	True negative	Moderate
Altman (2004)	WOMAC Stiffness	346	yes	26	NR	NR	NR	HA injections	Placebo	0.19 (- 0.02, 0.40)	No	True negative	Moderate
Huang (2011)	WOMAC Stiffness	198	yes	25	K-L 2-3	5	500- 730kda	Hyalgan	Placebo	-0.10 (- 0.38, 0.18)	No	True negative	High
Altman (2009)	WOMAC Stiffness	586	Yes	26	K-L 2-3	3	2.4-3.6 Million Daltons	HA injections	Placebo	-.14(-.30, .02)	No	negative	Moderate
Day (2004)	WOMAC Stiffness	240	Yes	18	NR	5	6.2- 11.7 x 10 ⁵ Da	HA injections	Placebo	-.24(-.5, .01)	No	Inconclusive	Moderate
Kahan	WOMAC	498	Yes	36	K-L	3	6	HA	Usual	-.5(-.68,	Favors	Possibly	Moderate

Study	Outcome	N	Power	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Differen ce When Indicate d)	Sig	Clinical Importance	Strength of Evidence
(2003)	Stiffness				1-4		million Da	Injections	care	-.32)	HA	clinically significant	
Petrella (2006)	WOMAC Stiffness	106	No	6	NR	6	NR	HA injections	Placebo	-.22(-.6, .16)	No	Inconclusive	Moderate

Table 184. High Versus Low Molecular Weight: WOMAC Stiffness

Study	Outcome	N	Power to Detect MCH	Week	Group 1	Group 2	Severity	# Of Injections	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Juni (2009)	WOMAC Stiffness	657	Unclear	26	High Molecular Weight HA (6 million Da)	Medium or Low Molecular Weight HA	K-L 2+	3	Mean Difference= .1(-.3, .4)	No	True negative	High
Berenbaum (2012)	WOMAC Stiffness	426	Yes	26	Medium MW HA (800-1500kDa)	Low MW HA (500-700 kDa)	K-L 2-3	3	-.22 (-.41, -.02)	Favors MMW	Possibly clinically significant	Moderate
Pavelka (2011)	WOMAC stiffness	380	unclear	26	synvisc (6 million da)	Sinovial (800kda-1200kda)	K-L 2-3	3	mean difference = -0.1 p>.05	no	n/a	moderate

Table 185. Hyaluronic Acid Versus Conventional Treatment: WOMAC Total (Kahan et al., 2003)

Outcome	N	Sufficient Power	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
WOMAC Total	495	Yes	36	K-L 1-4	3	6 million Da	Hyaluronic Acid (HA) injection	Conventional Treatment	-.6(-.78, -.42)	Favors HA	Clinically important	Moderate

Table 186. High Versus Low Molecular Weight: WOMAC Total (Juni et al., 2007)

Study	N	Power	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Juni (2007)	657	Unclear	26	K-L 2+	3	High Molecular Weight HA (6 million Da)	Medium or Low Molecular Weight HA	Mean difference= .1(-.2, .4)	No	True negative	High
Berenbaum (2012)	426	Yes	26	K-L 2-3	3	Medium MW HA (800- 1500kDa)	Low MW HA (500-700 kDa)	-.31 (-.5, -.11)	Favors MMW	Possibly clinically significant	Moderate
Pavelka (2011)	380	unclear	26	K-L 2-3	3	Synvisc (6 million da)	Sinovial (800kda- 1200kda)	mean difference = 0 p>.05	no	n/a	Moderate

Table 187. Hyaluronic Acid Versus Control: Lequesne Index

Study	N	Power	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Puhl (1993)	195	Yes	10	NR	NR	NR	25mg/2.5 ml Sodium Hyaluronate	.25mg/2.5 ml Sodium Hyaluronate	Mean difference=.9 (p=.0088)	Favors 25mg Sodium HA	N/A	High
Puhl (1993)	195	Yes	14	NR	NR	NR	25mg/2.5 ml Sodium Hyaluronate	.25mg/2.5 ml Sodium Hyaluronate	mean difference=1.6 (p=.0053)	Favors 25mg Sodium HA	N/A	High
Kahan (2003)	506	Yes	36	K-L 1-4	3	6 million Da	HA injection	Conventional treatment	-.49(-.67,-.32)	No	N/A	Moderate
Karlsson (2002)	134	Unclear	20	Ahlback 1-2	3	7 million Da	HA injection	Placebo	.22(-.12,.57)	No	N/A	Moderate
Karlsson (2002)	133	Unclear	20	Ahlback 1-2	3	10 ⁶ Da	HA injection	Placebo	.05(-.29,.39)	No	N/A	Moderate

Study	N	Power	Week	Severity	# Of Injections	Weight	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Karlsson (2002)	134	Unclear	26	Ahlback 1-2	3	7 million Da	HA injection	Placebo	.18(-.17, .52)	No	N/A	Moderate
Karlsson (2002)	133	Unclear	26	Ahlback 1-2	3	10 ⁶ Da	HA injection	Placebo	.07(-.27, .41)	No	N/A	Moderate
Jorgenson (2010)	298	Unclear	13	NR	5	NR	HA injection	Placebo	Raw mean difference= 0.16(-.45, .78)	No	N/A	Moderate
Jorgenson (2010)	298	Unclear	26	NR	5	NR	HA injection	Placebo	Raw mean difference= 0.44(-.42, 1.3)	No	N/A	Moderate
Jorgenson (2010)	298	Unclear	52	NR	5	NR	HA injection	Placebo	Raw mean difference= 0.81 (-.75, 2.37)	No	N/A	Moderate
Lohmander (1996)	189	Yes	20	Ahlback 1-2	5	1000 kDa	HA injection	Placebo	Mean difference= 1.6 (p<.05)	Favors HA	N/A	Moderate

Table 188. High Versus Low Molecular Weight: Other Outcomes

Study	Outcome	N	Sufficient Power	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Karlsson (2002)	Lequesne Index	153	Unclear	20	Ahlback 1-2	3	High Molecular Weight HA	Low Molecular Weight HA (10 ⁶ Da)	.05 (-.29, .39)	No	N/A	Moderate
Karlsson (2002)	Lequesne Index	153	Unclear	26	Ahlback 1-2	3	High Molecular Weight HA	Low Molecular Weight HA (10 ⁶ Da)	.07 (-.27, .41)	No	N/A	Moderate
Berenbaum (2012)	Lequesne Index	426	Yes	26	K-L 2-3	3	Medium MW HA (800-1500kDa)	Low MW HA (500-700 kDa)	-.34 (-.53, -.15)	Favors MMW	Unclear	Moderate
Maheu (2011)	Lequesne index	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	SMD=0.04 (-0.21 ,0.3)	no	n/a	high

Study	Outcome	N	Sufficient Power	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Maheu (2011)	Investigator's assessment (change Baseline - W24)	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	SMD=0 (-0.26, 0.25)	no	n/a	high
Maheu (2011)	OARSI OMERAC T Responder	236	unclear	12	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	OR=1.19 (0.7 ,2.01)	no	n/a	high
Maheu (2011)	OARSI OMERAC T Responder	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	OR=0.88 (0.51 ,1.51)	no	n/a	high
Maheu (2011)	Rescue medication : Patients who did NOT take Paracetamol during the study period	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	OR=1.24 (0.68 ,2.27)	no	n/a	high

Study	Outcome	N	Sufficient Power	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Maheu (2011)	Rescue medication : Patients who did NOT take Paracetamol during the study period	236	unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	synsivic (6 million daltons)	OR=0.91 (0.52 ,1.58)	no	n/a	high
Pavelka (2011)	Lequesne index	380	unclear	4	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	mean difference = -0.2 P>.05	no	n/a	moderate
Pavelka (2011)	Lequesne index	380	unclear	12	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	mean difference = -0.5 p=.049	synvisc (6 million da)	n/a	moderate
Pavelka (2011)	Lequesne index	380	unclear	26	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	mean difference = -0.3 p>.05	no	n/a	moderate

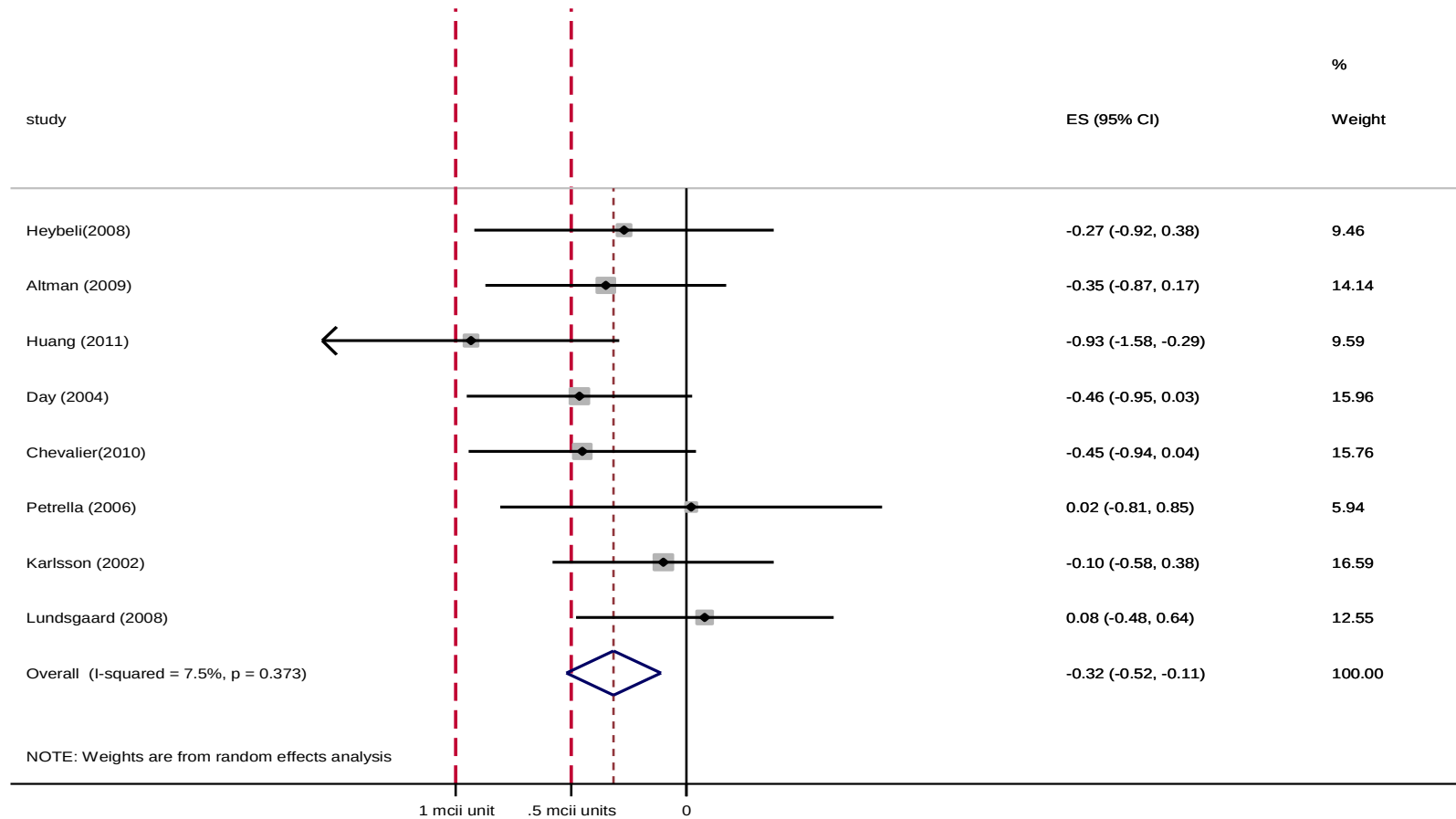
Study	Outcome	N	Sufficient Power	Week	Severity	# Of Injections	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Pavelka (2011)	percent using rescue medication	380	unclear	4 weeks	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	OR=0.74 (0.49 ,1.12)	no	n/a	moderate
Pavelka (2011)	percent using rescue medication	380	unclear	4 to 12 weeks	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	OR=0.77 (0.52 ,1.16)	no	n/a	moderate
Pavelka (2011)	percent using rescue medication	380	unclear	12-26 weeks	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	OR=0.77 (0.52 ,1.16)	no	n/a	moderate
Pavelka (2011)	percent using rescue medication	380	unclear	baseline to 26 weeks	K-L 2-3	3	synvisc (6 million da)	Sinovial (800kda-1200kda)	OR=0.64 (0.41 ,1.01)	no	n/a	moderate

Table 189. High Versus Low Molecular Weight Hyaluronic Acid: Adverse Events

Study	Outcome	N	Power	Week	Severity	# Of Injections	Group 1	Group 2	Odds Ratio	Sig	Clinical Importance	Strength of Evidence
Juni (2007)	Local adverse event	660	Unclear	26	K-L 2+	3	High Molecular Weight HA (6 million Da)	Medium or Low MW HA	1.33 (0.75, 2.36)	No	N/A	High
Karlsson (2001)	Adverse events	176	Unclear	26	Ahlback 1-2	3	High Molecular Weight HA (7x10 ⁶ Da)	Low Molecular Weight HA(10 ⁶ Da)	1.50 (0.82, 2.73)	No	N/A	Moderate
Lee (2006)	Adverse events	145	Unclear	12	K-L 1-3	5	High Molecular weight (3000 kDa)	Low molecular weight (750kD)	0.83 (0.42, 1.66)	No	N/A	Low
Maheu (2011)	Patients with one or more AE	279	Unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	Synsivic (6 million daltons)	0.88 (0.43, 1.81)	No	N/A	High
Maheu (2011)	Patients with treatment emergent AE	279	Unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	Synsivic (6 million daltons)	1.11 (0.69, 1.79)	No	N/A	High

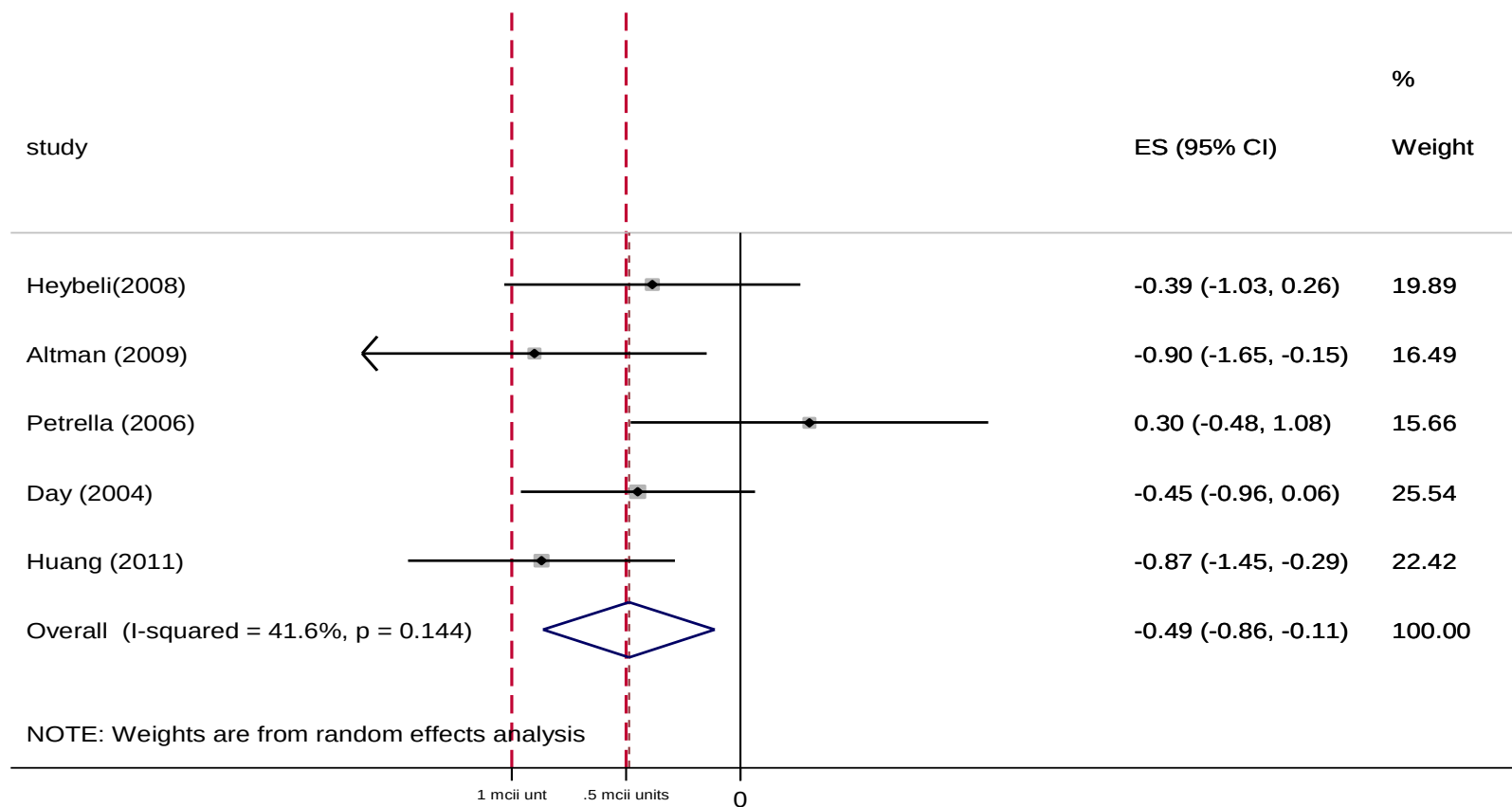
Study	Outcome	N	Power	Week	Severity	# Of Injections	Group 1	Group 2	Odds Ratio	Sig	Clinical Importance	Strength of Evidence
Maheu (2011)	Patients with serious AE	279	Unclear	24	K-L 2-3	3	Structovial (2.2-2.7 mda)	Synsivic (6 million daltons)	5.11 (0.59, 44.32)	No	N/A	High
Pavelka (2011)	Patients with treatment related adverse events	381	Unclear	26	K-L 2-3	3	Synvisc (6 million da)	Sinovial (800kda- 1200kda)	4.13 (0.46, 37.29)	No	N/A	Moderate
Pavelka (2011)	Patients with severe adverse events	381	Unclear	26	K-L 2-3	3	Synvisc (6 million da)	Sinovial (800kda- 1200kda)	6.26 (0.75, 52.52)	No	N/A	Moderate
Raman (2008)	Treatment related adverse events	392	Unclear	52	60% with K-L 3	3	Hylan G-F 20 (6 million Daltons)	Sodium Hyalurona te (.5 to .73 Daltons)	1.32 (0.78, 2.24)	No	N/A	Moderate

Figure 85. Hyaluronic Acid Versus Placebo: Pain in MID Units



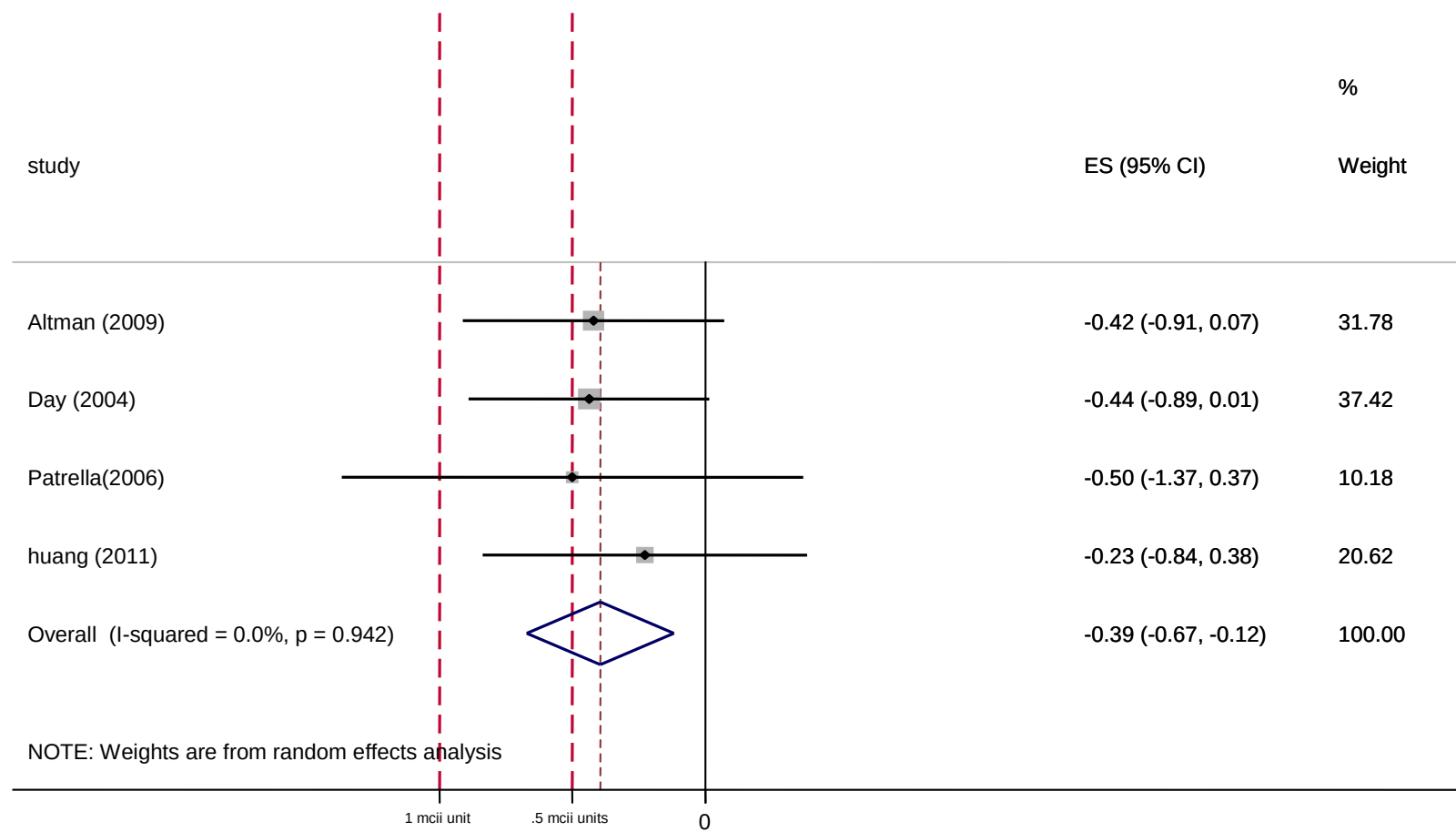
the red line is the threshold where some patients may benefit from treatment

Figure 86. Hyaluronic Acid Versus Placebo: WOMAC Function in MID Units



the red line is the threshold where some patients may benefit from treatment

Figure 87. Hyaluronic Acid Versus Placebo: WOMAC Stiffness in MID Units



the red line is the threshold where some patients may benefit from treatment

Figure 88. Hyaluronic Acid Versus Placebo: WOMAC Pain

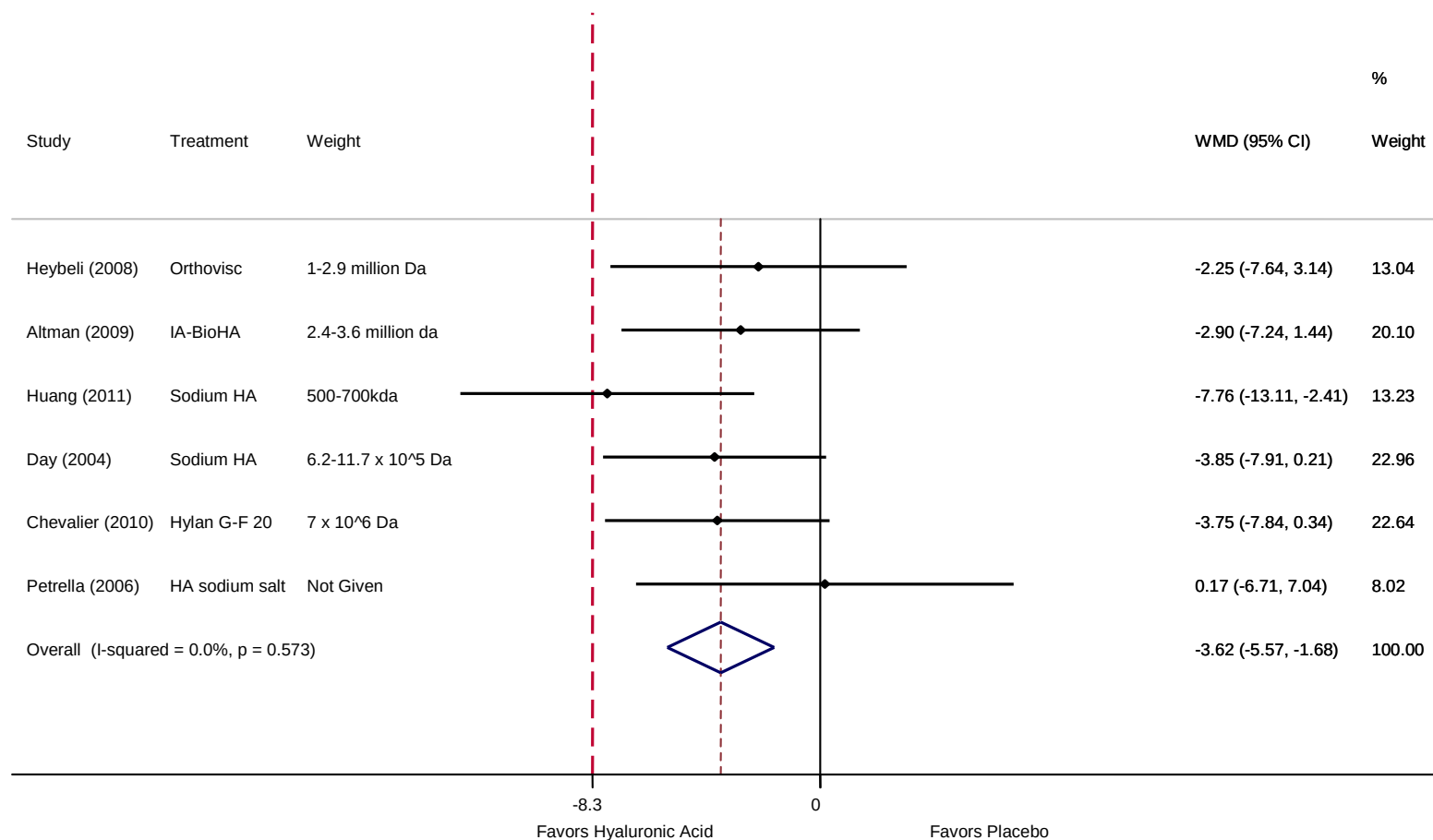


Figure 89. Hyaluronic Acid Versus Placebo: VAS Weight Bearing Pain

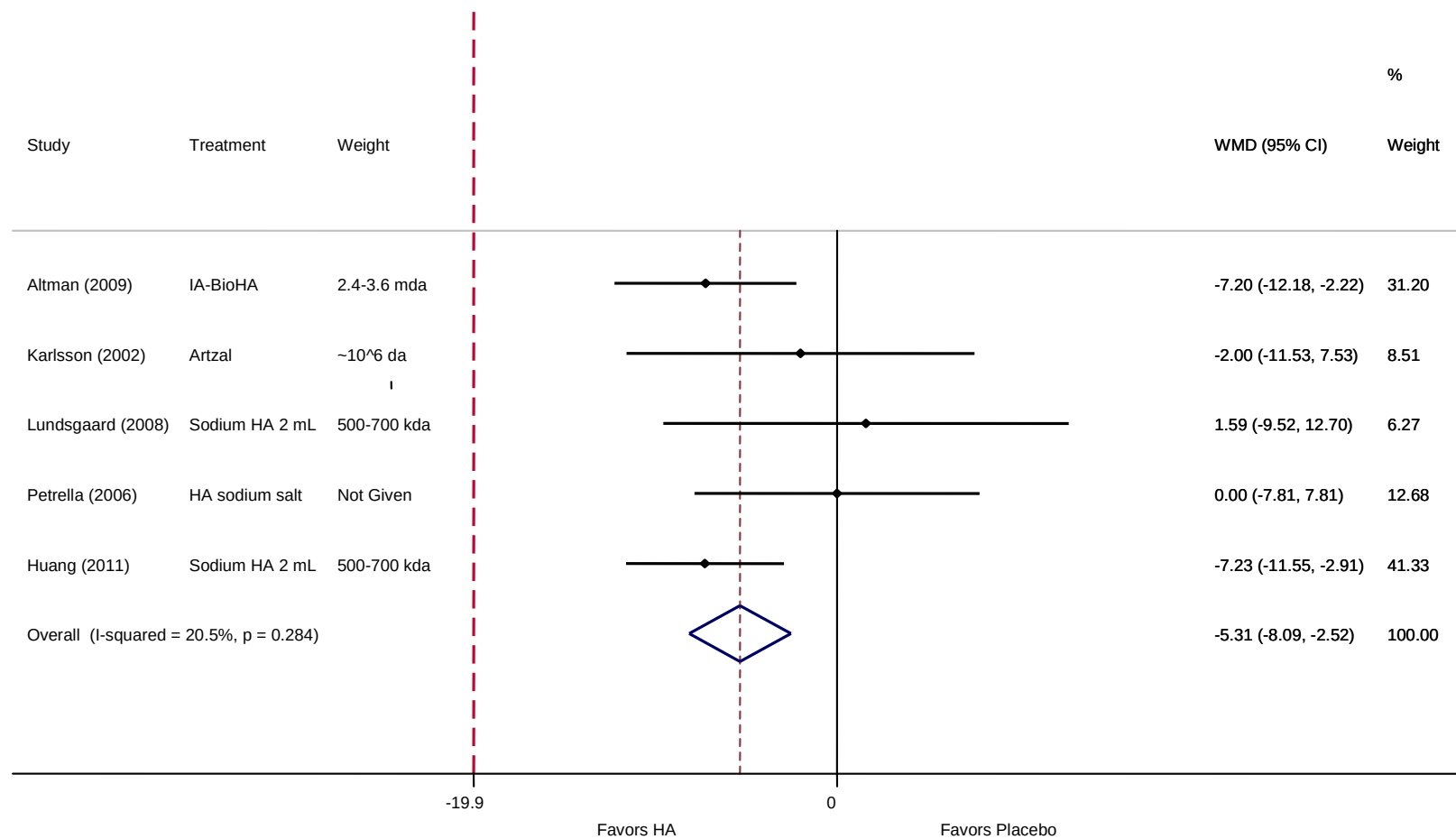


Figure 90. Hyaluronic Acid Versus Placebo: Function

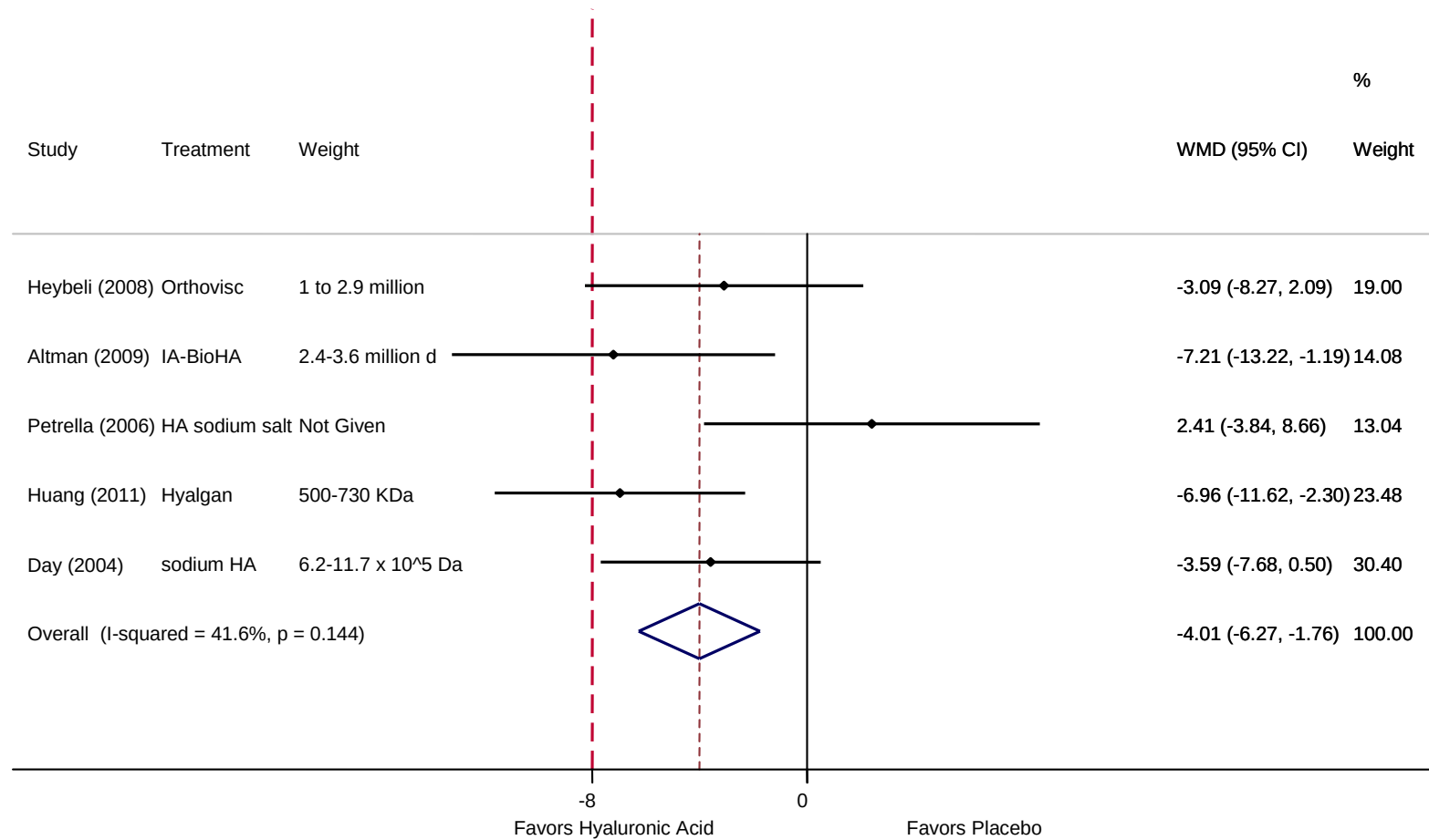
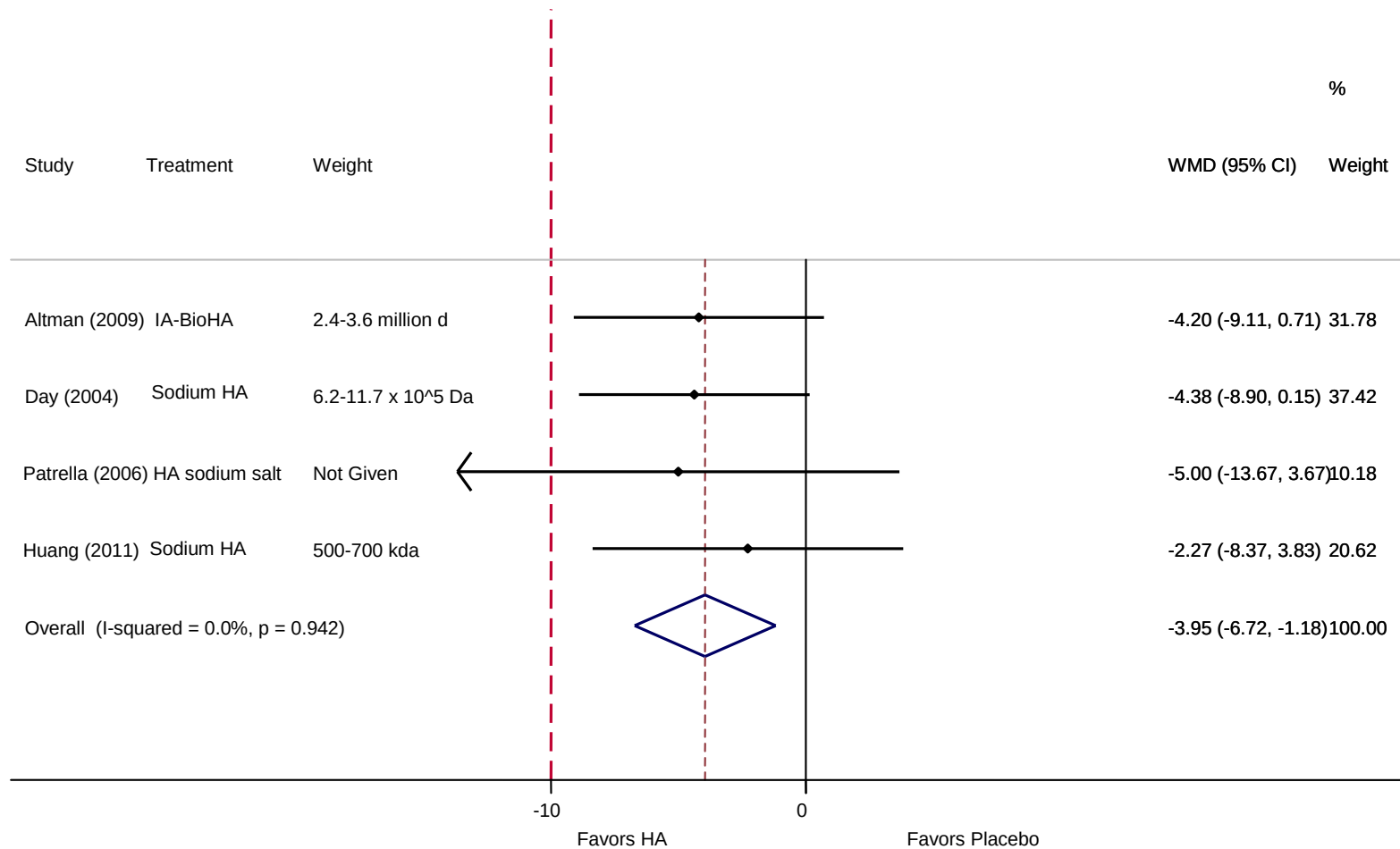


Figure 91. Hyaluronic Acid Versus Placebo: WOMAC Stiffness



RECOMMENDATION 10

We are unable to recommend for or against growth factor injections and/or platelet rich plasma for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

There was a paucity of articles on the use of platelet concentrates in the treatment of osteoarthritis. Sanchez et al.^{119;120} used activated platelet aggregates in a fibrin matrix and Spakova et al.¹²¹ used a platelet concentrate. None of the studies controlled for platelet volume. All studies used hyaluronic acid as the control group.

The studies showed decreased levels of pain in the post injection period but they were not constructed to allow for a comparative analysis of clinical effectiveness. The lack of controlled prospective blinded randomized clinical trials with a placebo control prevent the work group from making any recommendation on the use of platelets or platelet derived growth factor concentrates in the treatment of osteoarthritis of the knee.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 190](#), [Table 191](#)

Three studies were evaluated as part of this recommendation. Sanchez et al.^{119;120} compared growth factor injections to hyaluronic acid; the other compared platelet rich plasma to hyaluronic acid.¹²¹ Sanchez et al.¹¹⁹ was retrospective and had flaws in the investigator bias, blinding and group assignment domains. There was also questionable group comparability at baseline. The quality rating was determined to be low. The second study by Sanchez et al.¹²⁰ was of high quality; it was not flawed in any domain.

The platelet rich plasma (PRP) study by Spakova et al.¹²¹ was of moderate quality. There was uncertain allocation concealment causing the group assignment domain to be flawed as well as potential for investigator bias.

APPLICABILITY

Relevant Tables: [Table 190](#), [Table 191](#)

The participants might not have been representative of the typical patient population in all included studies. In the growth factor studies, the treatment administration might not have been reflective. Patient compliance and adherence were similar to general clinical settings in all studies and there were a sufficient percentage of originally enrolled patients in the final analyses.

FINAL STRENGTH OF EVIDENCE

Because of their moderate applicability, all studies had the same quality and strength of evidence ratings. Sanchez et al.¹¹⁹ was of low strength of evidence, and the second Sanchez et al.¹²⁰ was of high strength. Spakova et al.¹²¹ was of moderate strength of evidence.

Table 190. Quality and Applicability Summary: Growth Factor and Platelet Rich Plasma

Study	Outcome	Duration (Weeks)	Quality	Applicability	Strength of Evidence
Sanchez (2008)	40% WOMAC Pain subscale	4	Low	Moderate	Low
Sanchez (2008)	WOMAC Function	4	Low	Moderate	Low
Sanchez (2008)	WOMAC Total	4	Low	Moderate	Low
Sanchez (2012)	50% decrease in WOMAC pain	24	High	Moderate	Low
Sanchez (2012)	20% decrease in WOMAC pain	24	High	Moderate	Low
Sanchez (2012)	OARSI responders	24	High	Moderate	Low
Sanchez (2012)	WOMAC stiffness	24	High	Moderate	Low
Sanchez (2012)	WOMAC function	24	High	Moderate	Low
Sanchez (2012)	WOMAC total	24	High	Moderate	Low
Sanchez (2012)	Lequesne index	24	High	Moderate	Low
Sanchez (2012)	Acetaminophen use (g/day)	24	High	Moderate	Low
Spakova (2012)	WOMAC Total	13	Moderate	Moderate	Moderate
Spakova (2012)	WOMAC Total	26	Moderate	Moderate	Moderate
Spakova (2012)	NRS Pain	13	Moderate	Moderate	Moderate
Spakova (2012)	NRS Pain	26	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Table 192](#), [Table 193](#)

Sanchez et al.¹²⁰ compared growth factor injections to hyaluronic acid. The authors found that patients receiving growth factor were significantly more likely to achieve a 40% improvement in WOMAC pain. WOMAC function and total scores were significantly better in the group treated with growth factor than the group treated with hyaluronic acid. However, another study by Sanchez et al.¹¹⁹ found conflicting results, in which only 1 of 8 outcomes favored growth factor treatments.

Spakova et al.¹²¹ found that patients who received platelet rich plasma reportedly significantly lower pain at 13 and 26 weeks than those who received hyaluronic acid. WOMAC total scores were also significantly lower in the PRP group. The difference was possibly clinically significant at 13 weeks and clinically significant at 26 weeks.

EVIDENCE TABLES AND FIGURES

QUALITY AND APPLICABILITY

Table 191. Quality and Applicability: Platelet Rich Plasma and Growth Factor Injections

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Sanchez (2008)	40% WOMAC Pain subscale	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Sanchez (2008)	WOMAC Function	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Sanchez (2008)	WOMAC Total	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Sanchez (2012)	50% decrease in WOMAC pain	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Sanchez (2012)	20% decrease in WOMAC pain	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Sanchez (2012)	OARSI responders	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Sanchez (2012)	WOMAC stiffness	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Sanchez (2012)	WOMAC function	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Sanchez (2012)	WOMAC total	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Sanchez (2012)	Lequesne index	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Sanchez (2012)	Acetaminophen use (g/day)	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Spakova (2012)	WOMAC Total week 13	●	●	○	●	●	●	●	○	Moderate	○	●	●	●	Moderate
Spakova (2012)	WOMAC Total week 26	●	●	○	●	●	●	●	○	Moderate	○	●	●	●	Moderate
Spakova (2012)	NRS Pain week 13	●	●	○	●	●	●	●	○	Moderate	○	●	●	●	Moderate
Spakova	NRS Pain week 26	●	●	○	●	●	●	●	○	Moderate	○	●	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability</i> <i>Study</i>
(2012)															

FINDINGS

Table 192. Growth Factor Injections Versus Hyaluronic Acid (Sanchez et al., 2008 and Sanchez et al., 2012)

Study	Outcome	N	Powered	Week	Severity	Group 1	Group 2	Standardized Mean Difference(or Odds ratio or P value)	Sig	Clinical Importance	Strength of Evidence
Sanchez (2008)	40% WOMAC Pain subscale	60	Yes	4	Ahlback 1-4	Growth factor	Hyaluronic Acid	4.50 (1.09, 18.50)	Favors growth factor	Unclear	Low
Sanchez (2008)	WOMAC Function	60	Yes	4	Ahlback 1-4	Growth factor	Hyaluronic Acid	p=.043	Favors growth factor	Unclear	Low
Sanchez (2008)	WOMAC Total	60	Yes	4	Ahlback 1-4	Growth factor	Hyaluronic Acid	p=.01	Favors growth factor	Unclear	Low
Sanchez (2012)	50% decrease in WOMAC pain	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	OR=1.94(1.01, 3.73)	Favors growth factor	Unclear	High
Sanchez (2012)	20% decrease in WOMAC pain	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	OR=1.2(.66, 2.2)	No	Unclear	High
Sanchez (2012)	OARSI responders	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	OR=1.15(.63, 2.07)	No	Unclear	High
Sanchez (2012)	WOMAC stiffness	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	-0.02 (-0.31, 0.28)	No	True Negative	High
Sanchez (2012)	WOMAC function	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	-0.07 (-0.36, 0.23)	No	True Negative	High
Sanchez (2012)	WOMAC total	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	-0.09 (-0.39, 0.20)	No	True Negative	High

Study	Outcome	N	Powered	Week	Severity	Group 1	Group 2	Standardized Mean Difference(or Odds ratio or P value)	Sig	Clinical Importance	Strength of Evidence
Sanchez (2012)	Lequesne index	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	-0.06 (-0.35, 0.24)	No	True Negative	High
Sanchez (2012)	Acetaminophen use (g/day)	176	Yes	24	Ahlback 1-3	Growth factor	Hyaluronic Acid	p>.05	No	Unclear	High

Table 193. Platelet Rich Plasma (PRP) Versus Hyaluronic Acid (Spakova et al., 2012)

Outcome	N	Powered	Week	Severity	Group 1	Group 2	Effect size	Sig	Clinical Importance	Strength of Evidence
WOMAC Total	60	Yes	13	K-L 1-3	Platelet rich plasma	Hyaluronic Acid	-0.74 (-1.11, -0.37)	Favors PRP	Possibly clinically important	Moderate
WOMAC Total	60	Yes	26	K-L 1-3	Platelet rich plasma	Hyaluronic Acid	-0.78 (-1.15, -0.41)	Favors PRP	Clinically significant	Moderate
NRS Pain	60	Yes	13	K-L 1-3	Platelet rich plasma	Hyaluronic Acid	-0.89 (-1.26, -0.51)	Favors PRP	Unclear	Moderate
NRS Pain	60	Yes	26	K-L 1-3	Platelet rich plasma	Hyaluronic Acid	-0.81 (-1.19, -0.44)	Favors PRP	Unclear	Moderate

RECOMMENDATION 11

We cannot *suggest* that the practitioner use needle lavage for patients with symptomatic osteoarthritis of the knee.

Strength of Recommendation: Moderate

Description: A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

RATIONALE

This recommendation is based on one high strength study by Bradley et al.¹²² and one moderate strength study by Vad et al.¹²³ The evidence showed little or no benefit from needle lavage in the treatment of osteoarthritis of the knee. Fourteen of 15 outcomes were not statistically significant, including three pain and three functional outcomes, indicating no measurable benefit to patients from needle lavage.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 194](#), [Table 197](#), [Table 198](#)

Two studies compared patients undergoing needle lavage to a control group. The Bradley et al.¹²² study did not contain flaws in any of the quality domains and was rated as high quality. The study by Vad et al.¹²³ was a moderate quality non-randomized control trial. Patients were able to choose their treatment creating a flaw in the group assignment domain. There was also questionable comparability of the groups at baseline; the authors did not use a test of statistical significance when comparing the pre-test outcome scores.

Arden et al.¹⁰⁷ compared needle lavage and intraarticular corticosteroids using a research design that resulted in a moderate quality study. There was questionable comparability of the groups at baseline and potential for investigator bias.

APPLICABILITY

Relevant Tables: [Table 194](#), [Table 197](#), [Table 198](#)

All studies were of moderate applicability. Compliance and adherence reflected typical clinical practice. The studies included all originally enrolled patients in the final analyses. However, treatment interventions were applied in a manner that might have been unrepresentative of typical clinical settings in each study. The patients might not have been typical of the osteoarthritis of the knee population in the Bradley et al.¹²² and Arden et al.¹⁰⁷ studies.

FINAL STRENGTH OF EVIDENCE

The included studies were of moderate applicability so their strength of evidence ratings were comparable to their study quality ratings. The Bradley et al.¹²² study was rated as high strength of evidence, and the Arden et al.¹⁰⁷ study was of moderate strength.

Table 194. Quality and Applicability Summary: Needle Lavage

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Bradley (2002)	WOMAC Pain	12 weeks	High	Moderate	High
Bradley (2002)	WOMAC Pain	24 weeks	High	Moderate	High
Bradley (2002)	WOMAC Pain	52 weeks	High	Moderate	High
Bradley (2002)	WOMAC Function	12 weeks	High	Moderate	High
Bradley (2002)	WOMAC Function	24 weeks	High	Moderate	High
Bradley (2002)	WOMAC Function	52 weeks	High	Moderate	High
Bradley (2002)	Acetaminophen/day	12 weeks	High	Moderate	High
Bradley (2002)	Acetaminophen/day	24 weeks	High	Moderate	High
Bradley (2002)	Acetaminophen/day	52 weeks	High	Moderate	High
Bradley (2002)	Quality of Well-Being	24 weeks	High	Moderate	High
Bradley (2002)	Quality of Well-Being	52 weeks	High	Moderate	High
Bradley (2002)	50 ft. Walk time	12 weeks	High	Moderate	High
Bradley (2002)	50 ft. Walk time	24 weeks	High	Moderate	High

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Bradley (2002)	50 ft. Walk time	52 weeks	High	Moderate	High
Vad (2003)	VAS Pain	1.1 years	Moderate	Moderate	Moderate

Table 195. Quality and Applicability Summary: Needle Lavage Versus Corticosteroids

Study	Outcome	Weeks	Quality	Applicability	Strength of Evidence
Arden (2008)	WOMAC Pain	4	Moderate	Moderate	Moderate
Arden (2008)	WOMAC Pain	12	Moderate	Moderate	Moderate
Arden (2008)	WOMAC Pain	26	Moderate	Moderate	Moderate
Arden (2008)	WOMAC Total Function	12	Moderate	Moderate	Moderate
Arden (2008)	WOMAC Total Function	26	Moderate	Moderate	Moderate
Arden (2008)	WOMAC Total Stiffness	12	Moderate	Moderate	Moderate
Arden (2008)	WOMAC Total Stiffness	26	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Table 196](#), [Table 199-Table 203](#)

Fourteen of 15 outcomes were not statistically significant suggesting that there was not any benefit in needle lavage compared to the control group. Pain, function and quality of life provided the critical outcomes. Three of four pain outcomes were not statistically significant. WOMAC function scores were not statistically significant at 12, 24 and 52 weeks. The quality of well-being scores were not statistically significant at 24 weeks and after one year.

There were seven total outcomes comparing needle lavage and IA corticosteroids. Six were possibly clinically significant in favor of lavage. WOMAC pain was the only critical outcome. While not statistically significant at 4 weeks, pain scores at 12 and 26 weeks were significantly lower in patients who received lavage than those treated with corticosteroids.

Table 196. Results Summary: Needle Lavage Versus Sham

		4 weeks	12 weeks	24 weeks	26 weeks	52 weeks	1.1 years
Needle Lavage Versus Control	WOMAC Pain			○	○	●	
	VAS Pain						●
	WOMAC Function			○	○	○	
	Quality of Well-Being				●	●	
	50-feet walk			○	○	○	
	Acetaminophen use			○	○	○	
Needle Lavage Versus IA Corticosteroids	WOMAC Pain	○		●	●		
	WOMAC Stiffness			●	●		
	WOMAC Total			●	●		

○ = Not statistically significant; ● = Possibly Clinically Important;

● = Possibly Clinically Significant in Favor of Lavage;

● = Statistically Significant in Favor of Lavage

EVIDENCE TABLES AND FIGURES

QUALITY AND APPLICABILITY

Table 197. Quality and Applicability: Needle Lavage Versus Control

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Bradely (2002)	WOMAC Pain score 12 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	WOMAC Pain score 24 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	WOMAC Pain score 52 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	WOMAC Physical Function 12 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	WOMAC Physical Function 24 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bradely (2002)	WOMAC Physical Function 52 weeks	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	Acetaminophen/day 12 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	Acetaminophen/day 24 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	Acetaminophen/day 52 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	Quality of Well-Being 24 Weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	Quality of Well-Being 52 Weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bradely (2002)	50 foot walk time 12 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	50 foot walk time 24 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bradely (2002)	50 foot walk time 52 weeks	●	◐	●	●	●	●	●	●	High	○	○	●	●	Moderate
Vad (2003)	VAS pain 1.1 years	●	●	○	●	○	●	●	●	Moderate	●	○	●	●	Moderate

Table 198. Quality and Applicability: Needle Lavage Versus IA Corticosteroid

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Week</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Arden (2008)	WOMAC Pain	4	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Pain	12	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Function	12	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Stiffness	12	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Pain	26	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Function	26	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Arden (2008)	WOMAC Stiffness	26	●	●	●	●	○	●	●	○	Moderate	○	○	●	●	Moderate

FINDINGS

Table 199. Needle Lavage Versus Control: WOMAC Pain

Study	Outcome	N	Sufficient Power	Week	K-L Grade	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bradely (2002)	WOMAC Pain	178	Yes	12	1 to 4	Needle Lavage	Sham	MD = -.8(p>.05)	No	Inconclusive	High
Bradely (2002)	WOMAC Pain	176	Yes	24	1 to 4	Needle Lavage	Sham	MD = -.7(p>.05)	No	Inconclusive	High
Bradely (2002)	WOMAC Pain	177	Yes	52	1 to 4	Needle Lavage	Sham	MD = -1.5(p>.05)	No	Inconclusive	High
Vad (2003)	VAS Pain	81	Yes	57.2	1 to 4	Needle Lavage plus Hylan GF-20	Hylan GF-20	-0.83 (-1.29, -0.37)	Yes	Possibly Clinically Important	Moderate

Table 200. Needle Lavage Versus Sham: Function

Study	Outcome	N	Sufficient Power	Week	K-L Grade	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bradely (2002)	WOMAC Function	178	Yes	12	1 to 4	Needle Lavage	Sham	MD = -.4 (p>.05)	No	Inconclusive	High
Bradely (2002)	WOMAC Function	176	Yes	24	1 to 4	Needle Lavage	Sham	MD = -3.9 (p>.05)	No	Inconclusive	High
Bradely (2002)	WOMAC Function	177	Yes	52	1 to 4	Needle Lavage	Sham	MD = -2.8 (p>.05)	No	Inconclusive	High
Bradely (2002)	50 ft. Walk time	178	Unclear	12	1 to 4	Needle Lavage	Sham	MD = -.4 (p>.05)	No	N/A	High
Bradely (2002)	50 ft. Walk time	176	Unclear	24	1 to 4	Needle Lavage	Sham	MD = -.3 (p>.05)	No	N/A	High
Bradely (2002)	50 ft. Walk time	177	Unclear	52	1 to 4	Needle Lavage	Sham	MD = -.7 (p>.05)	No	N/A	High

Table 201. Needle Lavage Versus Sham: Quality of Well-Being Score

Study	Outcome	N	Sufficient Power	Week	K-L grade	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bradely (2002)	Quality of Well-Being Score	176	Unclear	24	1 to 4	Needle Lavage	Sham	MD = .02 (p>.05)	No	N/A	High
Bradely (2002)	Quality of Well-Being Score	177	Unclear	52	1 to 4	Needle Lavage	Sham	MD = .02 (p>.05)	No	N/A	High

Table 202. Needle Lavage Versus Sham: Acetaminophen Consumption

Study	Outcome	N	Sufficient Power	Week	K-L grade	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Bradely (2002)	Acetaminophen Consumption	178	Unclear	12	1 to 4	Needle Lavage	Sham	MD = -.3 (p>.05)	No	N/A	High
Bradely (2002)	Acetaminophen Consumption	176	Unclear	24	1 to 4	Needle Lavage	Sham	MD = -.4 (p>.05)	No	N/A	High
Bradely (2002)	Acetaminophen Consumption	177	Unclear	52	1 to 4	Needle Lavage	Sham	MD = -.1 (p>.05)	No	N/A	High

Table 203. Needle Lavage Versus Corticosteroids

Study	Outcome	N	Sufficient Power	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Arden (2008)	WOMAC Pain	146	Yes	4	K-L 1-4	Needle Lavage	IA Corticosteroid	0.24(-0.09, 0.56)	No	Inconclusive	Moderate
Arden (2008)	WOMAC Pain	146	Yes	12	K-L 1-4	Needle Lavage	IA Corticosteroid	0.35(0.02, 0.67)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total Function	145	Yes	12	K-L 1-4	Needle Lavage	IA Corticosteroid	0.34(0.01, 0.66)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total Stiffness	138	Yes	12	K-L 1-4	Needle Lavage	IA Corticosteroid	0.4(0.06, 0.74)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Pain	146	Yes	26	K-L 1-4	Needle Lavage	IA Corticosteroid	0.52(0.19, 0.85)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total Function	145	Yes	26	K-L 1-4	Needle Lavage	IA Corticosteroid	0.44(0.11, 0.77)	Favors Needle Lavage	Possibly clinically significant	Moderate
Arden (2008)	WOMAC Total Stiffness	138	Yes	26	K-L 1-4	Needle Lavage	IA Corticosteroid	0.45(0.11, 0.79)	Favors Needle Lavage	Possibly clinically significant	Moderate

RECOMMENDATION 12

We cannot recommend performing arthroscopy with lavage and/or debridement in patients with a primary diagnosis of symptomatic osteoarthritis of the knee.

Strength of Recommendation: Strong

Description: A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RATIONALE

There were three studies that met the inclusion criteria for this recommendation. The Kirkley et al.¹²⁴ and Kalunian et al.¹²⁵ studies comparing arthroscopic lavage to placebo were rated as moderate strength and the Moseley et al.¹²⁶ study comparing arthroscopic lavage to sham arthroscopic surgery was rated as a high strength study.

Kirkley et al.¹²⁴ reported that a large number of patients were not eligible for participation in their study (38%) largely due to the exclusion criteria of substantial knee malalignment. In some cases, patients declined participation. Kirkely et al.¹²⁴ compared arthroscopic surgery to lavage and debridement combined with usual physical therapy and medical treatment, usual care. The authors used the pain, functional status and other symptoms subscales of the Arthritis Self-Efficacy Scale (ASES) and the McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) at multiple time points (ranging from three months to two years). Out of 20 outcomes, only two were statistically significant in favor of surgery with lavage. Differences in AIMS pain were statistically significant at three months and differences in AIMS-Other Arthritis Symptoms subscale scores remained significant after two years. In summary, this randomized controlled trial demonstrated no benefit of arthroscopic surgery compared to physical therapy and medical treatment for osteoarthritis of the knee.

Kalunian et al.¹²⁵ included a large number of enrolled patients from one institution with intraarticular crystals in their knee. They compared arthroscopic lavage with 3,000 ml saline to lavage with 250 ml saline. There were not any statistically significant differences in VAS and WOMAC pain scores between the two treatment groups.

The Moseley et al.¹²⁶ study raised questions regarding its limited sampling (mostly male veterans) as well as the number of potential study participants who declined randomization into a treatment group. In this RCT, the effects of arthroscopy with debridement or lavage were not statistically significant in the vast majority of patient oriented outcome measures for pain and function, at multiple time points from one week to two years following surgery.

Collectively all three included studies did not demonstrate clinical benefit of arthroscopic debridement or lavage. The work group also considered the potential risks to patients (anesthesia intolerance, infection, and venous thrombosis) associated with surgical intervention.

It was agreed that the lacking evidence for treatment benefit and increased risks from surgery were sufficient reasons to recommend against arthroscopic debridement and/or lavage in patients with a primary diagnosis of osteoarthritis of the knee.

None of the evidence we examined specifically included patients who had a primary diagnosis of meniscal tear, loose body, or other mechanical derangement, with concomitant diagnosis of osteoarthritis of the knee. The present recommendation does not apply to such patients.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 204](#), [Table 205](#)

Three studies met the inclusion criteria for this recommendation. The Moseley et al.¹²⁶ study was of high quality. The studies by Kirkely et al.¹²⁴ and Kalunian et al.¹²⁵ were of moderate quality. The Moseley et al.¹²⁶ study was not flawed in any quality domain. Both moderate quality studies^{124;125} were flawed in the group assignment and group comparability domains and the Kalunian et al. study was also flawed in treatment integrity.

APPLICABILITY

Relevant Tables: [Table 204](#), [Table 205](#)

In all three studies, the participants might not have been representative of the osteoarthritis of the knee patient population. Furthermore, the application of the intervention might not have been the same as what is practiced in regular clinical settings. At the same time, compliance and adherence were typical. Two of the three studies included all originally enrolled patients in the final analyses.^{124;125}

FINAL STRENGTH OF EVIDENCE

All moderate and high quality outcomes were paired with comparable ratings for strength of evidence since all study applicability ratings were moderate.

Table 204. Quality and Applicability Summary: Arthroscopy with Lavage and/or Debridement

Study	Outcome	Duration (Weeks)	Comparison	Quality	Applicability	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Debridement versus Placebo	High	Moderate	High
Kalunian (2000)	WOMAC Pain	52	Full irrigation versus minimal irrigation	Moderate	Moderate	Moderate
Kalunian (2000)	VAS Pain	52	Full irrigation versus minimal irrigation	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	13	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	26	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	52	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy	78	Arthroscopic surgery with debridement and	Moderate	Moderate	Moderate

	Scale: Pain		lavage versus usual care			
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	104	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	13	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	26	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	52	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	78	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	104	Arthroscopic surgery with debridement and lavage versus usual	Moderate	Moderate	Moderate

			care			
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	13	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	26	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	52	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	78	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	104	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate

Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	13	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	26	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	52	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	78	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	104	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	13	Debridement versus Placebo	High	Moderate	High
Moseley (2000)	Arthritis Impact Measurement Scale:	26	Debridement versus Placebo	High	Moderate	High

Pain						
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	52	Debridement versus Placebo	High	Moderate	High
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	78	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	104	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	6	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	13	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	26	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	52	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale:	78	Debridement versus	High	Moderate	High

	Walking-Bending		Placebo			
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	104	Debridement versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	13	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	26	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	52	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	78	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	104	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale:	6	Debridement versus	High	Moderate	High

	Walking-Bending		lavage			
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	13	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	26	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	52	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	78	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	104	Debridement versus lavage	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	13	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale:	26	Lavage versus Placebo	High	Moderate	High

Pain						
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	52	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	78	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	104	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	6	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	13	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	26	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	52	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale:	78	Lavage versus Placebo	High	Moderate	High

	Walking-Bending					
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	104	Lavage versus Placebo	High	Moderate	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Debridement versus Placebo	High	Moderate	High
Kalunian (2000)	WOMAC Pain	52	Full irrigation versus minimal irrigation	Moderate	Moderate	Moderate
Kalunian (2000)	VAS Pain	52	Full irrigation versus minimal irrigation	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	13	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	26	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	52	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate

Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	78	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	104	Arthroscopic surgery with debridement and lavage versus usual care	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Figure 92](#), [Table-206](#)- [Table 215](#)

Moseley et al.¹²⁶ compared arthroscopic debridement and arthroscopic lavage to placebo using the AIMS-pain and AIMS-walking and bending instruments. Each outcome was measured at six weeks, 13 weeks, 26 weeks, 1 year, 78 weeks, and 2 years. Neither debridement nor lavage was associated with statistically significant treatment effects over placebo at any follow-up time. Also, debridement was not statistically better than lavage.

As indicated above, Kirkley et al.¹²⁴ compared arthroscopic surgery with lavage and debridement combined with usual physical and medical therapy to a control group who only received usual care. The authors used the pain, functional status and other symptoms subscales of the Arthritis Self-Efficacy Scale (ASES) and the McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR). The follow up periods were three months, six months, one year, 18 months and two years. Out of 20 outcomes, only two were statistically significant in favor of surgery with lavage. Differences in AIMS pain were statistically significant at three months and differences in AIMS-Other Arthritis Symptoms scores remained significant after two years.

Kalunian et al.¹²⁵ compared arthroscopic lavage with 3,000 ml saline to lavage with 250 ml saline. There were not any statistically significant differences in VAS and WOMAC pain scores between the two groups.

Figure 92. Results Summary: Arthroscopic Surgery, Lavage, and Debridement Versus Control

	Outcome	6	13	26	52	78	104
Debridement	Arthritis Impact Measurement Scale: Pain	●	●	●	●	●	●
	Arthritis Impact Measurement Scale: Walking-Bending	●	●	●	●	●	●
Lavage	Arthritis Impact Measurement Scale: Pain	●	●	●	●	●	●
	Arthritis Impact Measurement Scale: Walking-Bending	●	●	●	●	●	●
Arthroscopic Surgery with Debridement and Lavage	Arthritis Self-Efficacy Scale: Functional Status		●	●	●	●	●
	Arthritis Self-Efficacy Scale: Other Symptoms		●	●	●	●	●
	Arthritis Self-Efficacy Scale: Pain		●	●	●	●	●
	McMaster-Toronto Arthritis Patient Preference		●	●	●	●	●
Full Versus Minimal Irrigation	VAS Pain				●		
	WOMAC Pain				●		

Key: ●=Not Significant; ●=Statistically Significant

EVIDENCE TABLES AND FIGURES

QUALITY AND APPLICABILITY

Table 205. Quality and Applicability: Arthroscopy with Lavage and/or Debridement

●: Domain free of flaws ○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Kalunian (2000)	WOMAC Pain	52	Full irrigation versus minimal irrigation	●	●	○	●	○	○	●	●	Moderate	○	○	●	●	Moderate
Kalunian (2000)	VAS Pain	52	Full irrigation versus minimal irrigation	●	●	○	●	○	○	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	13	Arthroscopic surgery with debridement and lavage versus usual care	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	26	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	52	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	78	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	104	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	13	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	26	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	52	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	78	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	104	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	13	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	26	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	52	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	78	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	104	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	13	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	26	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	52	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	78	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Score: Other Arthritis Related Symptoms	104	Arthroscopic surgery with debridement and lavage versus usual care	●	◐	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	13	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence	Analysis	Applicability Study
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	26	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	52	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate
Moseley (2000)	Arthritis Impact Measurement Scale: Pain	78	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	104	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	6	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	13	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	26	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	52	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain free of flaws ○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	78	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	104	Debridement versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	13	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	26	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	52	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	78	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	104	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	6	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	13	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	26	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	52	Debridement versus lavage	●	○	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	78	Debridement versus lavage	●	○	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ◐: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	104	Debridement versus lavage	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	6	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	13	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	26	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	52	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	78	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○ ○ ● ○		Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	104	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	6	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	13	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

○: Domain flaws present ●: Moderate power																	
Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study	
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	26	Lavage versus Placebo	●	○	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	52	Lavage versus Placebo	●	○	●	●	●	●	●	●	High	○	○	●	○	Moderate

●: Domain
free of flaws

○: Domain
flaws present

◐: Moderate
power

Study	Outcome	Week	Comparison	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	78	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	104	Lavage versus Placebo	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate

FINDINGS

Table 206. Debridement Versus Placebo: Pain

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	116	Unclear	6	K-L 0-4	Debridement	Placebo	-0.04 (-0.40, 0.33)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	114	Unclear	13	K-L 0-4	Debridement	Placebo	-0.01 (-0.38, 0.36)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	112	Unclear	26	K-L 0-4	Debridement	Placebo	0.10 (-0.27, 0.47)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	105	Unclear	52	K-L 0-4	Debridement	Placebo	-0.01 (-0.40, 0.37)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	103	Unclear	78	K-L 0-4	Debridement	Placebo	-0.20 (-0.59, 0.18)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	108	Unclear	104	K-L 0-4	Debridement	Placebo	0.06 (-0.32, 0.44)	No	N/A	High

Table 207. Debridement Versus Placebo: Function

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	116	Unclear	6	K-L 0-4	Debridement	Placebo	0.10 (-0.27, 0.46)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	114	Unclear	13	K-L 0-4	Debridement	Placebo	0.14 (-0.23, 0.51)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	112	Unclear	26	K-L 0-4	Debridement	Placebo	0.12 (-0.25, 0.49)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	105	Unclear	52	K-L 0-4	Debridement	Placebo	0.26 (-0.13, 0.64)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	103	Unclear	78	K-L 0-4	Debridement	Placebo	-0.09 (-0.48, 0.30)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	108	Unclear	104	K-L 0-4	Debridement	Placebo	0.09 (-0.29, 0.47)	No	N/A	High

Table 208. Debridement Versus Lavage: Pain

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	116	Unclear	6	K-L 0-4	Debridement	Lavage	-0.11 (-0.47, 0.25)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	114	Unclear	13	K-L 0-4	Debridement	Lavage	-0.17 (-0.53, 0.19)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	112	Unclear	26	K-L 0-4	Debridement	Lavage	-0.13 (-0.50, 0.24)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	105	Unclear	52	K-L 0-4	Debridement	Lavage	-0.18 (-0.56, 0.20)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	103	Unclear	78	K-L 0-4	Debridement	Lavage	-0.19 (-0.57, 0.19)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	108	Unclear	104	K-L 0-4	Debridement	Lavage	-0.11 (-0.49, 0.26)	No	N/A	High

Table 209. Debridement Versus Lavage: Function

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	116	Unclear	6	K-L 0-4	Debridement	Lavage	0.09 (-0.27, 0.45)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	114	Unclear	13	K-L 0-4	Debridement	Lavage	0.19 (-0.17, 0.55)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	112	Unclear	26	K-L 0-4	Debridement	Lavage	0.12 (-0.24, 0.49)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	105	Unclear	52	K-L 0-4	Debridement	Lavage	0.23 (-0.14, 0.61)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	103	Unclear	78	K-L 0-4	Debridement	Lavage	0.09 (-0.29, 0.47)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	108	Unclear	104	K-L 0-4	Debridement	Lavage	0.18 (-0.19, 0.56)	No	N/A	High

Table 210. Arthroscopic Lavage Versus Placebo: Pain

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	114	Unclear	6	K-L 0-4	Lavage	Placebo	0.07 (-0.30, 0.44)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	115	Unclear	13	K-L 0-4	Lavage	Placebo	0.16 (-0.21, 0.53)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	116	Unclear	26	K-L 0-4	Lavage	Placebo	0.23 (-0.14, 0.59)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	111	Unclear	52	K-L 0-4	Lavage	Placebo	0.18 (-0.19, 0.56)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	109	Unclear	78	K-L 0-4	Lavage	Placebo	-0.01 (-0.38, 0.37)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Pain	111	Unclear	104	K-L 0-4	Lavage	Placebo	0.17 (-0.20, 0.54)	No	N/A	High

Table 211. Arthroscopic Lavage Versus Placebo: Function

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	114	Unclear	6	K-L 0-4	Lavage	Placebo	-0.00 (-0.37, 0.36)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	115	Unclear	13	K-L 0-4	Lavage	Placebo	-0.08 (-0.44, 0.29)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	116	Unclear	26	K-L 0-4	Lavage	Placebo	-0.01 (-0.38, 0.35)	No	N/A	High

Study	Outcome	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	111	Unclear	52	K-L 0-4	Lavage	Placebo	0.01 (-0.36, 0.38)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	109	Unclear	78	K-L 0-4	Lavage	Placebo	-0.18 (-0.56, 0.19)	No	N/A	High
Moseley (2002)	Arthritis Impact Measurement Scale: Walking-Bending	111	Unclear	104	K-L 0-4	Lavage	Placebo	-0.10 (-0.47, 0.28)	No	N/A	High

Table 212. Arthroscopic Surgery with Lavage and Debridement Versus Usual Care: Pain

Study	Outcome	N	Sufficient Power	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	170	Yes	13	K-L 2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.32 (0.02, 0.63)	Favors surgery with lavage and debridement	N/A	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	163	Unclear	26	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.21 (-0.10, 0.52)	No	N/A	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	157	Unclear	52	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.05 (-0.26, 0.37)	No	N/A	Moderate

Study	Outcome	N	Sufficient Power	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	148	Unclear	78	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.17 (-0.16, 0.49)	No	N/A	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Pain	168	Unclear	104	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.26 (-0.04, 0.56)	No	N/A	Moderate

Table 213. Arthroscopic Surgery with Lavage and Debridement Versus Usual Care: Function

Study	Outcome	N	Powered	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	170	Unclear	13	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	-0.06 (-0.37, 0.25)	No	N/A	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	163	Unclear	26	2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.04 (-0.27, 0.35)	No	N/A	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	157	Unclear	52	2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	-0.17 (-0.48, 0.14)	No	N/A	Moderate
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	148	Unclear	78	2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	-0.06 (-0.39, 0.26)	No	N/A	Moderate

Study	Outcome	N	Powered	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	Arthritis Self-Efficacy Scale: Functional Status	168	Unclear	104	2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.09 (-0.21, 0.39)	No	N/A	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	170	Unclear	13	2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.07 (-0.23, 0.37)	No	N/A	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	163	Unclear	26	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	-0.10 (-0.41, 0.21)	No	N/A	Moderate

Study	Outcome	N	Powered	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	157	Unclear	52	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.06 (-0.26, 0.37)	No	N/A	Moderate
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	148	Unclear	78	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	0.23 (-0.09, 0.55)	No	N/A	Moderate

Study	Outcome	N	Powered	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)	168	Unclear	104	2 to 4	Arthroscopic surgery with debridement and lavage	Usual care	-0.04 (-0.35, 0.26)	No	N/A	Moderate

Table 214. Arthroscopic Surgery with Lavage and Debridement Versus Usual Care: Arthritis Self-Efficacy Score (Other Arthritis Related Symptoms)

Study	N	Sufficient Power to Detect MCII	Week	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kirkley (2008)	148	Unclear	13	K-L 2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.16 (-0.14, 0.47)	No	N/A	Moderate
Kirkley (2008)	148	Unclear	26	K-L 2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.26 (-0.05, 0.57)	No	N/A	Moderate
Kirkley (2008)	148	Unclear	52	K-L 2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.13 (-0.18, 0.44)	No	N/A	Moderate
Kirkley (2008)	148	Unclear	78	K-L 2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.18 (-0.14, 0.51)	No	N/A	Moderate
Kirkley (2008)	148	Unclear	104	K-L 2 to 4	Arthroscopic Surgery with debridement and lavage	Usual care	0.31 (0.01, 0.62)	Favors surgery	N/A	Moderate

Table 215. Full Versus Minimal Irrigation at One Year

Study	Outcome	N	Powered	Severity	Group 1	Group 2	SMD (Odds Ratio or Raw Mean Difference When Indicated)	Sig	Clinical Importance	Strength of Evidence
Kalunian (2000)	WOMAC Pain	90	Yes	K-L 0-2	Full irrigation	Minimal irrigation	-0.15 (-0.56, 0.27)	No	Inconclusive	Low
Kalunian (2000)	VAS Pain	90	Yes	K-L 0-2	Full irrigation	Minimal irrigation	-0.23 (-0.65, 0.19)	No	True negative	Low

RECOMMENDATION 13

We are unable to recommend for or against arthroscopic partial meniscectomy in patients with osteoarthritis of the knee with a torn meniscus.

Strength of Recommendation: Inconclusive

Description: An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

Currently, arthroscopic partial meniscectomy is routinely performed in patients with symptomatic osteoarthritis of the knee who also have primary signs and symptoms of a torn meniscus.

Herrlin et al.¹²⁷ compared arthroscopic partial meniscectomy followed by supervised exercise to supervised exercise alone and measured KOOS pain, symptoms, activities of daily life, sports/recreation, and quality of life subscales scores as outcomes. The study was downgraded from moderate- to low- strength because 40% of patients declined participation and the arthroscopic group had non-homogeneous preoperative KOOS scores. The authors reported no significant treatment benefits of meniscectomy using any of the outcomes at eight weeks and six months. Since there was only one low-strength study, the recommendation was graded inconclusive.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 216-Table 217](#)

One moderate quality study by Herrlin et al.¹²⁷ met the inclusion criteria for this recommendation. The study was flawed in the group assignment, group comparability and investigator bias domains.

APPLICABILITY

Relevant Tables: [Table 216-Table 217](#)

The patients and the treatment administration might not have been representative of typical clinical practice settings.

FINAL STRENGTH OF EVIDENCE

Ratings of moderate quality and applicability resulted in a moderate strength of evidence rating for all included outcomes in the study.

Table 216. Quality and Applicability Summary: Arthroscopic Partial Meniscectomy

Study	Outcome	Quality	Applicability	Strength of Evidence
Herrlin (2007)	KOOS Pain Week 8	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Symptoms Week 8	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Activities of Daily Life Week 8	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Sports/Rec Week 8	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Quality of Life Week 8	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Pain 6 months	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Symptoms 6 months	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Activities of Daily Life 6 months	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Sports/Rec 6 months	Moderate	Moderate	Moderate
Herrlin (2007)	KOOS Quality of Life 6 months	Moderate	Moderate	Moderate

RESULTS

Relevant Tables: [Table 218](#)

KOOS pain, symptoms, activities of daily life, sports/recreation, and quality of life subscales were the outcomes studied by Herrlin et al.¹²⁷ The authors reported no significant treatment benefits of meniscectomy using any of the outcomes at eight weeks and six months.

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 217. Quality and Applicability: Partial Meniscectomy with Exercise Versus Exercise Only

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Herrlin (2007)	KOOS Pain Week 8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Symptoms Week 8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Activities of Daily Life Week 8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Sports/Rec Week 8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Quality of Life Week 8	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Herrlin (2007)	KOOS Pain 6 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Symptoms 6 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Activities of Daily Life 6 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Sports/Rec 6 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Herrlin (2007)	KOOS Quality of Life 6 months	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

FINDINGS

Table 218. Exercise and Meniscectomy Versus Exercise Only (Herrlin et al., 2007)

Outcome	N	Sufficient Power	Week	Age	Ahlback Grade	Meniscal Tear	Loose Bodies	Group 1	Group 2	Author Reported Results
KOOS Pain	90	Unclear	8	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Symptoms	90	Unclear	8	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Activities of Daily Life	90	Unclear	8	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Sports/Rec	90	Unclear	8	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Quality of Life	90	Unclear	8	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Pain	90	Unclear	26	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant

Outcome	N	Sufficient Power	Week	Age	Ahlback Grade	Meniscal Tear	Loose Bodies	Group 1	Group 2	Author Reported Results
KOOS Symptoms	90	Unclear	26	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Activities of Daily Life	90	Unclear	26	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Sports/Rec	90	Unclear	26	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant
KOOS Quality of Life	90	Unclear	26	45-64	0-1	Yes	No	Exercise plus meniscectomy	Exercise only	Not Statistically Significant

RECOMMENDATION 14

The practitioner might perform a valgus producing proximal tibial osteotomy in patients with symptomatic medial compartment osteoarthritis of the knee.

Strength of Recommendation: Limited

Description: A **Limited** recommendation means that the quality of the supporting evidence is unconvincing, or that well-conducted studies show little clear advantage to one approach over another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might counter the current findings. Patient preference should have a substantial influencing role.

RATIONALE

Nine low-strength case series studies found nine out of 10 outcomes significantly improved from baseline. A cross-sectional time series regression analysis was used to predict the placebo effect on VAS pain for comparison to that of the treatment group. Compared to the predicted placebo effect on VAS pain, the proximal tibial osteotomy group reported decreased pain on the VAS.

Based on a lack of appropriate studies, distal femoral (varus producing) osteotomy was not evaluated.

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 219-Table 220](#), [Table 221-Table 222](#)

Data on 48 outcomes in nine studies were analyzed for this recommendation. Eight studies were prospective case series, and were flawed in the group assignment, blinding, group comparability, and treatment integrity domains. Six included studies had some form of investigator bias. All studies used valid measurements for the outcomes. All eight case series studies were given low quality ratings.

Two additional studies were included that compared closed to open wedge osteotomy. Brouwer et al.¹²⁸ was not flawed in six of the seven quality domains, giving it a high rating. Its only quality flaw was that the evaluators were not blinded to the treatment patients received. The Song et al.¹²⁹ study was of low quality, and was flawed in every domain except treatment integrity and measurement validity.

APPLICABILITY

Relevant Tables: [Table 219-Table 220](#), [Table 221-Table 222](#)

All case series studies were rated as having moderate applicability. Each study raised uncertainty about whether or not the treatment and practitioners who administered them were typical of those encountered in clinical practice. Patients in four out of eight case series studies might not have been representative of the treatment seeking population. Two case series studies did not include all enrolled patients in the final data analyses of its outcomes. The applicability of the studies comparing open to closed wedge osteotomy

was rated as moderate. There was uncertainty regarding whether the treatment and practitioners who administered them were similar to those seen in typical clinical practice.

FINAL STRENGTH OF EVIDENCE

Since all the case series osteotomy outcomes were of low quality and were paired with moderate applicability ratings, they were evaluated as comprising low strength of evidence. Of the studies that compared open to closed wedge osteotomy, one was of high and the other was of low strength of evidence.

Table 219. Quality and Applicability Summary: Osteotomy

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Bachhal (2005)	Pin tract infection	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Lateral cortex fracture	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Delayed union	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Knee stiffness	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Ring sequestrum	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Deep infection/chronic osteomyelitis	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Intraarticular fractures	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Neurovascular injury	Final follow-up	Low	Moderate	Low
Bachhal (2005)	Symptomatic deep-vein thrombosis	Final follow-up	Low	Moderate	Low
El-Azab (2011)	Lysholm-Gillquist	Baseline-post-op	Low	Moderate	Low

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
El-Azab (2011)	Lysholm-Gillquist 3 months	3 months	Low	Moderate	Low
El-Azab (2011)	Lysholm-Gillquist 6 months	6 months	Low	Moderate	Low
El-Azab (2011)	Lysholm-Gillquist 3 years	3 years	Low	Moderate	Low
Flamme (2003)	N cases of distal deep vein thrombosis (DVT)	10 years	Low	Moderate	Low
Flamme (2003)	N cases of proximal deep vein thrombosis (DVT)	10 years	Low	Moderate	Low
Flamme (2003)	N cases of bony non-union	10 years	Low	Moderate	Low
Flamme (2003)	N cases of lesions of the fibular nerve	10 years	Low	Moderate	Low
Flamme (2003)	N cases of superficial wound infections	10 years	Low	Moderate	Low
Flamme (2003)	Percentage with adverse events	10 years	Low	Moderate	Low
Flamme (2003)	N cases of bony non-union	10 years	Low	Moderate	Low
Flamme (2003)	International Knee Score	Final follow-up	Low	Moderate	Low

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Niemeyer (2010)	International Knee Documentation Committee Score	Final follow-up	Low	Moderate	Low
Niemeyer (2010)	Lysholm-Tenger Score	Final follow-up	Low	Moderate	Low
Niemeyer (2010)	Intraarticular fractures	3 years	Low	Moderate	Low
Niemeyer (2010)	Over correction	3 years	Low	Moderate	Low
Niemeyer (2010)	Delayed union	3 years	Low	Moderate	Low
Niemeyer (2010)	Overall adverse events	3 years	Low	Moderate	Low
Pongsoipetch (2009)	Superficial incision wound infection	2 years	Low	Moderate	Low
Pongsoipetch (2009)	Knee Society Score	1 year	Low	Moderate	Low
Pongsoipetch (2009)	Knee Society Score	2 years	Low	Moderate	Low
Pongsoipetch (2009)	VAS Pain	3 months	Low	Moderate	Low
Pongsoipetch (2009)	VAS Pain	6 months	Low	Moderate	Low
Pongsoipetch (2009)	VAS Pain	1 year	Low	Moderate	Low
Pongsoipetch (2009)	VAS Pain	2 years	Low	Moderate	Low

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Rudan (1990)	Hospital for Special Surgery-Pain	Final follow-up	Low	Moderate	Low
Rudan (1990)	Hospital for Special Surgery-Function	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Lysholm-Tenger Score	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Knee Outcome Osteoarthritis score	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Lateral tibial plateau fractures	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Deep vein thrombosis (DVT)	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Pulmonary embolism	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Failure of fixation (screw breakage)	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	Loss of angulation	Final follow-up	Low	Moderate	Low
Saragaglia (2010)	TKA Revision	Final follow-up	Low	Moderate	Low
Schroter (2011)	Improvement in Lysholm-Gillquist	1 year	Low	Moderate	Low
Schroter (2011)	Improvement in Tenger activity level	1 year	Low	Moderate	Low

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Schroter (2011)	Improvement in International Knee Documentation Committee Subjective score	1 year	Low	Moderate	Low

Table 220. Quality and Applicability Summary: Lateral Closing Wedge Versus Medial Open Wedge with Puddu Plate

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Song (2012)	40+ VAS Pain Score	Final follow-up	Low	Moderate	Low
Brouwer (2006)	VAS Pain	Final follow-up	High	Moderate	High
Brouwer (2006)	Walking distance	Final follow-up	High	Moderate	High
Brouwer (2006)	Wound infection	Final follow-up	High	Moderate	High
Brouwer (2006)	Nonunion	Final follow-up	High	Moderate	High
Brouwer (2006)	Palsy of the common peroneal nerve	Final follow-up	High	Moderate	High
Brouwer (2006)	Pain in proximal tibiofibular joint	Final follow-up	High	Moderate	High
Brouwer (2006)	Iliac-crest morbidity	Final follow-up	High	Moderate	High
Brouwer (2006)	Fracture of the tibial plateau	Final follow-up	High	Moderate	High

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Brouwer (2006)	Re-operation (further valgus correction)	Final follow-up	High	Moderate	High
Brouwer (2006)	Re-operation (reduction of valgus correction)	Final follow-up	High	Moderate	High
Brouwer (2006)	Revision to joint replacement	Final follow-up	High	Moderate	High
Brouwer (2006)	Removal of osteosynthesis material	Final follow-up	High	Moderate	High

RESULTS

Relevant Tables: [Figure 93-Figure 103](#), [Table 223-Table 226](#)

Pongsoipetch et al.¹³⁰ measured VAS pain at 3, 6, 12, and 24 months. El-Azab et al.¹³¹ also measured VAS pain in patients three years after receiving osteotomy. A cross sectional time series regression equation computed from the placebo data allowed the prediction of expected reduction in pain based on these two studies, given the average age of the sample, average baseline score, and follow-up duration if osteotomy were no more effective than a placebo. At each follow-up period, pain scores were significantly lower than predicted placebo scores in the Pongsoipetch et al. study.¹³⁰ The predicted placebo VAS pain score after three years for the patient population was 40.35(34.33, 46.35). The actual VAS pain score after three years in the osteotomy group was 23(13.3, 32.7), which was significantly lower than the predicted placebo score.

Another study measured the Hospital for Special Surgery pain and function scores.¹³² While pain was found to have significantly improved from baseline, function did not. Other outcomes included the International Knee Documentation Subjective Score, Knee Society Score, and the International Knee Society Score. All outcomes were associated with statistically significant improvements from baseline. The remaining outcomes were used to indicate prevalence of the different types of adverse events among patients who underwent osteotomy (see [Table 224](#)).

VAS pain and walking distance (in km) were not significantly different in patients who received open wedge osteotomy compared to those who underwent the closed procedure. However, patients who underwent closed wedge osteotomy were at significantly lower odds of iliac crest morbidity and of requiring removal of osteosynthesis material

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY
Table 221. Quality and Applicability: Osteotomy

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Rudan (1990)	HSS pain	●	◐	○	○	○	○	●	○	Low	●	○	●	●	Moderate
Rudan (1990)	HSS function	●	◐	○	○	○	○	●	○	Low	●	○	●	●	Moderate
Saragaglia (2010)	Lysholm-Tenger Score	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Saragaglia (2010)	KOOS	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Saragaglia (2010)	Lateral tibial plateau fractures	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Saragaglia (2010)	Deep vein thrombosis (DVT)	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Saragaglia (2010)	Pulmonary embolism	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Saragaglia (2010)	Failure of fixation (screw breakage)	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Saragaglia (2010)	Loss of angulation	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Saragaglia (2010)	Revised to TKA	●	◐	○	○	○	○	●	○	Low	●	○	●	○	Moderate
Niemeyer (2010)	IKDC Score	●	◐	○	○	○	○	●	○	Low	○	○	●	○	Moderate
Niemeyer (2010)	Lysholm-Tenger Score	●	◐	○	○	○	○	●	○	Low	○	○	●	○	Moderate
Niemeyer (2010)	Intraarticular fractures	●	◐	○	○	○	○	●	○	Low	○	○	●	○	Moderate
Niemeyer (2010)	Over correction	●	◐	○	○	○	○	●	○	Low	○	○	●	○	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Niemeyer (2010)	Delayed union	●	◐	○	○	○	○	●	○	Low	○	○	●	○	Moderate
Niemeyer (2010)	Adverse events	●	◐	○	○	○	○	●	○	Low	○	○	●	○	Moderate
Pongsoipetch (2009)	KSS 2 years	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Pongsoipetch (2009)	KSS 1 year	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Pongsoipetch (2009)	VAS 24 months	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Pongsoipetch (2009)	VAS 1 year	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Pongsoipetch (2009)	VAS 6 months	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Pongsoipetch (2009)	VAS 3 months	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Pongsoipetch (2009)	Superficial incision wound infection	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
El-Azab (2011)	Lysholm-Gillquist 3 months	●	◐	○	○	○	○	●	○	Low	●	○	●	●	Moderate
El-Azab (2011)	Lysholm-Gillquist 6 months	●	◐	○	○	○	○	●	○	Low	●	○	●	●	Moderate
El-Azab (2011)	Lysholm-Gillquist 3 years	●	◐	○	○	○	○	●	○	Low	●	○	●	●	Moderate
Schroter (2011)	Improvement in Lysholm-Gillquist	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Schroter (2011)	Improvement in Tenger activity level	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Schroter	Improvement in International Knee	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
(2011)	Documentation Committee Subjective score														
Flamme (2003)	International Knee Society Score	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Flamme (2003)	N cases of distal deep vein thrombosis (DVT)	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Flamme (2003)	N cases of Proximal deep vein thrombosis (DVT)	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Flamme (2003)	N cases of bony non-union	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Flamme (2003)	N cases of lesions of the fibular nerve	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Flamme (2003)	N cases of superficial wound infections	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Flamme (2003)	Percentage with adverse events	●	◐	○	○	○	○	●	○	Low	○	○	●	●	Moderate
Bachhal (2005)	Pin tract infection	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Lateral cortex fracture	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Delayed union	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Bachhal (2005)	Knee stiffness	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Ring sequestrum	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Deep infection/chronic osteomyelitis	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Intraarticular fractures	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Neurovascular injury	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate
Bachhal (2005)	Symptomatic deep-vein Thrombosis	●	◐	○	○	○	○	●	●	Low	●	○	●	●	Moderate

Table 222. Quality and Applicability: Closing Wedge Versus Open Wedge Osteotomy

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Song(2012)	VAS Pain	○	●	○	○	○	●	●	○	Low	○	○	●	●	Moderate
Brouwer (2006)	VAS Pain	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Walking distance	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Walking distance	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Wound infection	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Nonunion	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Palsy of the common peroneal nerve	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate

- : Domain free of flaws
- : Domain flaws present
- ◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Brouwer (2006)	Pain in proximal tibiofibular joint	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Iliac-crest morbidity	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Fracture of the tibial plateau	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Re-operation (further valgus correction)	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Re-operation (reduction of valgus correction)	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate
Brouwer (2006)	Revision to joint replacement	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate

●: Domain free of flaws

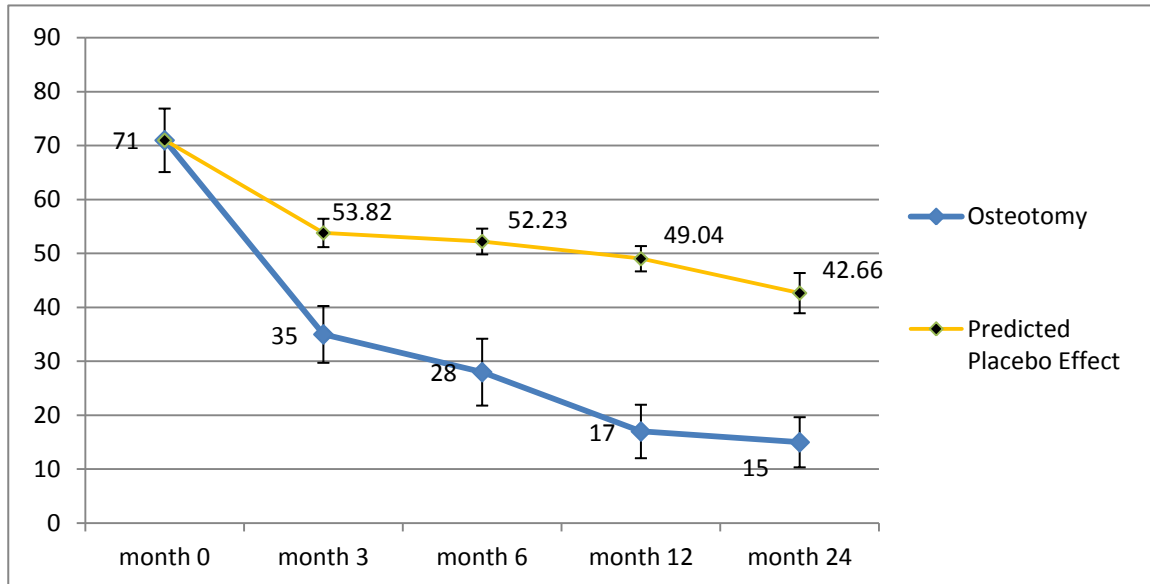
○: Domain flaws present

◐: Moderate power

<i>Study</i>	<i>Outcome</i>	<i>Prospective</i>	<i>Power</i>	<i>Group Assignment</i>	<i>Blinding</i>	<i>Group Comparability</i>	<i>Treatment Integrity</i>	<i>Measurement</i>	<i>Investigator Bias</i>	<i>Quality</i>	<i>Participants</i>	<i>Intervention and Expertise</i>	<i>Compliance and Adherence</i>	<i>Analysis</i>	<i>Applicability Study</i>
Brouwer (2006)	Removal of osteosynthesis material	●	◐	●	○	●	●	●	●	High	●	○	●	●	Moderate

FINDINGS

Figure 93. Open-Wedge High Tibial Osteotomy: VAS Pain Change from Baseline (Pongsoipetch et al., 2009)



*The predicted placebo effect is based on a cross-sectional time series regression analysis of all extracted placebo data.

Figure 94. Open Wedge High Tibial Osteotomy with TomoFix Plate: VAS Pain at 3 Year Follow-Up (El-Azab et al., 2011)

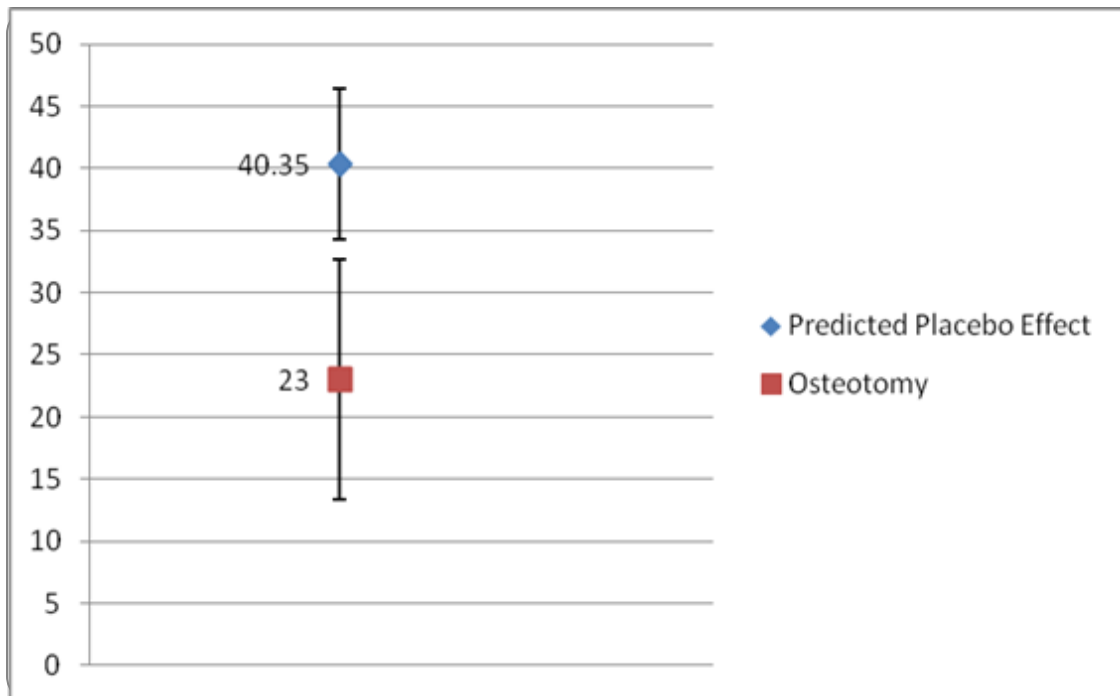
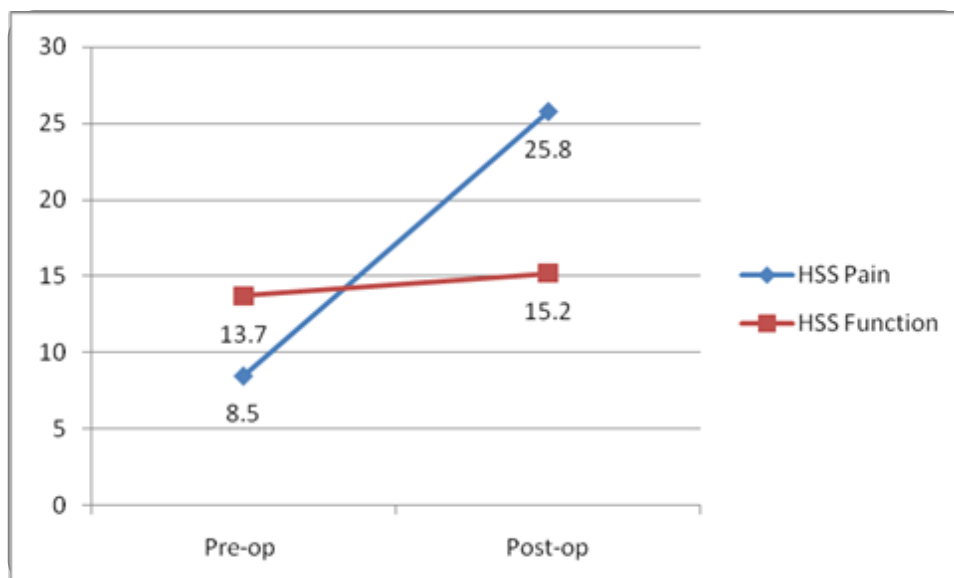
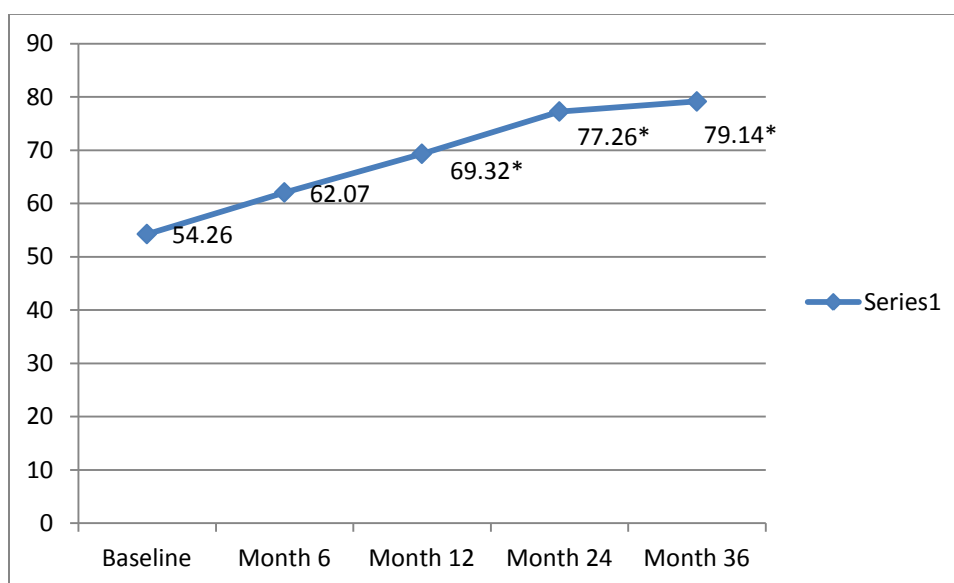


Figure 95. Hospital for Special Surgery: Pain and Function (Rudan and Simurda, 1990)



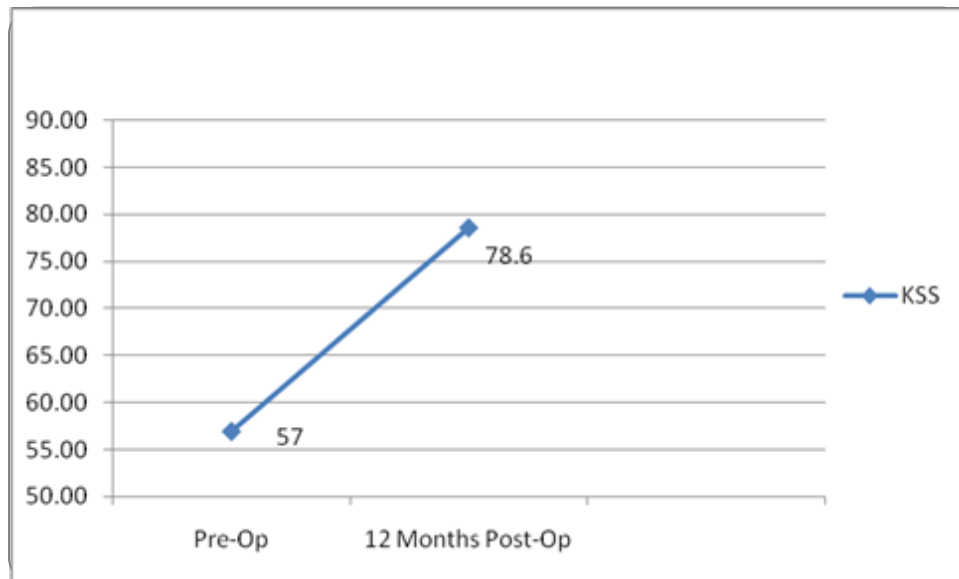
Author reported HSS Pain is statistically significant $p < .001$.

Figure 96. International Knee Documentation Committee Score: Open-Wedge HTO with Internal Fixator Plate (Niemeyer et al., 2010)



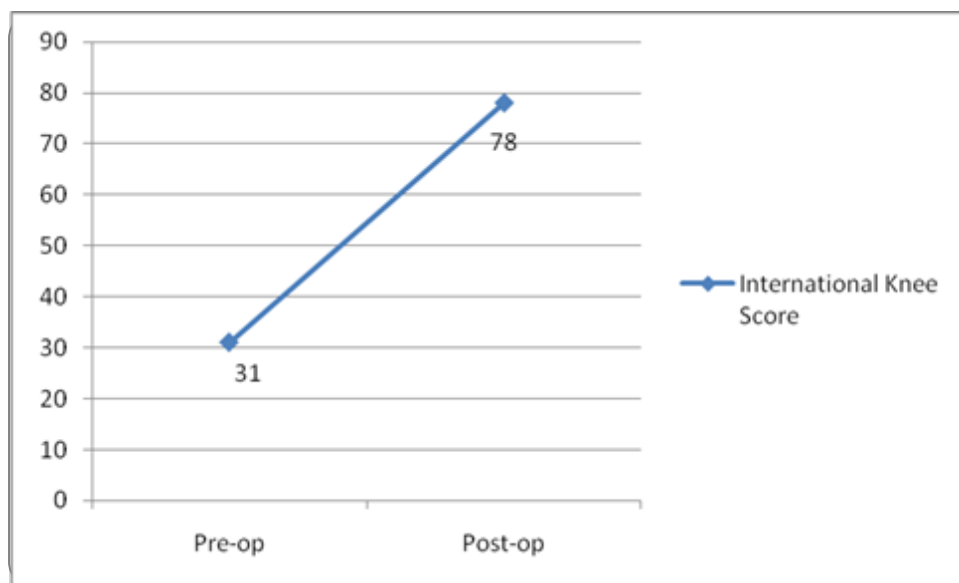
*Author reported Mann Whitney Test was significant ($P < .05$) for both outcomes at month 12, 24 and 36.

Figure 97. Open-Wedge High Tibial Osteotomy: Knee Society Score (Pongsoipetch et al., 2009)



Author results from a paired t-test. $P < .001$

Figure 98. High Tibial Osteotomy: International Knee Society Score (Flamme et al., 2003)



The authors reported results of a t-test, where $P < .05$

Table 223. High Tibial Osteotomy: Other Outcomes

Study	Treatment	Follow-Up	Outcome	Mean (95% CI)	P-Value
Schroter (2011)	Biplanar Open Wedge HTO with spacer plate	1 year	Improvement in Tenger activity level	1.1 (1.7 , 0.5)	p< .02
Schroter (2011)	Biplanar Open Wedge HTO with spacer plate	1 year	Improvement in International Knee Documentation Committee Subjective Score	23.7 (28.6 , 18.8)	p< .0001

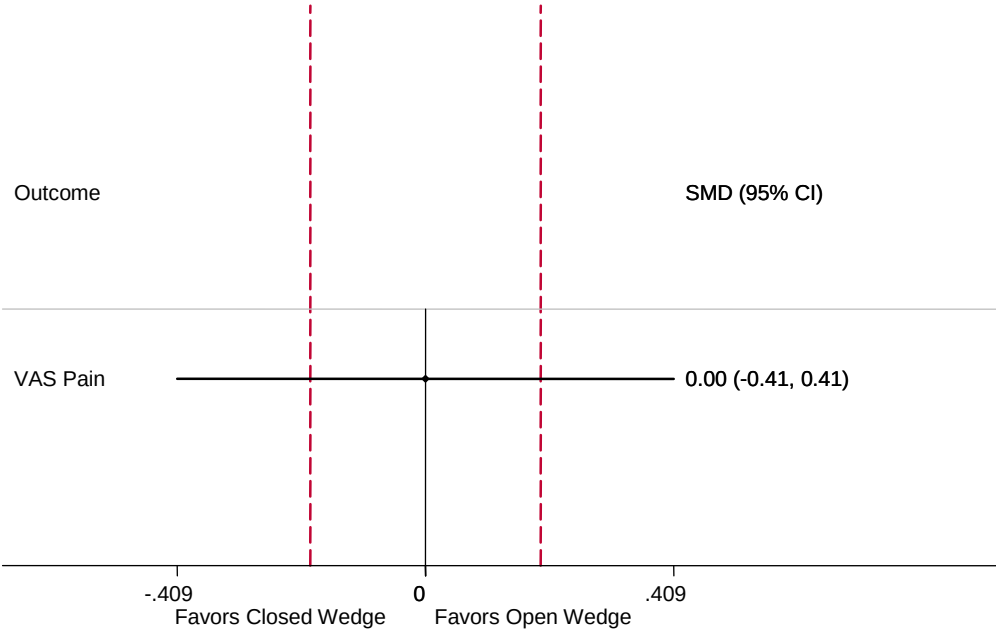
Table 224. Osteotomy: Adverse Events

Study	Treatment	Duration/Follow-Up	Adverse Event	Incidence of Adverse Events
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Pin tract infection	62.20%
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Lateral cortex fracture	2.70%
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Delayed union	5.40%
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Knee stiffness	10.8
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Ring sequestrum	2.70%
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Deep infection/chronic osteomyelitis	0%
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Intraarticular fractures	0%

Study	Treatment	Duration/Follow-Up	Adverse Event	Incidence of Adverse Events
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Neurovascular injury	0%
Bachhal (2005)	HTO with dynamic axial fixator	Final follow-up	Symptomatic deep-vein thrombosis	0%
Niemeyer (2010)	HTO with Internal Fixator Plate	3 years	Intraarticular fractures	1.45
Niemeyer (2010)	HTO with Internal Fixator Plate	3 years	Over correction	4.35
Niemeyer (2010)	HTO with Internal Fixator Plate	3 years	Delayed union	2.9
Niemeyer (2010)	HTO with Internal Fixator Plate	3 years	Overall adverse events	8.60%
Saragaglia (2010)	HTO with T-shaped Plate	Final follow-up	Lateral tibial plateau fractures	5.20%
Saragaglia (2010)	HTO with T-shaped Plate	Final follow-up	Deep vein thrombosis (DVT)	1.10%
Saragaglia (2010)	HTO with T-shaped Plate	Final follow-up	Pulmonary embolism	1.70%
Saragaglia (2010)	HTO with T-shaped Plate	Final follow-up	Failure of fixation (screw breakage)	1.70%
Saragaglia (2010)	HTO with T-shaped Plate	Final follow-up	Loss of angulation	0.60%
Saragaglia (2010)	HTO with T-shaped Plate	Final follow-up	Revised to TKA	12.90%
Flame (2003)	High Tibial Osteotomy	10 years	N cases of distal deep vein thrombosis (DVT)	2

Study	Treatment	Duration/Follow-Up	Adverse Event	Incidence of Adverse Events
Flame (2003)	High Tibial Osteotomy	10 years	N cases of proximal deep vein thrombosis (DVT)	2
Flame (2003)	High Tibial Osteotomy	10 years	N cases of bony non-union	3
Flame (2003)	High Tibial Osteotomy	10 years	N cases of lesions of the fibular nerve	2
Flame (2003)	High Tibial Osteotomy	10 years	N cases of superficial wound infections	3
Flame (2003)	High Tibial Osteotomy	10 years	Percentage with adverse events	11.20%
Pongsiopetch (2009)	Medial Open-Wedge High Tibial Osteotomy	2 years	Superficial incision wound infection	7.50%

Figure 99. Closed Versus Open Osteotomy: VAS Pain (Brouwer et al., 2006)



The red line indicates the MCII

Figure 100. Open Versus Closed Wedge Osteotomy: Mild to Severe Knee Pain on Stair Climb (Song et al., 2012)

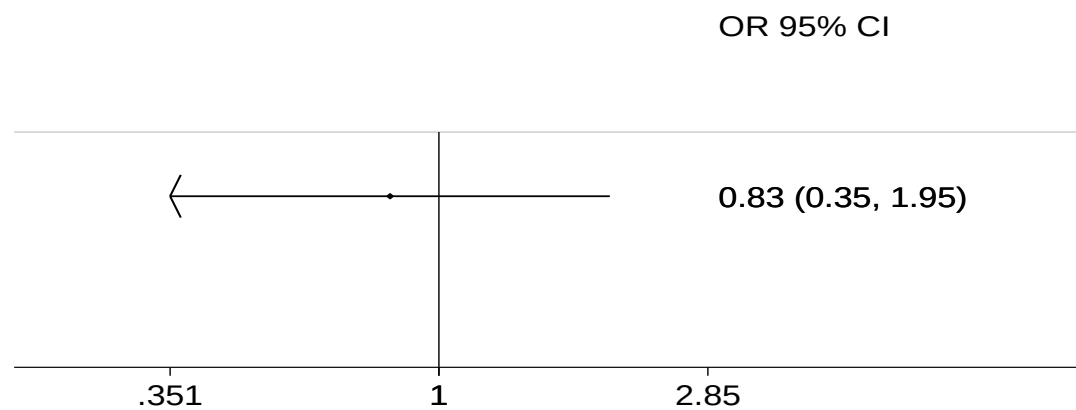


Figure 101. Open Versus Closed Wedge Osteotomy (Brouwer et al., 2006)

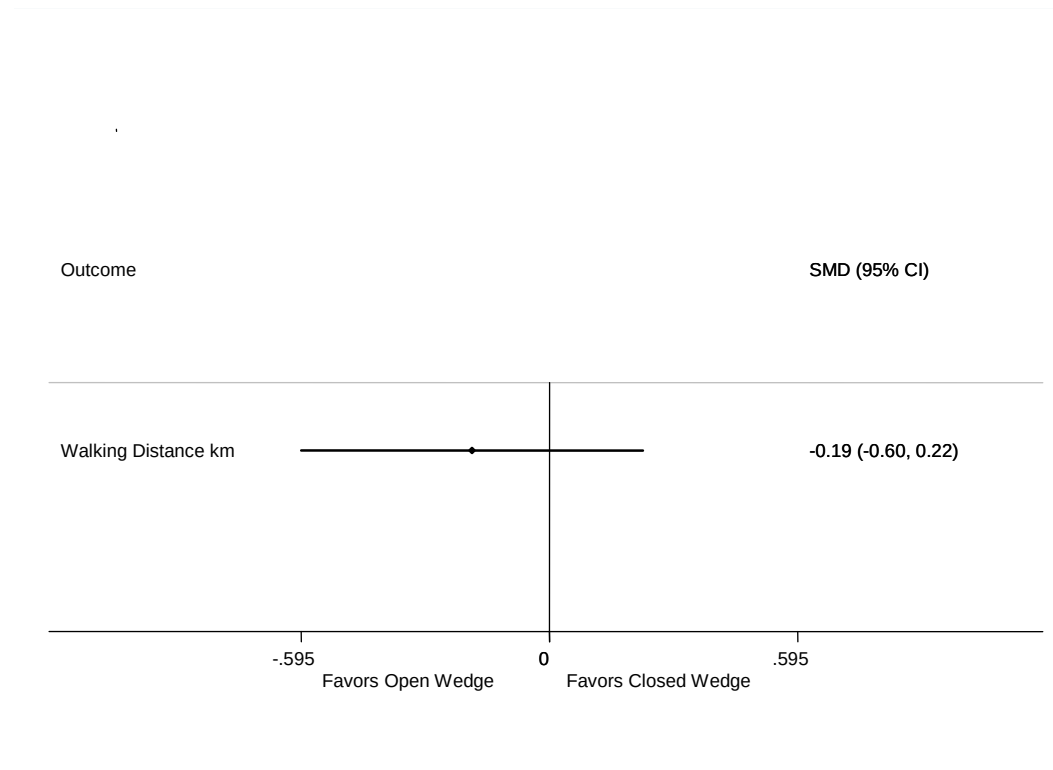


Table 225. Open Versus Closed Wedge Osteotomy

Study	Outcome	N	Group 1	Group 2	Effect size	Sig.	Clinical Significance	Strength of Evidence
Brouwer (2006)	VAS Pain	92	Open wedge	Closed wedge	0 (-.41, .41)	No	True negative	High
Brouwer (2006)	Walk distance (km)	92	Open wedge	Closed wedge	-.19 (-.6, .22)	No	Unclear	High
Song (2012)	40+ VAS Pain rating	100	Open wedge	Closed wedge	Or= 0.85 (0.28, 2.57)	No	Unclear	Low

Figure 102. Adverse Events: Open Versus Closed Wedge Osteotomy (Brouwer et al., 2006)

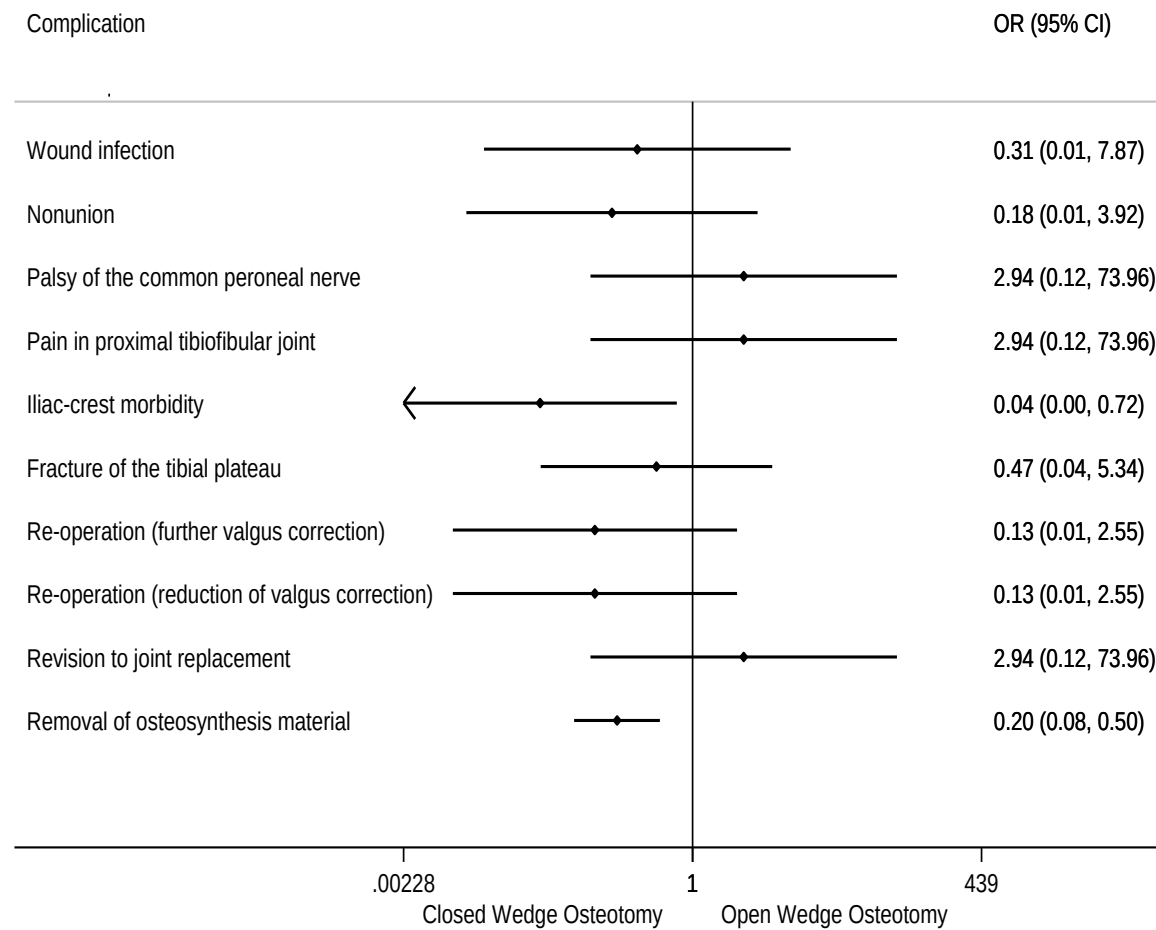
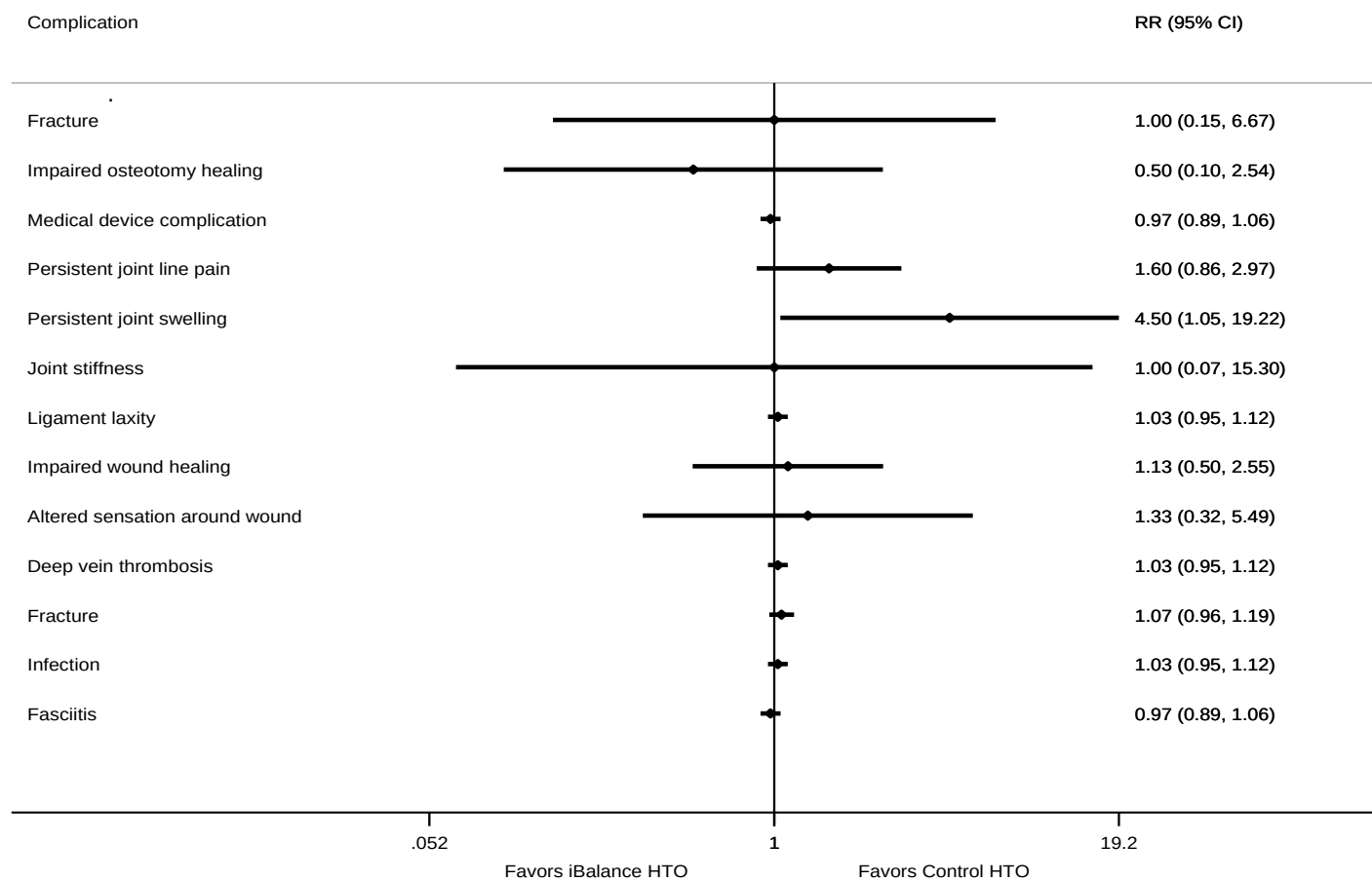


Table 226. iBalance HTO Versus Control HTO (Getgood et al., 2011)

Outcome	Duration	Results
KOOS Pain	6	Not statistically significant
KOOS Pain	12	Not statistically significant
KOOS Other Symptoms	6	Not statistically significant
KOOS Other Symptoms	12	Not statistically significant
KOOS Functions of Daily Life	6	Not statistically significant
KOOS Functions of Daily Life	12	Not statistically significant
KOOS Sports and Recreation	6	Not statistically significant
KOOS Sports and Recreation	12	Not statistically significant
KOOS Quality of Life	6	Not statistically significant
KOOS Quality of Life	12	Not statistically significant
SF-36 Physical Health	6	Not statistically significant
SF-36 Physical Health	12	Not statistically significant
SF-36 Mental Health	6	Not statistically significant
SF-36 Mental Health	12	Not statistically significant

Figure 103. iBalance HTO Versus Control HTO: Adverse Events (Getgood et al., 2011)



RECOMMENDATION 15

In the absence of reliable evidence, it is the opinion of the work group not to use the free-floating (un-fixed) interpositional device in patients with symptomatic medial compartment osteoarthritis of the knee.

Strength of Recommendation: Consensus

Description: A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus**, although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

RATIONALE

One published case series reported the results of free-floating (un-fixed) interpositional device surgery for treatment of medial unicompartmental OA of the knee.¹²⁹ We determined that the evidence was low-strength.

The evidence indicated high reoperation rates in the patients who were followed. Thirty-two percent of patients were revised to total knee arthroplasty. The evidence showed differences from baseline that were not clinically or statistically significant for increased pain measured with the VAS two years postoperatively. Knee Society Score function subscale scores were “poor” postoperatively.

The AAOS workgroup modified the grade of this recommendation to consensus, because of the high revision rates in this study, increased pain, and the potential harm associated with this intervention (anesthesia risks, VTE, infection, and reoperation).

SUPPORTING EVIDENCE

QUALITY

Relevant Tables: [Table 227](#), [Table 228](#)

All four of the included outcomes were from a study by Sisto and Mitchell¹³³ that followed a prospective case series design. Every outcome was flawed in the group assignment, blinding, group comparability and treatment integrity domains. Consequently, they were all rated as low quality.

APPLICABILITY

Relevant Tables: [Table 227](#), [Table 228](#)

The Sisto and Mitchell¹³³ study was of moderate applicability because of uncertainty regarding whether the treatment was delivered in the same manner as in regular clinical practice, and the enrolled patients might not have been representative of patients typically seen in clinical practice.

FINAL STRENGTH OF EVIDENCE

The moderate applicability of the Sisto and Mitchell¹³³ study in combination with low quality of its outcomes resulted in a low strength of evidence rating.

Table 227. Quality and Applicability Summary: Free-floating Interpositional Device

Study	Outcome	Duration	Quality	Applicability	Strength of Evidence
Sisto (2005)	Knee Society Objective Score	Average follow-up of 26 months	Low	Moderate	Low
Sisto (2005)	Knee Society Function Score	Average follow-up of 26 months	Low	Moderate	Low
Sisto (2005)	Percent needing TKA revision	Average follow-up of 26 months	Low	Moderate	Low
Sisto (2005)	VAS Pain	Average follow-up of 26 months	Low	Moderate	Low

RESULTS

Relevant Tables: [Figure 104](#)-[Figure 106](#)

The included study did not support the use of free-floating interpositional devices for medial compartment OA knee.¹³³ The authors reported results of a Wilcoxon Signed-Rank test assessing the effect of the Unispacer interpositional device on Knee Society Objective and functional scores. Neither outcome showed significant improvement. Two year post-operative VAS Pain scores were actually higher than pre-operative scores and 32.4 % of knees had to be revised with total knee arthroplasty.

EVIDENCE TABLES AND FIGURES
QUALITY AND APPLICABILITY

Table 228. Quality and Applicability: Free-Floating Interpositional Device

●: Domain free of flaws

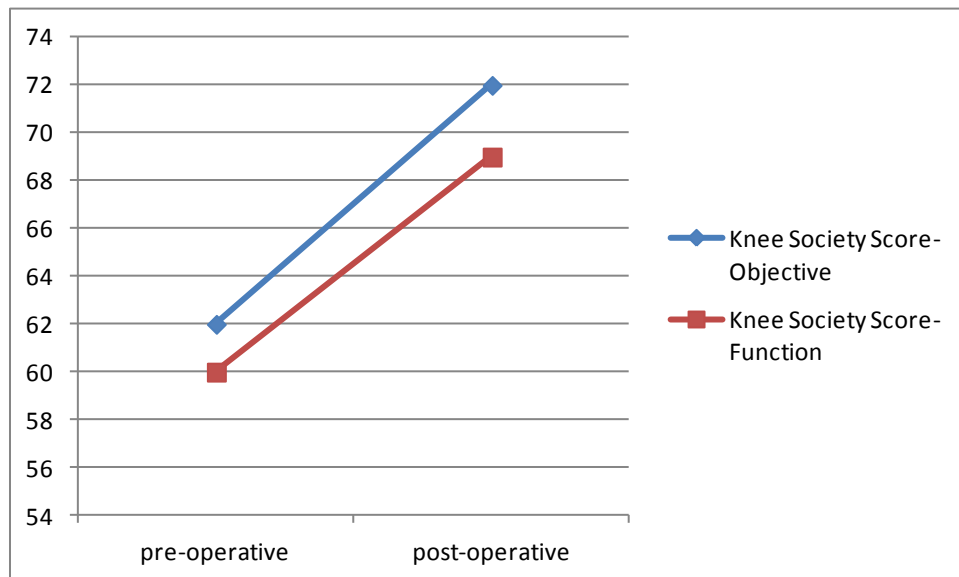
○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	Quality	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	Applicability Study
Sisto 2005	Knee Society Objective Score	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Sisto 2005	Knee Society Function Score	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Sisto 2005	Percent revised to Total Knee Arthroplasty	●	◐	○	○	○	○	●	●	Low	○	○	●	●	Moderate

FINDINGS

Figure 104. Knee Society Scores (Sisto and Mitchell 2005)



*These are author reported results of a Wilcoxon Signed-Rank test. The results are not significantly improved from baseline

Figure 105. VAS Pain (Sisto and Mitchell, 2005)

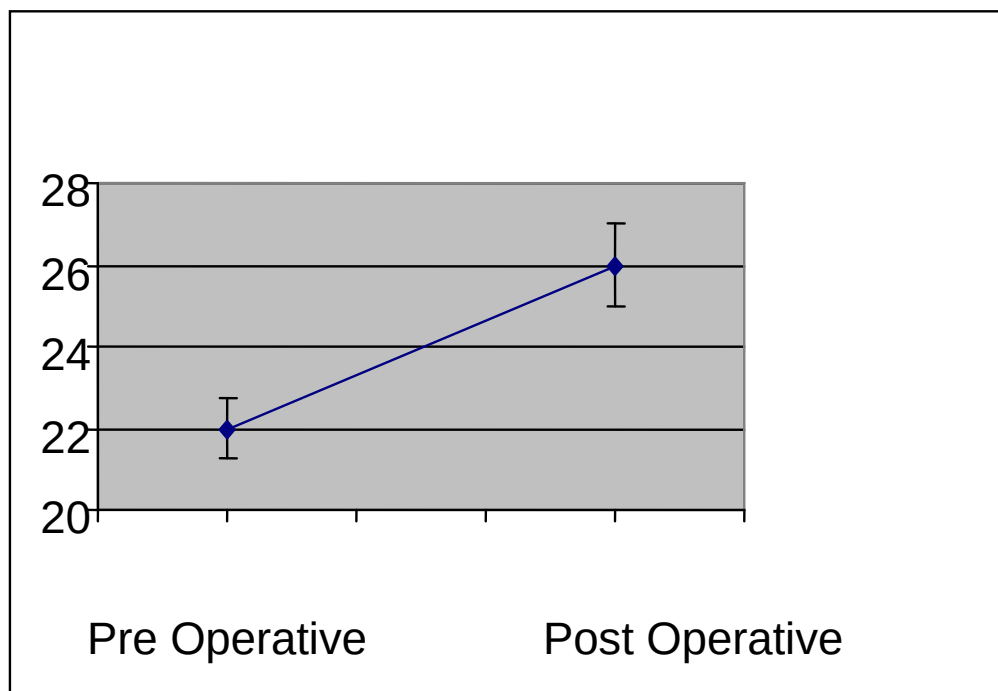
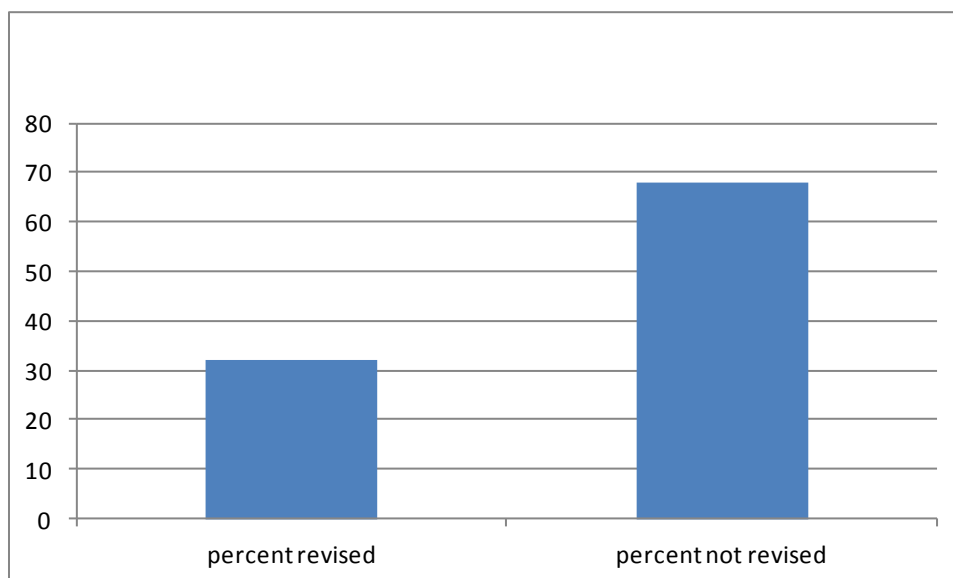


Figure 106. Percent Revised to Total Knee Arthroplasty (Sisto and Mitchell, 2005)



FUTURE RESEARCH

Many treatments for osteoarthritis of the knee are addressed by randomized controlled trials. The quality of these trials is, in some cases, questionable. To achieve a high quality literature base, clinicians and scientists should invest their time and effort in studies designed to avoid bias. Some techniques to limit bias include stochastic randomization and blinding of investigators or evaluators and patients. Future studies should include a priori power analyses to adequately power the studies to be able to detect minimum clinically important improvements (MCII; improvements that matters to the patient). Studies should likewise utilize patient reported outcomes (i.e. Oxford Knee Score, EQ-5D, and Visual Analog Scales) whose measurement properties have been validated. The use of standardized pain and function measures will ensure that efficacy evaluated in future studies can be analyzed on the basis of clinical significance to offset the limitations of interpreting only the p-value. Commensurate with these steps, investigators should better define the hypotheses of the treatment studies. For example, does a two year follow-up analysis accurately reflect the expected outcomes of one intraarticular corticosteroid injection?

While some of the non-operative treatments of knee osteoarthritis have higher level clinical evidence, the availability of strong evidence is not consistent across interventions. Several of the relatively commonly prescribed treatments, such as the use of acetaminophen and intraarticular corticosteroid injections, are in need of higher strength studies to support and define their use and indications. Better and higher strength evidence for surgical treatment (up to but not including knee arthroplasty) of knee osteoarthritis has been published since the original CPG, but is still insufficient to answer the questions that patients and orthopaedic surgeons have regarding their use. The resource difficulties and ethical concerns about conducting placebo controlled studies of operative interventions compromise the quality of these studies. To improve the quality of future studies of operative treatments, the use of nonsurgical, non-placebo control groups should be considered. Surgical treatments for knee osteoarthritis are often indicated in patients exhibiting unique symptoms from other pathologies (i.e. loose body, meniscal tear) in addition to the symptoms from osteoarthritis of the knee, or in patients with a specific characteristics (i.e. young age, high activity level, or end-stage severity of the osteoarthritis). Investigators should develop rigorous patient inclusion criteria to ensure that patients who typically receive the surgical intervention in clinical practice are adequately represented in the study population (including adequate statistical power of key patient subgroups to allow subgroup analyses).

The evidence analysis of this second edition raised specific questions for the clinicians who were either directly involved in its development or indirectly involved through peer review. The lack of clinically significant outcomes in viscosupplementation treatment groups could be due to the inability to distinguish responders from non-responders. Additionally, it might be that current widely used outcome measures are not broad enough in scope to detect such improvements as, for example, family reported gains in functional autonomy in patients who themselves report no effect. Higher statistically powered studies are needed to allow for these types of subgroup analyses. Without an

evidence-based method of identifying prognostic characteristics of patients who might benefit from the treatment, non-operative treatment options for patients with serious medical co-morbidities and who are not candidates for knee arthroplasty are limited.

There are valid concerns about the side effect profile of nonsteroidal anti-inflammatory drugs and tramadol (addiction and withdrawal). As future measures are developed it might be possible to evaluate gastrointestinal bleeds and infection not detected in Oxford Knee Score, EQ-5D, and VAS outcomes. Currently, the adverse effects of tramadol have not been adequately reported in the knee osteoarthritis literature, perhaps because efficacy studies have focused on short-term outcomes (up to 13 weeks). The data reported in this guideline focuses on treatment efficacy.

Reviewing the potential risks of every medication was beyond the scope of this clinical practice guideline from the beginning. Physicians must be knowledgeable about the potential side effects of the treatments they prescribe especially when using them long term. Complicating this task is that tramadol is studied less frequently than other medications. Additionally, randomized clinical trials cannot reliably identify uncommon and serious adverse reactions or the effects of long term use. Observational studies and registries are needed to provide robust estimates of adverse event rates based on patient demographics and co-morbidities. Empirical evidence will always be limited by the “rules” of evidence-based medicine.

It is the hope of this Work Group that the detailed review of knee osteoarthritis treatment evidence will provide a background for future high-quality clinical trials to improve our evidence base and improve the clinical treatment of patients with osteoarthritis of the knee.

APPENDIX I
WORK GROUP
REVISION WORK GROUP

David Jevsevar MD, MBA Chair
652 S Medical Center Drive, Suite 400
Saint George, UT 84790

**Gregory Alexander Brown MD PhD,
Co-Chair**
Park Nicollet Clinic-Meadowbrook
Department of Orthopaedic Surgery
6490 Excelsior Boulevard Suite E400
St Louis Park, MN 55426

Dina L. Jones, PT, PhD
West Virginia University
Department of Orthopaedics
PO Box 9196, 1 Medical Center Drive
Morgantown, WV 26506-9196

Elizabeth G. Matzkin, MD
Tufts – New England Medical Center
Department of Orthopaedics
750 Washington Street
Boston, MA 02111

Paul Manner MD, FRCSC
University of Washington
Box 356500
1959 NE Pacific Street
Seattle WA 98195-6500

Pekka Mooar MD
3401 N. Broad Street
6th Fl Outpatient Building
Philadelphia, PA 19140

John T. Schousboe MD PhD
University of Minnesota
Consultant Rheumatologist
Park Nicollet Health Services
Adjunct Assistant Professor

Division of Health Policy and
Management
3800 Park Nicollet Boulevard
Minneapolis MN 55416

Steven Stovitz, MD
University of Minnesota
Sports Medicine and Family Practice
Department of Family Medicine and
Community Health
717 Delaware Street SE, Room 421
Minneapolis, MN 55414

Guidelines Oversight Chair
Michael J. Goldberg MD
Seattle Children's Hospital & Regional
Center
4800 Sand Point Way NE, #W7706
P.O. Box 5371
Seattle WA 98105-5371

Guidelines Oversight Vice Chair
James O. Sanders MD
University of Rochester
Department of Orthopaedics
601 Elmwood Avenue
Rochester, NY

Council on Research and Quality
Kevin J. Bozic MD, MBA Chair
University of California, San Francisco
500 Parnassus, MU 320W
San Francisco, CA 94143-0728

AAOS Staff:

William R Martin, III MD

AAOS Medical Director

6300 N River Road Rosemont, IL 60018

Deborah S. Cummins PhD

Director of Research and Scientific Affairs

6300 N River Road Rosemont, IL 60018

Patrick Donnelly, MA

Lead Research Analyst

Anne Woznica MLS

Medical Librarian

Former AAOS Staff

Patrick Sluka MPH

Janet L Wies MPH

Kevin Boyer MPH

Charles M Turkelson PhD

Sharon Song PhD

ORIGINAL WORK GROUP

John Richmond MD, Chair

New England Baptist Hospital 125
Parker Hill Avenue Boston, MA 02120

David Hunter MBBS, MSc, PhD

New England Baptist Hospital
125 Parker Hill Avenue
Boston, MA 02120

James Irrgang PT, Ph.D, ATC

Director of Clinical Research, Dept of
Orthopaedic Surgery
Univ. of Pittsburgh School of Medicine
Kaufmann Medical Building, Suite 911
3471 Fifth Ave.
Pittsburgh, PA 15213

Morgan H. Jones MD

9500 Euclid Ave. A41
Cleveland, OH 44195

Lynn Snyder-Mackler PT, ATC, SCS, ScD

Department of Physical Therapy
University of Delaware
309 McKinly Lab
Newark, DE 19716

Daniel Van Durme MD

Dept. of Family Med. and Rural Health
Florida State University, Suite 3200
1115 W. Call Street
Tallahassee, Florida 32306-4300

Cheryl Rubin, MD

Rockland Orthopedics & Sports
Medicine
327 Route 59, #2
Airmont, NY 10952

Elizabeth G. Matzkin, MD

Tufts – New England Medical Center
Department of Orthopaedics
750 Washington Street
Boston, MA 02111

Robert G Marx, MD
Hospital for Special Surgery
535 E 70th St
New York, NY 10021

Bruce A Levy, MD

Mayo Clinic
200 First St SW
Rochester, MN 55905

Guidelines and Technology Oversight

Chair:

William C. Watters III MD

6624 Fannin #2600
Houston, TX 77030

Guidelines and Technology Oversight

Vice-Chair:

Michael J. Goldberg, MD

Department of Orthopaedics
Seattle Children's Hospital
4800 Sand Point Way NE
Seattle, WA 98105

Evidence Based Practice Committee

Chair:

Michael Keith, MD

2500 Metro Health Drive
Cleveland, OH 44109-1900

AAOS Staff:

Robert H. Haralson III, MD, MBA

Medical Director 6300 N River Road
Rosemont, IL 60018

Charles M. Turkelson, PhD

Director of Research and Scientific
Affairs
6300 N River Road Rosemont, IL 60018

Janet L. Wies MPH

Clinical Practice Guidelines Manager
6300 N River Road Rosemont, IL 60018

Research Analysts

Sara Anderson MPH

Kevin Boyer

Patrick Sluka MPH

Justin St. Andre MS

Medical Librarian

Richard McGowan, MLS

2007 -2008 Intern

Michelle Scott, MA

APPENDIX II

DECISION-MAKERS WHO APPROVE THIS CLINICAL PRACTICE GUIDELINE

Committee on Evidence Based Quality and Value

The committee on Evidence Based Quality and Value (EBQV) consists of twenty AAOS members who implement evidence-based quality initiatives such as clinical practice guidelines (CPGs) and appropriate use criteria (AUCs). They also oversee the dissemination of related educational materials and promote the utilization of orthopaedic value products by the Academy's leadership and its members.

Council on Research and Quality

The Council on Research and Quality promotes ethically and scientifically sound clinical and translational research to sustain patient care in musculoskeletal disorders. The Council also serves as the primary resource for educating its members, the public, and public policy makers regarding evidenced-based medical practice, orthopaedic devices and biologics, regulatory pathways and standards development, patient safety, occupational health, technology assessment, and other related important errors.

The Council is comprised of the chairs of the committees on Biological Implants, Biomedical Engineering, Occupational Health and Workers' Compensation, Patient Safety, Research Development, U.S. Bone and Joint Decade, and chair and Appropriate Use Criteria and Clinical Practice Guideline section leaders of the Evidence Based Quality and Value committee. Also on the Council are the second vice-president, three members at large, and representatives of the Diversity Advisory Board, Women's Health Issues Advisory Board, Board of Specialty Societies (BOS), Board of Councilors (BOC), Communications Cabinet, Orthopaedic Research Society (ORS), Orthopedic Research and Education Foundation (OREF).

Board of Directors

The 17 member Board of Directors manage the affairs of the AAOS, set policy, and oversee the Strategic Plan.

APPENDIX III

DETERMINING CRITICAL OUTCOMES

WORK GROUP PARTICIPATION

The first task of the work group is to identify the critical outcomes for the guideline. Members are asked to construct a preliminary list of important outcomes prior to attending the introductory meeting. They participate in three Delphi rounds, completing the “Critical Outcomes Form” shown below.

CRITICAL OUTCOMES FORM

DETERMINING OUTCOMES

The first task as a guideline work group member is to determine outcomes. List the variables you think are relevant and rank them in order of importance. Appropriate outcomes are patient-centered and consider the benefits and potential harm of the treatments being measured.

Criticality

Some outcomes are more important than others. The *most* important ones are considered critical. Critical outcomes are vital for determining whether or not you should offer a treatment or diagnostic test to a patient. Without knowing what the essential outcomes are and how the treatment or test influences them, efficacy cannot be determined.

Patient-Oriented Outcomes

In general, good practice and good evidence-based medicine give priority to the outcomes that patients care about. Patient-oriented outcomes:

- Help the patient live longer or better
- Are typically something the patient experiences
- Are often the patient’s diagnostic or treatment goal(s)
- Do not require extrapolation or interpolation to determine their importance to the patient

Examples of patient-oriented outcomes are:

- Survival/mortality
- Pain relief
- Fracture prevention
- Functional status
- Quality of life

Surrogate Outcomes

Patient-oriented outcomes contrast surrogate ones in that the latter:

- Substitute measures for patient-oriented outcomes
- Are typically not experienced by the patient
- Are typically not the patient's goals for treatment
- Require extrapolation or interpolation to determine their relationship to (or effect on) patient-oriented outcomes

Examples of surrogate outcomes are:

- Blood cholesterol (a surrogate for survival)
- Bone mineral density (a surrogate for fractures)
- All imaging results (often surrogates for pain or functional status but they can also be surrogates for other patient-oriented outcomes)

Benefit versus Harm

Potential benefit to patients is based on the patient-oriented outcomes that they desire and potential harm can be thought of as patient-oriented outcomes unwanted to them. For example, avoiding harm (e.g. fractures or death) is considered a benefit.

For Consideration

Not taking the time to develop appropriate critical outcomes has been known to detrimentally affect the strength of the final recommendations, and on occasion prevent being able to make a recommendation for a treatment or diagnostic test of clinical importance.

Rating Outcomes

In addition to identifying patient outcomes, work group members rated the importance of each one using a scale of 1 to 9. The rating categories are shown in the table below:

<i>Rating</i>	<i>Importance</i>
9	Critical
8	
7	
6	Important
5	
4	
3	Not Important
2	
1	

Work group members were advised to note that:

1. Unless you are interested in measures of diagnostic test performance (i.e., sensitivity and specificity), surrogate outcomes may not be rated as “Critical” (7-9).
2. If all outcomes are rated as critically important, then it will not be possible to prioritize the ones that are more likely to generate a comprehensive list of initial recommendations.

Final Determinations

To determine which outcomes to include and designate as critical, three rounds of the Delphi method were used.

The form below was used by the work group.

Please list up to 10 outcomes that you think this guideline should address, and rate them in order of importance on a scale from 1-9. Do not consult with other members of the work group during this step.

Outcome Number	Outcome	Rating
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

This form was circulated three times.

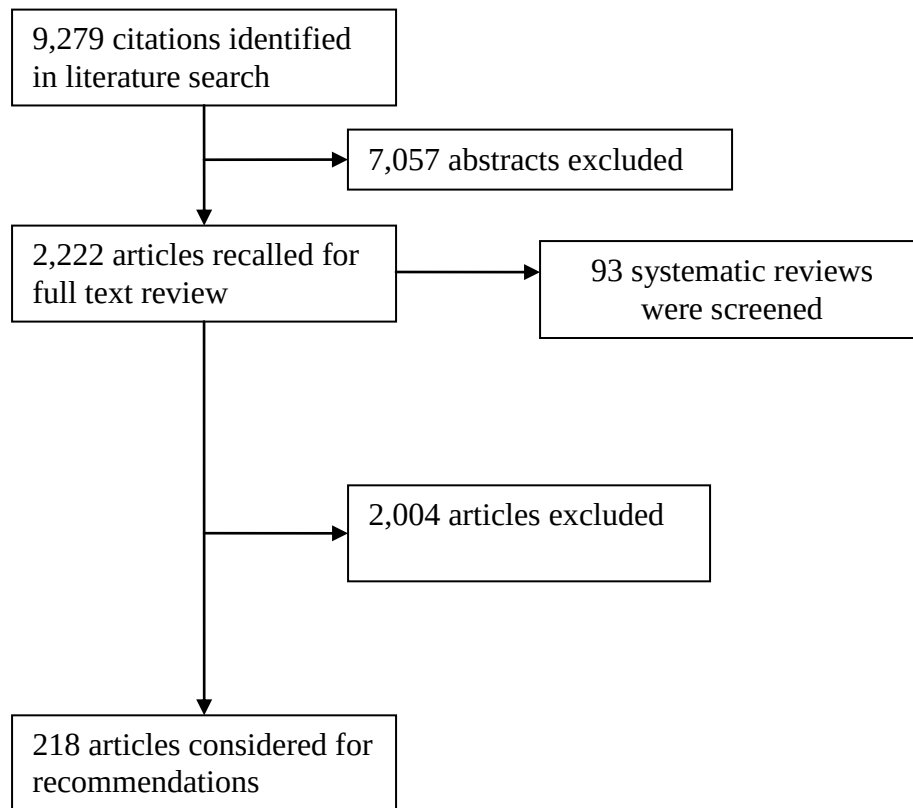
In the present guideline, the work group identified six critical outcomes: knee pain, activities of daily living, quality of life, functional status, activity tolerance, and self-reported physical function.

The work group identified the following outcomes as important: performance based physical function, serious GI bleed, ability to perform recreational activities, survival, treatment side effects, surgical complications, night time pain affecting sleep, major surgery complications, revision surgery, ability to earn income, ability to drive, social role function, joint stiffness, stability, range of motion, minor GI bleed, avoidance of need for knee replacement, strength, limpness, prevention of disease progression, deformity, joint alignment and stability, and joint swelling/effusion.

The work group identified the following outcomes as unimportant: radiographic improvement, MRI findings, and biomarker improvement.

APPENDIX IV STUDY ATTRITION FLOWCHART

Attrition chart



APPENDIX V

LITERATURE SEARCH STRATEGIES

PUBMED/MEDLINE

Search Strategy

#1

"Osteoarthritis, Knee"[mh] OR gonitis[tiab] OR gonarthrit[tiab] OR gonarthros*[tiab]

#2

"Knee Joint"[mh] OR "Knee"[mh] OR knee*[tiab]

#3

Osteoarthritis[mh:noexp] OR Arthritis[mh:noexp] OR osteoarthrit*[tiab]

#4

(#1 OR (#2 AND #3)) NOT arthroplasty[majr]

#5

"1966"[PDat]:"2012"[PDat] AND English[lang] AND "2011/4/22"[edat]:"2012"[edat]

#6

(animal[mh] NOT human[mh]) OR cadaver[mh] OR cadaver*[titl] OR comment[pt] OR editorial[pt] OR letter[pt] OR "historical article"[pt] OR addresses[pt] OR news[pt] OR "newspaper article"[pt] OR "in vitro"[pt] OR "case report"[title]

#7

#4 AND #5 NOT #6

#8

Nonarthroplasty[tiab] OR nonsurgical[tiab] OR non-surgical[tiab] OR ((conservative[tiab] OR medical[tiab]) AND management[tiab])

#9

Walking[mh] OR "Exercise therapy"[mh:noexp] OR "Exercise"[mh:noexp] OR "Exercise Movement Techniques"[mh] OR "Muscle Stretching Exercises"[mh] OR exercise*[tiab] OR yoga[tiab] OR aerobic*[tiab] OR fitness[tw] OR conditioning[tiab] OR reconditioning[tiab] OR "tai chi" OR "tai ji" OR aquatic[tiab] OR ((balanc*[tiab] OR flexib*[tiab] OR gait[tiab] OR proprioception OR sensorimotor[tiab] OR endurance[tiab]) AND training[tiab]) OR "Self care" OR "self-management" OR strengthen*[tiab] OR isokinetic[tiab] OR isotonic[tiab] OR isometric[tiab] OR stretch*[tiab]

#10

"weight loss" OR "Diet, reducing"[mh] OR BMI OR "Body mass index"[mh] OR Obesity[mh:noexp] OR "Obesity, morbid"[mh] OR "Overweight"[mh:noexp] OR overweight[tiab] OR obese[tiab] OR obesity[tiab]

#11

"Musculoskeletal Manipulations"[mh] OR "manual therapy" OR mobiliz*[tiab] OR chiropract* OR manipulation*[tiab] OR physiotherap*[tiab] OR "physical therapy modalities"[mh:noexp] OR taping[tiab] OR "Transcutaneous Electric Nerve Stimulation" OR "Transcutaneous Electric Nerve Stimulation"[mh] OR TENS[tiab] OR "neuromuscular electrical stimulation" OR NMES[tiab] OR laser*[tiab] OR "Laser Therapy, Low-Level"[mh] OR "Acupuncture therapy"[mh] OR acupunctur* OR "dry needling" OR electroacupunctur*[tiab] OR ultrasound[tiab] OR ultrasonography[tw] OR Ultrasonography[mh] OR phonophoresis[tw] OR cryotherapy[tw] OR ice[tiab] OR "cold pack" OR heat[tiab] OR "Hot temperature"[mh] OR "hot pack" OR hydrotherapy[tw] OR electromagnet*[tiab] OR balneology[tw] OR iontophoresis[tw]

#12

"Orthotic devices"[mh] OR brace[tiab] OR bracing[tiab] OR orthotic*[tiab] OR wedge[tiab] OR wedges[tiab] OR viscoelastic*[tiab] OR shoes[tw] OR shoe[tw]

#13

"dietary supplements" OR neutraceutic*[tiab] OR vitamin*[tw] OR herbal[tiab] OR "Plant extracts"[mh] OR methylsulfonylmethane[tiab] OR "omega 3" OR "Fish oils"[mh] OR "fish oil" OR "fatty acids" OR glucosamine OR chondroitin OR gelatin[tiab] OR "vitamin d" OR "dimethyl sulfoxide" OR Antioxidants[pa] OR antioxidant*[tiab] OR "coenzyme q"[tiab] OR "coenzyme q10"[tiab] OR CoQ10[tiab] OR Ubiquinone[mh]

#14

"Osteoarthritis, knee/drug therapy"[mh] OR NSAID*[tiab] OR "Anti-Inflammatory Agents"[mh] OR "Anti-Inflammatory Agents, Non-Steroidal"[pa] OR "Analgesics, Non-Narcotic"[mh] OR "Analgesics, Non-Narcotic"[pa] OR opiod*[tiab] OR "Analgesics, Opioid"[mh] OR "Analgesics, Opioid"[pa] OR analges*[tiab] OR narcotics[pa] OR "Cyclooxygenase 2 Inhibitors"[pa] OR Cox-2[tiab] OR Celecoxib OR "Phenylpropionates"[mh] OR patch*[tiab] OR gel[tiab] OR cream[tiab] OR lidocaine[tw] OR Acetaminophen[tw] OR naprox*[tw] OR tramadol[tiab]

#15

"Injections, Intraarticular"[mh] OR corticosteroid*[tiab] OR glucocorticoid*[tw] OR hyaluron*[tw] OR viscosupplement* OR "platelet-rich plasma" OR "Fibroblast Growth Factors"[mh] OR fibroblast*[tw] OR "growth factor" OR "Stem cells"[mh] OR "stem cells" OR mesenchymal OR prolotherap*[tiab] OR "Hypertonic Solutions"[mh]

#16

lavage[tiab] OR irrigat* OR debridement OR meniscectom* OR (loose[tiab] AND (body[tiab] OR bodies[tiab])) OR ((torn[tiab] OR tear[tiab]) AND menisc*[tiab])

#17

Osteotomy[mh:noexp] OR osteotom*[tiab]

#18

unispace[tiab] OR (interpositional[tiab] AND device[tiab])

#19

#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

#20

#7 AND #19

#21

Medline[tw] OR systematic review[tiab] OR Meta-analysis[pt]

#22

#7 AND #21

#23

"Clinical Trial"[pt] OR (clinical[tiab] AND trial[tiab]) OR random*[tw] OR "Therapeutic use"[sh]

#24

(#20 AND #23) NOT #21

#25

#20 NOT (#21 OR #23)

EMBASE

Search strategy

#1

'knee osteoarthritis'/de OR 'knee arthritis'/de OR gonitis OR gonarthriti OR gonarthros*

#2

Knee/de OR 'knee meniscus'/de OR knee*:ti OR (joint*:ti AND knee*)

#3

arthriti/de OR osteoarthrit* OR arthriti*:ti

#4

(#1 OR (#2 AND #3)) NOT arthroplasty/exp

#5

English:la AND [humans]/lim AND [embase]/lim AND [22/4/2011]/sd

#6

cadaver/de OR 'in vitro study'/exp OR 'abstract report'/de OR book/de OR editorial/de OR note/de OR letter/de OR 'case report':ti

#7

#4 AND #5 NOT #6

#8

Nonarthroplasty OR nonsurgical OR non-surgical OR 'conservative treatment'/exp

#9

Walking/de OR exercise/exp OR kinesiotherapy/exp OR 'muscle stretching'/de OR stretching/de OR conditioning OR fitness/de OR ((balanc* OR flexib* OR gait OR proprioception OR sensorimotor OR endurance) AND training) OR 'self care'/de OR 'self-management' OR 'muscle training'/de

#10

'body weight'/de OR 'weight reduction'/de OR 'weight control'/de OR 'body mass'/de OR BMI:ti,ab OR obesity/de OR 'morbid obesity'/de OR overweight

#11

'physical medicine'/de OR balneotherapy/exp OR balneology OR cryotherapy/exp OR 'electrostimulation therapy'/exp OR 'hyperthermic therapy'/exp OR 'manipulative medicine'/exp OR magnetotherapy/de OR physiotherapy/de OR 'joint mobilization'/de OR ultrasound therapy/exp OR 'athletic tape'/de OR taping OR 'cold pack' OR 'hot pack' OR 'electromagnetic radiation'/exp OR iontophoresis/de OR 'neuromuscular electrical stimulation'/de OR ultrasound/de

#12

Orthotics/de OR 'heel wedge' OR brace/de OR viscoelastic* OR 'orthopedic shoe'/de OR shoe/de

#13

'diet supplementation'/de OR nutraceutical* OR vitamin/exp OR 'medicinal plant'/exp OR 'plant extract'/exp OR 'dimethyl sulfone'/de OR methylsulfonylmethane OR 'dimethyl sulfoxide'/de OR 'dimethyl sulfoxide reductase'/de OR 'omega 3 fatty acid'/de OR 'fish oil'/de OR glucosamine/de OR 'chondroitin sulfate'/de OR 'chondroitin 4 sulfate'/de OR 'chondroitin 6 sulfate'/de OR gelatin/de OR antioxidant/exp OR ubiquinone/de OR 'coenzyme q'

#14

'nonsteroid antiinflammatory agent'/exp OR NSAID*:ti,ab OR Paracetamol /de OR Acetaminophen OR 'analgesic agent'/exp OR 'cyclooxygenase 2 inhibitor'/exp OR 'transdermal patch'/de OR cream/de OR gel/exp lidocaine/de OR opioid*

#15

'intraarticular drug administration'/de OR corticosteroid/exp OR 'hyaluronic acid'/de OR viscosupplementation/de OR 'thrombocyte rich plasma'/de OR 'platelet rich plasma' OR 'growth factor'/exp OR 'mesenchymal stem cell transplantation'/de OR 'stem cell transplantation'/de OR prolotherap* OR 'hypertonic solution'/de

#16

lavage/de OR 'needle lavage' OR 'arthroscopic debridement'/de OR debridement/de OR meniscectomy/de OR 'loose bodies' OR 'loose body' OR 'knee meniscus rupture'/de

#17

Osteotomy/de OR 'tibia osteotomy'/de OR 'tibia proximal osteotomy'/de

#18

Unispacer OR uni-spacer OR 'interpositional device'

#19

#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

#20

#7 AND #19

#21

'meta analysis':ti,ab,de OR 'systematic review':ti,ab,de OR medline:ti,ab,de

#22

#7 AND #21

#23

random*:ti,ab,de OR 'clinical trial':ti,ab,de OR 'health care quality'/exp

#24

(#20 AND #23) NOT #21

#25

#20 NOT (#21 OR #23)

COCHRANE LIBRARY (WILEY INTERFACE)

Search strategy

Knee*:ti,ab AND osteoarthritis*:ti,ab AND (nonsurgical OR non-surgical OR exercise OR walking OR 'gait training' OR conditioning OR 'self care' OR 'self-management' OR obesity OR BMI OR 'weight loss' OR manipulation* OR chiropract* OR 'manual therapy' OR physiotherapy* OR taping OR 'transcutaneous electric nerve stimulation' OR 'neuromuscular electrical stimulation' OR laser OR acupuncture OR electroacupuncture OR 'dry needling' OR ultrasound OR ultrasonography OR phonophoresis OR cryotherapy OR 'cold pack' OR 'hot pack' OR 'heat therapy' OR hydrotherapy OR electromagnet* OR

balneology OR iontophoresis OR orthotic OR brace OR 'heel wedge' OR 'heel wedges'
OR supplement OR vitamin OR nutraceutical* OR herbal OR methylsulfonylmethane OR
'omega 3' OR 'fish oil' OR glucosamine OR chondroitin OR gelatin OR 'dimethyl
sulfoxide' OR antioxidant* OR 'coenzyme q' OR CoQ10 OR ubiquinone OR NSAID*
OR 'Non-steroidal anti-inflammatory drugs' OR 'anti-inflammatory' OR analgesic* OR
opiod* OR 'cyclooxygenase 2 inhibitors' OR 'Cox-2' OR lidocaine OR 'pain patch' OR
Acetaminophen OR Paracetamol OR Tramadol OR corticosteroid* OR glucocorticoid*
OR hyaluron* OR viscosupplement* OR 'platelet rich plasma' OR 'growth factor' OR
'stem cells' OR prolotherapy OR 'hypertonic solution' OR lavage OR debridement OR
meniscectom* OR 'loose bodies' OR osteotomy* OR unispacer OR uni-spacer OR
'interpositional device') NOT (arthroplasty OR replacement):ti

APPENDIX VI

QUALITY AND APPLICABILITY QUESTIONS

STUDIES OF INTERVENTIONS

QUALITY

Quality questions are asked for every outcome reported in a study. They vary according to the rigor of a study's research design. Different questions are asked depending on if a study uses a controlled design with a no-treatment comparison group, is a crossover or historically controlled study, or case series. A total of 20 questions are asked for each type of research design and are described below:

Quality Questions and Domains for Four Designs of Studies of Interventions

Domain	Question:	Parallel, Contemporary Controls	Crossover Trials	Historical Controls	Case Series
Group Assignment	Stochastic	Yes	Yes	No	No
Group Assignment	Quasi-random Assignment	No	No	No	*NA
Group Assignment	Matched Groups	No	No	Yes	No
Group Assignment	Consecutive Enrollment	NA	NA	NA	Yes
Prospective	Prospective	Yes	Yes	Yes	Yes
Blinding	Blinded Patients	Yes	Yes	No	No
Blinding	Blinded Assessors	Yes	Yes	No	No
Blinding	Blinding Verified	Yes	Yes	No	No
Group Comparability	Allocation Concealment	Yes	Yes	No	No
Group Comparability	>80% Follow-up	Yes	Yes	No	Yes
Group Comparability	<20% Completion Difference	Yes	Yes	No	No
Group Comparability	Similar Baseline Outcome Values	Yes	NA	Yes	No
Group Comparability	Comparable Pt. Characteristics	Yes	NA	Yes	No
Group Comparability	Same Control Group Results	NA	Yes	NA	NA
Group Comparability	Same Experimental Group Results	NA	Yes	NA	NA
Treatment Integrity	Same Centers	Yes	Yes	Yes	No
Treatment Integrity	Same Treatment Duration in and across All Groups	Yes	Yes	Yes	No
Treatment Integrity	Same Concomitant Treatment to All Groups (controlled studies only)	Yes	Yes	Yes	NA
Treatment Integrity	No Confounding Treatment (case series only)	NA	NA	NA	Yes
Measurement	Same Instruments	Yes	Yes	Yes	Yes
Measurement	Valid Instrument	Yes	Yes	Yes	Yes

Domain	Question:	Parallel, Contemporary Controls	Crossover Trials	Historical Controls	Case Series
Bias	Article & Abstract Agree	Yes	Yes	Yes	Yes
Bias	All Outcomes Reported	Yes	Yes	Yes	Yes
Bias	A Priori Analysis	Yes	Yes	Yes	Yes
Statistical Power	Statistically Significant	High	High	High	High
Statistical Power	Number of patients in analysis	See below for further information			

*"NA" means "not asked."

The statistical power domain is assessed differently from the other domains. We characterize this domain as free from flaws if any one of the following is true:

- The results of a statistical test on the outcome of interest are statistically significant (statistical significance is indicative of adequate statistical power).
- The results of a statistical test of the outcome of interest are not statistically significant (or it is unclear whether the results are statistically significant), and the study is either an uncontrolled study in which data from 34 or more patients are included in the statistical analysis of the outcome of interest OR a controlled study in which data from 128 or more patients are included in the analysis of the outcome of interest.
- The study's results for the outcome of interest are used in a meta-analysis. We make this assumption because one reason for performing a meta-analysis is to compensate for the low statistical power of individual studies. Implicit in this assumption is a second assumption; that the power of the meta-analysis will be sufficient to detect an effect as statistically significant.

We term the power domain as flawed if all of the following are true:

- The results of a statistical test on the outcome of interest are either not statistically significant or it is unclear whether the results of statistical test on the outcome of interest are statistically significant.
- The study is an uncontrolled study in which data from fewer than 15 patients are included in the analysis of the outcome of interest OR the study is a controlled study in which data from fewer than 52 patients were included in the analysis of the outcome of interest.
- The results on the outcome of interest will not be used in a meta-analysis.

The numbers used to determine whether a study is of sufficient power are based on Cohen's¹³⁴ definitions of small, medium, and large effects. To compute the number of patients needed for an uncontrolled study using a pretest/posttest design, we consider a two-tailed paired samples t-test. We then determine whether or not sample size is sufficient to detect a large effect (defined as a standardized mean difference of ≥ 0.8) with alpha = 0.05 significance level and power = 80%. If a study does not have the ability to detect even a large effect as statistically significant, we characterize it as underpowered and the domain flawed.

To compute the number of patients needed for a controlled study, we consider a two-tailed independent samples t-test with equal size groups, and then determine if sample size is adequate for detecting a large effect, again with alpha = 0.05 and power = 80%. Similar to the above, we term a study as underpowered and the domain flawed if it does not enroll enough patients to detect a large effect size. It is viewed as adequately powered if it enrolls enough patients to detect a small effect.

APPLICABILITY

We determine the applicability of a study using the PRECIS instrument.¹³⁵ This instrument consists of 10 questions. The domains that each question applies to are shown in the table below.

Applicability Questions and the Domains for Studies of Interventions

Question	Domain
All Types of Patients Enrolled	Participants
Flexible Instructions to Practitioners	Interventions and Expertise
Full Range of Expt'l Practitioners	Interventions and Expertise
Usual Practice Control	Interventions and Expertise
Full Range of Control Practitioners	Interventions and Expertise
No Formal Follow-up	Interventions and Expertise
Usual and Meaningful Outcome	Interventions and Expertise
Compliance Not Measured	Compliance and Adherence
No Measure of Practitioner Adherence	Compliance and Adherence
All Patients in Analysis	Analysis

APPENDIX VII
FORM FOR ASSIGNING STRENGTH OF RECOMMENDATION
GUIDELINE RECOMMENDATION _____

PRELIMINARY GRADE OF RECOMMENDATION: _____

STEP 1: LIST BENEFITS AND HARMS

Please list the benefits (as demonstrated by the systematic review) of the intervention.

Please list the harms (as demonstrated by the systematic review) of the intervention.

Please list the benefits for which the systematic review is not definitive.

Please list the harms for which the systematic review is not definitive.

STEP 2: IDENTIFY CRITICAL OUTCOMES

Please circle the above outcomes that are critical for determining whether the intervention is beneficial and whether it is harmful.

Are data about critical outcomes lacking to such a degree that you would lower the preliminary strength of the recommendation?

What is the resulting strength of recommendation?

STEP 3: EVALUATE APPLICABILITY OF THE EVIDENCE

Is the applicability of the evidence for any of the critical outcomes so low that substantially worse results are likely to be obtained in actual clinical practice?

Please list the critical outcomes backed by evidence of doubtful applicability.

Should the strength of recommendation be lowered because of low applicability?

What is the resulting strength of recommendation?

STEP 4: BALANCE BENEFITS AND HARMS

Are there tradeoffs between benefits and harms that alter the strength of recommendation obtained in STEP 3?

What is the resulting strength of recommendation?

STEP 5: CONSIDER STRENGTH OF EVIDENCE

Does the strength of the existing evidence alter the strength of recommendation obtained in STEP 4?

What is the resulting strength of recommendation?

NOTE: Because we are not performing a formal cost analyses, you should only consider costs if their impact is substantial.

APPENDIX VIII

OPINION BASED RECOMMENDATIONS

RULES FOR MAKING OPINION BASED RECOMMENDATIONS

A guideline can contain recommendations for which there is no evidence. Work groups might make the decision to issue opinion-based recommendations. Although expert opinion is a form of evidence, it is also important to avoid liberal use in a guideline since research shows that expert opinion can be incorrect.

Opinion-based recommendations are developed only if they address a vitally important aspect of patient care. For example, constructing an opinion-based recommendation in favor of taking a history and physical is warranted. Constructing an opinion-based recommendation in favor of a specific modification of a surgical technique is less commonly warranted. To ensure that an opinion-based recommendation is absolutely necessary, the AAOS has adopted rules to guide the content of the rationales that are based on those outlined by the U.S. Preventive Services Task Force (USPSTF).¹³⁶ Specifically, rationales based on expert opinion must:

- Not contain references to or citations from articles not included in the systematic review.
- Not contain the AAOS guideline language “We Recommend”, “We suggest” or “The practitioner might.”
- Contain an explanation of the potential preventable burden of disease. This involves considering both the incidence and/or prevalence of the disease, disorder, or condition and the associated burden of suffering. To paraphrase the USPSTF, when evidence is insufficient, provision of a treatment (or diagnostic) for a serious condition might be viewed more favorably than provision of a treatment (or diagnostic) for a condition that does not cause as much suffering. The AAOS understands that evaluating the “burden of suffering” is subjective and involves judgment. This evaluation should be informed by patient values and concerns. It is not appropriate for a guideline to recommend widespread use of a technology backed by little data and for which there is limited experience. Such technologies are addressed in the AAOS’ Technology Overviews.
- Address potential harms.
- Address apparent discrepancies in the logic of different recommendations. If there are no relevant data for several recommendations and the work group chooses to issue an opinion-based recommendation in some cases but not in other cases, the rationales must explain why.
- Consider current practice. The USPSTF specifically states that clinicians justifiably fear not providing a service that is practiced on a widespread basis will lead to litigation.¹³⁶ Not providing a service that is not widely available or commonly used has less serious consequences than not providing a treatment accepted by the medical profession that patients expect. The patient’s “expectation of treatment” must be tempered by the treating physician’s guidance about the reasonable outcomes that the patient can expect.
- Justify when applicable why a more costly device, drug, or procedure is being recommended.

Work group members write the rationales for opinion based recommendations on the first day of the final work group meeting. When the work group reconvenes on the second day, members approve the rationales. If the work group cannot adopt a rationale after three votes, the rationale and the opinion-based recommendation will be withdrawn, and a “recommendation” stating that the group can neither recommend for or against the recommendation in question will appear in the guideline.

Sometimes work group members change their views. At any time during the discussion of the rationales, any member of the work group can make a motion to withdraw a recommendation. The guideline will state that the work group can neither recommend for or against the recommendation in question.

CHECKLIST FOR VOTING ON OPINION BASED RECOMMENDATIONS

When voting on the rationale, please consider the following:

1. Does the recommendation affect a substantial number of patients or address treatment (or diagnosis) of a condition that causes death and/or considerable suffering?
2. Does the recommendation address the potential harms that will be incurred if it is implemented and, if these harms are serious, does the recommendation justify:
 - a. why the potential benefits outweigh the potential harm
 - b. why an alternative course of treatment (or diagnostic workup) that involves less serious or fewer harms is not being recommended
3. Does the rationale explain why the work group chose to make a recommendation when presented with minimal evidence when it might not have in other cases?
4. Does the rationale explain that the recommendation is consistent with current practice?
5. If applicable, does the rationale justify why a less costly device, drug, or procedure is not being recommended?

VOTING BY THE NOMINAL GROUP TECHNIQUE

Voting on guideline recommendations will be conducted using a modification of the nominal group technique (NGT), a method previously used in guideline development.¹³⁷ Each work group member ranks his or her agreement with a recommendation or performance measure on a scale of 1 to 9 (where 1 = “extremely inappropriate” and 9 = “extremely appropriate”). Consensus is obtained if the number of individuals who do not rate a measure as 7, 8, or 9 is statistically non-significant (as determined using the binomial distribution). Because the number of work group members who are allowed to dissent with the recommendation depends on statistical significance, the number of permissible dissenters varies with the size of the work group. The number of permissible dissenters for several work group sizes is given in the table below:

Work Group Size	Number of Permissible Dissenters
≤ 3	Not allowed. Statistical significance cannot be obtained
4-5	0
6-8	1
9	1 or 2

The NGT is conducted by first having members vote on a given recommendation/performance measure without discussion. If the number of dissenters is “permissible”, the recommendation/measure is adopted. If the number of dissenters is not permissible, then there is discussion to see if the disagreement(s) can be resolved. Three rounds of voting are held to attempt to resolve differences. If agreement is not reached after three voting rounds, the recommendation is not adopted.

APPENDIX IX

STRUCTURED PEER REVIEW FORM

Review of any AAOS confidential draft allows us to improve the overall guideline but does not imply endorsement by any given individual or any specialty society who participates in our review processes. The AAOS review process may result in changes to the documents; therefore, endorsement cannot be solicited until the AAOS Board of Directors officially approves the final guideline.

Reviewer Information:

Name of Reviewer _____

Address _____

City _____ State _____ Zip Code _____

Phone _____ Fax _____ E-mail _____

Specialty Area/Discipline: _____

Work setting: _____ Credentials: _____

May we list you as a Peer Reviewer in the final Guidelines (GL)?

☐ Yes ☐ No

*If you do not wish to be listed, your name will be removed for identification purposes.
However, your COI will still be available for review with the comments you have made.*

Are you reviewing this guideline as a representative of a professional society?

☐ Yes ☐ No

If yes, may we list your society as a reviewer of this guideline?

☐ Yes ☐ No

Society Name: _____

(Listing the specialty society as a reviewing society does not imply or otherwise indicate endorsement of this guideline.)

Conflicts of Interest (COI): All Reviewers must declare their conflicts of interest.

If the boxes below are not checked and/or the reviewer does not attach his/her conflicts of interest, the reviewer's comments will not be addressed by the AAOS nor will the reviewer's name or society be listed as a reviewer of this GL. If a committee reviews the guideline, only the chairperson/or lead of the review must declare their relevant COI.

☐ I have declared my conflicts of interest on page 2 of this form.

☐ I have declared my conflicts of interest in the AAOS database; my customer # is _____

☐ I understand that the AAOS will post my declared conflicts of interest with my comments concerning review of this guideline or technology overview on the AAOS website.

REVIEWER CONFLICT OF INTEREST - The Orthopaedic Disclosure Program

Each item below requires an answer. Please report information for the last 12-months as required by the Accreditation Council for Continuing Medical Education (ACCME) guidelines.

Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device? If YES, please identify product or device:	☐ Yes ☐ No
Within the past twelve months, have you or a member of your immediate family served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company? If YES, please identify company:	☐ Yes ☐ No
Are you or a member of your immediate family a PAID EMPLOYEE for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Are you or a member of your immediate family a PAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Are you or a member of your immediate family an UNPAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family own stock or stock options in any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds)? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive research or institutional support as a principal investigator from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive any other financial or material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive any royalties, financial or material support from any medical and/or orthopaedic publishers? If YES, please identify publisher:	☐ Yes ☐ No
Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication? If YES, please identify:	☐ Yes ☐ No
Do you or a member of your immediate family serve on the Board of Directors or a committee of any medical and/or orthopaedic professional society? If YES, please identify:	☐ Yes ☐ No

Guidelines Peer Review Form

Reviewer Instructions

Please read and review this Draft Clinical Practice Guideline and its associated Technical Report with particular focus on your area of expertise. Your responses are confidential and will be used only to assess the validity, clarity and accuracy of the interpretation of the evidence. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on overall structure and content of the guideline and Technical Report. If you need more space than is provided, please attach additional pages.

Please indicate your level of agreement with each of the following statements by placing an “X” in the appropriate box.

	Disagree	Somewhat Disagree	Somewhat Agree	Agree
1. The recommendations are clearly stated	☐	☐	☐	☐
2. There is an explicit link between the recommendations and the supporting evidence	☐	☐	☐	☐
3. Given the nature of the topic and the data, all clinically important outcomes are considered	☐	☐	☐	☐
4. The guideline's target audience is clearly described	☐	☐	☐	☐
5. The patients to whom this guideline is meant to apply are specifically described	☐	☐	☐	☐
6. The criteria used to select articles for inclusion are appropriate	☐	☐	☐	☐
7. The reasons why some studies were excluded are clearly described	☐	☐	☐	☐
8. All important studies that met the article inclusion criteria are included	☐	☐	☐	☐
9. The validity of the studies is appropriately appraised	☐	☐	☐	☐
10. The methods are described in such a way as to be reproducible.	☐	☐	☐	☐
11. The statistical methods are appropriate to the material and the objectives of this guideline	☐	☐	☐	☐
12. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed	☐	☐	☐	☐
13. Health benefits, side effects, and risks are adequately addressed	☐	☐	☐	☐
14. The writing style is appropriate for health care professionals.	☐	☐	☐	☐
15. The grades assigned to each recommendation are appropriate	☐	☐	☐	☐

COMMENTS

Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the guideline and Technical Report

OVERALL ASSESSMENT

Would you recommend these guidelines for use in practice? (check one)

- ☐ Strongly recommend
- ☐ Recommend (with provisions or alterations)
- ☐ Would not recommend
- ☐ Unsure

APPENDIX X

PARTICIPATING PEER REVIEW ORGANIZATIONS

Peer review of the guideline is completed by interested external organizations. The AAOS solicits reviewers for each guideline. They consist of experts in the topic area and represent professional societies other than AAOS. Review organizations are nominated by the work group at the introductory meeting. For this guideline, nineteen organizations were invited to review the full guideline. Fifteen societies participated in the review of the guideline on treatment of osteoarthritis of the knee and have given consent to be listed below:

American Academy of Family Physicians (AAFP)

American Association of Hip and Knee Surgeons (AAHKS)

Arthroscopy Association of North America (AANA)

American Orthopaedic Society for Sports Medicine (AOSSM)

American Academy of Physical Medicine and Rehabilitation (AAPMR)

American Physical Therapy Association (APTA)

Eastern Orthopaedic Association (EOA)

Orthopaedic Trauma Association (OTA)

Arthritis Foundation

Knee Society

American College of Sports Medicine (ACSM)

Southern Orthopaedic Association (SOA)

Mid-America Orthopaedic Association

Western Orthopaedic Association (WOA)

Peer review comments will be available on aaos.org.

Participation in the AAOS guideline peer review process does not constitute an endorsement nor does it imply that the reviewer supports this document.

APPENDIX XI

INTERPRETING THE FOREST PLOTS

We use descriptive diagrams known as forest plots to present data from studies comparing the differences in outcomes between two treatment groups when a meta-analysis has been performed (combining results of multiple studies into a single estimate of overall effect). The overall effect is shown at the bottom of the graph as a diamond to illustrate the confidence intervals. The standardized mean difference or odds ratio are measures used to depict differences in outcomes between treatment groups. The horizontal line running through each point represents the 95% confidence interval for that point estimate. The solid vertical line represents “no effect” and is where the standardized mean difference = 0 or odds ratio = 1.

ABBREVIATIONS USED IN THIS REPORT

Abbreviation	Term
95% CI	95% Confidence interval
AAOS	American Academy of Orthopaedic Surgeons
AIMS	Arthritis Impact Management Scale
ASES	Arthritis Self-Efficacy Scale
BMI	Body mass index
BOC	AAOS Board of Councilors
BOD	AAOS Board of Directors
BOS	AAOS Board of Specialty Societies
COI	Conflict of interest
CORQ	AAOS Council on Research and Quality
Cox-2	Cyclooxygenase-2
CPG	Clinical practice guidelines
Da	Daltons
EBM	Evidence-based medicine
EBP	Evidence-based practice
EBPC	AAOS Evidence-Based Practice Committee
FDA	United States Food and Drug Administration
GI	Gastrointestinal
GOC	AAOS Guidelines Oversight Committee
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HA	Hyaluronic Acid
HAD	Hospital Anxiety and Depression
HAQ	Health Assessment Questionnaire
HMW	High Molecular Weight
HSS	Hospital for Special Surgery
IOM	Institute of Medicine
kDa	Kilo-Daltons
KOOS	Knee Injury and Osteoarthritis Outcome Score

KSS	Knee Society Score
LMW	Low Molecular Weight
MACTAR	McMaster Toronto Arthritis Patient Preference Disability questionnaire
MCII	Minimal Clinically Important Improvement
MR	Magnetic resonance
NR	Not reported
NRS	Numerical Rating Scale
NS	Not significant
NSAID	Non-steroidal anti-inflammatory drug
OARSI	Osteoarthritis Research Society International
OR	Odds ratio
OREF	Orthopaedic Research and Education Foundation
ORS	Orthopaedic Research Society
PQLC	Profile of Quality of Life in the Chronically Ill
PRECIS	Pragmatic-explanatory continuum indicator summary
QUADAS	Quality Assessment of Diagnostic Accuracy Studies instrument
SF	Short Form
SMD	Standardized Mean Difference
TKA	Total knee arthroplasty
VAS	Visual Analogue Scale
WMD	Weighted Mean Difference
WOMAC	Western Ontario and McMaster Universities Index

APPENDIX XII

CONFLICT OF INTEREST

Prior to the development of this guideline, work group members disclose conflicts of interest. They disclose COIs in writing to the American Academy of Orthopaedic Surgeons via a private on-line reporting database and also verbally at the recommendation approval meeting.

Disclosure Items: (n) = Respondent answered 'No' to all items indicating no conflicts. 1 = Board member/owner/officer/committee appointments; 2 = Medical/Orthopaedic Publications; 3 = Royalties; 4 = Speakers bureau/paid presentations; 5A = Paid consultant; 5B = Unpaid consultant; 6 = Research or institutional support from a publisher; 7 = Research or institutional support from a company or supplier; 8 = Stock or Stock Options; 9 = Other financial/material support from a publisher; 10 = Other financial/material support from a company or supplier.

APPENDIX XIII

NETWORK META ANALYSIS CHECKS FOR CONSISTENCY

Table 229. Network Meta-Analysis Consistency Check: WOMAC Pain

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean Difference	Direct Effect SD	Omega (Direct Minus Indirect Effect)	Z	p-value (For Omega)
Celecoxib versus Placebo	-6.665	1.663	-6.31	58.31655	0.355289	0.00609	0.995141
Diacerein versus Placebo	-6.122	3.458	-4.4	41.94362	1.733785	0.041195	0.96714
Diclofenac versus Placebo	-8.824	2.655	-9.5	42.4978	-0.67865	-0.01594	0.987284
Lumiracoxib versus Placebo	-6.552	2.021	-5.02	43.89235	1.535255	0.034941	0.972127
Naproxen versus Piroxicam	1.271	3.652	2	44.09972	0.734034	0.016588	0.986766
Naproxen versus Placebo	-9.29	2.813	-10.24	32.95406	-0.95697	-0.02893	0.976918
Naproxinod versus Placebo	-8.87	3.866	-10.71	53.3577	-1.84971	-0.03458	0.972419
Piroxicam versus Diclofenac	-1.737	4.073	-0.44	49.16689	1.305962	0.026471	0.978882
Piroxicam versus Tenidap	-0.1768	3.947	-0.2	43.75281	-0.02339	-0.00053	0.999575
Rofecoxib versus Placebo	-12.4	2.867	-14.12	40.93851	-1.72848	-0.04212	0.966405
Topical Diclofenac versus Placebo	-8.218	3.161	-8.17	45.51421	0.048233	0.001057	0.999157
Topical Eltenac versus Placebo	-3.099	5.568	-3.13	46.37836	-0.03145	-0.00067	0.999463
Tramadol versus Diclofenac	1.075	6.142	-0.2	49.14379	-1.29523	-0.02615	0.979138
Valdecoxib versus Placebo	-8.433	3.68	-6.73	46.67269	1.713654	0.036602	0.970802
Diclofenac versus Tramadol	-0.2052	3.966	-0.2	43.75281	0.005243	0.000119	0.999905
Tenoxicam versus Placebo	-1.805	3.347	-1.8	8.532672	0.005909	0.000637	0.999492

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean Difference	Direct Effect SD	Omega (Direct Minus Indirect Effect)	Z	p-value (For Omega)
Acetaminophen versus Aceclofenac	7.656	4.979	7.64	73.5249	-0.01607	-0.00022	0.999826
Topical Ketoprofen versus Placebo	-7.361	3.814	-7	41.19538	0.364121	0.008801	0.992978
Topical Ketoprofen versus Celecoxib	-0.6956	4.161	0.6	43.92958	1.307329	0.029626	0.976365
Tramadol versus Placebo	-8.619	3.929	-9.7	64.54882	-1.08502	-0.01678	0.986614

Table 230. Network Meta-Analysis Consistency Check: WOMAC Function

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean Difference	Direct Effect SD	Omega	Z	p
Lumiracoxib versus Celecoxib	-0.1848	0.7628	-0.45	24.76538	-0.13283	-0.00536	0.837689
Celecoxib versus Diclofenac	2.405	1.486	1.9	26.66777	0.816794	0.030581	0.923854
Tramadol versus Diclofenac	1.294	2.412	1.07	34.52125	0.852826	0.024644	0.87909
Celecoxib versus Lumiracoxib	0.1848	0.7628	0.2	1416.932	-0.1176	-8.3E-05	0.909168
Naproxen versus Naproxcinod	-2.222	2.014	-2.21	35.80515	-1.66921	-0.04655	0.995723
Diacerein versus Piroxicam	3.004	2.323	3.01	25.76558	2.477993	0.095783	0.975604
Tenidap versus Piroxicam	-1.026	1.828	-1.02	29.44944	-0.71691	-0.0243	0.980339
Celecoxib versus Placebo	-4.009	0.6665	-3.79	25.53272	5.232178	0.204851	0.999934
Diacerein versus Placebo	-3.315	2.567	-3.32	29.62268	-2.84205	-0.09558	0.962875
Diclofenac versus Placebo	-6.414	1.466	-7	26.49743	-4.03707	-0.15212	0.923693
Lumiracoxib versus Placebo	-4.193	0.7906	-3.79	25.53509	2.914644	0.114088	0.980616
Naproxcinod versus Placebo	-7.137	2.031	-7.15	35.82434	-5.44286	-0.15169	0.837689
Naproxen versus Placebo	-9.359	2.026	-9.36	35.81259	-7.10997	-0.19821	0.923854

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean Difference	Direct Effect SD	Omega	Z	p
Rofecoxib versus Placebo	-3.914	1.654	-5.4	27.69695	-3.98862	-0.14375	0.87909
Topical Diclofenac versus Placebo	-5.806	1.594	-5.75	30.02551	-3.48118	-0.11578	0.909168
Celecoxib versus Placebo	-0.09485	1.626	-1.1	27.51334	-1.06798	-0.03875	0.879433
Tramadol versus Placebo	-5.12	2.308	-4.97	29.58248	-4.03927	-0.13613	0.842877
Topical Ketoprofen versus Placebo	-2.816	1.801	-2.99	28.15572	-2.13411	-0.07564	0.885696
Topical Ketoprofen versus Celecoxib	1.193	1.806	1.36	28.42009	0.999747	0.035106	0.907829

Table 231. Network Meta-Analysis Consistency Check: WOMAC Stiffness

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean difference	Direct Effect SD	Omega	Z	p
Lumiracoxib versus Celecoxib	0.01963	-0.11	3.736156	3.009356	- 0.13042	-0.03480101	0.972238
Celecoxib versus Diclofenac	0.3448	0.3	3.562489	3.866677	- 0.04565	-0.01269421	0.989872
Tramadol versus Diclofenac	0.7592	0.43	4.346562	3.465048	- 0.33706	-0.07663726	0.938912
Valdecoxib versus Naproxen	0.081	0.08	3.491004	3.663208	- 0.00102	-0.00028997	0.999769
Diacerein versus Piroxicam	0.2447	0.24	2.913194	3.508201	- 0.00488	-0.00164401	0.998688
Tenidap versus Piroxicam	-0.03978	-0.04	4.121328	3.654279	- 0.00022	-5.3858E-05	0.999957
Celecoxib versus Placebo	-0.6101	-0.49	3.009357	4.005223	0.120964	0.040052235	0.968051
Diacerein versus Placebo	-0.4014	-0.4	3.866677	3.317778	0.001434	0.000366376	0.999708
Diclofenac versus Placebo	-0.9549	-1	3.465048	3.495311	-0.046	-0.01314553	0.989512
Lumiracoxib versus Placebo	-0.5905	-0.39	3.663208	3.736156	0.202042	0.054943476	0.956183
Naproxen versus Placebo	-0.419	-0.42	3.508201	3.562489	0.00102	-0.00028847	0.99977
Rofecoxib versus Placebo	-1.017	-1.09	3.654279	4.346562	- 0.07376	-0.02007989	0.98398
Topical Diclofenac versus Placebo	-0.6398	-0.61	4.005223	3.491004	0.030108	0.007478655	0.994033
Tramadol versus Placebo	-0.1957	-0.68	3.317778	2.913194	- 0.49347	-0.1473462	0.882859
Valdecoxib versus Placebo	-0.338	-0.34	3.495311	4.121328	- 0.00205	-0.00057914	0.999538

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean difference	Direct Effect SD	Omega	Z	p
Celecoxib versus Rofecoxib	0.4069	-0.1	2.781132	2.7811 32	- 0.5175 6	-0.1841701	0.85388

Table 232. Network Meta-Analysis Consistency Check: WOMAC Total

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean Difference	Direct Effect SD	Omega	Z	p
Lumiracoxib versus Celecoxib	-0.4188	1.111	-0.47	34.0524	-0.05125	-0.0015	0.9988
Diclofenac versus Diacerein	-0.1763	1.818	-0.42	17.27515	-0.63141	-0.03635	0.971006
Celecoxib versus Diclofenac	2.502	2.031	2.6	36.43917	0.098305	0.002694	0.997851
Valdecoxib versus Naproxen	1.041	3.395	0.82	37.78499	-0.2228	-0.00587	0.995314
Diacerein versus Piroxicam	2.513	3.079	2.53	32.56303	0.017153	0.000524	0.999582
Tenidap versus Piroxicam	-0.4035	2.635	-0.38	41.27031	0.023596	0.000571	0.999545
Celecoxib versus Placebo	-5.996	1.09	-6.2	47.90869	-0.20411	-0.00426	0.996602
Diacerein versus Placebo	-8.321	2.303	-5.92	41.48486	2.408422	0.057966	0.953776
Diclofenac versus Placebo	-8.498	1.965	-9.9	36.68875	-1.40603	-0.03827	0.969474
Lumiracoxib versus Placebo	-6.414	1.29	-4.7	34.83313	1.716354	0.04924	0.960728
Naproxcinod versus Placebo	-6.069	2.835	-8.43	47.669	-2.36938	-0.04962	0.960428
Naproxen versus Placebo	-7.109	1.948	-7.74	86.35239	-0.63132	-0.00731	0.994168
Valdecoxib versus Placebo	-5.028	2.38	-3.74	37.7288	1.293146	0.034207	0.972712

Comparison	MTC Mean Difference	MTC SD	Direct Weighted Mean Difference	Direct Effect SD	Omega	Z	p
Tramadol versus Placebo	-8.453	3.993	-8.448	41.28798	0.005047	0.000122	0.999903

Table 233. Network Meta-Analysis Consistency Check: Adverse Events

Comparison	MTC LN Odds Ratio	MTC SD	Direct Effect LN Odds Ratio	Direct Effect SD	Omega	Z	p
Lumiracoxib 100mg versus Placebo	0.3026	0.3692	0.23	4.002017	-0.14039	-0.03493	0.972134
Lumiracoxib 100mg WLD versus Placebo	0.3403	0.37	0.27	4.076128	-0.10083	-0.02463	0.980346
Naproxcinod 750mg versus Placebo	0.2079	0.4476	-0.08	4.248963	-0.53352	-0.12487	0.90063
Naproxen 500mg versus Placebo	0.1992	0.4479	0.21	5.219101	-0.23967	-0.04575	0.963508
Celecoxib 100mg versus Placebo	-0.07778	0.2717	0.08	4.167209	-0.19252	-0.0461	0.963231
Celecoxib 200mg versus Placebo	0.1848	0.1959	0.35	4.146549	0.154445	0.037205	0.970322
High Dose Diflunisal versus Placebo	0.2966	0.4752	0.29	4.634799	-0.18717	-0.04017	0.967957
Low Dose Diflunisal versus Placebo	0.1956	0.478	0.19	4.669442	-0.29105	-0.062	0.95056
Lumiracoxib 200mg versus Placebo	-0.2919	0.2712	0.13	4.330409	-0.14176	-0.03267	0.973937
Lumiracoxib 400mg versus Placebo	0.1176	0.2718	0.09	8.483219	-0.18199	-0.02144	0.982893

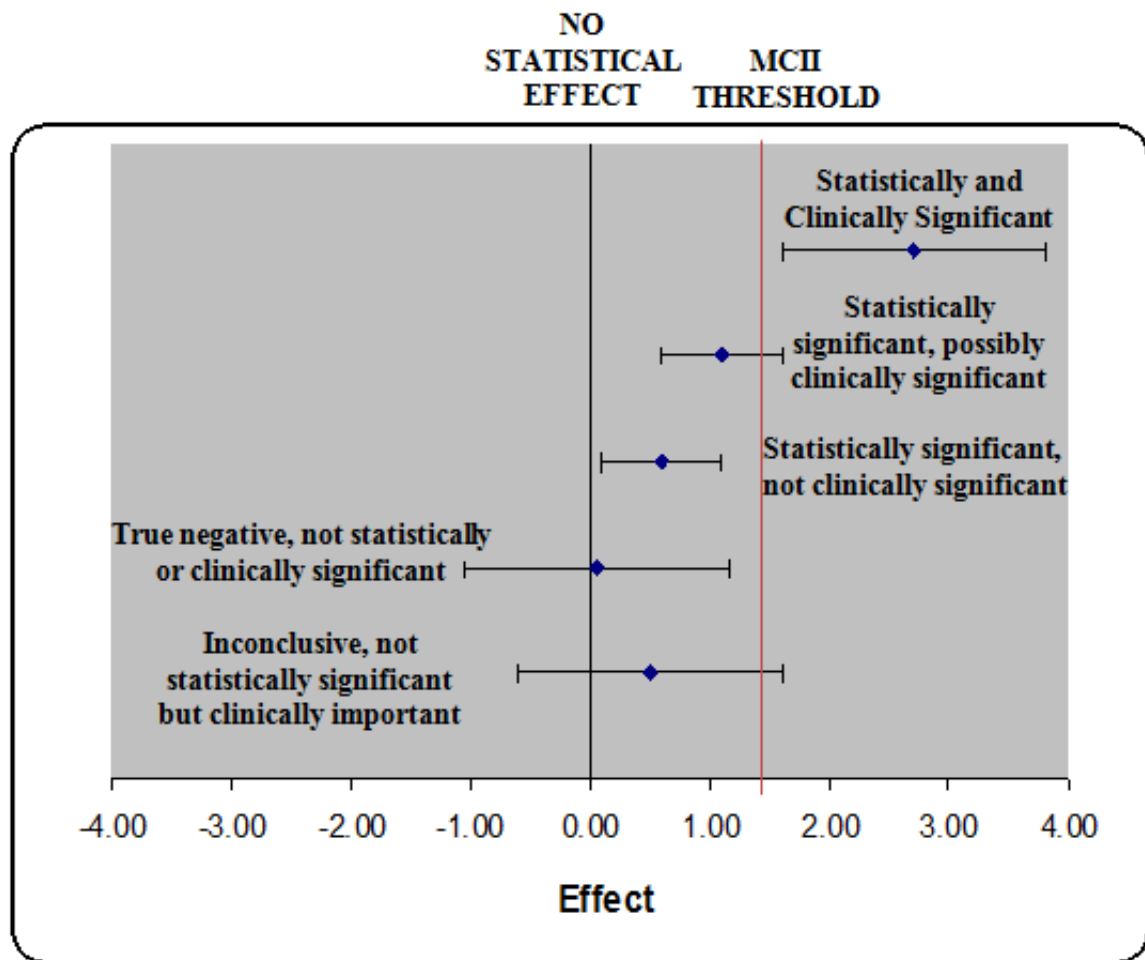
Comparison	MTC LN Odds Ratio	MTC SD	Direct Effect LN Odds Ratio	Direct Effect SD	Omega	Z	p
Rofecoxib 12.5mg versus Placebo	0.16	0.3016	0	4.232689	-0.30314	-0.07144	0.94305
Rofecoxib 25mg versus Placebo	0.2956	0.3019	0.52	4.491048	0.21909	0.048673	0.96118
Rofecoxib 12.5mg versus Nabumetone	0.1536	0.3865	0.08	3.978238	-0.30942	-0.07741	0.938297
Naproxcinod 750mg versus Naproxen 500mg	0.008678	0.4152	0.01	4.398402	-0.40884	-0.09254	0.926271
Acetaminophen versus Aceclofenac	-0.124	0.5135	-0.12	4.331515	-0.64253	-0.14729	0.882901
Lumiracoxib 100mg WLD versus Celecoxib 200mg	0.1555	0.3692	0.23	3.992522	-0.1404	-0.03502	0.972068
Celecoxib 100mg versus Celecoxib 200mg	-0.2626	0.2901	-0.17	3.990409	-0.46254	-0.11561	0.907964
Lumiracoxib 200mg versus Celecoxib 200mg	-0.4767	0.2906	0.08	4.787857	-0.21138	-0.04407	0.964851
Lumiracoxib 400mg versus Celecoxib 200mg	-0.06717	0.291	-0.04	4.112072	-0.33267	-0.0807	0.935683
High dose diflunisal versus low dose diflunisal	0.101	0.4724	0.1	4.516707	-0.37652	-0.0829	0.933928
Celecoxib 100mg versus Lumiracoxib 200mg	0.2141	0.3175	-0.17	4.047825	-0.49052	-0.12081	0.903844

Comparison	MTC LN Odds Ratio	MTC SD	Direct Effect LN Odds Ratio	Direct Effect SD	Omega	Z	p
Lumiracoxib 400mg versus Lumiracoxib 200mg	0.4096	0.2897	0.05	4.06868	-0.24092	-0.05906	0.952902
Celecoxib 100mg versus Lumiracoxib 400mg	-0.1954	0.3179	-0.22	3.976647	-0.54136	-0.1357	0.892059
Acetaminophen versus Rofecoxib 12.5mg	0.1747	0.3989	0.09	4.044641	-0.31193	-0.07675	0.938825
Celecoxib 200mg versus Rofecoxib 12.5mg	0.02484	0.305	-0.13	3.029447	-0.43945	-0.14432	0.885245
Acetaminophen versus Rofecoxib 25mg	0.03899	0.388	0.04	4.318388	-0.35083	-0.08091	0.935511
Celecoxib 200mg versus Rofecoxib 25mg	-0.1108	0.2803	-0.12	3.554488	-0.4028	-0.11297	0.910054
Rofecoxib 12.5mg versus Rofecoxib 25mg	-0.1357	0.3395	0.12	4.195686	-0.22095	-0.05249	0.95814

APPENDIX XIV

CONFIDENCE INTERVALS OF TREATMENT EFFECTS THAT RANGE IN STATISTICAL AND CLINICAL SIGNIFICANCE

- Treatment effects that do not contain zero, i.e. are higher than the black line, are statistically significant
- Treatment effects that contain zero, i.e. cross the black line, are not statistically significant
- Treatment effects that are higher than the red line are clinically significant
- If only a portion of the confidence interval lies above the minimum threshold for clinical significance, its impact on patients cannot be determined
- If the entire confidence interval lies below the minimum threshold for clinical significance, i.e. is below the red line, it is not meaningful to patients
- Inconclusive treatment effects are not consistent in statistical and clinical significance
- True negative treatment effects are neither statistically or clinically significant



APPENDIX XV

BIBLIOGRAPHY

Studies Included in the Guideline

Allen KD, Oddone EZ, Coffman CJ, Datta SK, Juntilla KA, Lindquist JH, Walker TA, Weinberger M, Bosworth HB. Telephone-based self-management of osteoarthritis: A randomized trial. *Ann Intern Med* 2010 Nov 2;153(9):570-579.

Altman RD, Akermark C, Beaulieu AD, Schnitzer T. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage* 2004;12(8):642-649.

Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum* 2001;44(11):2531-2538.

Altman RD, Rosen JE, Bloch DA, Hatoum HT, Korner P. A double-blind, randomized, saline-controlled study of the efficacy and safety of EUFLEXXA for treatment of painful osteoarthritis of the knee, with an open-label safety extension (the FLEXX trial). *Semin Arthritis Rheum* 2009;39(1):1-9.

Altman RD, Rosen JE, Bloch DA, Hatoum HT. Safety and efficacy of retreatment with a bioengineered hyaluronate for painful osteoarthritis of the knee: Results of the open-label extension study of the flexx trial. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S144.

Arden NK, Reading IC, Jordan KM, Thomas L, Platten H, Hassan A, Ledingham J. A randomised controlled trial of tidal irrigation versus corticosteroid injection in knee osteoarthritis: the KIVIS Study. *Osteoarthritis Cartilage* 2008;16(6):733-739.

Atamaz FC, Durmaz B, Baydar M, Demircioglu OY, Iyiyapici A, Kuran B, Oncel S, Sendur OF. Comparison of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled, multicenter study. *Arch Phys Med Rehabil* 2012 May;93(5):748-756.

Ayral X, Mackillop N, Genant HK, Kirkpatrick J, Beaulieu A, Pippingskiold P, Will RK, Alava S, Dougados M. Arthroscopic evaluation of potential structure-modifying drug in osteoarthritis of the knee. A multicenter, randomized, double-blind comparison of Tenidap sodium versus Piroxicam. *Osteoarthritis Cartilage* 2003;11(3):198-207.

Azad AK, Nabi G, Shakoor MA, Moyeenuzzaman M. Role of muscle strengthening exercise on osteoarthritis of the knee joint. *J Med* 2011;12(2):120-124.

Babul N, Noveck R, Chipman H, Roth SH, Gana T, Albert K. Efficacy and safety of extended-release, once-daily Tramadol in chronic pain: a randomized 12-week clinical trial in osteoarthritis of the knee. *J Pain Symptom Manage* 2004;28(1):59-71.

Bachhal V, Sankhala SS, Jindal N, Dhillon MS. High tibial osteotomy with a dynamic axial fixator: precision in achieving alignment. *J Bone Joint Surg Br* 2011 Jul;93(7):897-903.

Baer PA, Thomas LM, Shainhouse Z. Treatment of osteoarthritis of the knee with a topical Diclofenac solution: a randomised controlled, 6-week trial [ISRCTN53366886]. *BMC Musculoskelet Disord* 2005;6:44.

- Baker K, Goggins J, Xie H, Szumowski K, Lavalley M, Hunter DJ, Felson DT. A randomized crossover trial of a wedged insole for treatment of knee osteoarthritis. *Arthritis Rheum* 2007;56(4):1198-1203.
- Barthel HR, Haselwood D, Longley S, Gold MS, Altman RD. Randomized controlled trial of Diclofenac sodium gel in knee osteoarthritis. *Semin Arthritis Rheum* 2009;39(3):203-212.
- Batlle-Gualda E, Roman IJ, Martin-Mola E, Carbonell AJ, Linares Ferrando LF, Tornero MJ, Raber BA, Fortea BJ. Aceclofenac versus Paracetamol in the management of symptomatic osteoarthritis of the knee: a double-blind 6-week randomized controlled trial. *Osteoarthritis Cartilage* 2007;15(8):900-908.
- Battisti E, Piazza E, Rigato M, Nuti R, Bianciardi L, Scribano A, Giordano N. Efficacy and safety of a musically modulated electromagnetic field (TAMMEF) in patients affected by knee osteoarthritis. *Clin Exp Rheumatol* 2004;22(5):568-572.
- Beaulieu AD, Peloso PM, Haraoui B, Bensen W, Thomson G, Wade J, Quigley P, Eisenhoffer J, Harsanyi Z, Darke AC. Once-daily, controlled-release Tramadol and sustained-release Diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial. *Pain Res Manag* 2008;13(2):103-110.
- Bellamy N, Buchanan WW, Chalmers A, Ford PM, Kean WF, Kraag GR, Gercz-Simon E, Campbell J. A multicenter study of tenoxicam and Diclofenac in patients with osteoarthritis of the knee. *J Rheumatol* 1993;20(6):999-1004.
- Bennell KL, Bowles KA, Payne C, Cicuttini F, Williamson E, Forbes A, Hanna F, Davies-Tuck M, Harris A, Hinman RS. Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial. *BMJ* 2011;342:d2912.
- Bennell KL, Hinman RS, Metcalf BR, Buchbinder R, McConnell J, McColl G, Green S, Crossley KM. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis* 2005;64(6):906-912.
- Bennell KL, Hunt MA, Wrigley TV, Hunter DJ, McManus FJ, Hodges PW, Li L, Hinman RS. Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomised controlled trial. *Osteoarthritis Cartilage* 2010;18(5):621-628.
- Bensen WG, Fiechtner JJ, McMillen JJ, Zhao WW, Yu SS, Woods EM, Hubbard RC, Isakson PC, Verburg KM, Geis GS. Treatment of osteoarthritis with Celecoxib, a cyclooxygenase-2 inhibitor: a randomized controlled trial. *Mayo Clin Proc* 1999;74(11):1095-1105.
- Berenbaum F, Grifka J, Cazzaniga S, D'Amato M, Giacobelli G, Chevalier X, Rannou F, Rovati LC, Maheu E. A randomised, double-blind, controlled trial comparing two intra-articular hyaluronic acid preparations differing by their molecular weight in symptomatic knee osteoarthritis. *Ann Rheum Dis* 2012 Jan 31.
- Berenbaum F, Grifka J, Cazzaniga S, D'Amato M, Giacobelli G, Chevalier X, Rannou F, Rovati LC, Maheu E. A randomised, double-blind, controlled trial comparing two intra-articular hyaluronic acid preparations differing by their molecular weight in symptomatic knee osteoarthritis. *Annals of the Rheumatic Diseases* 2011;. Date of Publication(31 Jan 2012).
- Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 2004;141(12):901-910.

Berman BM, Singh BB, Lao L, Langenberg P, Li H, Hadhazy V, Bareta J, Hochberg M. A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. *Rheumatology (Oxford)* 1999;38(4):346-354.

Bin S, Wu SS, Zeng X, Moore A, Frank N. Efficacy of Lumiracoxib in relieving pain associated with knee osteoarthritis: A 6-week, randomized, double-blind, parallel-group study. *APLAR Journal of Rheumatology* 2007;10:190-197.

Bingham CO, Buckland-Wright JC, Garner P, Cohen SB, Dougados M, Adami S, Clauw DJ, Spector TD, Pelletier JP, Raynauld JP, Strand V, Simon LS, Meyer JM, Cline GA, Beary JF. Risedronate decreases biochemical markers of cartilage degradation but does not decrease symptoms or slow radiographic progression in patients with medial compartment osteoarthritis of the knee: results of the two-year multinational knee osteoarthritis study. *Arthritis Rheum* 2006;54(11):3494-3507.

Bliddal H, Leeds AR, Stigsgaard L, Astrup A, Christensen R. Weight loss as treatment for knee osteoarthritis symptoms in obese patients: 1-year results from a randomised controlled trial. *Ann Rheum Dis* 2011 Oct;70(10):1798-1803.

Bookman AA, Williams KS, Shainhouse JZ. Effect of a topical Diclofenac solution for relieving symptoms of primary osteoarthritis of the knee: a randomized controlled trial. *CMAJ* 2004;171(4):333-338.

Borjesson M, Robertson E, Weidenhielm L, Mattsson E, Olsson E. Physiotherapy in knee osteoarthritis: effect on pain and walking. *Physiother Res Int* 1996;1(2):89-97.

Bourgeois P, Chales G, Dehais J, Delcambre B, Kuntz JL, Rozenberg S. Efficacy and tolerability of chondroitin sulfate 1200mg/day versus chondroitin sulfate 3 x 400 mg/day versus placebo. *Osteoarthritis Cartilage* 1998;6 Suppl A:25-30.

Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Comparison of an antiinflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and Acetaminophen in the treatment of patients with osteoarthritis of the knee. *N Engl J Med* 1991;325(2):87-91.

Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Treatment of knee osteoarthritis: relationship of clinical features of joint inflammation to the response to a nonsteroidal antiinflammatory drug or pure analgesic. *J Rheumatol* 1992;19(12):1950-1954.

Bradley JD, Heilman DK, Katz BP, Gsell P, Wallick JE, Brandt KD. Tidal irrigation as treatment for knee osteoarthritis: a sham-controlled, randomized, double-blinded evaluation. *Arthritis Rheum* 2002;46(1):100-108.

Brouwer RW, Bierma-Zeinstra SM, van Raaij TM, Verhaar JA. Osteotomy for medial compartment arthritis of the knee using a closing wedge or an opening wedge controlled by a Puddu plate. A one-year randomised, controlled study. *J Bone Joint Surg Br* 2006;88(11):1454-1459.

Brouwer RW, van Raaij TM, Verhaar JA, Coene LN, Bierma-Zeinstra SM. Brace treatment for osteoarthritis of the knee: a prospective randomized multi-centre trial. *Osteoarthritis Cartilage* 2006;14(8):777-783.

Brown BL, Johnson JH, Herron MS. Double-blind comparison of flurbiprofen and sulindac for the treatment of osteoarthritis. *Am J Med* 1986;80(3A):112-117.

Bucsi L, Poor G. Efficacy and tolerability of oral chondroitin sulfate as a symptomatic slow-acting drug for osteoarthritis (SYSADOA) in the treatment of knee osteoarthritis. *Osteoarthritis Cartilage* 1998;6 Suppl A:31-36.

Burch F, Fishman R, Messina N, Corser B, Radulescu F, Sarbu A, Craciun-Nicodin MM, Chiriac R, Beaulieu A, Rodrigues J, Beignot-Devalmont P, Duplan A, Robertson S, Fortier L, Bouchard S. A comparison of the analgesic efficacy of Tramadol Contramid OAD versus placebo in patients with pain due to osteoarthritis. *J Pain Symptom Manage* 2007;34(3):328-338.

Caborn D, Rush J, Lanzer W, Parenti D, Murray C. A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. *J Rheumatol* 2004;31(2):333-343.

Chao J, Wu C, Sun B, Hose MK, Quan A, Hughes TH, Boyle D, Kalunian KC. Inflammatory characteristics on ultrasound predict poorer longterm response to intraarticular corticosteroid injections in knee osteoarthritis. *J Rheumatol* 2010;37(3):650-655.

Chevalier X, Goupille P, Beaulieu AD, Burch FX, Bensen WG, Conrozier T, Loeuille D, Kivitz AJ, Silver D, Appleton BE. Intraarticular injection of anakinra in osteoarthritis of the knee: a multicenter, randomized, double-blind, placebo-controlled study. *Arthritis Rheum* 2009;61(3):344-352.

Chevalier X, Jerosch J, Goupille P, van DN, Luyten FP, Scott DL, Bailleul F, Pavelka K. Single, intra-articular treatment with 6 ml hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee: a randomised, multicentre, double-blind, placebo controlled trial. *Ann Rheum Dis* 2010;69(1):113-119.

Christensen R, Astrup A, Bliddal H. Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. *Osteoarthritis Cartilage* 2005;13(1):20-27.

Chubick AJ, Worley WE, Berman RS, Dobrinska MR. A double-blind multicenter study of sulindac once daily versus sulindac twice daily in osteoarthritis of the knee. *CURR THER RES, CLIN EXP* 1987;41:692-705.

Cibere J, Kopec JA, Thorne A, Singer J, Canvin J, Robinson DB, Pope J, Hong P, Grant E, Esdaile JM. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *Arthritis Rheum* 2004;51(5):738-745.

Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, Bradley JD, Bingham CO, Weisman MH, Jackson CG, Lane NE, Cush JJ, Moreland LW, Schumacher HR, Oddis CV, Wolfe F, Molitor JA, Yocum DE, Schnitzer TJ, Furst DE, Sawitzke AD, Shi H, Brandt KD, Moskowitz RW, Williams HJ. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006;354(8):795-808.

Coleman S, Briffa NK, Carroll G, Inderjeeth C, Cook N, McQuade J. A randomised controlled trial of a self-management education program for osteoarthritis of the knee delivered by health care professionals. *Arthritis Res Ther* 2012 Jan 27;14(1):R21.

Coleman S, Briffa NK, Carroll G, Inderjeeth C, Cook N, McQuade J. Effects of self-management, education and specific exercises, delivered by health professionals, in patients with osteoarthritis of the knee. *BMC Musculoskelet Disord* 2008;9:133.

Das A, Hammad TA. Efficacy of a combination of FCHG49 glucosamine hydrochloride, TRH122 low molecular weight sodium chondroitin sulfate and manganese ascorbate in the management of knee osteoarthritis. *Osteoarthritis Cartilage* 2000;8(5):343-350.

Day R, Brooks P, Conaghan PG, Petersen M. A double blind, randomized, multicenter, parallel group study of the effectiveness and tolerance of intraarticular hyaluronan in osteoarthritis of the knee. *J Rheumatol* 2004;31(4):775-782.

Deyle GD, Henderson NE, Matekel RL, Ryder mg, Garber MB, Allison SC. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med* 2000;132(3):173-181.

Dick WC, Bulstra S, Schardijn GH, Feenstra RM. Safety and efficacy of etodolac compared with Piroxicam in patients with degenerative joint disease of the knee. *Clin Ther* 1992;14(4):517-526.

Diracoglu D, Aydin R, Baskent A, Celik A. Effects of kinesthesia and balance exercises in knee osteoarthritis. *J Clin Rheumatol* 2005;11(6):303-310.

Ebnezar J, Nagarathna R, Bali Y, Nagendra HR. Effect of an integrated approach of yoga therapy on quality of life in osteoarthritis of the knee joint: A randomized control study. *Int J Yoga* 2011 Jul;4(2):55-63.

Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effect of integrated yoga therapy on pain, morning stiffness and anxiety in osteoarthritis of the knee joint: A randomized control study. *Int J Yoga* 2012 Jan;5(1):28-36.

Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effects of an integrated approach of hatha yoga therapy on functional disability, pain, and flexibility in osteoarthritis of the knee joint: a randomized controlled study. *J Altern Complement Med* 2012 May;18(5):463-472.

Ehrich EW, Schnitzer TJ, McIlwain H, Levy R, Wolfe F, Weisman M, Zeng Q, Morrison B, Bolognese J, Seidenberg B, Gertz BJ. Effect of specific COX-2 inhibition in osteoarthritis of the knee: a 6 week double blind, placebo controlled pilot study of Rofecoxib . Rofecoxib Osteoarthritis Pilot Study Group. *J Rheumatol* 1999;26(11):2438-2447.

El-Azab HM; Morgenstern M; Ahrens P; Schuster T; Imhoff AB; Lorenz SGF. Limb alignment after open-wedge high tibial osteotomy and its effect on the clinical outcome. *Orthopedics* 2011; 34(10):e622-e628.

Ettinger WH, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;277(1):25-31.

Ettinger WH, Burns R, Messier SP. Exercise programs for seniors with knee osteoarthritis. *Clin J Sport Med* 1997;7(3):231.

Evcik D, Maralcan G, Kuru I. The efficacy of intra-articular tenoxicam in the treatment of knee osteoarthritis. *Pain Clinic* 2003;15(4):405-408.

Fary RE. The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: results of a double-blind, randomized, placebo-controlled, repeated-measures trial. 2011;.

Fishman RL, Kistler CJ, Ellerbusch MT, Aparicio RT, Swami SS, Shirley ME, Jain AK, Fortier L, Robertson S, Bouchard S. Efficacy and safety of 12 weeks of osteoarthritic pain therapy with once-daily Tramadol (Tramadol Contramid OAD). *J Opioid Manag* 2007;3(5):273-280.

Fitzgerald GK, Piva SR, Gil AB, Wisniewski SR, Oddis CV, Irrgang JJ. Agility and perturbation training techniques in exercise therapy for reducing pain and improving function in people with knee osteoarthritis: a randomized clinical trial. *Phys Ther* 2011;91:452-469.

Flamme CH, Ruhmann O, Schmolke S, Wichmann R. Long-term outcome following high tibial osteotomy with tension bend principle. *Arch Orthop Trauma Surg* 2003;123(1):12-16.

Fleischmann R, Sheldon E, Maldonado-Cocco J, Dutta D, Yu S, Sloan VS. Lumiracoxib is effective in the treatment of osteoarthritis of the knee: a prospective randomized 13-week study versus placebo and Celecoxib. *Clin Rheumatol* 2006;25(1):42-53.

Fleischmann RM, Caldwell JR, Roth SH, Tesser JRP, Olson W, Kamin M. Tramadol for the treatment of joint pain associated with osteoarthritis: A randomized, double-blind, placebo-controlled trial. *Current Therapeutic Research, Clinical & Experimental* 2001;62:113-128.

Fleischmann RM, Flint K, Constantine G, Kolecki B. A double-masked comparison of Naprelan and nabumetone in osteoarthritis of the knee. Naprelan Study Group. *Clin Ther* 1997;19(4):642-655.

Focht BC, Rejeski WJ, Ambrosius WT, Katula JA, Messier SP. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum* 2005;53(5):659-665.

Forestier R, Desfour H, Tessier JM, Francon A, Foote AM, Genty C, Rolland C, Roques CF, Bosson JL. Spa therapy in the treatment of knee osteoarthritis: a large randomised multicentre trial. *Ann Rheum Dis* 2010;69(4):660-665.

Fransen M, Crosbie J, Edmonds J. Physical therapy is effective for patients with osteoarthritis of the knee: a randomized controlled clinical trial. *J Rheumatol* 2001;28(1):156-164.

Gaffney K, Ledingham J, Perry JD. Intra-articular triamcinolone hexacetonide in knee osteoarthritis: factors influencing the clinical response. *Ann Rheum Dis* 1995;54(5):379-381.

Getgood A, Collins B, Slynarski K, Kurowska E, Parker D, Engebretsen L, Macdonald PB, Litchfield R. Short-term safety and efficacy of a novel high tibial osteotomy system: a case controlled study. *Knee Surg Sports Traumatol Arthrosc* 2011 Oct 18.

Gibofsky A, Williams GW, McKenna F, Fort JG. Comparing the efficacy of cyclooxygenase 2-specific inhibitors in treating osteoarthritis: appropriate trial design considerations and results of a randomized, placebo-controlled trial. *Arthritis Rheum* 2003;48(11):3102-3111.

Giordano N, Fioravanti A, Papakostas P, Montella A, Giorgi G, Nuti R. The efficacy and tolerability of glucosamine sulfate in the treatment of knee osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Current Therapeutic Research Clinical and Experimental* 2009;70:185-196.

Goregaonkar A, Mathiazhagan KJ, Shah RR, Kapoor PS, Taneja P, Sharma A, Bolmall C, Baliga VP. Comparative assessment of the effectiveness and tolerability of Lornoxicam 8mg BID and Diclofenac 50 mg TID in adult indian patients with osteoarthritis of the hip or knee: a 4-week, double-blind, randomized, comparative, multicenter study. *Current Therapeutic Research Clinical and Experimental* 2009;70:56-68.

Gur A, Cosut A, Sarac AJ, Cevik R, Nas K, Uyar A. Efficacy of different therapy regimes of low-power laser in painful osteoarthritis of the knee: a double-blind and randomized-controlled trial. *Lasers Surg Med* 2003;33(5):330-338.

Guyatt GH, Thorlund K, Oxman AD, et al. Grade Guidelines 13. Preparing Summary of Findings Tables and Evidence Profiles—Continuous Outcomes. *Journal of Clinical Epidemiology* 2013; 66(2): 173-183.

Herrera JA, Millan A, Ramos R, Fuentes P, Gonzalez M. Evaluation of the effectiveness and tolerability of controlled-release Diclofenac-potassium versus immediate-release Diclofenac-potassium in the treatment of knee osteoarthritis. *Current Therapeutic Research Clinical and Experimental* 2007;68:82-93.

Herrlin S, Hallander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. *Knee Surg Sports Traumatol Arthrosc* 2007;15(4):393-401.

Heybeli N, Doral MN, Atay OA, lu G, Uz^mmcⁿgil A. [Intra-articular sodium hyaluronate injections after arthroscopic debridement for osteoarthritis of the knee: a prospective, randomized, controlled study]. *Acta orthopaedica et traumatologica turcica* 2008;42:221-227.

Haupt JB, McMillan R, Wein C, Paget-Dellio SD. Effect of glucosamine hydrochloride in the treatment of pain of osteoarthritis of the knee. *J Rheumatol* 1999;26(11):2423-2430.

Huang MH, Chen CH, Chen TW, Weng MC, Wang WT, Wang YL. The effects of weight reduction on the rehabilitation of patients with knee osteoarthritis and obesity. *Arthritis Care Res* 2000;13(6):398-405.

Huang MH, Lin YS, Yang RC, Lee CL. A comparison of various therapeutic exercises on the functional status of patients with knee osteoarthritis. *Semin Arthritis Rheum* 2003;32(6):398-406.

Huang MH, Yang RC, Lee CL, Chen TW, Wang MC. Preliminary results of integrated therapy for patients with knee osteoarthritis. *Arthritis Rheum* 2005;53(6):812-820.

Huang TL, Chang CC, Lee CH, Chen SC, Lai CH, Tsai CL. Intra-articular injections of sodium hyaluronate (Hyalgan(R)) in osteoarthritis of the knee. a randomized, controlled, double-blind, multicenter trial in the asian population. *BMC Musculoskelet Disord* 2011;12:221.

Hughes R, Carr A. A randomized, double-blind, placebo-controlled trial of glucosamine sulphate as an analgesic in osteoarthritis of the knee. *Rheumatology (Oxford)* 2002;41(3):279-284.

Hurley MV; Walsh NE; Mitchell HL; Pimm TJ; Patel A; Williamson E; Jones RH; Dieppe PA; Reeves BC. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster randomized trial. *Arthritis Rheum.* 2007; 57(7): 1211-1219.

Jan MH,Lin CH,Lin YF,Lin JJ,Lin DH. Effects of weight-bearing versus nonweight-bearing exercise on function, walking speed, and position sense in participants with knee osteoarthritis: a randomized controlled trial. *Arch Phys Med Rehabil* 2009;90(6):897-904.

Jan MH,Lin JJ,Liau JJ,Lin YF,Lin DH. Investigation of clinical effects of high- and low-resistance training for patients with knee osteoarthritis: a randomized controlled trial. *Phys Ther* 2008;88(4):427-436.

Jones A,Doherty M. Intra-articular corticosteroids are effective in osteoarthritis but there are no clinical predictors of response. *Ann Rheum Dis* 1996;55(11):829-832.

Jorgensen A,Stengaard-Pedersen K,Simonsen O,Pfeiffer-Jensen M,Eriksen C,Bliddal H,Pedersen NW,Bodtker S,Horslev-Petersen K,Snerum LO,Egund N,Frimer-Larsen H. Intra-articular hyaluronan is without clinical effect in knee osteoarthritis: a multicentre, randomised, placebo-controlled, double-blind study of 337 patients followed for 1 year. *Ann Rheum Dis* 2010.

Juni P,Reichenbach S,Trelle S,Tschannen B,Wandel S,Jordi B,Zullig M,Guetg R,Hauselmann HJ,Schwarz H,Theiler R,Ziswiler HR,Dieppe PA,Villiger PM,Egger M. Efficacy and safety of intraarticular hylan or hyaluronic acids for osteoarthritis of the knee: a randomized controlled trial. *Arthritis Rheum* 2007;56(11):3610-3619.

Kahan A,Uebelhart D,De VF,Delmas PD,Reginster JY. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2009;60(2):524-533.

Kalunian KC,Moreland LW,Klashman DJ,Brion PH,Concoff AL,Myers S,Singh R,Ike RW,Seeger LL,Rich E,Skovron ML. Visually-guided irrigation in patients with early knee osteoarthritis: a multicenter randomized, controlled trial. *Osteoarthritis Cartilage* 2000;8(6):412-418.

Karbowski A. Double-blind, parallel comparison of etodolac and indomethacin in patients with osteoarthritis of the knee. *Curr Med Res Opin* 1991;12(5):309-317.

Karlsson J,Sjogren LS,Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. *Rheumatology (Oxford)* 2002;41(11):1240-1248.

Kirkley A,Birmingham TB,Litchfield RB,Giffin JR,Willits KR,Wong CJ,Feagan BG,Donner A,Griffin SH,D'Ascanio LM,Pope JE,Fowler PJ. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2008;359(11):1097-1107.

Kirkley A,Webster-Bogaert S,Litchfield R,Amendola A,MacDonald S,McCalden R,Fowler P. The effect of bracing on varus gonarthrosis. *J Bone Joint Surg Am* 1999;81(4):539-548.

Kivitz A,Eisen G,Zhao WW,Bevirt T,Recker DP. Randomized placebo-controlled trial comparing efficacy and safety of Valdecoxib with Naproxen in patients with osteoarthritis. *J Fam Pract* 2002;51(6):530-537.

Kivitz AJ,Greenwald MW,Cohen SB,Polis AB,Najarian DK,Dixon ME,Moidel RA,Green JA,Baraf HS,Petruschke RA,Matsumoto AK,Geba GP. Efficacy and safety of Rofecoxib 12.5mg versus nabumetone 1,000 mg in patients with osteoarthritis of the knee: a randomized controlled trial. *J Am Geriatr Soc* 2004;52(5):666-674.

Kovar PA,Allegrente JP,MacKenzie CR,Peterson mg,Gutin B,Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med* 1992;116(7):529-534.

La mg,Tirri G,Cacace E,Perpignano G,Covelli M,Pipitone V,D'Agostino P,Magaro M,Ferraccioli G,Mascia MT,Manzini E,Minari C,Barreca C,Marcolongo R,Paresce E,Colombo B. Quality of life assessment during six months of NSAID treatment [Gonarthrosis and Quality of Life (GOAL) Study]. *Clin Exp Rheumatol* 1998;16(1):49-54.

Lane NE,Schnitzer TJ,Birbara CA,Mokhtarani M,Shelton DL,Smith MD,Brown MT. Tanezumab for the treatment of pain from osteoarthritis of the knee. *N Engl J Med* 2010 Oct 14;363(16):1521-1531.

Le Graverand MP,Brandt K,Mazzuca SA,Raunig D,Vignon E. Progressive increase in body mass index is not associated with a progressive increase in joint space narrowing in obese women with osteoarthritis of the knee. *Ann Rheum Dis* 2009;68(11):1734-1738.

Lee P,Davis P,Prat A. The efficacy of diflunisal in osteoarthritis of the knee. A Canadian Multicenter Study. *J Rheumatol* 1985;12(3):544-548.

Lee P,Davis P,Prat A. The efficacy of diflunisal in osteoarthritis of the knee: an extended study. *J Rheumatol* 1986;13(3):666-667.

Lee PB,Kim YC,Lim YJ,Lee CJ,Sim WS,Ha CW,Bin SI,Lim KB,Choi SS,Lee SC. Comparison between high and low molecular weight hyaluronates in knee osteoarthritis patients: open-label, randomized, multicentre clinical trial. *J Int Med Res* 2006;34(1):77-87.

Lehmann R,Brzosko M,Kopsa P,Nischik R,Kreisse A,Thurston H,Litschig S,Sloan VS. Efficacy and tolerability of Lumiracoxib 100mg once daily in knee osteoarthritis: a 13-week, randomized, double-blind study versus placebo and Celecoxib . *Curr Med Res Opin* 2005;21(4):517-526.

Levy RM,Khokhlov A,Kopenkin S,Bart B,Ermolova T,Kantemirova R,Mazurov V,Bell M,Caldron P,Pillai L,Burnett BP. Efficacy and safety of flavocoxid, a novel therapeutic, compared with Naproxen: a randomized multicenter controlled trial in subjects with osteoarthritis of the knee. *Adv Ther* 2010 Oct;27(10):731-742.

Liang TH,Hsu PN. Double-blind, randomised, comparative trial of etodolac SR versus Diclofenac in the treatment of osteoarthritis of the knee. *Curr Med Res Opin* 2003;19(4):336-341.

Lin DH,Lin CH,Lin YF,Jan MH. Efficacy of 2 non-weight-bearing interventions, proprioception training versus strength training, for patients with knee osteoarthritis: a randomized clinical trial. *J Orthop Sports Phys Ther* 2009;39(6):450-457.

Lohmander LS,Dalen N,Englund G,Hamalainen M,Jensen EM,Karlsson K,Odensten M,Ryd L,Sernbo I,Suomalainen O,Tegnander A. Intra-articular hyaluronan injections in the treatment of osteoarthritis of the knee: a randomised, double blind, placebo controlled multicentre trial. Hyaluronan Multicentre Trial Group. *Ann Rheum Dis* 1996;55(7):424-431.

Lohmander LS,McKeith D,Svensson O,Malmenas M,Bolin L,Kalla A,Genti G,Szechinski J,Ramos-Remus C. A randomised, placebo controlled, comparative trial of the gastrointestinal safety and efficacy of AZD3582 versus Naproxen in osteoarthritis. *Ann Rheum Dis* 2005;64(3):449-456.

- Louthrenoo W, Nilganuwong S, Aksaranugraha S, Asavatanabodee P, Saengnipanthkul S, Thai Study Group. The efficacy, safety and carry-over effect of Diacerein in the treatment of painful knee osteoarthritis: a randomised, double-blind, NSAID-controlled study. *Osteoarthritis Cartilage* 2007;15(6):605-614.
- Lucker PW, Pawlowski C, Friedrich I, Faiella F, Magni E. Double-blind, randomised, multi-centre clinical study evaluating the efficacy and tolerability of nimesulide in comparison with etodolac in patients suffering from osteoarthritis of the knee. *Eur J Rheumatol Inflamm* 1994;14(2):29-38.
- Lundsgaard C, Dufour N, Fallentin E, Winkel P, Gluud C. Intra-articular sodium hyaluronate 2 mL versus physiological saline 20 mL versus physiological saline 2 mL for painful knee osteoarthritis: a randomized clinical trial. *Scand J Rheumatol* 2008;37(2):142-150.
- Luyten FP, Geusens P, Malaise M, De CL, Westhovens R, Raeman F, Vander MD, Mathy L, Hauzeur JP, De KF, Van den Bosch F. A prospective randomised multicentre study comparing continuous and intermittent treatment with Celecoxib in patients with osteoarthritis of the knee or hip. *Ann Rheum Dis* 2007;66(1):99-106.
- Maheu E, Zaim M, Appelboom T, Jeka S, Trc T, Berenbaum F, Maasalu K, Berenbaum F. Comparative efficacy and safety of two different molecular weight (MW) hyaluronans F60027 and Hylan G-F20 in symptomatic osteoarthritis of the knee (KOA). Results of a non inferiority, prospective, randomized, controlled trial. *Clin Exp Rheumatol* 2011 May;29(3):527-535.
- Maillefert JF, Hudry C, Baron G, Kieffert P, Bourgeois P, Lechevalier D, Coutaux A, Dougados M. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis: a prospective randomized controlled study. *Osteoarthritis Cartilage* 2001;9(8):738-745.
- Manheimer E, Lim B, Lao L, Berman B. Acupuncture for knee osteoarthritis--a randomised trial using a novel sham. *Acupunct Med* 2006;24 Suppl:S7-14.
- Matts SGF, Hazleman BL, Houben H, Dhondt E, Tebbs VM. Controlled study of once-daily, sustained release ibuprofen in osteoarthritis. *Current Therapeutic Research, Clinical & Experimental* 1993;53:394-400.
- Maurer BT, Stern AG, Kinossian B, Cook KD, Schumacher HR. Osteoarthritis of the knee: isokinetic quadriceps exercise versus an educational intervention. *Arch Phys Med Rehabil* 1999;80(10):1293-1299.
- Mazieres B, Combe B, Phan VA, Tondut J, Grynfeldt M. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study. *J Rheumatol* 2001;28(1):173-181.
- Mazieres B, Hucher M, Zaim M, Garnerio P. Effect of chondroitin sulphate in symptomatic knee osteoarthritis: a multicentre, randomised, double-blind, placebo-controlled study. *Ann Rheum Dis* 2007;66(5):639-645.
- McAlindon T, Formica M, Lavalley M, Lehmer M, Kabbara K. Effectiveness of glucosamine for symptoms of knee osteoarthritis: results from an internet-based randomized double-blind controlled trial. *Am J Med* 2004;117(9):643-649.

- McCarthy CJ,Mills PM,Pullen R,Roberts C,Silman A,Oldham JA. Supplementing a home exercise programme with a class-based exercise programme is more effective than home exercise alone in the treatment of knee osteoarthritis. *Rheumatology (Oxford)* 2004;43(7):880-886.
- McIlwain H,Silverfield JC,Cheatum DE,Poiley J,Taborn J,Ignaczak T,Multz CV. Intra-articular orpotein in osteoarthritis of the knee: a placebo-controlled efficacy, safety, and dosage comparison. *Am J Med* 1989;87(3):295-300.
- McKenna F,Borenstein D,Wendt H,Wallemark C,Lefkowitz JB,Geis GS. Celecoxib versus Diclofenac in the management of osteoarthritis of the knee. *Scand J Rheumatol* 2001;30(1):11-18.
- McKenna F,Weaver A,Fiechtner JJ,Bello AE,Fort JG. COX-2 specific inhibitors in the management of osteoarthritis of the knee: a placebo-controlled, randomized, double-blind study. *J Clin Rheumatol* 2001;7(3):151-159.
- Mehta K,Gala J,Bhasale S,Naik S,Modak M,Thakur H,Deo N,Miller MJ. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial [ISRCTN25438351]. *BMC Complement Altern Med* 2007;7:34.
- Meng CR,Fan L,Fu WB,Li Y. Clinical research on abdominal acupuncture plus conventional acupuncture for knee osteoarthritis. *J Tradit Chin Med* 2009;29(4):249-252.
- Miceli-Richard C,Le BM,Schmidely N,Dougados M. Paracetamol in osteoarthritis of the knee. *Ann Rheum Dis* 2004;63(8):923-930.
- Miller GD,Nicklas BJ,Davis C,Loeser RF,Lenchik L,Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring)* 2006;14(7):1219-1230.
- Miller GD,Rejeski WJ,Williamson JD,Morgan T,Sevick MA,Loeser RF,Ettinger WH,Messier SP. The Arthritis, Diet and Activity Promotion Trial (ADAPT): design, rationale, and baseline results. *Control Clin Trials* 2003;24(4):462-480.
- Minns Lowe CJ,Barker KL,Holder R,Sackley CM. Comparison of postdischarge physiotherapy versus usual care following primary total knee arthroplasty for osteoarthritis: an exploratory pilot randomized clinical trial. *Clin Rehabil* 2011 Dec 16.
- Moller I,Perez M,Monfort J,Benito P,Cuevas J,Perna C,Domenech G,Herrero M,Montell E,Verges J. Effectiveness of chondroitin sulphate in patients with concomitant knee osteoarthritis and psoriasis: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage* 2010.
- Moseley JB,O'Malley K,Petersen NJ,Menke TJ,Brody BA,Kuykendall DH,Hollingsworth JC,Ashton CM,Wray NP. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002;347(2):81-88.
- Navarro-Sarabia F,Coronel P,Collantes E,Navarro FJ,de la Serna AR,Naranjo A,Gimeno M,Herrero-Beaumont G. A 40-month multicentre, randomised placebo-controlled study to assess the efficacy and carry-over effect of repeated intra-articular injections of hyaluronic acid in knee osteoarthritis: the AMELIA project. *Ann Rheum Dis* 2011 Nov;70(11):1957-1962.

Niemeyer P,Schmal H,Hauschild O,von HJ,Sudkamp NP,Kostler W. Open-wedge osteotomy using an internal plate fixator in patients with medial-compartment gonarthrosis and varus malalignment: 3-year results with regard to preoperative arthroscopic and radiographic findings. *Arthroscopy* 2010 Dec;26(12):1607-1616.

Nigg BM,Emery C,Hiemstra LA. Unstable shoe construction and reduction of pain in osteoarthritis patients. *Med Sci Sports Exerc* 2006;38(10):1701-1708.

Noack W,Fischer M,Forster KK,Rovati LC,Setnikar I. Glucosamine sulfate in osteoarthritis of the knee. *Osteoarthritis Cartilage* 1994;2(1):51-59.

O'Reilly SC,Muir KR,Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. *Ann Rheum Dis* 1999;58(1):15-19.

Ottlinger B,Gomor B,Michel BA,Pavelka K,Beck W,Elsasser U. Efficacy and safety of eltenac gel in the treatment of knee osteoarthritis. *Osteoarthritis Cartilage* 2001;9(3):273-280.

Paul S,Das N,Ghosh S. The effects of Aceclofenac and nabumetone in osteoarthritis. *JNMA J Nepal Med Assoc* 2009;48(174):121-125.

Pavelka K,Coste P,Geher P,Krejci G. Efficacy and safety of piascledine 300 versus chondroitin sulfate in a 6 months treatment plus 2 months observation in patients with osteoarthritis of the knee. *Clin Rheumatol* 2010;29(6):659-670.

Pavelka K,Coste P,Geher P,Krejci G. Erratum to: Efficacy and safety of piascledine 300 versus chondroitin sulfate in a 6 months treatment plus 2 months observation in patients with osteoarthritis of the knee. *Clin Rheumatol* 2010.

Pavelka K,Gatterova J,Olejarova M,Machacek S,Giacovelli G,Rovati LC. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind study. *Arch Intern Med* 2002;162(18):2113-2123.

Pavelka K,Sedlackova M,Gatterova J,Becvar R,Pavelka K. Glycosaminoglycan polysulfuric acid (GAGPS) in osteoarthritis of the knee. *Osteoarthritis Cartilage* 1995;3(1):15-23.

Pavelka K,Trc T,Karpas K,Vitek P,Sedlackova M,Vlasakova V,Bohmova J,Rovensky J. The efficacy and safety of Diacerein in the treatment of painful osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled study with primary end points at two months after the end of a three-month treatment period. *Arthritis Rheum* 2007;56(12):4055-4064.

Pavelka K,Uebelhart D. Efficacy evaluation of highly purified intra-articular hyaluronic acid (Sinovial((R))) versus hylan G-F20 (Synvisc((R))) in the treatment of symptomatic knee osteoarthritis. A double-blind, controlled, randomized, parallel-group non-inferiority study. *Osteoarthritis Cartilage* 2011 Nov;19(11):1294-1300.

Pavelka K,Uebelhart D. Efficacy evaluation of highly purified intra-articular hyaluronic acid (Sinovial(registered trademark)) versus hylan G-F20 (Synvisc(registered trademark)) in the treatment of symptomatic knee osteoarthritis. A double-blind, controlled, randomized, parallel-gr. *Osteoarthritis and Cartilage* 2011 Nov;19(11):1294-1300.

Perlman AI, Sabina A, Williams AL, Njike VY, Katz DL. Massage therapy for osteoarthritis of the knee: a randomized controlled trial. *Arch Intern Med* 2006;166(22):2533-2538.

Petrella RJ, Petrella M. A prospective, randomized, double-blind, placebo controlled study to evaluate the efficacy of intraarticular hyaluronic acid for osteoarthritis of the knee. *J Rheumatol* 2006;33(5):951-956.

Pham T, Maillefert JF, Hudry C, Kieffert P, Bourgeois P, Lechevalier D, Dougados M. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis. A two-year prospective randomized controlled study. *Osteoarthritis Cartilage* 2004;12(1):46-55.

Pongsoipetch B, Tantikul C. Open-wedge high tibial osteotomy in varus knee osteoarthritis: a 5-year prospective cohort study. *J Med Assoc Thai* 2009;92 Suppl 6:S109-S114.

Puhl W, Bernau A, Greiling H, Kopcke W, Pforringer W, Steck KJ, Zacher J, Scharf HP. Intra-articular sodium hyaluronate in osteoarthritis of the knee: a multicenter, double-blind study. *Osteoarthritis Cartilage* 1993;1(4):233-241.

Puopolo A, Boice JA, Fidelholtz JL, Littlejohn TW, Miranda P, Berrocal A, Ko A, Cichanowitz N, Reicin AS. A randomized placebo-controlled trial comparing the efficacy of Etoricoxib 30 mg and ibuprofen 2400 mg for the treatment of patients with osteoarthritis. *Osteoarthritis Cartilage* 2007;15(12):1348-1356.

Queiros MV. Piroxicam and oxaprozin: A crossover comparison in the management of osteoarthritis. *Curr Ther Res Clin Exp* 1990;47:466-474.

Rai J, Pal SK, Gul A, Senthil R, Singh H. Efficacy of chondroitin sulfate and glucosamine sulfate in the progression of symptomatic knee osteoarthritis: A randomized, placebo-controlled, double blind study. *Bulletin, Postgraduate Institute of Medical Education and Research, Chandigarh* 2004;38(1):18-22.

Raman R, Dutta A, Day N, Sharma HK, Shaw CJ, Johnson GV. Efficacy of Hylan G-F 20 and Sodium Hyaluronate in the treatment of osteoarthritis of the knee -- a prospective randomized clinical trial. *Knee* 2008;15(4):318-324.

Ravaud P, Flipo RM, Boutron I, Roy C, Mahmoudi A, Giraudeau B, Pham T. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *BMJ* 2009;338:b421.

Raynauld JP, Buckland-Wright C, Ward R, Choquette D, Haraoui B, Martel-Pelletier J, Uthman I, Khy V, Tremblay JL, Bertrand C, Pelletier JP. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2003;48(2):370-377.

Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, Giacovelli G, Henrotin Y, Dacre JE, Gossett C. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet* 2001;357(9252):251-256.

Reichelt A, Forster KK, Fischer M, Rovati LC, Setnikar I. Efficacy and safety of intramuscular glucosamine sulfate in osteoarthritis of the knee. A randomised, placebo-controlled, double-blind study. *Arzneimittelforschung* 1994;44(1):75-80.

- Rejeski WJ,Focht BC,Messier SP,Morgan T,Pahor M,Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol* 2002;21(5):419-426.
- Rindone JP,Hiller D,Collacott E,Nordhaugen N,Arriola G. Randomized, controlled trial of glucosamine for treating osteoarthritis of the knee. *West J Med* 2000;172(2):91-94.
- Roth SH,Shainhouse JZ. Efficacy and safety of a topical Diclofenac solution (pennsaid) in the treatment of primary osteoarthritis of the knee: a randomized, double-blind, vehicle-controlled clinical trial. *Arch Intern Med* 2004;164(18):2017-2023.
- Rother M,Lavins BJ,Kneer W,Lehnhardt K,Seidel EJ,Mazgareanu S. Efficacy and safety of epicutaneous Ketoprofen in Transfersome (IDEA-033) versus oral Celecoxib and placebo in osteoarthritis of the knee: multicentre randomised controlled trial. *Ann Rheum Dis* 2007;66(9):1178-1183.
- Rudan JF,Simurda MA. High tibial osteotomy. A prospective clinical and roentgenographic review. *Clin Orthop Relat Res* 1990;(255):251-256.
- Rudan JF,Simurda MA. Valgus high tibial osteotomy. A long-term follow-up study. *Clin Orthop Relat Res* 1991;(268):157-160.
- Sanchez M,Anitua E,Azofra J,Aguirre JJ,Andia I. Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. *Clin Exp Rheumatol* 2008;26(5):910-913.
- Sangdee C,Teekachunhatean S,Sananpanich K,Sugandhavesa N,Chiewchantanakit S,Pojchamarnwiputh S,Jayasvasti S. Electroacupuncture versus Diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *BMC Complement Altern Med* 2002;2:3.
- Saragaglia D,Blaysat M,Inman D,Mercier N. Outcome of opening wedge high tibial osteotomy augmented with a Biosorb(R) wedge and fixed with a plate and screws in 124 patients with a mean of ten years follow-up. *Int Orthop* 2010 Jul 29:.
- Schnitzer TJ,Hochberg MC,Marrero CE,Duquesroix B,Frayssinet H,Beekman M. Efficacy and safety of Naproxen in patients with osteoarthritis of the knee: a 53-week prospective randomized multicenter study. *Semin Arthritis Rheum* 2011 Feb;40(4):285-297.
- Schnitzer TJ,Kamin M,Olson WH. Tramadol allows reduction of Naproxen dose among patients with Naproxen-responsive osteoarthritis pain: a randomized, double-blind, placebo-controlled study. *Arthritis Rheum* 1999;42(7):1370-1377.
- Schnitzer TJ, Kivitz A, Frayssinet H, Duquesroix B. Efficacy and safety of Naproxen in the treatment of patients with osteoarthritis of the knee: a 13-week prospective, randomized, multicenter study. *Osteoarthritis Cartilage* 2010;18(5):629-639.
- Schnitzer TJ,Kivitz AJ,Lipetz RS,Sanders N,Hee A. Comparison of the COX-inhibiting nitric oxide donator AZD3582 and Rofecoxib in treating the signs and symptoms of Osteoarthritis of the knee. *Arthritis Rheum* 2005;53(6):827-837.

Schnitzer TJ, Pelletier JP, Haselwood DM, Ellison WT, Ervin JE, Gordon RD, Lisse JR, Archambault WT, Sampson AR, Fezatte HB, Phillips SB, Bernstein JE. Civamide Cream 0.075% in Patients with Osteoarthritis of the Knee: A 12-Week Randomized Controlled Clinical Trial with a Longterm Extension. *J Rheumatol* 2011 Nov 15:.

Schnitzer TJ, Pelletier JP, Haselwood DM, Ellison WT, Ervin JE, Gordon RD, Lisse JR, Archambault WT, Sampson AR, Fezatte HB, Phillips SB, Bernstein JE. Civamide cream 0.075% in patients with osteoarthritis of the knee: a 12-week randomized controlled clinical trial with a longterm extension. *J Rheumatol* 2012 Mar;39(3):610-620.

Schnitzer TJ, Tesser JR, Cooper KM, Altman RD. A 4-week randomized study of Acetaminophen extended-release versus Rofecoxib in knee osteoarthritis. *Osteoarthritis Cartilage* 2009;17(1):1-7.

Schnitzer TJ, Weaver AL, Polis AB, Petruschke RA, Geba GP. Efficacy of Rofecoxib, Celecoxib, and Acetaminophen in patients with osteoarthritis of the knee. A combined analysis of the VACT studies. *J Rheumatol* 2005;32(6):1093-1105.

Schroter S, Gonser CE, Konstantinidis L, Helwig P, Albrecht D. High complication rate after biplanar open wedge high tibial osteotomy stabilized with a new spacer plate (Position HTO plate) without bone substitute. *Arthroscopy* 2011 May; 27(5):644-652.

Schroter S, Gonser CE, Konstantinidis L, Helwig P, Albrecht D. High complication rate after biplanar open wedge high tibial osteotomy stabilized with a new spacer plate (position HTO plate) without bone substitute. *Arthroscopy - Journal of Arthroscopic and Related Surgery* 2011 May;27(5):644-652.

Shakoor MA, Rahman MS, Azad AK, Islam MS. Effects of isometric quadriceps muscle strengthening exercise on chronic osteoarthritis of the knee. *Bangladesh Med Res Counc Bull* 2010 Apr;36(1):20-22.

Silva LE, Valim V, Pessanha AP, Oliveira LM, Myamoto S, Jones A, Natour J. Hydrotherab vpy versus conventional land-based exercise for the management of patients with osteoarthritis of the knee: a randomized clinical trial. *Phys Ther* 2008;88(1):12-21.

Sisto DJ, Mitchell IL. UniSpacer arthroplasty of the knee. *J Bone Joint Surg Am* 2005;87(8):1706-1711.

Smith MD, Wetherall M, Darby T, Esterman A, Slavotinek J, Roberts-Thomson P, Coleman M, Ahern MJ. A randomized placebo-controlled trial of arthroscopic lavage versus lavage plus intra-articular corticosteroids in the management of symptomatic osteoarthritis of the knee. *Rheumatology (Oxford)* 2003;42(12):1477-1485.

Song IH, Song EK, Seo HY, Lee KB, Yim JH, Seon JK. Patellofemoral Alignment and Anterior Knee Pain After Closing- and Opening-Wedge Valgus High Tibial Osteotomy. *Arthroscopy* 2012 Apr 19.

Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *Am J Phys Med Rehabil* 2012 May;91(5):411-417.

Suarez-Almazor ME, Looney C, Liu Y, Cox V, Pietz K, Marcus DM, Street RL. A randomized controlled trial of acupuncture for osteoarthritis of the knee: effects of patient-provider communication. *Arthritis Care Res (Hoboken)* 2010 Sep;62(9):1229-1236.

Taechaarpornkul W,Suvapan D,Theppanom C,Chanthipwaree C,Chirawatkul A. Comparison of the effectiveness of six and two acupuncture point regimens in osteoarthritis of the knee: a randomised trial. *Acupunct Med* 2009;27(1):3-8.

Tannenbaum H,Berenbaum F,Reginster JY,Zacher J,Robinson J,Poor G,Bliddal H,Uebelhart D,Adami S,Navarro F,Lee A,Moore A,Gimona A. Lumiracoxib is effective in the treatment of osteoarthritis of the knee: a 13 week, randomised, double blind study versus placebo and Celecoxib . *Ann Rheum Dis* 2004;63(11):1419-1426.

Tao QW,Xu Y,Jin DE,Yan XP. Clinical efficacy and safety of Gubitong Recipe () in treating osteoarthritis of knee joint. *Chin J Integr Med* 2009;15(6):458-461.

Teixeira PE,Piva SR,Fitzgerald GK. Effects of Impairment-Based Exercise on Performance of Specific Self-Reported Functional Tasks in Individuals With Knee Osteoarthritis. *Phys Ther* 2011 Oct 14:.

Toda Y,Tsukimura N. A comparative study on the effect of the insole materials with subtalar strapping in patients with medial compartment osteoarthritis of the knee. *Modern Rheumatology* 2004;14(6):459-465.

Toda Y,Tsukimura N. A six-month followup of a randomized trial comparing the efficacy of a lateral-wedge insole with subtalar strapping and an in-shoe lateral-wedge insole in patients with varus deformity osteoarthritis of the knee. *Arthritis Rheum* 2004;50(10):3129-3136.

Toda Y,Tsukimura N. Influence of concomitant heeled footwear when wearing a lateral wedged insole for medial compartment osteoarthritis of the knee. *Osteoarthritis Cartilage* 2008;16(2):244-253.

Topp R,Woolley S,Hornyak J,Khuder S,Kahaleh B. The effect of dynamic versus isometric resistance training on pain and functioning among adults with osteoarthritis of the knee. *Arch Phys Med Rehabil* 2002;83(9):1187-1195.

Torri G,Vignati C,Agrifoglio E,Benvenuti M,Ceciliani L,Raschella BF,Letizia G,Martorana U,Tessari L,Thovez G,Siclari A. Aceclofenac versus Piroxicam in the management of osteoarthritis of the knee: A double-blind controlled study. *Curr Ther Res Clin Exp* 1994;55:576-583.

Trc T,Bohmova J. Efficacy and tolerance of enzymatic hydrolysed collagen (EHC) versus glucosamine sulphate (GS) in the treatment of knee osteoarthritis (KOA). *Int Orthop* 2010.

Trc T,Bohmova J. Efficacy and tolerance of enzymatic hydrolysed collagen (EHC) versus glucosamine sulphate (GS) in the treatment of knee osteoarthritis (KOA). *Int Orthop* 2011;35:341-348.

Trock DH. The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee and cervical spine. Report of randomized, double blind, placebo controlled trials. 1994;.

Tunay VB,Baltaci G,Atay AO. Hospital-based versus home-based proprioceptive and strengthening exercise programs in knee osteoarthritis. *Acta Orthop Traumatol Turc* 2010;44(4):270-277.

Tyson VC,Glynn A. A comparative study of Benoxaprofen and ibuprofen in osteoarthritis in general practice. *J Rheumatol Suppl* 1980;6:132-138.

Uebelhart D,Malaise M,Marcolongo R,De VF,Piperno M,Mailleux E,Fioravanti A,Matoso L,Vignon E. Intermittent treatment of knee osteoarthritis with oral chondroitin sulfate: a one-year, randomized, double-blind, multicenter study versus placebo. *Osteoarthritis Cartilage* 2004;12(4):269-276.

Vad VB,Bhat AL,Sculco TP,Wickiewicz TL. Management of knee osteoarthritis: knee lavage combined with hylan versus hylan alone. *Arch Phys Med Rehabil* 2003;84(5):634-637.

van-Raaij TM,Reijman M,Brouwer RW,Bierma-Zeinstra SM,Verhaar JA. Medial knee osteoarthritis treated by insoles or braces: a randomized trial. *Clin Orthop* 2010;468:1926-1932.

Vas J,Mendez C,Perea-Milla E,Vega E,Panadero MD,Leon JM,Borge MA,Gaspar O,Sanchez-Rodriguez F,Aguilar I,Jurado R. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. *BMJ* 2004;329(7476):1216.

Walker AF,Bundy R,Hicks SM,Middleton RW. Bromelain reduces mild acute knee pain and improves well-being in a dose-dependent fashion in an open study of otherwise healthy adults. 2002;9(8):681-686.

Weiner DK,Rudy TE,Morone N,Glick R,Kwoh CK. Efficacy of periosteal stimulation therapy for the treatment of osteoarthritis-associated chronic knee pain: an initial controlled clinical trial. *J Am Geriatr Soc* 2007;55(10):1541-1547.

Williams GW,Ettlinger RE,Ruderman EM,Hubbard RC,Lonien ME,Yu SS,Zhao W,Geis GS. Treatment of osteoarthritis with a once-daily dosing regimen of Celecoxib : a randomized, controlled trial. *J Clin Rheumatol* 2000;6(2):65-74.

Williams GW,Hubbard RC,Yu SS,Zhao W,Geis GS. Comparison of once-daily and twice-daily administration of Celecoxib for the treatment of osteoarthritis of the knee. *Clin Ther* 2001;23(2):213-227.

Williamson L,Wyatt MR,Yein K,Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology (Oxford)* 2007; 46(9):1445-1449

Witt C,Brinkhaus B,Jena S,Linde K,Streng A,Wagenpfeil S,Hummelsberger J,Walther HU,Melchart D,Willich SN. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet* 2005;366(9480):136-143.

Wobig M,Bach G,Beks P,Dickhut A,Runzheimer J,Schwieger G,Vetter G,Balazs E. The role of comparison of hylan G-F 20 and a lower-molecular-weight hyaluronan. *Clin Ther* 1999;21(9):1549-1562.

Wobig M,Dickhut A,Maier R,Vetter G. Viscosupplementation with hylan G-F 20: a 26-week controlled trial of efficacy and safety in the osteoarthritic knee. *Clin Ther* 1998;20(3):410-423.

Yang PF,Li D,Zhang SM,Wu Q,Tang J,Huang LK,Liu W,Xu XD,Chen SR. Efficacy of ultrasound in the treatment of osteoarthritis of the knee. *Orthop Surg* 2011 Aug;3(3):181-187.

Yip YB,Sit JW,Fung KK,Wong DY;Chong SY;Chung LH;Ng TP. Effects of a self-management arthritis programme with an added exercise component for osteoarthritic knee: randomized controlled trial. *J Adv Nur.* 2007; 59(1): 5-20

Zakeri Z,Izadi S,Bari Z,Soltani F,Narouie B,Ghasemi-Rad M. Evaluating the effects of ginger extract on knee pain, stiffness and difficulty in patients with knee osteoarthritis. *Journal of Medicinal Plant Research* 2011;5(15):3375-3379.

Zheng W,Tang F,Li J,Zhang F,Li Z,Su Y,Wu D,Ma L,Zhou H,Huang F,Zhang J,Liang D,Zhou Y,Xu H. Efficacy and safety of Diacerein in osteoarthritis of the knee: A randomized, multicenter, double-dummy, Diclofenac-controlled trial in China. *APLAR Journal of Rheumatology* 2006;9(1):64-69.

Zizic TM,Hoffman KC,Holt PA,Hungerford DS,O'Dell JR,Jacobs MA,Lewis CG,Deal CL,Caldwell JR,Cholewczynski JG,Free SM. The treatment of osteoarthritis of the knee with pulsed electrical stimulation. *J Rheumatol* 1995;22(9):1757-1761.

ADDITIONAL REFERENCES

- (1) Zhang W., Moskowitz R.W., Nuki M.B. et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part I: Critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis Cartilage* 2007 June 16;15:981-1000.
- (2) Zhang W., Moskowitz R.W., Nuki M.B. et al. OARSI recommendations for management of hip and knee osteoarthritis, Part II:OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2007 December 20;16:137-62.
- (3) Samson D.J., Grant M.D., Ratko T.A., Bonnell C.J., Ziegler K.M., Aronson N. Treatment of Primary and Secondary Osteoarthritis of the Knee. Rockville, MD: Agency for Healthcare Research and Quality; 2007 Sep 1. Report No.: 157.
- (4) Shaneyfelt TM, Centor RM. Reassessment of clinical practice guidelines: go gently into that good night. *JAMA* 2009;301(8):868-869.
- (5) Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, D.C.: National Academies Press; 2011.
- (6) Conflict of Interest in Medical Research, Education, and Practice. Washington, D.C.: National Academies Press; 2009.
- (7) Hirsh J, Guyatt G. Clinical experts or methodologists to write clinical guidelines? *Lancet* 2009;374(9686):273-275.
- (8) Atkins D, Eccles M, Flottorp S et al. Systems for grading the quality of evidence and the strength of recommendations I: critical appraisal of existing approaches The GRADE Working Group. *BMC Health Serv Res* 2004; 4(1):38.
- (9) GRADE handbook for grading quality of evidence and strength of recommendation. Schunemann H, Brozek JL, Oxman AD, editors. [Version 3.2]. 2009. The GRADE Working Group 1-1-2011.
- (10) Moher D, Dulberg CS, Wells GA. Statistical power, sample size, and their reporting in randomized controlled trials. *JAMA*. 1994;272(2):122-124.
- (11) Treadwell JR, Tregear SJ, Reston JT, Turkelson CM. A system for rating the stability and strength of medical evidence. *BMC Med Res Methodol* 2006;6:5
- (12) Higgins J, Altman D. Assessing risk of bias in included studies. In: Higgins J, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions*. John Wiley & Sons; 2008. 187-241.
- (13) Armitage P., Berry G., Matthews J.N.S *Statistical Methods in Medical Research*. 4 ed. Malden, MA: Blackwell Science; 2002
- (14) Angst F, Aeschlimann A, Michel BA, Stucki G. Minimal clinically important rehabilitation effects in patients with osteoarthritis of the lower extremities. *J Rheumatol* 2002 January;29(1):131-8.

- (15) Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. *Arthritis Rheum* 2001 August;45(4):384-91.
- (16) Tubach F, Wells GA, Ravaud P, Dougados M. Minimal clinically important difference, low disease activity state, and patient acceptable symptom state: methodological issues. *J Rheumatol* 2005 October;32(10):2025-9.
- (17) Petitti DB, Teutsch SM, Barton MB, Sawaya GF, Ockene JK, DeWitt T. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. *Ann Intern Med* 2009;150(3):199-205.
- (18) Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med*. 2004;23(20):3105-3124.
- (19) Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med*. 2010; 29(7-8): 932-944.
- (20) Lorig K, Lubeck D, Kraines RG, Seleznick M, Holan HR. Outcomes of self-help education for patients with arthritis. *Arthritis Rheum* 1985;28:680-685
- (21) Coleman S, Briffa NK, Carroll G, Inderjeeth C, Cook N, McQuade J. A randomised controlled trial of a self-management education program for osteoarthritis of the knee delivered by health care professionals. *Arthritis Res Ther* 2012;14(1):R21. PM:22284848
- (22) Fransen M, Crosbie J, Edmonds J. Physical therapy is effective for patients with osteoarthritis of the knee: a randomized controlled clinical trial. *J Rheumatol* 2001;28(1):156-164. PM:11196518
- (23) Bennell KL, Hinman RS, Metcalf BR et al. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis* 2005;64(6):906-912. PM:15897310
- (24) Borjesson M, Robertson E, Weidenhielm L, Mattsson E, Olsson E. Physiotherapy in knee osteoarthritis: effect on pain and walking. *Physiother Res Int* 1996;1(2):89-97. PM:9238726
- (25) Deyle GD, Henderson NE, Matekel RL, Ryder MG, Garber MB, Allison SC. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med* 2000;132(3):173-181. PM:10651597
- (26) Huang MH, Lin YS, Yang RC, Lee CL. A comparison of various therapeutic exercises on the functional status of patients with knee osteoarthritis. *Semin Arthritis Rheum* 2003;32(6):398-406. PM:12833248
- (27) Jan MH, Lin CH, Lin YF, Lin JJ, Lin DH. Effects of weight-bearing versus nonweight-bearing exercise on function, walking speed, and position sense in participants with knee osteoarthritis: a randomized controlled trial. *Arch Phys Med Rehabil* 2009;90(6):897-904. PM:19480863
- (28) Jan MH, Lin JJ, Liao JJ, Lin YF, Lin DH. Investigation of clinical effects of high- and low-resistance training for patients with knee osteoarthritis: a randomized controlled trial. *Phys Ther* 2008;88(4):427-436. PM:18218827

- (29) Ebnezar J, Nagarathna R, Bali Y, Nagendra HR. Effect of an integrated approach of yoga therapy on quality of life in osteoarthritis of the knee joint: A randomized control study. *Int J Yoga* 2011;4(2):55-63. PM:22022123
- (30) Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effects of an integrated approach of hatha yoga therapy on functional disability, pain, and flexibility in osteoarthritis of the knee joint: a randomized controlled study. *J Altern Complement Med* 2012;18(5):463-472. PM:22537508
- (31) Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effect of integrated yoga therapy on pain, morning stiffness and anxiety in osteoarthritis of the knee joint: A randomized control study. *Int J Yoga* 2012;5(1):28-36. PM:22346063
- (32) Silva LE, Valim V, Pessanha AP et al. Hydrotherapy versus conventional land-based exercise for the management of patients with osteoarthritis of the knee: a randomized clinical trial. *Phys Ther* 2008;88(1):12-21. PM:17986497
- (33) O'Reilly SC, Muir KR, Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. *Ann Rheum Dis* 1999;58(1):15-19. PM:10343535
- (34) Kovar PA, Allegrante JP, MacKenzie CR, Peterson MG, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med* 1992;116(7):529-534. PM:1543305
- (35) Fitzgerald GK, Piva SR, Gil AB, Wisniewski SR, Oddis CV, Irrgang JJ. Agility and perturbation training techniques in exercise therapy for reducing pain and improving function in people with knee osteoarthritis: a randomized clinical trial. *Phys Ther* 2011;91(4):452-469.
- (36) Lin DH, Lin CH, Lin YF, Jan MH. Efficacy of 2 non-weight-bearing interventions, proprioception training versus strength training, for patients with knee osteoarthritis: a randomized clinical trial. *J Orthop Sports Phys Ther* 2009;39(6):450-457. PM:19531879
- (37) Topp R, Woolley S, Hornyak J, III, Khuder S, Kahaleh B. The effect of dynamic versus isometric resistance training on pain and functioning among adults with osteoarthritis of the knee. *Arch Phys Med Rehabil* 2002;83(9):1187-1195. PM:12235596
- (38) Bennell KL, Hunt MA, Wrigley TV et al. Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomised controlled trial. *Osteoarthritis Cartilage* 2010;18(5):621-628. PM:20175973
- (39) Shakoor MA, Rahman MS, Azad AK, Islam MS. Effects of isometric quadriceps muscle strengthening exercise on chronic osteoarthritis of the knee. *Bangladesh Med Res Counc Bull* 2010;36(1):20-22. PM:21280554
- (40) Maurer BT, Stern AG, Kinossian B, Cook KD, Schumacher HR, Jr. Osteoarthritis of the knee: isokinetic quadriceps exercise versus an educational intervention. *Arch Phys Med Rehabil* 1999;80(10):1293-1299. PM:10527090
- (41) Azad AK, Nabi G, Shakoor MA, Moyeenuzzaman M. Role of muscle strengthening exercise on osteoarthritis of the knee joint. *J Med* 2011;12(2):120-124.

- (42) Ettinger WH, Jr., Burns R, Messier SP et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;277(1):25-31. PM:8980206
- (43) Diracoglu D, Aydin R, Baskent A, Celik A. Effects of kinesthesia and balance exercises in knee osteoarthritis. *J Clin Rheumatol* 2005;11(6):303-310. PM:16371799
- (44) Teixeira PE, Piva SR, Fitzgerald GK. Effects of Impairment-Based Exercise on Performance of Specific Self-Reported Functional Tasks in Individuals With Knee Osteoarthritis. *Phys Ther* 2011. PM:22003157
- (45) Yip YB, Sit JW, Fung KK et al. Effects of a self-management arthritis programme with an added exercise component for osteoarthritic knee: randomized controlled trial. *J Adv Nurs* 2007;59(1):20-28. PM:17559610
- (46) Focht BC, Rejeski WJ, Ambrosius WT, Katula JA, Messier SP. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum* 2005;53(5):659-665. PM:16208674
- (47) Rejeski WJ, Focht BC, Messier SP, Morgan T, Pahor M, Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol* 2002;21(5):419-426. PM:12211508
- (48) McCarthy CJ, Mills PM, Pullen R, Roberts C, Silman A, Oldham JA. Supplementing a home exercise programme with a class-based exercise programme is more effective than home exercise alone in the treatment of knee osteoarthritis. *Rheumatology (Oxford)* 2004;43(7):880-886. PM:15113993
- (49) Tunay VB, Baltaci G, Atay AO. Hospital-based versus home-based proprioceptive and strengthening exercise programs in knee osteoarthritis. *Acta Orthop Traumatol Turc* 2010;44(4):270-277. PM:21252603
- (50) Allen KD, Oddone EZ, Coffman CJ et al. Telephone-based self-management of osteoarthritis: A randomized trial. *Ann Intern Med* 2010;153(9):570-579. PM:21041576
- (51) Hurley MV, Walsh NE, Mitchell HL et al. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster randomized trial. *Arthritis Rheum* 2007;57(7):1211-1219. PM:17907147
- (52) Ravaud P, Flipo RM, Boutron I et al. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *BMJ* 2009;338:b421. PM:19237406
- (53) Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord* 2008;9:132. PM:18831740
- (54) Lee R, Kean WF. Obesity and knee osteoarthritis. *Inflammopharmacology* 2012;20(2):53-58. PM:22237485

- (55) Muthuri SG, Hui M, Doherty M, Zhang W. What if we prevent obesity? Risk reduction in knee osteoarthritis estimated through a meta-analysis of observational studies. *Arthritis Care and Research* 2011;63(7):982-990.
- (56) Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring)* 2006;14(7):1219-1230. PM:16899803
- (57) Bliddal H, Leeds AR, Stigsgaard L, Astrup A, Christensen R. Weight loss as treatment for knee osteoarthritis symptoms in obese patients: 1-year results from a randomised controlled trial. *Ann Rheum Dis* 2011;70(10):1798-1803. PM:21821622
- (58) Riecke BF, Christensen R, Christensen P et al. Comparing two low-energy diets for the treatment of knee osteoarthritis symptoms in obese patients: a pragmatic randomized clinical trial. *Osteoarthritis Cartilage* 2010;18(6):746-754. PM:20206314
- (59) Christensen R, Astrup A, Bliddal H. Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. *Osteoarthritis Cartilage* 2005;13(1):20-27. PM:15639633
- (60) Jenkinson CM, Doherty M, Avery AJ et al. Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. *BMJ* 2009;339:b3170. PM:19690345
- (61) Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 2004;141(12):901-910. PM:15611487
- (62) Suarez-Almazor ME, Looney C, Liu Y et al. A randomized controlled trial of acupuncture for osteoarthritis of the knee: effects of patient-provider communication. *Arthritis Care Res (Hoboken)* 2010;62(9):1229-1236. PM:20506122
- (63) Weiner DK, Rudy TE, Morone N, Glick R, Kwok CK. Efficacy of periosteal stimulation therapy for the treatment of osteoarthritis-associated chronic knee pain: an initial controlled clinical trial. *J Am Geriatr Soc* 2007;55(10):1541-1547. PM:17908057
- (64) Williamson L, Wyatt MR, Yein K, Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology (Oxford)* 2007;46(9):1445-1449. PM:17604311
- (65) Taechaarpornkul W, Suvapan D, Theppanom C, Chanthipwaree C, Chirawatkul A. Comparison of the effectiveness of six and two acupuncture point regimens in osteoarthritis of the knee: a randomised trial. *Acupunct Med* 2009;27(1):3-8. PM:19369186
- (66) Sangdee C, Teekachunhatean S, Sananpanich K et al. Electroacupuncture versus diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *BMC Complement Altern Med* 2002;2:3. PM:11914160
- (67) Vas J, Mendez C, Perea-Milla E et al. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. *BMJ* 2004;329(7476):1216. PM:15494348

- (68) Witt C, Brinkhaus B, Jena S et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet* 2005;366(9480):136-143. PM:16005336
- (69) Berman BM, Singh BB, Lao L et al. A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. *Rheumatology (Oxford)* 1999;38(4):346-354. PM:10378713
- (70) Fary RE, Carroll GJ, Briffa TG, Briffa NK. The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: results of a double-blind, randomized, placebo-controlled, repeated-measures trial. 2011. <http://dx.doi.org/10.1002/art.30258>; <http://www.ncbi.nlm.nih.gov/pubmed/21312188>; <http://onlinelibrary.wiley.com/journal/10.1002/%28ISSN%291529-0131/issues>
- (71) Zizic TM, Hoffman KC, Holt PA et al. The treatment of osteoarthritis of the knee with pulsed electrical stimulation. 1995. https://www.cebp.nl/vault_public/filesystem/?ID=2503; <http://www.ncbi.nlm.nih.gov/pubmed/8523357>; <http://www.jrheum.com/>
- (72) Trock DH, Bollet AJ, Markoll R. The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee and cervical spine. Report of randomized, double blind, placebo controlled trials. *J Rheumatol* 1994;21(10):1903-1911. PM:7837158
- (73) Atamaz FC, Durmaz B, Baydar M et al. Comparison of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled, multicenter study. *Arch Phys Med Rehabil* 2012;93(5):748-756. PM:22459699
- (74) Battisti E, Piazza E, Rigato M et al. Efficacy and safety of a musically modulated electromagnetic field (TAMMEF) in patients affected by knee osteoarthritis. *Clin Exp Rheumatol* 2004;22(5):568-572. PM:15485009
- (75) Huang MH, Yang RC, Lee CL, Chen TW, Wang MC. Preliminary results of integrated therapy for patients with knee osteoarthritis. *Arthritis Rheum* 2005;53(6):812-820. PM:16342083
- (76) Yang PF, Li D, Zhang SM et al. Efficacy of ultrasound in the treatment of osteoarthritis of the knee. *Orthop Surg* 2011;3(3):181-187. PM:22009649
- (77) Perlman AI, Sabina A, Williams AL, Njike VY, Katz DL. Massage therapy for osteoarthritis of the knee: a randomized controlled trial. *Arch Intern Med* 2006;166(22):2533-2538. PM:17159021
- (78) Kirkley A, Webster-Bogaert S, Litchfield R et al. The effect of bracing on varus gonarthrosis. *J Bone Joint Surg Am* 1999;81(4):539-548. PM:10225800
- (79) van-Raaij TM, Reijman M, Brouwer RW, Bierma-Zeinstra SM, Verhaar JA. Medial knee osteoarthritis treated by insoles or braces: a randomized trial. *Clin Orthop* 2010;468):1926-1932.
- (80) Brouwer RW, van Raaij TM, Verhaar JA, Coene LN, Bierma-Zeinstra SM. Brace treatment for osteoarthritis of the knee: a prospective randomized multi-centre trial. *Osteoarthritis Cartilage* 2006;14(8):777-783. PM:16563810
- (81) Bennell KL, Bowles KA, Payne C et al. Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial. *BMJ* 2011;342):d2912. PM:21593096

- (82) Baker K, Goggins J, Xie H et al. A randomized crossover trial of a wedged insole for treatment of knee osteoarthritis. *Arthritis Rheum* 2007;56(4):1198-1203. PM:17393448
- (83) Maillefert JF, Hudry C, Baron G et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis: a prospective randomized controlled study. *Osteoarthritis Cartilage* 2001;9(8):738-745. PM:11795993
- (84) Pham T, Maillefert JF, Hudry C et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis. A two-year prospective randomized controlled study. *Osteoarthritis Cartilage* 2004;12(1):46-55. PM:14697682
- (85) Toda Y, Tsukimura N. A comparative study on the effect of the insole materials with subtalar strapping in patients with medial compartment osteoarthritis of the knee. *Modern Rheumatology* 2004;14(6):459-465.
- (86) Clegg DO, Reda DJ, Harris CL et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006;354(8):795-808. PM:16495392
- (87) Mehta K, Gala J, Bhasale S et al. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial [ISRCTN25438351]. *BMC Complement Altern Med* 2007;7:34. PM:17974032
- (88) Trc T, Bohmova J. Efficacy and tolerance of enzymatic hydrolysed collagen (EHC) vs. glucosamine sulphate (GS) in the treatment of knee osteoarthritis (KOA). *Int Orthop* 2010. PM:20401752
- (89) Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum* 2001;44(11):2531-2538. PM:11710709
- (90) Zakeri Z, Izadi S, Bari Z, Soltani F, Narouie B, Ghasemi-Rad M. Evaluating the effects of ginger extract on knee pain, stiffness and difficulty in patients with knee osteoarthritis. *Journal of Medicinal Plant Research* 2011;5(15):3375-3379.
- (91) Pavelka K, Jr., Sedlackova M, Gatterova J, Becvar R, Pavelka K, Sr. Glycosaminoglycan polysulfuric acid (GAGPS) in osteoarthritis of the knee. *Osteoarthritis Cartilage* 1995;3(1):15-23. PM:7536623
- (92) Cibere J, Kopec JA, Thorne A et al. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *Arthritis Rheum* 2004;51(5):738-745. PM:15478160
- (93) Mazieres B, Combe B, Phan VA, Tondut J, Grynfeldt M. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study. *J Rheumatol* 2001;28(1):173-181. PM:11196521
- (94) Pavelka K, Coste P, Geher P, Krejci G. Efficacy and safety of piascledine 300 versus chondroitin sulfate in a 6 months treatment plus 2 months observation in patients with osteoarthritis of the knee. *Clin Rheumatol* 2010;29(6):659-670. PM:20179981
- (95) Fishman RL, Kistler CJ, Ellerbusch MT et al. Efficacy and safety of 12 weeks of osteoarthritic pain therapy with once-daily tramadol (Tramadol Contramid OAD). *J Opioid Manag* 2007;3(5):273-280. PM:18181382

- (96) Beaulieu AD, Peloso PM, Haraoui B et al. Once-daily, controlled-release tramadol and sustained-release diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial. *Pain Res Manag* 2008;13(2):103-110. PM:18443672
- (97) Miceli-Richard C, Le BM, Schmidely N, Dougados M. Paracetamol in osteoarthritis of the knee. *Ann Rheum Dis* 2004;63(8):923-930. PM:15249319
- (98) Schnitzer TJ, Weaver AL, Polis AB, Petruschke RA, Geba GP. Efficacy of rofecoxib, celecoxib, and acetaminophen in patients with osteoarthritis of the knee. A combined analysis of the VACT studies. *J Rheumatol* 2005;32(6):1093-1105. PM:15940774
- (99) Evcik D, Maralcan G, Kuru I. The efficacy of intra-articular tenoxicam in the treatment of knee osteoarthritis. *Pain Clinic* 2003;15(4):405-408.
- (100) Ottlinger B, Gomor B, Michel BA, Pavelka K, Beck W, Elsasser U. Efficacy and safety of eltenac gel in the treatment of knee osteoarthritis. *Osteoarthritis Cartilage* 2001;9(3):273-280. PM:11300751
- (101) Rother M, Lavins BJ, Kneer W, Lehnhardt K, Seidel EJ, Mazgareanu S. Efficacy and safety of epicutaneous ketoprofen in Transfersome (IDEA-033) versus oral celecoxib and placebo in osteoarthritis of the knee: multicentre randomised controlled trial. *Ann Rheum Dis* 2007;66(9):1178-1183. PM:17363401
- (102) Chao J, Wu C, Sun B et al. Inflammatory characteristics on ultrasound predict poorer longterm response to intraarticular corticosteroid injections in knee osteoarthritis. *J Rheumatol* 2010;37(3):650-655. PM:20080918
- (103) Gaffney K, Ledingham J, Perry JD. Intra-articular triamcinolone hexacetonide in knee osteoarthritis: factors influencing the clinical response. *Ann Rheum Dis* 1995;54(5):379-381. PM:7794044
- (104) Raynauld JP, Buckland-Wright C, Ward R et al. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2003;48(2):370-377. PM:12571845
- (105) Jones A, Doherty M. Intra-articular corticosteroids are effective in osteoarthritis but there are no clinical predictors of response. *Ann Rheum Dis* 1996;55(11):829-832. PM:8976640
- (106) Caborn D, Rush J, Lanzer W, Parenti D, Murray C. A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. *J Rheumatol* 2004;31(2):333-343. PM:14760806
- (107) Arden NK, Reading IC, Jordan KM et al. A randomised controlled trial of tidal irrigation vs corticosteroid injection in knee osteoarthritis: the KIVIS Study. *Osteoarthritis Cartilage* 2008;16(6):733-739. PM:18077189
- (108) Lundsgaard C, Dufour N, Fallentin E, Winkel P, Gluud C. Intra-articular sodium hyaluronate 2 mL versus physiological saline 20 mL versus physiological saline 2 mL for painful knee osteoarthritis: a randomized clinical trial. *Scand J Rheumatol* 2008;37(2):142-150. PM:18415773

- (109) Huang TL, Chang CC, Lee CH, Chen SC, Lai CH, Tsai CL. Intra-articular injections of sodium hyaluronate (Hyalgan(R)) in osteoarthritis of the knee. a randomized, controlled, double-blind, multicenter trial in the asian population. *BMC Musculoskelet Disord* 2011;12):221. PM:21978211
- (110) Puhl W, Bernau A, Greiling H et al. Intra-articular sodium hyaluronate in osteoarthritis of the knee: a multicenter, double-blind study. *Osteoarthritis Cartilage* 1993;1(4):233-241. PM:15449510
- (111) Day R, Brooks P, Conaghan PG, Petersen M. A double blind, randomized, multicenter, parallel group study of the effectiveness and tolerance of intraarticular hyaluronan in osteoarthritis of the knee. *J Rheumatol* 2004;31(4):775-782. PM:15088306
- (112) Juni P, Reichenbach S, Trelle S et al. Efficacy and safety of intraarticular hylan or hyaluronic acids for osteoarthritis of the knee: a randomized controlled trial. *Arthritis Rheum* 2007;56(11):3610-3619. PM:17968921
- (113) Maheu E, Zaim M, Appelboom T et al. Comparative efficacy and safety of two different molecular weight (MW) hyaluronans F60027 and Hylan G-F20 in symptomatic osteoarthritis of the knee (KOA). Results of a non inferiority, prospective, randomized, controlled trial. *Clin Exp Rheumatol* 2011;29(3):527-535. PM:21722501
- (114) Lee PB, Kim YC, Lim YJ et al. Comparison between high and low molecular weight hyaluronates in knee osteoarthritis patients: open-label, randomized, multicentre clinical trial. *J Int Med Res* 2006;34(1):77-87. PM:16604827
- (115) Raman R, Dutta A, Day N, Sharma HK, Shaw CJ, Johnson GV. Efficacy of Hylan G-F 20 and Sodium Hyaluronate in the treatment of osteoarthritis of the knee -- a prospective randomized clinical trial. *Knee* 2008;15(4):318-324. PM:18430574
- (116) Karlsson J, Sjogren LS, Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. *Rheumatology (Oxford)* 2002;41(11):1240-1248. PM:12421996
- (117) Kahan A, Lleu PL, Salin L. Prospective randomized study comparing the medicoeconomic benefits of Hylan GF-20 vs. conventional treatment in knee osteoarthritis. *Joint Bone Spine* 2003;70(4):276-281. PM:12951310
- (118) Altman RD, Akemark C, Beaulieu AD, Schnitzer T. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage* 2004;12(8):642-649. PM:15262244
- (119) Sanchez M, Fiz N, Azofra J et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy* 2012;28(8):1070-1078. PM:22840987
- (120) Sanchez M, Anitua E, Azofra J, Aguirre JJ, Andia I. Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. *Clin Exp Rheumatol* 2008;26(5):910-913. PM:19032827

- (121) Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *Am J Phys Med Rehabil* 2012;91(5):411-417. PM:22513879
- (122) Bradley JD, Heilman DK, Katz BP, Gsell P, Wallick JE, Brandt KD. Tidal irrigation as treatment for knee osteoarthritis: a sham-controlled, randomized, double-blinded evaluation. *Arthritis Rheum* 2002;46(1):100-108. PM:11817581
- (123) Vad VB, Bhat AL, Sculco TP, Wickiewicz TL. Management of knee osteoarthritis: knee lavage combined with hylan versus hylan alone. *Arch Phys Med Rehabil* 2003;84(5):634-637. PM:12736873
- (124) Kirkley A, Birmingham TB, Litchfield RB et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2008;359(11):1097-1107. PM:18784099
- (125) Kalunian KC, Moreland LW, Klashman DJ et al. Visually-guided irrigation in patients with early knee osteoarthritis: a multicenter randomized, controlled trial. *Osteoarthritis Cartilage* 2000;8(6):412-418. PM:11069725
- (126) Moseley JB, O'Malley K, Petersen NJ et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002;347(2):81-88. PM:12110735
- (127) Herrlin S, Hallander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. *Knee Surg Sports Traumatol Arthrosc* 2007;15(4):393-401. PM:17216272
- (128) Brouwer RW, Bierma-Zeinstra SM, van Raaij TM, Verhaar JA. Osteotomy for medial compartment arthritis of the knee using a closing wedge or an opening wedge controlled by a Puudu plate. A one-year randomised, controlled study. *J Bone Joint Surg Br* 2006;88(11):1454-1459. PM:17075089
- (129) Song IH, Song EK, Seo HY, Lee KB, Yim JH, Seon JK. Patellofemoral Alignment and Anterior Knee Pain After Closing- and Opening-Wedge Valgus High Tibial Osteotomy. *Arthroscopy* 2012. PM:22520445
- (130) Pongsoipetch B, Tantikul C. Open-wedge high tibial osteotomy in varus knee osteoarthritis: a 5-year prospective cohort study. *J Med Assoc Thai* 2009;92 Suppl 6):S109-S114. PM:20128075
- (131) El-Azab HM, Morgenstern M, Ahrens P, Schuster T, Imhoff AB, Lorenz SGF. Limb alignment after open-wedge high tibial osteotomy and its effect on the clinical outcome. *Orthopedics* 2011;34(10):e622-e628.
- (132) Rudan JF, Simurda MA. High tibial osteotomy. A prospective clinical and roentgenographic review. *Clin Orthop Relat Res* 1990;(255):251-256. PM:2347159
- (133) Sisto DJ, Mitchell IL. UniSpacer arthroplasty of the knee. *J Bone Joint Surg Am* 2005;87(8):1706-1711. PM:16085608
- (134) Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Lawrence Erlbaum Associates, 1998.

- (135) Thorpe KE, Zwarenstein M, Oxman AD et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clin Epidemiol* 2009;62(5):464-475. PM:19348971
- (136) Petitti DB, Teutsch SM, Barton MB, Sawaya GF, Ockene JK, DeWitt T. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. *Ann Intern Med* 2009;150(3):199-205. PM:19189910
- (137) Murphy MK, Black LA, Lamping DL, McKee CM, Sanderson C.F., Askam J. Consensus development methods, and their use in clinical guideline development. *Health Technol Assess* 1998.

EXCLUDED STUDIES

A study of Naproxen and ibuprofen in patients with osteoarthritis seen in general practice. The Manchester General Practitioner Group. *Curr Med Res Opin* 1984;9(1):41-46.

Aaron RK,Skolnick AH,Reinert SE,Ciombor DM. Arthroscopic debridement for osteoarthritis of the knee. *J Bone Joint Surg Am* 2006;88(5):936-943.

Abbate LM,Stevens J,Schwartz TA,Renner JB,Helmick CG,Jordan JM. Anthropometric measures, body composition, body fat distribution, and knee osteoarthritis in women. *Obesity (Silver Spring)* 2006;14(7):1274-1281.

Abdel-Salam A,Eyres KS,Cleary J. Biological osteotomy: a technique for pain relief in the osteoarthritic knee. *Journal of Orthopaedic Rheumatology* 1991;4(1):37-45.

Abramson SB. Do nonsteroidal anti-inflammatory drugs accelerate disease progression in osteoarthritis?. *Nat Clin Pract Rheumatol* 2006;2(6):302-303.

Abu-Abeid S,Wishnitzer N,Szold A,Liebergall M,Manor O. The influence of surgically-induced weight loss on the knee joint. *Obes Surg* 2005;15(10):1437-1442.

Acebes JC,Sanchez-Pernaute O,Diaz-Oca A,Herrero-Beaumont G. Ultrasonographic assessment of Baker's cysts after intra-articular corticosteroid injection in knee osteoarthritis. *J Clin Ultrasound* 2006;34(3):113-117.

Acharya KKV,Pandey V,Rao SP. Prospective, randomized control study of use of arthroscopic debridement with or without visco supplementation in knee osteoarthritis. *Osteoporos Int* 2012 Mar;23 SUPPL. 2:S213.

Adami S,Pavelka K,Cline GA,Hosterman MA,Barton IP,Cohen SB,Bensen WG. Upper gastrointestinal tract safety of daily oral risedronate in patients taking NSAIDs: a randomized, double-blind, placebo-controlled trial. *Mayo Clin Proc* 2005;80(10):1278-1285.

Adams ME,Atkinson MH,Lussier AJ,Schulz JI,Siminovitch KA,Wade JP,Zummer M. The role of viscosupplementation with hylan G-F 20 (Synvisc) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan G-F 20 alone, hylan G-F 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone. *Osteoarthritis Cartilage* 1995;3(4):213-225.

Adams ME,Ely G. Comparison of Voltaren(TM) SR 75mg once daily with Voltaren(TM) 25mg EC three times daily in the treatment of mild to moderate osteoarthritis of the knee and hip. *CURR THER RES CLIN EXP* 1990;48:460-475.

Adams ME,Ely G. Comparison of Voltaren(TM) SR 75mg twice daily with Voltaren(TM) 50 mg EC three times daily in the treatment of moderate to severe osteoarthritis of the knee and hip. *CURR THER RES CLIN EXP* 1990;48:476-491.

Adedoyin RA,Olaogun MOB,Fagbeja OO. Effect of interferential current stimulation in management of osteo-arthritic knee pain. *Physiotherapy* 2002;88(8):493-499.

Adedoyin RA,Olaogun MOB,Oyeyemi AL. Transcutaneous electrical nerve stimulation and interferential current combined with exercise for the treatment of knee osteoarthritis: A randomised controlled trial. *Hong Kong Physiotherapy Journal* 2005;23:13-19.

- Adegbehingbe OO,Adesanya SA,Idowu TO,Okimi OC,Oyelami OA,Iwalewa EO. Clinical effects of *Garcinia kola* in knee osteoarthritis. *J Orthop Surg Res* 2008;3:34.
- Adegoke BO,Babatunde FO,Oyeyemi AL. Pain, balance, self-reported function and physical function in individuals with knee osteoarthritis. *Physiother Theory Pract* 2012 Jan;28(1):32-40.
- Adelowo OO,Chukwuani CM,Grange JJ,Ojeasebhulo EE,Onabowale BO. Comparative double blind study of the efficacy and safety of tenoxicam versus Piroxicam in osteoarthritis of knee and hip joints. *West Afr J Med* 1998;17(3):194-198.
- Afilalo M,Etropolski MS,Kuperwasser B,Kelly K,Okamoto A, Van H,Steup A,Lange B,Rauschkolb C,Haeussler J. Efficacy and safety of Tapentadol extended release compared with oxycodone controlled release for the management of moderate to severe chronic pain related to osteoarthritis of the knee: a randomized, double-blind, placebo- and active-controlled phase III study. *Clin Drug Investig* 2010;30(8):489-505.
- Agarwala S,Shah SB. Staple versus locking compression plate fixation after lateral closing wedge high tibial osteotomy. *J Orthop Surg (Hong Kong)* 2008;16(3):303-307.
- Ageberg E,Link A,Roos EM. Feasibility of neuromuscular training in patients with severe hip or knee OA: the individualized goal-based NEMEX-TJR training program. *BMC Musculoskelet Disord* 2010;11:126.
- Aglamis B,Toraman NF,Yaman H. Change of quality of life due to exercise training in knee osteoarthritis: SF-36 and WOMAC. *J Back Musculoskelet Rehabil* 2009;22(1):43-8, 46.
- Aglamis B,Toraman NF,Yaman H. The effect of a 12-week supervised multicomponent exercise program on knee OA in Turkish women. *Journal of Back and Musculoskeletal Rehabilitation* 2008;21(2):121-128.
- Aglietti P,Buzzi R,Vena LM,Baldini A,Mondaini A. High tibial valgus osteotomy for medial gonarthrosis: a 10- to 21-year study. *J Knee Surg* 2003;16(1):21-26.
- Ahlberg A,Scham S,Unander-Scharin L. Osteotomy in degenerative and rheumatoid arthritis of the knee joint. *Acta Orthop Scand* 1968;39(3):379-388.
- Ahmad N,Boutron I,Moher D,Pitrou I,Roy C,Ravaud P. Neglected external validity in reports of randomized trials: The example of hip and knee osteoarthritis. *Arthritis Care and Research* 2009;61(3):361-369.
- Akamatsu Y,Koshino T,Saito T,Wada J. Changes in osteosclerosis of the osteoarthritic knee after high tibial osteotomy. *Clin Orthop Relat Res* 1997;(334):207-214.
- Akermark C,Berg P,Bjorkman A,Malm P. Non-animal stabilised hyaluronic acid in the treatment of osteoarthritis of the knee: A tolerability study. *Clinical Drug Investigation* 2002;22(3):157-166.
- Akizuki S,Yasukawa Y,Takizawa T. Does arthroscopic abrasion arthroplasty promote cartilage regeneration in osteoarthritic knees with eburnation? A prospective study of high tibial osteotomy with abrasion arthroplasty versus high tibial osteotomy alone. *Arthroscopy* 1997;13(1):9-17.

Al Harfoushi FZA, Abou-Nouar AK, Pandey R. High tibial osteotomy for medial osteoarthritis of the knee. *Journal of Orthopaedic Surgery* 1996;4(1):41-44.

Al QM, Al HE, Hamadi T, Karar AH. Relationship between changes of body mass index and the pattern of osteoarthritis. *Journal of the Bahrain Medical Society* 2010;22(2):55-59.

Alarcon-Segovia D. Long-term treatment of symptomatic osteoarthritis with Benoxaprofen. Double-blind comparison with aspirin and ibuprofen. *J Rheumatol Suppl* 1980;6:89-99.

Al-Arfaj AS. Radiographic osteoarthritis and obesity. *Saudi Med J* 2002;23(8):938-942.

Alcidi L, Beneforti E, Maresca M, Santosuosso U, Zoppi M. Low power radiofrequency electromagnetic radiation for the treatment of pain due to osteoarthritis of the knee. 2007;59(2):140-145.

Alemдарoglu KB, Cimen O, Aydoğan NH, Atlihan D, İltar S. Early results of arthroscopic lateral retinacular release in patellofemoral osteoarthritis. *Knee* 2008;15(6):451-455.

Alentorn-Geli E, Seijas VR, Garcia BM, Alvarez DP, Steinbacher G, Cusco S, Rius VM, Cugat BR. Arthroscopic meniscal allograft transplantation without bone plugs. *Knee Surg Sports Traumatol Arthrosc* 2010;:.

Al-Jarallah KF, Shehab D, Al-Awadhi A, Nahar I, Haider MZ, Moussa MA. Are 25(OH)D Levels Related to the Severity of Knee Osteoarthritis and Function?. *Med Princ Pract* 2011 Oct 20;.

Alkire MR, Swank ML. Use of inpatient continuous passive motion versus no CPM in computer-assisted total knee arthroplasty. ;29(1):36-40.

Allen KD, Oddone EZ, Coffman CJ, Keefe FJ, Lindquist JH, Bosworth HB. Racial differences in osteoarthritis pain and function: potential explanatory factors. *Osteoarthritis Cartilage* 2010;18(2):160-167.

Allen KD, Oddone EZ, Stock JL, Coffman CJ, Lindquist JH, Juntilla KA, Lemmerman DS, Datta SK, Harrelson ML, Weinberger M, Bosworth HB. The Self-Management of OsteoArthritis in Veterans (SeMOA) Study: design and methodology. *Contemp Clin Trials* 2008;29(4):596-607.

Allen KD. Racial and ethnic disparities in osteoarthritis phenotypes. *Current Opinion in Rheumatology* 2010 Sep;22(5):528-532.

Almoammar IA, Al-Mansoor AS, Alamri NZ. Taping for knee osteoarthritis. *Almoammar Ibtesam A, Al Mansoor Afaf Saleh , Alamri Nadrah Z Taping for knee osteoarthritis Cochrane Database of Systematic Reviews: Protocols 2010 Issue 1 John Wiley & Sons , Ltd Chichester, UK DOI : 10 1002 /14651858 CD008275* 2010;.

Alok K. Combined effectiveness of Maitland's mobilization and patellar taping in patellofemoral osteoarthritis: a randomised clinical trial. 2011.

Al-Omran AS, Sadat-Ali M. Arthroscopic joint lavage in osteoarthritis of the knee. Is it effective?. *Saudi Med J* 2009;30(6):809-812.

Altman RD,Akermark C,Beaulieu AD,Schnitzer T. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage* 2004;12(8):642-649.

Altman RD,Moskowitz R. Intraarticular sodium hyaluronate (Hyalgan) in the treatment of patients with osteoarthritis of the knee: a randomized clinical trial. Hyalgan Study Group. *J Rheumatol* 1998;25(11):2203-2212.

Altman RD,Zinsenheim JR,Temple AR,Schweinle JE. Three-month efficacy and safety of Acetaminophen extended-release for osteoarthritis pain of the hip or knee: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage* 2007;15(4):454-461.

Altman RD. New guidelines for topical NSAIDs in the osteoarthritis treatment paradigm. *Curr Med Res Opin* 2010 Dec;26(12):2871-2876.

Alvarez-Nemegyei J,Bautista-Botello A,Davila-Velazquez J. Association of complementary or alternative medicine use with quality of life, functional status or cumulated damage in chronic rheumatic diseases. *Clin Rheumatol* 2009;28(5):547-551.

Al-Zahrani S,Zamzam M,Farooq M,Badr A. The evaluation of laser irradiation therapy in the treatment of osteoarthritic knee. *Bahrain Medical Bulletin* 1997;19(2):47-50.

Amadio PJ,Cummings DM. Evaluation of Acetaminophen in the management of osteoarthritis of the knee. *CURR THER RES , CLIN EXP* 1983;34:59-66.

Amendola A,Fowler PJ,Litchfield R,Kirkley S,Clatworthy M. Opening wedge high tibial osteotomy using a novel technique: early results and complications. *J Knee Surg* 2004;17(3):164-169.

Amendola A. Unicompartmental osteoarthritis in the active patient: the role of high tibial osteotomy. *Arthroscopy* 2003;19 Suppl 1:109-116.

Amor B,Benarrosh C. A method for comparing analgesics: glafenine and Paracetamol . Multicenter cross-over approach. *Clin Rheumatol* 1988;7(4):492-497.

An B,Dai K,Zhu Z,Wang Y,Hao Y,Tang T,Yan H. Baduanjin alleviates the symptoms of knee osteoarthritis. *J Altern Complement Med* 2008;14(2):167-174.

Anandacoomarasamy A,Bagga H,Ding C,Burkhardt D,Sambrook PN,March LM. Predictors of clinical response to intraarticular Hylan injections -- a prospective study using synovial fluid measures, clinical outcomes, and magnetic resonance imaging. *J Rheumatol* 2008;35(4):685-690.

Anandacoomarasamy A,Smith G,Leibman S,Caterson I,Giuffre B,Fransen M,Sambrook P,March L. Cartilage defects are associated with physical disability in obese adults. *Rheumatology (Oxford)* 2009;48(10):1290-1293.

Andelman S,Levin J,Simson J,Amadio P,Wenger M. A double-blind crossover comparison of zomepirac and placebo in pain secondary to osteoarthritis of the knee. *J Clin Pharmacol* 1980;20(5-6 Pt 1):364-370.

Anderson JJ,Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol* 1988;128(1):179-189.

- Andrews JR,Regan TP. Unicompartmental replacement for medial compartment gonarthrosis: preliminary report. *South Med J* 1979;72(6):675-680.
- Andrianakos AA,Kontelis LK,Karamitsos DG,Aslanidis SI,Georgountzos AI,Kaziolas GO,Pantelidou KV,Vafiadou EV,Dantis PC. Prevalence of symptomatic knee, hand, and hip osteoarthritis in Greece. The ESORDIG study. *J Rheumatol* 2006;33(12):2507-2513.
- Andrzejewski T,Golda W,Gruszka J,Jander P,Jeske P,Jozwik A,Kolban M,Kukielka R,Kurpik M,Kwiatkowski K,Marek M,Morawski G,Romaniuk W,Rusin Z,Scinski T,Swiatlowski T,Szawczukiewicz W,Tokarczuk K,Wojcik B. Assessment of Synvisc treatment in osteoarthritis. *Ortop Traumatol Rehabil* 2003;5(3):379-390.
- Angel JC,Liyanage SP,Griffiths WE. Double osteotomy for the relief of pain in arthritis of the knee. *Rheumatol Rehabil* 1974;13(3):109-119.
- Angst F,Aeschlimann A,Steiner W,Stucki G. Responsiveness of the WOMAC osteoarthritis index as compared with the SF-36 in patients with osteoarthritis of the legs undergoing a comprehensive rehabilitation intervention. *Ann Rheum Dis* 2001;60(9):834-840.
- Aoki T,Kaneda K,Sakurai M,Sugawara S,Nagaya I,Komatsubara Y,Shibata T,Sugioka Y,Nakashima M. [A Phase III Study of UHAC62 (Meloxicam) Capsule in Osteoarthritis of the Knee Joint]. *Rinsho Iyaku* 1997;13:973-1013.
- Aoki T,Kaneda K,Sakurai M,Sugawara S,Nagaya I,Komatsubara Y,Shibata T,Sugioka Y,Nakashima M. [Clinical Late Phase II Study of UHAC62 (Meloxicam) Capsule in Osteoarthritis of Knee Joint]. *Rinsho Iyaku* 1997;13:365-394.
- Aoki T,Kawaji W,Kuroki Y,Sugawara S,Miyoshi K,Murota K,Iwasaki Y. [Clinical Evaluation of RAK-591 on Osteoarthritis of the Knee: Double-Blind Study in Comparison with Indomethacin]. *Rinsho Iyaku* 1991;7:1543-1563.
- Aoki Y,Yasuda K,Mikami S,Ohmoto H,Majima T,Minami A. Inverted V-shaped high tibial osteotomy compared with closing-wedge high tibial osteotomy for osteoarthritis of the knee. Ten-year follow-up result. *J Bone Joint Surg Br* 2006;88(10):1336-1340.
- Appel H,Friberg S. The effect of high tibial osteotomy on pain in osteoarthritis of the knee joint. *Acta Orthop Scand* 1972;43(6):558-565.
- Appelboom T,Schuermans J,Verbruggen G,Henrotin Y,Reginster JY. Symptoms modifying effect of avocado/soybean unsaponifiables (ASU) in knee osteoarthritis. A double blind, prospective, placebo-controlled study. *Scand J Rheumatol* 2001;30(4):242-247.
- Arensi F. Comparison of efficacy and therapeutic safety of two treatments based on hyaluronic acid (Go-On and Hyalgan) in knee osteoarthritis. *Minerva Ortopedica e Traumatologica* 2006;57(3):105-111.
- Arichi S,Arichi H,Toda S. Acupuncture and rehabilitation (III) effects of acupuncture applied to the normal side on osteoarthritis deformans and rheumatoid arthritis of the knee and on disorders in motility of the knee joint after cerebral hemorrhage and thrombosis. *Am J Chin Med* 1983;11(1-4):146-149.

ARITOMI H,KAGEYAMA T,SUGAWARA S,KAWAJI W,IGARASHI M,AOKI T. Clinical Evaluation of EB-382 in the Treatment of Osteoarthritis of the Knee -A Double-Blind Comparative Study-. *Rinsho Hyoka* 1986;14:723-756.

Arjmandi BH,Khalil DA,Lucas EA,Smith BJ,Sinichi N,Hodges SB,Juma S,Munson ME,Payton ME,Tivis RD,Svanborg A. Soy protein may alleviate osteoarthritis symptoms. 2004;11(7-8):567-575.

Arroll B,Goodyear-Smith F,Shoor S. Review: Intra-articular corticosteroid injections are better than placebo for improving symptoms of knee osteoarthritis. *Evidence-Based Medicine* 2005;10(1):23.

Asai H,Nakamura R. Effect of non-steroidal anti-inflammatory drugs on osteoarthritis of the knee. With special reference to PSP clearance as an indicator. *Acta Rheumatol Scand* 1970;16(3):231-239.

Asik M,Sen C,Kilic B,Goksan SB,Ciftci F,Taser OF. High tibial osteotomy with Puddu plate for the treatment of varus gonarthrosis. *Knee Surg Sports Traumatol Arthrosc* 2006;14(10):948-954.

Assche DV,Caspel DV,Staes F,Saris DB,Bellemans J,Vanlauwe J,Luyten FP. Implementing one standardized rehabilitation protocol following autologous chondrocyte implantation or microfracture in the knee results in comparable physical therapy management. *Physiother Theory Pract* 2011 Feb;27(2):125-136.

Astephen Wilson JL,Deluzio KJ,Dunbar MJ,Caldwell GE,Hubley-Kozey CL. The association between knee joint biomechanics and neuromuscular control and moderate knee osteoarthritis radiographic and pain severity. *Osteoarthritis Cartilage* 2011 Feb;19(2):186-193.

Astorga PG,Baigun S,Galvao de FJ,Gomes de FG. Efficacy and tolerability comparison of etodolac and Piroxicam in the treatment of patients with osteoarthritis of the knee. *Curr Med Res Opin* 1991;12(6):401-412.

Atamaz F,Kirazli Y,Akkoc Y. A comparison of two different intra-articular hyaluronan drugs and physical therapy in the management of knee osteoarthritis. *Rheumatol Int* 2006;26(10):873-878.

Atra E,Metz CA,Brown BL,Teoh K. Flurbiprofen versus Diclofenac for the treatment of osteoarthritis of the knee. *DICP* 1990;24(10):920-923.

Aubin M,Marks R. The efficacy of short-term treatment with transcutaneous electrical nerve stimulation for osteo-arthritic knee pain. *Physiotherapy* 1995;81(11):669-675.

Auerbach B,Melzer C. [Cross-linked hyaluronic acid in the treatment of osteoarthritis of the knee--results of a prospective randomized trial]. *Zentralblatt für Chirurgie* 2002;127:895-899.

Avelar NB,Sim OA,Tossige-Gomes R,Neves CD,Rocha-Vieira E,Coimbra CN,Lacerda AC. The Effect of Adding Whole-Body Vibration to Squat Training on the Functional Performance and Self-Report of Disease Status in Elderly Patients with Knee Osteoarthritis: A Randomized, Controlled Clinical Study. *J Altern Complement Med* 2011 Nov 16;.

Avramidis K. Does electric stimulation of the vastus medialis muscle influence rehabilitation after total knee replacement?. 2011.

Ay S,Evcik D. The effects of pulsed electromagnetic fields in the treatment of knee osteoarthritis: a randomized, placebo-controlled trial. *Rheumatol Int* 2009;29(6):663-666.

Ayis S, Arden N, Doherty M, Pollard B, Johnston M, Dieppe P. Applying the impairment, activity limitation, and participation restriction constructs of the ICF model to osteoarthritis and low back pain trials: A reanalysis. *J Rheumatol* 2010 Sep;37(9):1923-1931.

Ayral X, Gicquere C, Duhalde A, Boucheny D, Dougados M. Effects of video information on preoperative anxiety level and tolerability of joint lavage in knee osteoarthritis. *Arthritis Rheum* 2002;47(4):380-382.

Baar-van ME. Effectiveness of exercise therapy for osteoarthritis of the hip or knee. *Nederlands Tijdschrift Fysiotherapie* 1999;Special:2-5.

Babis GC, An K, Chao EYS, Larson DR, Rand JA, Sim FH. Upper tibia osteotomy: Long term results - Realignment analysis using OASIS computer software. *J Orthop Sci* 2008;13(4):328-334.

Backstein D, Morag G, Hanna S, Safir O, Gross A. Long-term follow-up of distal femoral varus osteotomy of the knee. *J Arthroplasty* 2007;22(4 Suppl 1):2-6.

Bacon P, Luqmani RA, Bossingham DH, Daymond TJ, Grahame R, West J, Hazleman BL, Adebajo AO, Hughes GR, Abdullah M, ... A comparison of two formulations of indomethacin ('Flexin Continus' tablets and 'Indocid' capsules) in the treatment of osteoarthritis. *Curr Med Res Opin* 1990;12(2):128-134.

Bacon TH, Hole JG, North M, Burnett I. Analgesic efficacy of sustained release Paracetamol in patients with osteoarthritis of the knee. *Br J Clin Pharmacol* 2002;53(6):629-636.

Badria FA, El-Farahaty T, Shabana AA, Hawas SA, El-Batoty MF. Boswellia-curcumin preparation for treating knee osteoarthritis: A clinical evaluation. *Alternative and Complementary Therapies* 2002;8(6):341-348.

Bagga H, March L. Intra-articular hyaluronic acid for osteoarthritis of the knee. *Medicine Today* 2003;4(10):67-68.

Bagis S, Sahin G, Oztuna V, Milcan A, Erdogan C, Camdeviren H. The long-term effect of intra-articular hyaluronic acid on pain and functional status in knee osteoarthritis (one year follow-up). *Pain Clinic* 2002;14(4):331-337.

Bagnato G, De Filippis LG, Morgante S, Morgante ML, Farina G, Caliri A, Romano C, D'Avola G, Pinelli P, Calpona PR, Strega P, Resta ML, De LG, Di GR. Clinical improvement and serum amino acid levels after mud-bath therapy. *Int J Clin Pharmacol Res* 2004;24(2-3):39-47.

Bailey RE. Arthroscopic surgery ineffective for osteoarthritis of the knee. *J Fam Pract* 2002;51(10):813.

Baime MJ. Glucosamine and chondroitin sulphate did not improve pain in osteoarthritis of the knee. *Evidence-Based Medicine* 2006;11(4):115.

Baker JF, Solayar GN, Byrne DP, Moran R, Mulhall KJ. Analgesic control and functional outcome after knee arthroscopy: results of a randomized double-blinded trial comparing a hyaluronic acid supplement with bupivacaine. *Clin J Sport Med* 2012 Mar;22(2):109-115.

Baker KR, Nelson ME, Felson DT, Layne JE, Sarno R, Roubenoff R. The efficacy of home-based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial. *J Rheumatol* 2001;28(7):1655-1665.

Bakshi R,Ezzet N,Frey L,Lasry D,Salliere D. Efficacy and tolerability of Diclofenac dispersible in painful osteoarthritis. *Clin Rheumatol* 1993;12(1):57-61.

Bakshi R. Comparative efficacy and tolerability of two Diclofenac formulations in the treatment of painful osteoarthritis. *Br J Clin Pract* 1996;50(6):294-297.

Baliki MN,Geha PY,Jabakhanji R,Harden N,Schnitzer TJ,Apkarian AV. A preliminary fMRI study of analgesic treatment in chronic back pain and knee osteoarthritis. *Mol Pain* 2008;4:47.

Balint GP,Buchanan WW,Adam A,Ratko I,Poor L,Balint PV,Somos E,Tefner I,Bender T. The effect of the thermal mineral water of Nagybaracska on patients with knee joint osteoarthritis--a double blind study. *Clin Rheumatol* 2007;26(6):890-894.

Baltzer AW,Moser C,Jansen SA,Krauspe R. Autologous conditioned serum (Orthokine) is an effective treatment for knee osteoarthritis. *Osteoarthritis Cartilage* 2009;17(2):152-160.

Bannuru RR,Natov NS,Dasi UR,Schmid CH,McAlindon TE. Therapeutic trajectory following intra-articular hyaluronic acid injection in knee osteoarthritis: Meta-analysis. *Osteoarthritis and Cartilage* 2010;18 SUPPL. 2:S242-S243.

Bannuru RR,Natov NS,Obadan IE,Price LL,Schmid CH,McAlindon TE. Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: a systematic review and meta-analysis (Structured abstract). *Arthritis and Rheumatism* 2009;61:1704-1711.

Bannuru RR,Natov NS,Obadan IE,Schmid CH,McAlindon TE. Relative efficacy of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: Meta-analysis. *Osteoarthritis and Cartilage* 2009;17 SUPPL. 1:S269-S270.

Bannwarth B,Treves R,Euller-Ziegler L,Rolland D,Ravaud P,Dougados M. Adverse events associated with Rofecoxib therapy: results of a large study in community-derived osteoarthritic patients. *Drug Saf* 2003;26(1):49-54.

Bansil CK,Joshi JB. Effectiveness of shortwave diathermy and ultrasound in the treatment of osteoarthritis of the knee joint. *Med J Zambia* 1975;9(5):138-139.

Baraf HS,Gold MS,Clark MB,Altman RD. Safety and efficacy of topical Diclofenac sodium 1% gel in knee osteoarthritis: a randomized controlled trial. *Phys Sportsmed* 2010 Jun;38(2):19-28.

Barrack RL,Wolfe MW,Waldman DA,Milicic M,Bertot AJ,Myers L. Resurfacing of the patella in total knee arthroplasty. A prospective, randomized, double-blind study. *J Bone Joint Surg Am* 1997;79(8):1121-1131.

Barrios JA,Crenshaw JR,Royer TD,Davis IS. Walking shoes and laterally wedged orthoses in the clinical management of medial tibiofemoral osteoarthritis: a one-year prospective controlled trial. *Knee* 2009;16(2):136-142.

Bartels EM,Bliddal H,Schondorff PK,Altman RD,Zhang W,Christensen R. Symptomatic efficacy and safety of Diacerein in the treatment of osteoarthritis: a meta-analysis of randomized placebo-controlled trials. *Osteoarthritis and Cartilage* 2010;18(3):289-296.

Barthel HR,Axford-Gatley RA. Topical nonsteroidal anti-inflammatory drugs for osteoarthritis. *Postgrad Med* 2010 Nov;122(6):98-106.

Barton GR,Sach TH,Avery AJ,Jenkinson C,Doherty M,Whynes DK,Muir KR. A comparison of the performance of the EQ-5D and SF-6D for individuals aged ≥ 45 years. *Health Econ* 2008;17(7):815-832.

Bar-Ziv Y,Beer Y,Ran Y,Benedict S,Halperin N. A treatment applying a biomechanical device to the feet of patients with knee osteoarthritis results in reduced pain and improved function: a prospective controlled study. *BMC Musculoskelet Disord* 2010;11:179.

Bassett FH,Harrelson JM. Meniscectomy in osteoarthritis. *Clin Orthop Relat Res* 1974;(101):53-60.

Bassiouni M. Open study of flurbiprofen in the treatment of osteoarthritis of the knee. *Br J Clin Pract* 1985;39(10):393-394.

Battagliotti CA,Baetti EA. Clinical, double-blind long-term study of tenoxicam 20mg (Ro 12-0068) versus Piroxicam 20mg in patients with gonarthrosis. *Eur J Rheumatol Inflamm* 1987;9(2):74-76.

Bauer GC,Insall J,Koshino T. Tibial osteotomy in gonarthrosis (osteo-arthritis of the knee). *J Bone Joint Surg Am* 1969;51(8):1545-1563.

Bauer HW,Klasser M,von Hanstein KL,Rolinger H,Schladitz G,Henke HD,Gimbel W,Steinbach K. Oxaceprol is as effective as Diclofenac in the therapy of osteoarthritis of the knee and hip. *Clin Rheumatol* 1999;18(1):4-9.

Bauer T,Hardy P,Lemoine J,Finlayson DF,Tranier S,Lortat-Jacob A. Drop foot after high tibial osteotomy: a prospective study of aetiological factors. *Knee Surg Sports Traumatol Arthrosc* 2005;13(1):23-33.

Baumgaertner MR,Cannon WD,Vittori JM,Schmidt ES,Maurer RC. Arthroscopic debridement of the arthritic knee. *Clin Orthop Relat Res* 1990;(253):197-202.

Baumgartner H,Schwarz HA,Blum W,Bruhin A,Gallachi G,Goldinger G,Saxer M,Trost H. Ibuprofen and Diclofenac sodium in the treatment of osteoarthritis: a comparative trial of two once-daily sustained-release NSAID formulations. *Curr Med Res Opin* 1996;13(8):435-444.

Bayat N,Keen HI,Hill CL. Randomized clinical trials of osteoarthritis: A review. *APLAR Journal of Rheumatology* 2005;8(3):171-176.

Bayramoglu M,Karatas M,Cetin N,Akman N,Sozay S,Dilek A. Comparison of two different viscosupplements in knee osteoarthritis -- a pilot study. *Clin Rheumatol* 2003;22(2):118-122.

Bayramoglu M,Toprak R,Sozay S. Effects of osteoarthritis and fatigue on proprioception of the knee joint. *Arch Phys Med Rehabil* 2007;88(3):346-350.

Beaudreuil J,Bendaya S,Faucher M,Coudeyre E,Ribinik P,Revel M,Rannou F. Clinical practice guidelines for rest orthosis, knee sleeves, and unloading knee braces in knee osteoarthritis. *Joint Bone Spine* 2009;76(6):629-636.

Beckwee D, De HW, Lievens P, Bautmans I, Vaes P. Effect of tens on pain in relation to central sensitization in patients with osteoarthritis of the knee: study protocol of a randomized controlled trial. *Trials* 2012;13:21.

Becvar R, Urbanova Z, Vlasakova V, Vitova J, Rybar I, Malyk H, Filipowicz-Sosnowska A, Bernacka K, Mackiewicz S, Gomor B, Rojkovich B, Siro B, Bereczki J, Toth K, Sukenik S, Green L, Ehrenfeld M, Pavelka K. Nabumetone induces less gastrointestinal mucosal changes than Diclofenac retard. *Clin Rheumatol* 1999;18(4):273-278.

Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: A systematic search and summary of the literature. *BMC Musculoskeletal Disorders* 2008;9 Article Number(116. Date of Publication):.

Beer A, Wegener T. Willow bark extract (Salicis cortex) for gonarthrosis and coxarthrosis - Results of a cohort study with a control group. 2008;15(11):907-913.

Belcaro G, Cesarone MR, Dugall M, Pellegrini L, Ledda A, Grossi mg, Togni S, Appendino G. Product-evaluation registry of Meriva(R), a curcumin-phosphatidylcholine complex, for the complementary management of osteoarthritis. *Panminerva Med* 2010 Jun;52(2 Suppl 1):55-62.

Belcaro G, Cesarone MR, Dugall M, Pellegrini L, Ledda A, Grossi mg, Togni S, Appendino G. Efficacy and safety of Meriva(R), a curcumin-phosphatidylcholine complex, during extended administration in osteoarthritis patients. *Altern Med Rev* 2010 Dec;15(4):337-344.

Belcaro G, Cesarone MR, Errichi S, Zulli C, Errichi BM, Vinciguerra G, Ledda A, Di RA, Stuard S, Dugall M, Pellegrini L, Gizzi G, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M, Rohdewald P. Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol. *Redox Rep* 2008;13(6):271-276.

Bellamy N, Bell MJ, Goldsmith CH, Pericak D, Walker V, Raynauld JP, Torrance GW, Tugwell P, Polisson R. The effectiveness of hylan G-F 20 in patients with knee osteoarthritis: an application of two sets of response criteria developed by the OARSI and one set developed by OMERACT-OARSI. *Osteoarthritis Cartilage* 2005;13(2):104-110.

Bellamy N, Bell MJ, Goldsmith CH, Pericak D, Walker V, Raynauld JP, Torrance GW, Tugwell P, Polisson R. Evaluation of WOMAC 20, 50, 70 response criteria in patients treated with hylan G-F 20 for knee osteoarthritis. *Ann Rheum Dis* 2005;64(6):881-885.

Bellamy N, Bell MJ, Pericak D, Goldsmith CH, Torrance GW, Raynauld JP, Walker V, Tugwell P, Polisson R. BLISS index for analyzing knee osteoarthritis trials data. *J Clin Epidemiol* 2007;60(2):124-132.

Bellamy N, Bensen WG, Beaulieu A, Siminovitch KA, Kraag GR, Lussier A, Ahmad S, Khanna VN, Davis P, Bell MJ,.. A multicenter study of nabumetone and Diclofenac SR in patients with osteoarthritis. *J Rheumatol* 1995;22(5):915-920.

Bellamy N, Bensen WG, Ford PM, Huang SH, Lang JY. Double-blind randomized controlled trial of flurbiprofen-SR (ANSAID-SR) and Diclofenac sodium-SR (Voltaren-SR) in the treatment of osteoarthritis. *Clin Invest Med* 1992;15(5):427-433.

- Bellamy N,Goldstein LD,Tekanoff RA. Continuing medical education-driven skills acquisition and impact on improved patient outcomes in family practice setting. *J Contin Educ Health Prof* 2000;20(1):52-61.
- Beltran J,Martin-Mola E,Figueroa M,Granados J,Sanmarti R,Artigas R,Torres F,Forns M,Mauleon D. Comparison of dexKetoprofen trometamol and Ketoprofen in the treatment of osteoarthritis of the knee. *J Clin Pharmacol* 1998;38(12 Suppl):74S-80S.
- Ben Dallah SK,Lenghi M. Efficacy and tolerability of nabumetone in the treatment of osteoarthritis of the knee joint: an open trial. *J Int Med Res* 1994;22(4):218-224.
- Benedetto KP,Rangger C. Arthroscopic partial meniscectomy: 5-year follow-up. *Knee Surg Sports Traumatol Arthrosc* 1993;1(3-4):235-238.
- Benichou OD,Hunter DJ,Nelson DR,Guermazi A,Eckstein F,Kwoh K,Myers SL,Wirth W,Duryea J. One-year change in radiographic joint space width in patients with unilateral joint space narrowing: data from the Osteoarthritis Initiative. *Arthritis Care Res (Hoboken)* 2010 Jul;62(7):924-931.
- Benito RP,Camacho-Zambrano MM,Carrillo-Arcentales JN,Mestanza-Peralta MA,Vallejo-Flores CA,Vargas-Lopez SV,Villacis-Tamayo RA,Zurita-Gavilanes LA. A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort. *Int J Food Sci Nutr* 2009;60:99-113.
- Benito-Ruiz P,Camacho-Zambrano MM,Carrillo-Arcentales JN,Mestanza-Peralta MA,Vallejo-Flores CA,Vargas-Lopez SV,Villacis-Tamayo RA,Zurita-Gavilanes LA. A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort. *Int J Food Sci Nutr* 2009;60(SUPPL. 2):99-113.
- Benjamin A. Double osteotomy for the painful knee in rheumatoid arthritis and osteoarthritis. *J Bone Joint Surg Br* 1969;51(4):694-699.
- Benjamin A. Double osteotomy of the knee. *Scand J Rheumatol* 1974;3(2):65.
- Bennell KL,Bowles KA,Payne C,Cicuttini FM,Williamson E,Forbes A,Hanna F,Hinman RS. Effects of lateral wedge insoles on symptoms and structural disease progression in medial knee osteoarthritis: a 12-month randomised controlled trial [abstract]. *Osteoarthritis and Cartilage* 2010;18:S11.
- Bennell KL,Egerton T,Wrigley TV,Hodges PW,Hunt M,Roos EM,Kyriakides M,Metcalf B,Forbes A,Ageberg E,Hinman RS. Comparison of neuromuscular and quadriceps strengthening exercise in the treatment of varus malaligned knees with medial knee osteoarthritis: a randomised controlled trial protocol. *BMC Musculoskelet Disord* 2011;12:276.
- Bennell KL,Hinman RS. A review of the clinical evidence for exercise in osteoarthritis of the hip and knee. *J Sci Med Sport* 2011 Jan;14(1):4-9.
- Bennett AN,Crossley KM,Brukner PD,Hinman RS. Predictors of symptomatic response to glucosamine in knee osteoarthritis: an exploratory study. *Br J Sports Med* 2007;41(7):415-419.
- Bentley G,Goodfellow JW. Disorganisation of the knees following intra-articular hydrocortisone injections. *J Bone Joint Surg Br* 1969;51(3):498-502.

Benzakour T,Hefti A,Lemseffer M,El Ahmadi JD,Bouyarmene H,Benzakour A. High tibial osteotomy for medial osteoarthritis of the knee: 15 years follow-up. *Int Orthop* 2010;:.

Berenbaum F,Castillo JR,Conaghan P,Hochberg M,Moller I,Monfort J,Pap T,Pelletier JP,Sawitzke A,DuSouich P. Non-inferiority clinical trial on the efficacy and safety of chondroitin sulfate and glucosamine hydrochloride in combination versus Celecoxib in patients with knee osteoarthritis. *Basic and Clinical Pharmacology and Toxicology* 2011 Oct;109 SUPPL. 3:49.

Berger R,Nowak H. A new medical approach to the treatment of osteoarthritis. Report of an open phase IV study with ademetionine (Gumbaral). *Am J Med* 1987;83(5A):84-88.

Berkhout B,MacFarlane JD,Cats A. Symptomatic osteoarthrosis of the knee: A follow-up study. *Br J Rheumatol* 1985;24(1):40-45.

Berkovitz S,Cummings M,Perrin C,Ito R. High volume acupuncture clinic (HVAC) for chronic knee pain--audit of a possible model for delivery of acupuncture in the National Health Service. *Acupunct Med* 2008;26(1):46-50.

Berman BM,Lao L,Greene M,Anderson RW,Wong RH,Langenberg P,Hochberg MC. Efficacy of traditional Chinese acupuncture in the treatment of symptomatic knee osteoarthritis: a pilot study. *Osteoarthritis Cartilage* 1995;3(2):139-142.

Berman BM,Lao L,Langenberg P,Roumie CL. Is acupuncture effective for arthritis of the knee?. *Journal of Clinical Outcomes Management* 2005;12(2):81-82.

Bernard J,Lemon M,Patterson MH. Arthroscopic washout of the knee--a 5-year survival analysis. *Knee* 2004;11(3):233-235.

Bernardo MLR. A randomized controlled trial on the effects of oral collagen treatment on the medial knee joint space and functional outcome among patients diagnosed with osteoarthritis of the knee. *PM and R* 2011 Sep;3(10 SUPPL. 1):S164.

Bernhardt M,Plaster RL,Marsh HO. Proximal tibial valgus osteotomy. The Veterans Administration Hospital experience, Wichita, Kansas, 1977-82. *Kans Med* 1987;88(9):267-270.

Berry H,Bird HA,Black C,Blake DR,Freeman AM,Golding DN,Hamilton EB,Jayson MI,Kidd B,Kohn H,... A double blind, multicentre, placebo controlled trial of Lornoxicam in patients with osteoarthritis of the hip and knee. *Ann Rheum Dis* 1992;51(2):238-242.

Berry H,Bloom B,Hamilton EB. A comparative study of zomepirac and placebo in osteoarthritis. *Pharmatherapeutica* 1981;2:662-667.

Berry H,Liyanage SP,Durance RA,Goode JD,Swannell AJ. A double-blind study of benorylate and chlormezanone in musculoskeletal disease. *Rheumatol Rehabil* 1981;20(1):46-49.

Betsch M,Schneppendahl J,Dor L,Jungbluth P,Grassmann JP,Windolf J,Thelen S,Hakimi M,Rapp W,Wild M. Influence of foot positions on the spine and pelvis. *Arthritis Care Res (Hoboken)* 2011 Dec;63(12):1758-1765.

Bettin D,Karbowski A,Schwering L,Matthiass HH. Time-dependent clinical and roentgenographical results of Coventry high tibial valgisation osteotomy. *Archives of Orthopaedic and Trauma Surgery* 1998;117(1-2):53-57.

Beyaz SG,Arun O,Tufek A,Tokgoz O,Karaman H. Comparison of efficacy of intraarticularly applied morphine and steroid in patients with knee osteoarthritis. *Reg Anesth Pain Med* 2011;36(5 SUPPL. 2):E180-October.

Bhan S,Dave PK. High valgus tibial osteotomy for osteoarthritis of the knee. *Int Orthop* 1992;16(1):13-17.

Bhatnagar T,Jenkyn TR. Internal kinetic changes in the knee due to high tibial osteotomy are well-correlated with change in external adduction moment: an osteoarthritic knee model. *J Biomech* 2010 Aug 26;43(12):2261-2266.

Bianchi M,Broggini M,Balzarini P,Franchi S,Sacerdote P. Effects of nimesulide on pain and on synovial fluid concentrations of substance P, interleukin-6 and interleukin-8 in patients with knee osteoarthritis: comparison with Celecoxib . *Int J Clin Pract* 2007;61(8):1270-1277.

Bianchi M,Broggini M. A randomised, double-blind, clinical trial comparing the efficacy of nimesulide, Celecoxib and Rofecoxib in osteoarthritis of the knee. *Drugs* 2003;63 Suppl 1:37-46.

Bianchi M,Ferrario P,Balzarini P,Broggini M. Plasma and synovial fluid concentrations of nimesulide and its main metabolite after a single or repeated oral administration in patients with knee osteoarthritis. *J Int Med Res* 2006;34(4):348-354.

Bias P,Labrenz R,Rose P. Sustained-release dexamethasone palmitate: Pharmacokinetics and efficacy in patients with activated inflammatory osteoarthritis of the knee. *Clinical Drug Investigation* 2001;21(6):429-436.

Biegert C,Wagner I,Ludtke R,Kotter I,Lohmuller C,Gunaydin I,Taxis K,Heide L. Efficacy and safety of willow bark extract in the treatment of osteoarthritis and rheumatoid arthritis: results of 2 randomized double-blind controlled trials. *J Rheumatol* 2004;31(11):2121-2130.

Biehl G. Double-blind comparison of i.m. indomethacin-meglumine with a corticosteroid-containing combination preparation in osteoarthritis of the hip and knee. *Orthopadische Praxis* 1983;19:465-470.

Bilgen MS,Atici T,Bilgen OF. High tibial osteotomy for medial compartment osteoarthritis: a comparison of clinical and radiological results from closed wedge and focal dome osteotomies. *J Int Med Res* 2007;35(6):733-741.

Bin SI, Lee SH, Kim CW, Kim TH, Lee DH. Results of arthroscopic medial meniscectomy in patients with grade IV osteoarthritis of the medial compartment. *Arthroscopy* 2008;24(3):264-268.

Bingham CO,Bird SR,Smugar SS,Xu X,Tershakovec AM. Responder analysis and correlation of outcome measures: pooled results from two identical studies comparing etoricoxib, Celecoxib , and placebo in osteoarthritis. *Osteoarthritis Cartilage* 2008;16(11):1289-1293.

- Bingham CO, Sebba AI, Rubin BR, Ruoff GE, Kremer J, Bird S, Smugar SS, Fitzgerald BJ, O'Brien K, Tershakovec AM. Efficacy and safety of Etoricoxib 30 mg and Celecoxib 200mg in the treatment of osteoarthritis in two identically designed, randomized, placebo-controlled, non-inferiority studies. *Rheumatology (Oxford)* 2007;46(3):496-507.
- Birbara C, Ruoff G, Sheldon E, Valenzuela C, Rodgers A, Petruschke RA, Chang DJ, Tershakovec AM. Efficacy and safety of Rofecoxib 12.5mg and Celecoxib 200mg in two similarly designed osteoarthritis studies. *Curr Med Res Opin* 2006;22(1):199-210.
- Birchall D, Ismail AM, Peat G. Clinical outcomes from a physiotherapist-led intra-articular hyaluronic acid injection clinic. *Musculoskeletal Care* 2008;6(3):135-149.
- Bird HA, Hill J, Stratford ME, Fenn GC, Wright V. A double-blind cross-over study comparing the analgesic efficacy of Tramadol with pentazocine in patients with osteoarthritis. *Journal of Drug Development and Clinical Practice* 1995;7:181-188.
- Birmingham TB, Giffin JR, Chesworth BM, Bryant DM, Litchfield RB, Willits K, Jenkyn TR, Fowler PJ. Medial opening wedge high tibial osteotomy: a prospective cohort study of gait, radiographic, and patient-reported outcomes. *Arthritis Rheum* 2009;61(5):648-657.
- Bischoff HA, Roos EM. Effectiveness and safety of strengthening, aerobic, and coordination exercises for patients with osteoarthritis. *Curr Opin Rheumatol* 2003;15(2):141-144.
- Bishnoi M, Kumar A, Kulkarni SK. Prescription monitoring of management pattern of osteoarthritis with non-steroidal antiinflammatory drugs at PUHC, Chandigarh in India. *Indian Journal of Pharmaceutical Sciences* 2006;68(4):525-527.
- Bjorkenheim JM, Helland J, Peltonen J. A double-blind crossover evaluation of Naproxen and Piroxicam in osteoarthritis of hip or knee. *J Int Med Res* 1985;13(5):263-269.
- Blechman W, Willkens R, Boncaldo GL, Hoffmeister RT, Lockie LM, Multz C. Naproxen in osteoarthritis. Double-blind crossover trial. *Ann Rheum Dis* 1978;37(1):80-84.
- Bliddal H, Rosetzsky A, Schlichting P, Weidner MS, Andersen LA, Ibfelt HH, Christensen K, Jensen ON, Barslev J. A randomized, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. *Osteoarthritis Cartilage* 2000;8(1):9-12.
- Blotman F, Maheu E, Wulwik A, Caspard H, Lopez A. Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial. *Rev Rhum Engl Ed* 1997;64(12):825-834.
- Bohnsack M, Ruhmann O. [Arthroscopic meniscal repair with bioresorbable implants]. *Oper Orthop Traumatol* 2006;18(5-6):425-452.
- Bohorquez-Corona JD. High tibial osteotomy for osteoarthritis of the knee. *Am Surg* 1974;40(2):125-132.
- Boissier C, Perpoint B, Laporte-Simitsidis S, Mismetti P, Hocquart J, Gayet JL, Rambaud C, Queneau P, Decousus H. Acceptability and efficacy of two associations of Paracetamol with a central analgesic (dextropropoxyphene or codeine): comparison in osteoarthritis. *J Clin Pharmacol* 1992;32(11):990-995.

Bokhari SZH,Zahid S. The role of acupuncture in arthritis of the knee joint in addition to local steroid injection. *Journal of Postgraduate Medical Institute* 2006;20(1):36-39.

Bolnot-Delmas D,Buch JP,Zeidler H,Dougados M. Ro 15-8081 in osteoarthritis of hip and knee: a double-blind placebo-controlled multicentre dose-ranging study on analgesia. *Pain* 1996;64(1):99-105.

Bonamo JJ,Kessler KJ,Noah J. Arthroscopic meniscectomy in patients over the age of 40. *Am J Sports Med* 1992;20(4):422-428.

Boon AJ,Smith J,Dahm DL,Sorenson EJ,Larson DR,Fitz-Gibbon PD,Dykstra DD,Singh JA. Efficacy of intra-articular botulinum toxin type A in painful knee osteoarthritis: a pilot study. *PM R* 2010;2(4):268-276.

Borjesson M,Weidenhielm L,Elfving B,Olsson E. Tests of walking ability at different speeds in patients with knee osteoarthritis. *Physiother Res Int* 2007;12(2):115-121.

Borjesson M,Weidenhielm L,Mattsson E,Olsson E. Gait and clinical measurements in patients with knee osteoarthritis after surgery: a prospective 5-year follow-up study. *The Knee* 2005;12:121-127.

Boswell DJ,Ostergaard K,Philipson RS,Hodge RA,Blum D,Brown JC,Quessy SN. Evaluation of GW406381 for treatment of osteoarthritis of the knee: two randomized, controlled studies. *Medscape J Med* 2008;10(11):259.

Boswellia serrata. *Altern Med Rev* 2008;13(2):165-167.

Botha-Scheepers S,Riyazi N,Kroon HM,Scharloo M,Houwing-Duistermaat JJ,Slagboom E,Rosendaal FR,Breedveld FC,Kloppenburger M. Activity limitations in the lower extremities in patients with osteoarthritis: the modifying effects of illness perceptions and mental health. *Osteoarthritis Cartilage* 2006;14(11):1104-1110.

Boureau F,Schneid H,Zeghari N,Wall R,Bourgeois P. The IPSO study: ibuprofen, Paracetamol study in osteoarthritis. A randomised comparative clinical study comparing the efficacy and safety of ibuprofen and Paracetamol analgesic treatment of osteoarthritis of the knee or hip. *Ann Rheum Dis* 2004;63(9):1028-1034.

Br Med J 1969;3(5662):102-104.

Bradley JD,Flusser D,Katz BP,Schumacher HR,Brandt KD,Chambers MA,Zonay LJ. A randomized, double blind, placebo controlled trial of intravenous loading with S-adenosylmethionine (SAM) followed by oral SAM therapy in patients with knee osteoarthritis. *The Journal of rheumatology* 1994;21:905-911.

Bradley JD,Katz BP,Brandt KD. Severity of knee pain does not predict a better response to an antiinflammatory dose of ibuprofen than to analgesic therapy in patients with osteoarthritis. *J Rheumatol* 2001;28(5):1073-1076.

Bradley JD,Rudy AC,Katz BP,Ryan SI,Kalasinski LA,Brater DC,Hall SD,Brandt KD. Correlation of serum concentrations of ibuprofen stereoisomers with clinical response in the treatment of hip and knee osteoarthritis. *J Rheumatol* 1992;19(1):130-134.

Bragantini A, Cassini M, De B, Perbellini A. Controlled single-blind trial of intra-articularly injected hyaluronic acid (Hyalgan(registered trademark)) in osteo-arthritis of the knee. *Clin Trials J* 1987;24(4):333-340.

Braham R, Dawson B, Goodman C. The effect of glucosamine supplementation on people experiencing regular knee pain. *Br J Sports Med* 2003;37(1):45-49.

Brahmachari B, Chatterjee S, Ghosh A. Efficacy and safety of Diacerein in early knee osteoarthritis: a randomized placebo-controlled trial. *Clin Rheumatol* 2009;28(10):1193-1198.

Brand C, Buchbinder R, Wluka A, Jones K, Ruth D, McKenzie S, Bucknall T, Ung L, McColl G, Hinman R, Somers K, Jasper A, Haesler E, Rada J. Guideline for the non-surgical management of hip and knee osteoarthritis [with systematic review]. .

Brand C, Snaddon J, Bailey M, Cicuttini F. Vitamin E is ineffective for symptomatic relief of knee osteoarthritis: a six month double blind, randomised, placebo controlled study. *Ann Rheum Dis* 2001;60(10):946-949.

Brand CA, Amatya B, Gordon B, Tosti T, Gorelik A. Redesigning care for chronic conditions: Improving hospital-based ambulatory care for people with osteoarthritis of the hip and knee. *Internal Medicine Journal* 2010 Jun;40(6):427-436.

Brandao GDC, Korukian M, Brandao DDC, Mainine S, De S. [Association of glucosamine sulphate and chondroitin sulphate for patients with osteoarthritis of the knee] TO: Associacao de sulfato de glicosamina e sulfato de condroitina para pacientes portadores de osteoartrose de joelho LA: Por. *Rev Bras Med* 2009;66:405-408.

Brander VA, Stadler TS. Functional improvement with hylan G-F 20 in patients with knee osteoarthritis (Provisional abstract). *Physician and Sportsmedicine* 2009;37:38-48.

Brandon SCE, Deluzio KJ. Robust features of knee osteoarthritis in joint moments are independent of reference frame selection. *Clinical Biomechanics* 2011 Jan;26(1):65-70.

Brandt KD, Block JA, Michalski JP, Moreland LW, Caldwell JR, Lavin PT. Efficacy and safety of intraarticular sodium hyaluronate in knee osteoarthritis. ORTHOVISC Study Group. *Clin Orthop Relat Res* 2001;(385):130-143.

Brandt KD, Mazzuca SA, Katz BP, Lane KA, Buckwalter KA, Yocum DE, Wolfe F, Schnitzer TJ, Moreland LW, Manzi S, Bradley JD, Sharma L, Oddis CV, Hugenberg ST, Heck LW. Effects of doxycycline on progression of osteoarthritis: results of a randomized, placebo-controlled, double-blind trial. *Arthritis Rheum* 2005;52(7):2015-2025.

Brandt KD, Mazzuca SA. Lessons learned from nine clinical trials of disease-modifying osteoarthritis drugs. *Arthritis Rheum* 2005;52(11):3349-3359.

Breivik H, Ljosaa TM, Stengaard PK, Persson J, Aro H, Villumsen J, Tvinnemose D. A 6-months, randomised, placebo-controlled evaluation of efficacy and tolerability of a low-dose 7-day buprenorphine transdermal patch in osteoarthritis patients naive to potent opioids. *Scandinavian Journal of Pain* 2010;1:122-141.

Brennan SL, Cicuttini FM, Pasco JA, Henry MJ, Wang Y, Kotowicz MA, Nicholson GC, Wluka AE. Does an increase in body mass index over 10 years affect knee structure in a population-based cohort study of adult women?. *Arthritis Res Ther* 2010;12(4):R139.

Brennan SL, Cicuttini FM, Shortreed S, Forbes A, Jones G, Stuckey SL, Wluka AE. Women lose patella cartilage at a faster rate than men: a 4.5-year cohort study of subjects with knee OA. 2010 Nov;67(3):270-274.

Bridgman S, Richards PJ, Walley G, MacKenzie G, Clement D, McCall I, Griffiths D, Maffulli N. The Effect of Magnetic Resonance Imaging Scans on Knee Arthroscopy: Randomized Controlled Trial. *Arthroscopy - Journal of Arthroscopic and Related Surgery* 2007;23(11):1167-1173.

Briem K, Axe MJ, Snyder-Mackler L. Functional and perceived response to intra-articular hyaluronan injection in patients with knee osteoarthritis: persistence of treatment effects over 5 months. *Knee Surg Sports Traumatol Arthrosc* 2009;17(7):763-769.

Briem K, Axe MJ, Snyder-Mackler L. Medial knee joint loading increases in those who respond to hyaluronan injection for medial knee osteoarthritis. *J Orthop Res* 2009;27(11):1420-1425.

Brien S, Lewith G, Walker AF, Middleton R, Prescott P, Bundy R. Bromelain as an adjunctive treatment for moderate-to-severe osteoarthritis of the knee: a randomized placebo-controlled pilot study. *QJM* 2006;99(12):841-850.

Brien S, Lewith GT, McGregor G. Devil's Claw (*Harpagophytum procumbens*) as a treatment for osteoarthritis: A review of efficacy and safety. *J Altern Complement Med* 2006;12(10):981-993.

Brien S, Prescott P, Lewith G. Meta-analysis of the Related Nutritional Supplements Dimethyl Sulfoxide and Methylsulfonylmethane in the Treatment of Osteoarthritis of the Knee. *Evid Based Complement Alternat Med* 2009;:.

Brien S, Prescott P, Lewith G. Meta-analysis of the related nutritional supplements dimethyl sulfoxide and methylsulfonylmethane in the treatment of osteoarthritis of the knee. *Evidence-based Complementary and Alternative Medicine* 2011;2011 Article Number(528403. Date of Publication):.

Brighton S, Mody GM, Tikly M, Bouwer D. Osteoarthritis: clinical guideline 2003. *S Afr Med J* 2003;93(12 Pt 2):972-990.

Brinkhaus B, Becker-Witt C, Jena S, Linde K, Streng A, Wagenpfeil S, Irnich D, Hummelsberger J, Melchart D, Willich SN. Acupuncture Randomized Trials (ART) in patients with chronic low back pain and osteoarthritis of the knee - design and protocols. *Forsch Komplementarmed Klass Naturheilkd* 2003;10(4):185-191.

Brinkhaus B, Witt CM, Linde K, Streng A, Melchart Da. Efficacy of acupuncture in patients with osteoarthritis of the knee. A randomized controlled trial [German]. *Padiatrische Praxis* 2006;68:679-689.

Brinkman JM, Luites JW, Wymenga AB, van Heerwaarden RJ. Early full weight bearing is safe in open-wedge high tibial osteotomy. *Acta Orthop* 2010;81(2):193-198.

Brismee JM, Paige RL, Chyu MC, Boatright JD, Hagar JM, McCaleb JA, Quintela MM, Feng D, Xu KT, Shen CL. Group and home-based tai chi in elderly subjects with knee osteoarthritis: a randomized controlled trial. *Clin Rehabil* 2007;21(2):99-111.

- Brittberg M,Faxen E,Peterson L. Carbon fiber scaffolds in the treatment of early knee osteoarthritis. A prospective 4-year followup of 37 patients. *Clin Orthop Relat Res* 1994;(307):155-164.
- Brosseau L,MacLeay L,Robinson V,Casimiro L,Pelland L,Wells G,Tugwell P,McGowan J. Efficacy of balneotherapy for osteoarthritis of the knee: a systematic review. *Physical Therapy Reviews* 2002;7(4):209-222.
- Brosseau L,Pelland L,Wells G,MacLeay L,Lamothe C,Michaud G,Lambert J,Robinson V,Tugwell P. Efficacy of aerobic exercises for osteoarthritis (part II): a meta-analysis. *Physical Therapy Reviews* 2004;9(3):125-145.
- Brosseau L,Tugwell P,Wells GA,Robinson VA,Graham ID,Shea BJ,Osiri M,McGowan J,Peterson J,Corriveau H,Pelland L,Morin M,Poulin L,Tousignant M,Laferriere L,Casimiro L,Tremblay LE,Albright J,Allman R,Bonfiglio RP,Conill A,Dobkin B,Guccione AA,Hasson S,Russ. Philadelphia Panel evidence-based clinical practice guidelines on selected rehabilitation interventions for knee pain [with systematic review]. *Phys Ther* 2001;81(10):1675-1700.
- Brosseau L,Welch V,Wells GA,de BR,Gam A,Harman K,Morin M,Shea B,Tugwell P. Low level laser therapy (Classes III) for treating osteoarthritis. *Brosseau Lucie , Welch Vivian , Wells George A, de Bie Rob , Gam Arne , Harman Katherine , Morin Michelle , Shea Beverley , Tugwell Peter Low level laser therapy for treating osteoarthritis Cochrane Database of Systematic Reviews: Reviews 2007 Issue 1* 2007;:.
- Brosseau L,Yonge K,Marchand S,Robinson V,Osiri M,Wells G,Tugwell P. Efficacy of transcutaneous electrical nerve stimulation for osteoarthritis of the lower extremities: a meta-analysis. *Physical Therapy Reviews* 2004;9(4):213-233.
- Brosseau L,Yonge KA,Robinson V,Marchand S,Judd M,Wells G,Tugwell P. Thermotherapy for treatment of osteoarthritis. *Cochrane Database Syst Rev* 2003;(4):CD004522.
- Brosset T,Pasquier G,Migaud H,Gougeon F. Opening wedge high tibial osteotomy performed without filling the defect but with locking plate fixation (TomoFix) and early weight-bearing: prospective evaluation of bone union, precision and maintenance of correction in 51 cases. *Orthop Traumatol Surg Res* 2011 Nov;97(7):705-711.
- Broughton NS,Newman JH,Baily RA. Unicompartmental replacement and high tibial osteotomy for osteoarthritis of the knee. A comparative study after 5-10 years' follow-up. *J Bone Joint Surg Br* 1986;68(3):447-452.
- Brouwer GM,van Tol AW,Bergink AP,Belo JN,Bernsen RM,Reijman M,Pols HA,Bierma-Zeinstra SM. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis Rheum* 2007;56(4):1204-1211.
- Brouwer RW,Bierma-Zeinstra SM,van Koevinge AJ,Verhaar JA. Patellar height and the inclination of the tibial plateau after high tibial osteotomy. The open versus the closed-wedge technique. *J Bone Joint Surg Br* 2005;87(9):1227-1232.
- Bruhlmann P,De VF,Dreiser RL,Michel BA. Short-term treatment with topical Diclofenac epolamine plaster in patients with symptomatic knee osteoarthritis: pooled analysis of two randomised clinical studies. *Curr Med Res Opin* 2006;22(12):2429-2438.

- Bruhlmann P, Michel BA. Topical Diclofenac patch in patients with knee osteoarthritis: a randomized, double-blind, controlled clinical trial. *Clin Exp Rheumatol* 2003;21(2):193-198.
- Bruyere O, Honore A, Ethgen O, Rovati LC, Giacobelli G, Henrotin YE, Seidel L, Reginster JY. Correlation between radiographic severity of knee osteoarthritis and future disease progression. Results from a 3-year prospective, placebo-controlled study evaluating the effect of glucosamine sulfate. *Osteoarthritis Cartilage* 2003;11(1):1-5.
- Bruyere O, Honore A, Rovati LC, Giacobelli G, Henrotin YE, Seidel L, Reginster JY. Radiologic features poorly predict clinical outcomes in knee osteoarthritis. *Scand J Rheumatol* 2002;31(1):13-16.
- Bruyere O, Pavelka K, Rovati LC, Deroisy R, Olejarova M, Gatterova J, Giacobelli G, Reginster JY. Glucosamine sulfate reduces osteoarthritis progression in postmenopausal women with knee osteoarthritis: evidence from two 3-year studies. *Menopause* 2004;11(2):138-143.
- Bruyere O, Scholtissen S, Neuprez A, Hilgsmann M, Toukoui A, Reginster JY. Impact of chondroitin sulphate on health utility in patients with knee osteoarthritis: towards economic analysis. *J Med Econ* 2009;12(4):356-360.
- Bruyere O, Reginster J, Croisier J, Crielaard J, Maquet D. Rehabilitation in osteoarthritis. *Therapy* 2010 Nov;7(6):669-674.
- Bryk FF, de Jesus JF, Fukuda TY, Moreira EG, Marcondes FB, dos Santos mg. Immediate effect of the elastic knee sleeve use on individuals with osteoarthritis. *Revista Brasileira de Reumatologia* 2011;51(5):434-446.
- Bryk FF, Jesus JF, Fukuda TY, Moreira EG, Marcondes FB, Santos mg. Immediate effect of the elastic knee sleeve use on individuals with osteoarthritis. *Rev Bras Reumatol* 2011 Nov;51(5):440-446.
- Buchmann E. Mefenamic acid compared with indomethacin and placebo in osteoarthritis. *Ann Phys Med* 1966;Suppl:119-125.
- Buck RJ, Wyman BT, Hellio Le Graverand MP, Hunter D, Vignon E, Wirth W, Eckstein F. Using ordered values of subregional cartilage thickness change increases sensitivity in detecting risk factors for osteoarthritis progression. *Osteoarthritis Cartilage* 2011 Mar;19(3):302-308.
- Bulgheroni P, Murena L, Ratti C, Bulgheroni E, Ronga M, Cherubino P. Follow-up of collagen meniscus implant patients: Clinical, radiological, and magnetic resonance imaging results at 5 years. *Knee* 2010 Jun;17(3):224-229.
- Bulow PM, Jensen H, Danneskiold-Samsoe B. Low power Ga-Al-As laser treatment of painful osteoarthritis of the knee. A double-blind placebo-controlled study. *Scand J Rehabil Med* 1994;26(3):155-159.
- Bulstrode S, Clarke A, Harrison R. A controlled trial to study the effects of ice therapy on joint inflammation in chronic arthritis. *Physiotherapy Practice* 1986;2(3):104-108.
- Bulthuis Y, Drossaers-Bakker KW, Taal E, Rasker J, Oostveen J, van't Pad BP, Oosterveld F, van de Laar M. Arthritis patients show long-term benefits from 3 weeks intensive exercise training directly following hospital discharge. *Rheumatology (Oxford)* 2007;46(11):1712-1717.

Bunyaratavej N, Chan KM, Subramanian N. Treatment of painful osteoarthritis of the knee with hyaluronic acid. Results of a multicenter Asian study. *J Med Assoc Thai* 2001;84 Suppl 2:S576-S581.

Burch F, Coddling C, Patel N, Sheldon E. Lidocaine patch 5% improves pain, stiffness, and physical function in osteoarthritis pain patients. A prospective, multicenter, open-label effectiveness trial. *Osteoarthritis Cartilage* 2004;12(3):253-255.

Burch FX, Tarro JN, Greenberg JJ, Carroll WJ. Evaluating the benefits of patterned stimulation in the treatment of osteoarthritis of the knee: a multi-center, randomized, single-blind, controlled study with an independent masked evaluator. *Osteoarthritis Cartilage* 2008;16(8):865-872.

Burks RT, Metcalf MH, Metcalf RW. Fifteen-year follow-up of arthroscopic partial meniscectomy. *Arthroscopy* 1997;13(6):673-679.

Burns R, Graney MJ, Lummus AC, Nichols LO, Martindale-Adams J. Differences of self-reported osteoarthritis disability and race. *J Natl Med Assoc* 2007;99(9):1046-1051.

Busija L, Osborne RH, Nilsdotter A, Buchbinder R, Roos EM. Magnitude and meaningfulness of change in SF-36 scores in four types of orthopedic surgery. *Health Qual Life Outcomes* 2008;6:55.

Buszewicz M, Rait G, Griffin M, Nazareth I, Patel A, Atkinson A, Barlow J, Haines A. Self-management of arthritis in primary care: randomised controlled trial. *BMJ* 2006;333(7574):879.

Butler RJ, Barrios JA, Royer T, Davis IS. Effect of laterally wedged foot orthoses on rearfoot and hip mechanics in patients with medial knee osteoarthritis. *Prosthet Orthot Int* 2009;33(2):107-116.

Byeon GJ, Kim KH. Piriformis syndrome in knee osteoarthritis patients after wearing rocker bottom shoes. *Korean J Pain* 2011 Jun;24(2):93-99.

Cadmus L, Patrick MB, Maciejewski ML, Topolski T, Belza B, Patrick DL. Community-based aquatic exercise and quality of life in persons with osteoarthritis. *Medicine (Baltimore)* ;42(1):8-15.

Cahue S, Chmiel J, Hayes K, Almagor O, Moio K, Chang A, Colbert C, Saurel C, Zhang J, Sharma L. Relationship between aspects of the pain experience in knee osteoarthritis and function and disability. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S206-S207.

Calamia V, Ruiz-Romero C, Rocha B, Fernandez-Puente P, Mateos J, Montell E, Verges J, Blanco FJ. Pharmacoproteomic study of the effects of chondroitin and glucosamine sulfate on human articular chondrocytes. *Arthritis Res Ther* 2010;12(4):R138.

Callaghan M, Pye S. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 1. The effects of glucosamine on osteoarthritis of the knee joint. *Emerg Med J* 2008;25(5):285-287.

Callaghan MJ, Oldham JA, Hunt J. An evaluation of exercise regimes for patients with osteoarthritis of the knee: A single-blind randomized controlled trial. *Clin Rehabil* 1995;9(3):213-218.

Callaghan MJ, Whittaker PE, Grimes S, Smith L. An evaluation of pulsed shortwave on knee osteoarthritis using radioleucoscintigraphy: A randomised, double blind, controlled trial. *Joint Bone Spine* 2005;72(2):150-155.

- Camerlain M,McCarty DJ,Silcox DC,Jung A. Inorganic pyrophosphate pool size and turnover rate in arthritic joints. *J Clin Invest* 1975;55(6):1373-1381.
- Cameron HU,Botsford DJ,Park YS. Prognostic factors in the outcome of supracondylar femoral osteotomy for lateral compartment osteoarthritis of the knee. *Can J Surg* 1997;40(2):114-118.
- Campbell DG,Angel KR,Dobson PJ,Lewis PL,Tandon S. Experiences of viscosupplementation for knee osteoarthritis. *Aust Fam Physician* 2004;33(10):863-864.
- Campbell J,Bellamy N,Gee T. Differences between systematic reviews/meta-analyses of hyaluronic acid/hyaluronan/hylan in osteoarthritis of the knee. *Osteoarthritis Cartilage* 2007;15(12):1424-1436.
- Campbell J,Ruddock B. Hyaluronic acid products for osteoarthritis of the knee. *Canadian Pharmacists Journal* 2007;140(3):194-196.
- Campbell MK,Skea ZC,Sutherland AG,Cuthbertson BH,Entwistle VA,McDonald AM,Norrie JD,Carlson RV,Bridgman S. Effectiveness and cost-effectiveness of arthroscopic lavage in the treatment of osteoarthritis of the knee: a mixed methods study of the feasibility of conducting a surgical placebo-controlled trial (the KORAL study). *Health Technol Assess* 2010;14(5):1-180.
- Campbell MK,Skea ZC,Sutherland AG,Cuthbertson BH,Entwistle VA,McDonald AM,Norrie JD,Carlson RV,-Bridgman-SKORAL-study-group. Effectiveness and cost-effectiveness of arthroscopic lavage in the treatment of osteoarthritis of the knee: a mixed methods study of the feasibility of conducting a surgical placebo-controlled trial (the KORAL study) (Structured abstract). *Health Technology Assessment* 2010;:1.
- Campos GC. Evaluation of the effect of adding corticosteroid to viscosupplementation: A prospective and randomized study. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S236.
- Cannon GW,Caldwell JR,Holt P,McLean B,Seidenberg B,Bolognese J,Ehrich E,Mukhopadhyay S,Daniels B. Rofecoxib , a specific inhibitor of cyclooxygenase 2, with clinical efficacy comparable with that of Diclofenac sodium: results of a one-year, randomized, clinical trial in patients with osteoarthritis of the knee and hip. Rofecoxib Phase III Protocol 035. *Arthritis Rheum* 2000;43(5):978-987.
- Cantarini L,Leo G,Giannitti C,Cevenini G,Barberini P,Fioravanti A. Therapeutic effect of spa therapy and short wave therapy in knee osteoarthritis: a randomized, single blind, controlled trial. *Rheumatol Int* 2007;27(6):523-529.
- Cao L,Zhang XL,Gao YS,Jiang Y. Needle acupuncture for osteoarthritis of the knee. A systematic review and updated meta-analysis. *Saudi Med J* 2012 May;33(5):526-532.
- Cao Y,Shi Y,Zheng Y,Shi M,Lo SK. Blood-nourishing and hard-softening capsule costs less in the management of osteoarthritic knee pain: a randomized controlled trial. *Evid Based Complement Alternat Med* 2005;2(3):363-368.
- Cao Y,Zhan H,Pang J,Li F,Xu S,Gao J,Xu Z,Li G,Liu T,Guo C,Shi Y. Individually integrated traditional Chinese medicine approach in the management of knee osteoarthritis: study protocol for a randomized controlled trial. *Trials* 2011;12:160.
- Cardoe N,Hart FD. Double-blind multicentre UK hospital studies of isoxicam versus Naproxen. *Br J Clin Pharmacol* 1986;22 Suppl 2:167S-172S.

- Carr A, Keyes G, Miller R, O'Connor J, Goodfellow J. Medial unicompartmental arthroplasty. A survival study of the Oxford meniscal knee. *Clin Orthop Relat Res* 1993;(295):205-213.
- Carrabba M, Paresce E, Angelini M, Perbellini Franchini AS, Colombo B. Hyaluronic acid (HA) in short and middle-term treatment of osteoarthritis of the knee. Five years of clinical experience. 1990;42(SPEC. ISS. 1):184-185.
- Carrabba M, Paresce E, Angelini M, Re KA, Torchiana EEM, Perbellini A. The safety and efficacy of different dose schedules of hyaluronic acid in the treatment of painful osteoarthritis of the knee with joint effusion. *Eur J Rheumatol Inflamm* 1995;15(1):25-31.
- Carrabba M, Paresce E, Angelini M, Zamboni AM, Bragantini A, Paissan A, Molinaroli F, Perbellini A. The intra-articular treatment of osteoarthritis of the knee. A comparative study between hyaluronic acid (Hyalgan((registered trademark))) and orgotein. *Eur J Rheumatol Inflamm* 1992;12(3):47-57.
- Carratelli L, Antonini P, Messina E, Pica B. Proglumetacin in arthritis of the hip and the knee. Results of a post-marketing surveillance study. *Drugs Exp Clin Res* 1985;11(4):307-316.
- Caruso I, Pietrogrande V. Italian double-blind multicenter study comparing S-adenosylmethionine, Naproxen, and placebo in the treatment of degenerative joint disease. *Am J Med* 1987;83(5A):66-71.
- Carvalho NA, Bittar ST, Pinto FR, Ferreira M, Sitta RR. Manual for guided home exercises for osteoarthritis of the knee. *Clinics (Sao Paulo)* 2010 Jun;65(8):775-780.
- Case JP, Baliunas AJ, Block JA. Lack of efficacy of Acetaminophen in treating symptomatic knee osteoarthritis: a randomized, double-blind, placebo-controlled comparison trial with Diclofenac sodium. *Arch Intern Med* 2003;163(2):169-178.
- Cass JR, Bryan RS. High tibial osteotomy. *Clin Orthop* 1988;(230):196-199.
- Catagni MA, Guerreschi F, Ahmad TS, Cattaneo R. Treatment of genu varum in medial compartment osteoarthritis of the knee using the Ilizarov method. *Orthop Clin North Am* 1994;25(3):509-514.
- Cats A, van IJzerloo JA, Davinova Y, Werthauer-Rodrigues PM, Blakemore CB, Steiner FJ. The efficacy of intra-articularly administered MYC 2095, triamcinolone hexacetonide and placebo in gonarthrosis. A combined double-blind clinical trial. *Scand J Rheumatol* 1979;8(4):199-203.
- Causero A, Tcherkes-Zade T, Tcherkes-Zade D, Paschina E. The Ilizarov technique in the treatment of osteoarthritic genu varum. *Chir Organi Mov* 2002;87(4):235-240.
- Cederlof S, Jonson G. Intraarticular prednisolone injection for osteoarthritis of the knee. A double blind test with placebo. *Acta Chir Scand* 1966;132(5):532-537.
- Cefalu CA, Waddell DS. Viscosupplementation: treatment alternative for osteoarthritis of the knee. *Geriatrics* 1999;54(10):51-4, 57.
- Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis: A systematic review and metaanalysis. *J Rheumatol* 2007;34(3):543-555.
- Chadade WH, Federico WA. Multi-clinic controlled study comparing sulindac with aspirin during 96 weeks in outpatients with osteoarthritis of the hip and/or knee. *Scand J Rheumatol Suppl* 1975;:S02-S03.

Chahade WH, Marques GC. Tenoxicam or Diclofenac in the treatment of gonarthrosis. *Eur J Rheumatol Inflamm* 1987;9(2):77-80.

Chaipinyo K, Karoonsupcharoen O. No difference between home-based strength training and home-based balance training on pain in patients with knee osteoarthritis: a randomised trial. *Aust J Physiother* 2009;55(1):25-30.

Chakravarty EF, Hubert HB, Lingala VB, Zatarain E, Fries JF. Long distance running and knee osteoarthritis. A prospective study. *Am J Prev Med* 2008;35(2):133-138.

Chamberlain MA, Care G, Harfield B. Physiotherapy in osteoarthritis of the knees. A controlled trial of hospital versus home exercises. *Int Rehabil Med* 1982;4(2):101-106.

Chamchan U, Waikakul S, Pukanchana-Mo-Rakote C. Clinical efficacy of glycosaminoglycan polysulfate for the treatment of osteoarthritis of the knee joint: A double blind controlled study. *J Med Assoc Thai* 1989;72(3):123-128.

Chantre P, Cappelaere A, Leblan D, Guedon D, Vandermander J, Fournie B. Efficacy and tolerance of *Harpagophytum procumbens* versus diacerhein in treatment of osteoarthritis. 2000;7(3):177-183.

Chappell AS, Ossanna MJ, Liu-Seifert H, Iyengar S, Skljarevski V, Li LC, Bennett RM, Collins H. Duloxetine, a centrally acting analgesic, in the treatment of patients with osteoarthritis knee pain: a 13-week, randomized, placebo-controlled trial. *Pain* 2009;146(3):253-260.

Chard J, Lohmander S, Smith C, Scott D. Osteoarthritis of the knee. *Clin Evid* 2005;(14):1506-1522.

Chatain F, Adeleine P, Chambat P, Neyret P. A comparative study of medial versus lateral arthroscopic partial meniscectomy on stable knees: 10-year minimum follow-up. *Arthroscopy* 2003;19(8):842-849.

Chatzopoulos D, Moravidis E, Markou P, Makris V. Yttrium-90 radiation synovectomy in knee osteoarthritis: A prospective assessment at 6 and 12 months. *Nucl Med Commun* 2009;30(6):472-479.

Cheing GL, Hui-Chan CW, Chan KM. Does four weeks of TENS and/or isometric exercise produce cumulative reduction of osteoarthritic knee pain?. *Clin Rehabil* 2002;16(7):749-760.

Cheing GL, Hui-Chan CW. Would the addition of TENS to exercise training produce better physical performance outcomes in people with knee osteoarthritis than either intervention alone?. *Clin Rehabil* 2004;18(5):487-497.

Cheing GL, Tsui AY, Lo SK, Hui-Chan CW. Optimal stimulation duration of tens in the management of osteoarthritic knee pain. *J Rehabil Med* 2003;35(2):62-68.

Chen CY, Chen CL, Hsu SC, Chou SW, Wang KC. Effect of magnetic knee wrap on quadriceps strength in patients with symptomatic knee osteoarthritis. *Arch Phys Med Rehabil* 2008;89(12):2258-2264.

Chen KW, Perlman A, Liao JG, Lam A, Staller J, Sigal LH. Effects of external qigong therapy on osteoarthritis of the knee. A randomized controlled trial. *Clin Rheumatol* 2008;27(12):1497-1505.

Chen W, Li Z, Zhang J. Treating osteoarthritis of the knee joint by traditional Chinese medicine. *J Tradit Chin Med* 1994;14(4):279-282.

Chen W. Clinical application of double-hand needling manipulation. *J Tradit Chin Med* 2003;23(2):134-135.

Chen Y, Jobanputra P, Barton P, Bryan S, Fry-Smith A, Harris G, Taylor RS. Cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs (etodolac, meloxicam, Celecoxib, Rofecoxib, etoricoxib, Valdecoxib and lumiracoxib) for osteoarthritis and rheumatoid arthritis: A systematic review and economic evaluation. *Health Technology Assessment* 2008;12(11):iii-158.

Chen Y. Treatment of genua osteoarthritis by massotherapy. *J Tradit Chin Med* 2000;20(3):191-194.

Chen YL. Clinical observation of combined modality therapy for knee osteoarthritis in 82 cases. *Journal of Clinical Acupuncture and Moxibustion [Zhen Jiu Lin Chuang Za Zhi]* 1996;12:16.

Cheng OT, Souzdalnitski D, Vrooman B, Cheng J. Evidence-Based Knee Injections for the Management of Arthritis. *Pain Med* 2012 May 23.

Cheras PA, Myers SP, Paul-Brent P, Outerbridge KH, Nielsen GVL. Randomized double-blind placebo-controlled trial on the potential modes of action of SheaFlex70 (trademark) in osteoarthritis. *Phytotherapy Research* 2010 Aug;24(8):1126-1131.

Cheung PP, Gossec L, Dougados M. What are the best markers for disease progression in osteoarthritis (OA)? *Best Practice and Research* 2010;24(1):81-92.

Chevalier X, Giraudeau B, Conrozier T, Marliere J, Kiefer P, Goupille P. Safety study of intraarticular injection of interleukin 1 receptor antagonist in patients with painful knee osteoarthritis: a multicenter study. *J Rheumatol* 2005;32(7):1317-1323.

Chevallard M, Galanti A, Paresce E, Wolf A, Carrabba M. Efficacy and tolerability of galactosaminoglycuronoglycan-sulfate in osteoarthritis of the knee: an 11-month experience. *Int J Clin Pharmacol Res* 1993;13 Suppl:49-53.

Chew KTL, Lew HL, Date E, Fredericson M. Current evidence and clinical applications of therapeutic knee braces. *Am J Phys Med Rehabil* 2007;86(8):678-686.

Chikanza IC, Clarke B, Hopkins R, MacFarlane DG, Bird H, Grahame R. A comparative study of the efficacy and toxicity of etodolac and Naproxen in the treatment of osteoarthritis. *Br J Clin Pract* 1994;48(2):67-69.

Cho SH, Jung YB, Seong SC, Park HB, Byun KY, Lee DC, Song EK, Son JH. Clinical efficacy and safety of Lyprinol, a patented extract from New Zealand green-lipped mussel (*Perna Canaliculus*) in patients with osteoarthritis of the hip and knee: a multicenter 2-month clinical trial. *Eur Ann Allergy Clin Immunol* 2003;35(6):212-216.

Chodosh J, Morton SC, Mojica W, Maglione M, Suttrop MJ, Hilton L, Rhodes S, Shekelle P. Meta-analysis: chronic disease self-management programs for older adults. *Ann Intern Med* 2005;143(6):427-438.

Choi CB, Song JS, Kang YM, Suh CH, Lee J, Choe JY, Lee CK, Shim SC, Chung WT, Song GG, Kim HA, Ji JD, Nam EJ, Park SH, Hong YH, Sheen DH, Lim MK, Seo YI, Sung YK, Kim TH, Lee JT, Bae SC. A 2-week, multicenter, randomized, double-blind, double-dummy, add-on study of the effects of titration on tolerability of tramadol/Acetaminophen combination tablet in Korean adults with knee osteoarthritis pain. *Clin Ther* 2007;29(7):1381-1389.

Choi HR,Hasegawa Y,Kondo S,Shimizu T,Ida K,Iwata H. High tibial osteotomy for varus gonarthrosis: a 10- to 24-year follow-up study. *J Orthop Sci* 2001;6(6):493-497.

Chopra A,Bichile L,Rajadhyaksha AG,Gadgil D,Maroli S,Goregaonkar AB. Randomized double-blind clinical drug trials of meloxicam in rheumatoid arthritis and osteoarthritis knees: An Indian experience. *Journal* 2004;7:108-116.

Chopra A,Lavin P,Patwardhan B,Chitre D. A 32-week randomized, placebo-controlled clinical evaluation of RA-11, an Ayurvedic drug, on osteoarthritis of the knees. *J Clin Rheumatol* 2004;10(5):236-245.

Chopra A,Saluja M,Tillu G,Venugopalan A,Sarmukaddam S,Raut AK,Bichile L,Narsimulu G,Handa R,Patwardhan B. A Randomized Controlled Exploratory Evaluation of Standardized Ayurvedic Formulations in Symptomatic Osteoarthritis Knees: A Government of India NMITLI Project. *Evid Based Complement Alternat Med* 2011;2011:724291.

Choquette D,McCarthy TG,Rodrigues JF,Kelly AJ,Camacho F,Horbay GL,Husein-Bhabha FA. Transdermal fentanyl improves pain control and functionality in patients with osteoarthritis: an open-label Canadian trial. *Clin Rheumatol* 2008;27(5):587-595.

Chou CL,Li HW,Lee SH,Tsai KL,Ling HY. Effect of intra-articular injection of hyaluronic acid in rheumatoid arthritis patients with knee osteoarthritis. *J Chin Med Assoc* 2008;71(8):411-415.

Chou CW,Lue KH,Lee HS,Lin RC,Lu KH. Hylan G-F 20 has better pain relief and cost-effectiveness than sodium hyaluronate in treating early osteoarthritic knees in Taiwan. *J Formos Med Assoc* 2009;108(8):663-672.

Chou P,Chen S,Chou Y,Lee S,Su F,Lin T. Biomechanical analysis of knee osteoarthritis patients after the treatment of glucosamine. *Biomedical Engineering - Applications, Basis and Communications* 2003;15(1):32-37.

Christgau S,Henrotin Y,Tanko LB,Rovati LC,Collette J,Bruyere O,Deroisy R,Reginster JY. Osteoarthritic patients with high cartilage turnover show increased responsiveness to the cartilage protecting effects of glucosamine sulphate. *Clin Exp Rheumatol* 2004;22(1):36-42.

Christie A,Moe RH. Aerobic walking and strengthening exercises have similar effectiveness for knee osteoarthritis. *Aust J Physiother* 2005;51(3):193.

Christodoulou NA,Tsaknis RN,Sdrenias CV,Galanis KG,Mavrogenis AF. Improvement of proximal tibial osteotomy results by lateral retinacular release. *Clin Orthop Relat Res* 2005;441:340-345.

Chrubasik S,Chrubasik C,Kunzel O,Black A. Patient-perceived benefit during one year of treatment with Doloteffin. 2007;14(6):371-376.

Chrubasik S,Thanner J,Kunzel O,Conradt C,Black A,Pollak S. Comparison of outcome measures during treatment with the proprietary Harpagophytum extract doloteffin in patients with pain in the lower back, knee or hip. 2002;9(3):181-194.

Chua SD,Messier SP,Legault C,Lenz ME,Thonar EJ,Loeser RF. Effect of an exercise and dietary intervention on serum biomarkers in overweight and obese adults with osteoarthritis of the knee. *Osteoarthritis Cartilage* 2008;16(9):1047-1053.

- Chuang SH,Huang MH,Chen TW,Weng MC,Liu CW,Chen CH. Effect of knee sleeve on static and dynamic balance in patients with knee osteoarthritis. *Kaohsiung J Med Sci* 2007;23(8):405-411.
- Cibere J,Thorne A,Kopec JA,Singer J,Canvin J,Robinson DB,Pope J,Hong P,Grant E,Lobanok T,Ionescu M,Poole AR,Esdaile JM. Glucosamine sulfate and cartilage type II collagen degradation in patients with knee osteoarthritis: randomized discontinuation trial results employing biomarkers. *J Rheumatol* 2005;32(5):896-902.
- Cisar P,Jany R,Waczulikova I,Sumegova K,Muchova J,Vojtassak J,Durackova Z,Lisy M,Rohdewald P. Effect of pine bark extract (Pycnogenol) on symptoms of knee osteoarthritis. *Phytother Res* 2008;22(8):1087-1092.
- Clarius M,Becker JF,Schmitt H,Seeger JB. The UniSpacer: correcting varus malalignment in medial gonarthrosis. *Int Orthop* 2009;:.
- Clark BM. Rheumatology: 9. Physical and occupational therapy in the management of arthritis. *CMAJ* 2000;163(8):999-1005.
- Clarke GR,Willis LA,Stenners L,Nichols PJ. Evaluation of physiotherapy in the treatment of osteoarthrosis of the knee. *Rheumatol Rehabil* 1974;13(4):190-197.
- Clarke S,Lock V,Duddy J,Sharif M,Newman JH,Kirwan JR. Intra-articular hylan G-F 20 (Synvisc) in the management of patellofemoral osteoarthritis of the knee (POAK). *Knee* 2005;12(1):57-62.
- Cochrane DJ,Jarvis B,Keating GM. Etoricoxib. *Drugs* 2002;62(18):2637-2651.
- Cochrane GM. A double-blind comparison of Naproxen with indomethacin in osteoarthritis. *Scand J Rheumatol* 1973;:Suppl-93.
- Cochrane T,Davey RC,Matthes Edwards SM. Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis. *Health Technol Assess* 2005;9(31):iii-xi, 1.
- Cochrane T,Davey RC,Matthes Edwards SM. Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis. 2005;9(31):1-130.
- Coggon D,Croft P,Kellingray S,Barrett D,McLaren M,Cooper C. Occupational physical activities and osteoarthritis of the knee. *Arthritis Rheum* 2000;43(7):1443-1449.
- Coggon D,Reading I,Croft P,McLaren M,Barrett D,Cooper C. Knee osteoarthritis and obesity. *Int J Obes Relat Metab Disord* 2001;25(5):622-627.
- Cohen M,Wolfe R,Mai T,Lewis D. A randomized, double blind, placebo controlled trial of a topical cream containing glucosamine sulfate, chondroitin sulfate, and camphor for osteoarthritis of the knee. *J Rheumatol* 2003;30(3):523-528.
- Cohen M,Wolfe R,Mai T,Lewis D. A randomized, double blind, placebo controlled trial of a topical cream containing glucosamine sulfate, chondroitin sulfate, and camphor for osteoarthritis of the knee J Rheumatol. 2003 Nov;30(11):2512. *The Journal of rheumatology* 2003;30:523-528.
- Coleman S,McQuade J,Rose J,Inderjeeth C,Carroll G,Briffa NK. Self-management for osteoarthritis of the knee: does mode of delivery influence outcome?. *BMC Musculoskelet Disord* 2010;11:56.

Colen S,Haverkamp D,Mulier M,van den Bekerom MP. Hyaluronic acid for the treatment of osteoarthritis in all joints except the knee: what is the current evidence?. *BioDrugs* 2012 Apr 1;26(2):101-112.

Colker CM,Swain M,Lynch L,Gingerich DA. Effects of a milk-based bioactive micronutrient beverage on pain symptoms and activity of adults with osteoarthritis: a double-blind, placebo-controlled clinical evaluation. *Nutrition* 2002;18(5):388-392.

Collantes-Estevez E,Fernandez-Perez C. Improved control of osteoarthritis pain and self-reported health status in non-responders to Celecoxib switched to Rofecoxib : results of PAVIA, an open-label post-marketing survey in Spain. *Curr Med Res Opin* 2003;19(5):402-410.

Collins E,O'Connell S,Jelinek C,Miskevics S,Budiman-Mak E. Evaluation of psychometric properties of Walking Impairment Questionnaire in overweight patients with osteoarthritis of knee. *J Rehabil Res Dev* 2008;45(4):559-566.

Conaghan PG,O'Brien CM,Wilson M,Schofield JP. Transdermal buprenorphine plus oral Paracetamol versus an oral codeine-Paracetamol combination for osteoarthritis of hip and/or knee: a randomised trial. *Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society* 2011;19:930-938.

Conrozier T,Jerosch J,Beks P,Kemper F,Euller-Ziegler L,Bailleul F,Chevalier X. Prospective, multi-centre, randomised evaluation of the safety and efficacy of five dosing regimens of viscosupplementation with hylan G-F 20 in patients with symptomatic tibio-femoral osteoarthritis: a pilot study. *Arch Orthop Trauma Surg* 2009;129(3):417-423.

Conrozier T. [Anti-arthritis treatments: efficacy and tolerance of chondroitin sulfates (CS 4&6)]. *Presse mOdicale* 1998;27:1862-1865.

Contreras-Hernandez I,Mould-Quevedo JF,Torres-Gonzalez R,Goycochea-Robles MV,Pacheco-Dominguez RL,Sanchez-Garcia S,Mejia-Arangure JM,Garduno-Espinosa J. Cost-effectiveness analysis for joint pain treatment in patients with osteoarthritis treated at the Instituto Mexicano del Seguro Social (IMSS): Comparison of nonsteroidal anti-inflammatory drugs (NSAIDs) versus cyclooxygenase-2 selective inhibitors. *Cost Eff Resour Alloc* 2008;6:21.

Corbett M,Seifert MH,Hacking C,Webb S. Comparison between local injections of silicone oil and hydrocortisone acetate in chronic arthritis. *Br Med J* 1970;1(5687):24-25.

Cornhill J,Rowley-Jones D. Is sustained-release ibuprofen as effective as Piroxicam? A comparison in patients with osteoarthritis. *Eur J Rheumatol Inflamm* 1984;7(3):114-121.

Corts Giner JR,Garcia Borrás JJ. Double-blind, randomized and parallel comparison between droxicam and Diclofenac sodium in patients with coxarthrosis and gonarthrosis. *Eur J Rheumatol Inflamm* 1991;11(4):29-34.

Coupe VM,Veenhof C,van Tulder MW,Dekker J,Bijlsma JW,van den Ende CH. The cost effectiveness of behavioural graded activity in patients with osteoarthritis of hip and/or knee. *Ann Rheum Dis* 2007;66(2):215-221.

Coutts RD,Waddell DD. Viscosupplementation for osteoarthritis of the knee. *Orthopedics* 2004;27(5):470-471.

Covall DJ, Wasilewski SA. Roentgenographic changes after arthroscopic meniscectomy: five-year follow-up in patients more than 45 years old. *Arthroscopy* 1992;8(2):242-246.

Coventry MB, Ilstrup DM, Wallrichs SL. Proximal tibial osteotomy. A critical long-term study of eighty-seven cases. *J Bone Joint Surg Am* 1993;75(2):196-201.

Coventry MB. Osteotomy about the knee for degenerative and rheumatoid arthritis. *J Bone Joint Surg Am* 1973;55(1):23-48.

Coventry MB. Osteotomy of the upper portion of the tibia for degenerative arthritis of the knee. A preliminary report. *Clin Orthop* 1989;(248):4-8.

Coventry MB. Proximal tibial varus osteotomy for osteoarthritis of the lateral compartment of the knee. *J Bone Joint Surg Am* 1987;69(1):32-38.

Coventry MB. Upper tibial osteotomy for gonarthrosis. The evolution of the operation in the last 18 years and long term results. *Orthop Clin North Am* 1979;10(1):191-210.

Coventry MB. Upper tibial osteotomy for osteoarthritis. *J Bone Joint Surg Am* 1985;67(7):1136-1140.

Creaby MW, Wang Y, Bennell KL, Hinman RS, Metcalf BR, Bowles KA, Cicuttini FM. Dynamic knee loading is related to cartilage defects and tibial plateau bone area in medial knee osteoarthritis. *Osteoarthritis Cartilage* 2010 Nov;18(11):1380-1385.

Creamer P, Hochberg MC. Osteoarthritis. *Lancet* 1997;350(9076):503-509.

Creamer P, Hunt M, Dieppe P. Pain mechanisms in osteoarthritis of the knee: effect of intraarticular anesthetic. *J Rheumatol* 1996;23(6):1031-1036.

Creamer P, Lethbridge-Cejku M, Hochberg MC. Determinants of pain severity in knee osteoarthritis: effect of demographic and psychosocial variables using 3 pain measures. *J Rheumatol* 1999;26(8):1785-1792.

Creamer P, Singh BB, Hochberg MC, Berman BM. Are psychosocial factors related to response to acupuncture among patients with knee osteoarthritis?. *Altern Ther Health Med* 1999;5(4):72-76.

Crowley DC, Lau FC, Sharma P, Evans M, Guthrie N, Bagchi M, Bagchi D, Dey DK, Raychaudhuri SP. Safety and efficacy of undenatured type II collagen in the treatment of osteoarthritis of the knee: a clinical trial. *Int J Med Sci* 2009;6(6):312-321.

Cryer BL, Sostek MB, Fort JG, Svensson O, Hwang C, Hochberg MC. A fixed-dose combination of Naproxen and esomeprazole magnesium has comparable upper gastrointestinal tolerability to Celecoxib in patients with osteoarthritis of the knee: Results from two randomized, parallel-group, placebo-controlled trials. *Ann Med* 2011 Dec;43(8):594-605.

Cubukcu D, Ardic F, Karabulut N, Topuz O, Hylan G-F. Efficacy on articular cartilage quality in patients with knee osteoarthritis: clinical and MRI assessment. *Clin Rheumatol* 2005;24(4):336-341.

Cummings M. Modellvorhaben Akupunktur - a summary of the ART, ARC and GERAC trials. *Acupunct Med* 2009;27(1):26-30.

Cummings M. Six sessions of manual acupuncture do not seem to help when added to optimal exercise for knee osteoarthritis. *Focus on Alternative and Complementary Therapies* 2008;13(1):35-36.

Cunnington J, Marshall N, Hide G, Bracewell C, Isaacs J, Platt P, Kane D. A randomized, double-blind, controlled study of ultrasound-guided corticosteroid injection into the joint of patients with inflammatory arthritis. *Arthritis and Rheumatism* 2010 Jul;62(7):1862-1869.

Curran MP. Hyaluronic acid (Supartz(R)): a review of its use in osteoarthritis of the knee. *Drugs Aging* 2010 Nov 1;27(11):925-941.

Curran MP. Hyaluronic acid (Supartz(registered trademark)): A review of its use in osteoarthritis of the knee. *Drugs Aging* 2010;27(11):925-941.

Currier LL, Froehlich PJ, Carow SD, McAndrew RK, Cliborne AV, Boyles RE, Mansfield LT, Wainner RS. Development of a clinical prediction rule to identify patients with knee pain and clinical evidence of knee osteoarthritis who demonstrate a favorable short-term response to hip mobilization. *Phys Ther* 2007;87(9):1106-1119.

Curtis SP, Bockow B, Fisher C, Olaleye J, Compton A, Ko AT, Reicin AS. Etoricoxib in the treatment of osteoarthritis over 52-weeks: a double-blind, active-comparator controlled trial [NCT00242489]. *BMC Musculoskelet Disord* 2005;6:58.

Cusack T. A randomised controlled trial to evaluate the effects of short-wave diathermy and hydrotherapy on patients with osteoarthritis of their knees: a two-year report. *Physiotherapy Ireland* 2003;24:19.

Dagfinrud H. NSAIDS reduce osteoarthritic knee pain in the short term; long term effects are unknown. *Aust J Physiother* 2005;51(1):53.

Dahaghin S, Tehrani-Banihashemi SA, Faezi ST, Jamshidi AR, Davatchi F. Squatting, sitting on the floor, or cycling: Are life-long daily activities risk factors for clinical knee osteoarthritis? Stage III results of a community-based study. *Arthritis Care and Research* 2009;61(10):1337-1342.

Dahl A, Robertsson O, Lidgren L. Surgery for knee osteoarthritis in younger patients. *Acta Orthop* 2010;81(2):161-164.

Dahl A, Toksvig-Larsen S, Roos EM. A 2-year prospective study of patient-relevant outcomes in patients operated on for knee osteoarthritis with tibial osteotomy. *BMC Musculoskelet Disord* 2005;6:18.

Dahl A, Toksvig-Larsen S, Roos EM. Association between knee alignment and knee pain in patients surgically treated for medial knee osteoarthritis by high tibial osteotomy. A one year follow-up study. *BMC Musculoskelet Disord* 2009;10:154.

Dahlberg LE, Holme I, Hoyer K, Ringertz B. A randomized, multicentre, double-blind, parallel-group study to assess the adverse event-related discontinuation rate with Celecoxib and Diclofenac in elderly patients with osteoarthritis. *Scand J Rheumatol* 2009;38(2):133-143.

Dai QP, Qiu ML, Shao P. Clinical observation on treatment of 60 cases of osteoarthritis of knee joint by electroacupuncture. *J Acu Tuina Sci* 2003;1:38.

Damush TM, Perkins SM, Mikesky AE, Roberts M, O'Dea J. Motivational factors influencing older adults diagnosed with knee osteoarthritis to join and maintain an exercise program. *J Aging Phys Act* 2005;13(1):45-60.

- Danao-Camara T,Tabrah FL. The use of pulsed electromagnetic fields (PEMF) in osteoarthritis (OA) of the knee preliminary report. *Hawaii Med J* 2001;60(11):288, 300.
- Das A,Neher JO,Safranek S. Clinical inquiries. Do hyaluronic acid injections relieve OA knee pain?. *J Fam Pract* 2009;58(5):281c-281e.
- Das SK,Mishra K,Ramakrishnan S,Srivastava R,Agarwal GG,Singh R,Sircar AR. A randomized controlled trial to evaluate the slow-acting symptom modifying effects of a regimen containing colchicine in a subset of patients with osteoarthritis of the knee. *Osteoarthritis Cartilage* 2002;10(4):247-252.
- Das SK,Ramakrishnan S,Mishra K,Srivastava R,Agarwal GG,Singh R,Sircar AR. A randomized controlled trial to evaluate the slow-acting symptom-modifying effects of colchicine in osteoarthritis of the knee: a preliminary report. *Arthritis Rheum* 2002;47(3):280-284.
- Davis CL,Chandler WL. Thromboelastography for the prediction of bleeding after transplant renal biopsy. *J Am Soc Nephrol* 1995 Oct;6(4):1250-1255.
- Davis S. Tai Chi, water classes options for patients with osteoarthritis. *Geriatrics* 2007;62(6):12.
- Day R,Morrison B,Luza A,Castaneda O,Strusberg A,Nahir M,Helgetveit KB,Kress B,Daniels B,Bolognese J,Krupa D,Seidenberg B,Ehrich E. A randomized trial of the efficacy and tolerability of the COX-2 inhibitor Rofecoxib versus ibuprofen in patients with osteoarthritis. Rofecoxib /Ibuprofen Comparator Study Group. *Arch Intern Med* 2000;160(12):1781-1787.
- de AS,Fraenkel L,Volk RJ,Cox V,Suarez-Almazor ME. Impact of educational and patient decision aids on decisional conflict associated with total knee arthroplasty. *Arthritis Care Res (Hoboken)* 2011 Sep 27;.
- de Blecourt JJ. Double-blind controlled evaluation of Benoxaprofen for treatment of coxarthrosis and gonarthrosis. *Eur J Rheumatol Inflamm* 1981;4(3):408-411.
- De Filippis LG,Gulli S,Caliri A,D'Avola G,Lo GR,Morgante S,Romano C,Munao F,Trimarchi G,La TD,Fichera C,Pappalardo A,Triolo G,Gallo M,Valentini G,Bagnato G. Factors influencing pain, physical function and social functioning in patients with osteoarthritis in southern Italy. *Int J Clin Pharmacol Res* 2004;24(4):103-109.
- De GN,Zhu N,Keresteci M,Shi JE. Obesity and Joint Replacement Surgery in Canada: Findings from the Canadian Joint Replacement Registry (CJRR). *Healthc Policy* 2006;1(3):36-43.
- de Groot IB,Bussmann JB,Stam HJ,Verhaar JA. Actual everyday physical activity in patients with end-stage hip or knee osteoarthritis compared with healthy controls. *Osteoarthritis Cartilage* 2008;16(4):436-442.
- de Jong OR,Hopman-Rock M,Tak EC,Klazinga NS. An implementation study of two evidence-based exercise and health education programmes for older adults with osteoarthritis of the knee and hip. *Health Educ Res* 2004;19(3):316-325.
- de Miguel ME,Cobo IT,Uson JJ,Bonilla HG,Martin ME. Clinical and ultrasonographic findings related to knee pain in osteoarthritis. *Osteoarthritis Cartilage* 2006;14(6):540-544.

- Deal CL, Schnitzer TJ, Lipstein E, Seibold JR, Stevens RM, Levy MD, Albert D, Renold F. Treatment of arthritis with topical capsaicin: a double-blind trial. *Clin Ther* 1991;13(3):383-395.
- Debi R, Mor A, Segal O, Segal G, Debbi E, Agar G, Halperin N, Haim A, Elbaz A. Differences in gait patterns, pain, function and quality of life between males and females with knee osteoarthritis: a clinical trial. *BMC Musculoskelet Disord* 2009;10:127.
- Debi R, Robinson D, Agar G, Halperin N. [GAG for osteoarthritis of the knee--a prospective study]. 2000;138:451-3, 518.
- Debi R, Robinson D, Agar G, Halperin N. Glucosamine sulfate and chondroitin sulfates for degenerative joint disease. 2000;138:451-453+518.
- Decaria J, Petrella R, Petrella R, Wolfe D, Chesworth BM, Montero OM. Effect of intra-articular hyaluronic acid on gait variability in older adults with knee osteoarthritis. *J Am Geriatr Soc* 2011;59:949-951.
- Defrin R, Ariel E, Peretz C. Segmental noxious versus innocuous electrical stimulation for chronic pain relief and the effect of fading sensation during treatment. *Pain* 2005;115(1-2):152-160.
- Degenerative joint disease (osteoarthritis). *JAMA* 1973;224(5 Suppl):740-744.
- de-Jong OR, Hopman RM, Tak EC, Klazinga NS. An implementation study of two evidence-based exercise and health education programmes for older adults with osteoarthritis of the knee and hip. *Health Educ Res* 2004;19:316-325.
- Dekker J, Tola P, Aufdemkampe G, Winckers M. Categories of pain behaviour in osteoarthritis patients. *Physiotherapy Theory and Practice* 1993;9(3):157-163.
- Delarue Y, de Branch, Anract P, Revel M, Rannou F. Physical exercise supervised or not by a physiotherapist in the treatment of lower-limb osteoarthritis. Elaboration of French clinical practice guidelines. *Annales de Readaptation et de Medecine Physique* 2007;50(9):759-768.
- Delemos BP, Xiang J, Benson C, Gana TJ, Pascual ML, Rosanna R, Fleming B. Tramadol Hydrochloride Extended-Release Once-Daily in the Treatment of Osteoarthritis of the Knee and/or Hip: A Double-Blind, Randomized, Dose-Ranging Trial. *Am J Ther* 2010;:.
- DeLong JM, Beitzel K, Mazzocc AD, Shepard D, Roller BL, Hanypsiak BT. Update on platelet-rich plasma. *Current Orthopaedic Practice* 2011 Nov;22(6):514-523.
- Demetriades P, Seitanides V, Vezyroglou G, Mitseas C, Kontomerkos A. Double-blind trial of sulindac and ibuprofen in the treatment of osteoarthritis of the hip and/or knee. *Scand J Rheumatol Suppl* 1975;:S04-S04.
- Denegar CR, Schimizzi ME, Dougherty DR, Friedman JE, Clark JE, Comstock BA, Kraemer WJ. Responses to superficial heating and cooling differ in men and women with knee osteoarthritis. *Physiother Theory Pract* 2011 Aug 8;.
- Dennis DA, Komistek RD, Nadaud MC, Mahfouz M. Evaluation of off-loading braces for treatment of unicompartmental knee arthrosis. *J Arthroplasty* 2006;21(4 Suppl 1):2-8.

Dervin GF, Stiell IG, Rody K, Grabowski J. Effect of arthroscopic debridement for osteoarthritis of the knee on health-related quality of life. *J Bone Joint Surg Am* 2003;85-A(1):10-19.

Detora LM, Krupa D, Bolognese J, Sperling RS, Ehrich EW. Rofecoxib shows consistent efficacy in osteoarthritis clinical trials, regardless of specific patient demographic and disease factors. *J Rheumatol* 2001;28(11):2494-2503.

Detrembleur C, De NJ, van den Hecke A. Celecoxib improves the efficiency of the locomotor mechanism in patients with knee osteoarthritis. A randomised, placebo, double-blind and cross-over trial. *Osteoarthritis Cartilage* 2005;13(3):206-210.

Devas MB. High tibial osteotomy for arthritis of the knee. A method specially suitable for the elderly. *J Bone Joint Surg Br* 1969;51(1):95-99.

Dexter PA. Joint exercises in elderly persons with symptomatic osteoarthritis of the hip or knee. Performance patterns, medical support patterns, and the relationship between exercising and medical care. *Arthritis Care Res* 1992;5(1):36-41.

Deyle GD, Allison SC, Matekel RL, Ryder mg, Stang JM, Gohdes DD, Hutton JP, Henderson NE, Garber MB. Physical therapy treatment effectiveness for osteoarthritis of the knee: a randomized comparison of supervised clinical exercise and manual therapy procedures versus a home exercise program. *Phys Ther* 2005;85(12):1301-1317.

Deyle GD, Henderson NE, Matekel RL, Helewa A. Manual physical therapy and exercise improved function in osteoarthritis of the knee. *Evidence-Based Medicine* 2000;5(5):145.

Diamond HS. Double-blind crossover study of fenoprofen and aspirin in osteoarthritis. *J Rheumatol* 1976;2:67-70.

Dias RC, Dias JM, Ramos LR. Impact of an exercise and walking protocol on quality of life for elderly people with OA of the knee. *Physiother Res Int* 2003;8(3):121-130.

Diaz C, Rodriguez A, Geli C, Llobet JM, Tapounet R. Comparison of Aceclofenac and Diclofenac in osteoarthritic pain. *CURR THER RES , CLIN EXP* 1988;44:252-256.

Dickson DJ, Hosie G, English JR. A double-blind, placebo-controlled comparison of hylan G-F 20 against Diclofenac in knee osteoarthritis. *Journal of Clinical Research* 2001;4(41-52):41-52.

Dickson DJ. A double-blind evaluation of topical Piroxicam gel with oral ibuprofen in osteoarthritis of the knee. *Curr Ther Res Clin Exp* 1991;49:199-207.

Dienst M, Kohn D. [Allogenic meniscus transplantation]. *Oper Orthop Traumatol* 2006;18(5-6):463-480.

Dieppe P, Cushnaghan J, Jasani MK, McCrae F, Watt I. A two-year, placebo-controlled trial of non-steroidal anti-inflammatory therapy in osteoarthritis of the knee joint. *Br J Rheumatol* 1993;32(7):595-600.

Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991-94. *J Rheumatol* 2006;33(11):2271-2279.

- Dincer F,Linde K. Sham interventions in randomized clinical trials of acupuncture - A review. *Complement Ther Med* 2003;11(4):235-242.
- Dincer U,Cakar E,Ozdemir B,Kiralp MZ. Comparison of effects of combined physical therapy program and exercise on corrupted balance functions in patient with knee bilateral osteoarthritis. [Turkish]. *Journal* 2008;23:9-13.
- Ding C,Cicuttini F,Parameswaran V,Burgess J,Quinn S,Jones G. Serum levels of vitamin D, sunlight exposure, and knee cartilage loss in older adults: the Tasmanian older adult cohort study. *Arthritis Rheum* 2009;60(5):1381-1389.
- Diracoglu D,Alptekin K,Teksoz B,Yagci I,Ozcakar L,Aksoy C. Knee versus hip single-joint intra-articular hyaluronic acid injection in patients with both hip and knee osteoarthritis: a pilot study. *Clin Rheumatol* 2009;28(9):1021-1024.
- Diracoglu D,Baskent A,Celik A,Issever H,Aydin R. Long-term effects of kinesthesia/balance and strengthening exercises on patients with knee osteoarthritis: A one-year follow-up study. *Journal of Back and Musculoskeletal Rehabilitation* 2008;21(4):253-262.
- Diracoglu D,Baskent A,Yagci I,Ozcakar L,Aydin R. Isokinetic strength measurements in early knee osteoarthritis. *Acta Reumatol Port* 2009;34(1):72-77.
- Diracoglu D,Vural M,Baskent A,Dikici F,Aksoy C. The effect of viscosupplementation on neuromuscular control of the knee in patients with osteoarthritis. *J Back Musculoskelet Rehabil* 2009;22(1):1-9.
- Dixon AS,Jacoby RK,Berry H,Hamilton EB. Clinical trial of intra-articular injection of sodium hyaluronate in patients with osteoarthritis of the knee. *Curr Med Res Opin* 1988;11(4):205-213.
- Doherty M. The efficacy of Arthrotec in the treatment of osteoarthritis. *Scand J Rheumatol Suppl* 1992;96:15-21.
- Doi T,Akai M,Fujino K,Hoshino Y,Iwaya T,Sunami Y. Effect of nonsteroidal anti-inflammatory drug plasters for knee osteoarthritis in Japanese: a randomized controlled trial. *Mod Rheumatol* 2010;20(1):24-33.
- Doi T,Akai M,Fujino K,Iwaya T,Kurosawa H,Hayashi K,Marui E. Effect of home exercise of quadriceps on knee osteoarthritis compared with nonsteroidal antiinflammatory drugs: a randomized controlled trial. *Am J Phys Med Rehabil* 2008;87(4):258-269.
- Domotor E. Clinical examination of the synergistic effect of niflumic acid and tolperisone in genicular arthritis. *Ther Hung* 1979;27(3):129-133.
- Dore R,Ballard I,Constantine G,McDonald P. Efficacy and safety of etodolac and Naproxen in patients with osteoarthritis of the knee: a double-blind, placebo-controlled study. *Clin Ther* 1995;17(4):656-666.
- Dorsher PT. Clinical equivalence of laser needle to metal acupuncture needle in treating musculoskeletal pain: A pilot study. *Medical Acupuncture* 2010;22(1):11-17.

Dougados M, Leclaire P, van der Heijde D, Bloch DA, Bellamy N, Altman RD. Response criteria for clinical trials on osteoarthritis of the knee and hip: a report of the Osteoarthritis Research Society International Standing Committee for Clinical Trials response criteria initiative. *Osteoarthritis Cartilage* 2000;8(6):395-403.

Dougados M, Moore A, Yu S, Gitton X. Evaluation of the patient acceptable symptom state in a pooled analysis of two multicentre, randomised, double-blind, placebo-controlled studies evaluating Lumiracoxib and Celecoxib in patients with osteoarthritis. *Arthritis Res Ther* 2007;9(1):R11.

Dougados M, Nguyen M, Listrat V, Amor B. High molecular weight sodium hyaluronate (hyalectin) in osteoarthritis of the knee: a 1 year placebo-controlled trial. *Osteoarthritis Cartilage* 1993;1(2):97-103.

Dowling AV, Fisher DS, Andriacchi TP. Gait modification via verbal instruction and an active feedback system to reduce peak knee adduction moment. *J Biomech Eng* 2010 Jul;132(7):071007.

Draper DO, Anderson MB. Combining topical analgesics and ultrasound, part I. *Athletic Therapy Today* 2005;10(1):26-27.

Draper ER, Cable JM, Sanchez-Ballester J, Hunt N, Robinson JR, Strachan RK. Improvement in function after valgus bracing of the knee. An analysis of gait symmetry. *J Bone Joint Surg Br* 2000;82(7):1001-1005.

Dreiser RL, Tisne-Camus M. DHEP plasters as a topical treatment of knee osteoarthritis--a double-blind placebo-controlled study. *Drugs Exp Clin Res* 1993;19(3):117-123.

Drexler M, Elbaz A, Mor A, Debi R, Debbi EM, Haim A, Lador R, Salai M, Segal G. Effects of a customized biomechanical therapy on patients with medial compartment knee osteoarthritis. *Ann Phys Rehabil Med* 2012 May;55(4):213-228.

Duffy T, Belton O, Bresnihan B, FitzGerald O, FitzGerald D. Inhibition of PGE2 production by nimesulide compared with Diclofenac in the acutely inflamed joint of patients with arthritis. *Drugs* 2003;63 Suppl 1:31-36.

Duke Med Health News 2011 Apr;17(4):4-5.

Duncan R, Peat G, Thomas E, Wood L, Hay E, Croft P. Does isolated patellofemoral osteoarthritis matter?. *Osteoarthritis Cartilage* 2009;17(9):1151-1155.

Duncan R, Peat G, Thomas E, Wood L, Hay E, Croft P. How do pain and function vary with compartmental distribution and severity of radiographic knee osteoarthritis?. *Rheumatology (Oxford)* 2008;47(11):1704-1707.

Dunlop DD, Semanik P, Song J, Sharma L, Nevitt M, Jackson R, Mysiw J, Chang RW. Moving to Maintain Function in Knee Osteoarthritis: Evidence From the Osteoarthritis Initiative. *Archives of Physical Medicine and Rehabilitation* 2010;91(5):714-721.

Dunlop DD, Song J, Semanik PA, Sharma L, Chang RW. Physical activity levels and functional performance in the osteoarthritis initiative: A graded relationship. *Arthritis and Rheumatism* 2011 Jan;63(1):127-136.

- Durmus D, Alayli G, Canturk F. Effects of quadriceps electrical stimulation program on clinical parameters in the patients with knee osteoarthritis. *Clin Rheumatol* 2007;26(5):674-678.
- Earl RT, Jenkins R, Munro AJ. A double-masked comparison of the efficacy of once-daily sustained-release ibuprofen and once-daily Piroxicam for 24-hour control of arthralgia due to osteoarthritis in the elderly. *Current Therapeutic Research Clinical and Experimental* 1996;57:811-821.
- Eastwood DM. The failures of arthroscopic partial meniscectomy. *Injury* 1985;16(9):587-590.
- Eaton CB, Bertola M, Dobosz B, Driban J, McAlindon TA. Predictors of progression of knee OA: Osteoarthritis initiative. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S149.
- Eberhardt R, Zwingers T, Gerbershagen H, Nagyivanyi P. Analgesic efficacy and tolerability of lysine-clonixinate versus ibuprofen in patients with gonarthrosis. *Current Therapeutic Research - Clinical and Experimental* 1995;56(6):573-580.
- Eberle E, Ottlinger B. Clinically relevant change and clinically relevant difference in knee osteoarthritis. *Osteoarthritis Cartilage* 1999;7(5):502-503.
- Ebert JR, Fallon M, Zheng MH, Wood DJ, Ackland TR. A Randomized Trial Comparing Accelerated and Traditional Approaches to Postoperative Weightbearing Rehabilitation After Matrix-Induced Autologous Chondrocyte Implantation: Findings at 5 Years. *Am J Sports Med* 2012 Apr 26.
- Eckstein F, Maschek S, Wirth W, Hudelmaier M, Hitzl W, Wyman B, Nevitt M, Le Graverand MP. One year change of knee cartilage morphology in the first release of participants from the Osteoarthritis Initiative progression subcohort: association with sex, body mass index, symptoms and radiographic osteoarthritis status. *Ann Rheum Dis* 2009;68(5):674-679.
- Edelson R, Burks RT, Bloebaum RD. Short-term effects of knee washout for osteoarthritis. *Am J Sports Med* 1995;23(3):345-349.
- Ediz L, Hiz O, Toprak M, Tekeoglu I. Effect of weekly alendronate on knee symptoms in patients with osteoporosis and knee osteoarthritis coexistence. *Osteoporoz Dunyasindan* 2010 Apr;16(1):17-21.
- Edworthy SM, Devins GM. Improving medication adherence through patient education distinguishing between appropriate and inappropriate utilization. Patient Education Study Group. *J Rheumatol* 1999;26(8):1793-1801.
- Efe T, Heyse TJ, Boese C, Timmesfeld N, Fuchs-Winkelmann S, Schmitt J, Theisen C, Schofer MD. TKA following high tibial osteotomy versus primary TKA--a matched pair analysis. *BMC Musculoskeletal Disord* 2010;11:207.
- Ehrich EW, Davies GM, Watson DJ, Bolognese JA, Seidenberg BC, Bellamy N. Minimal perceptible clinical improvement with the Western Ontario and McMaster Universities osteoarthritis index questionnaire and global assessments in patients with osteoarthritis. *J Rheumatol* 2000;27(11):2635-2641.
- El Amrani MH, Levy B, Scharycki S, Asselineau A. Patellar height relevance in opening-wedge high tibial osteotomy. 2009;.

El Amrani MH, Levy B, Scharycki S, Asselineau A. Patellar height relevance in opening-wedge high tibial osteotomy. *Orthopaedics and Traumatology* 2010;96(1):36-42.

El-Azab H, Halawa A, Anetzberger H, Imhoff AB, Hinterwimmer S. The effect of closed- and open-wedge high tibial osteotomy on tibial slope: a retrospective radiological review of 120 cases. *J Bone Joint Surg Br* 2008;90(9):1193-1197.

Elbaz A, Debbi EM, Segal G, Haim A, Halperin N, Agar G, Mor A, Debi R. Sex and body mass index correlate with Western Ontario and McMaster Universities Osteoarthritis Index and quality of life scores in knee osteoarthritis. *Arch Phys Med Rehabil* 2011 Oct;92(10):1618-1623.

Elbaz A, Mor A, Segal G, Debbi E, Haim A, Halperin N, Debi R. APOS therapy improves clinical measurements and gait in patients with knee osteoarthritis. *Clin Biomech (Bristol, Avon)* 2010 Nov;25(9):920-925.

Elleuch MH, Guermazi M, Mezghanni M, Ghroubi S, Fki H, Mefteh S, Baklouti S, Sellami S. Knee osteoarthritis in 50 former top-level soccer players: a comparative study. *Ann Readapt Med Phys* 2008;51(3):174-178.

El-Mehairy MM, Shaker A, Bahgat NE, Hamza S, Salam MS. A double-blind comparison of niflumic acid with phenylbutazone, oxyphenylbutazone and placebo in the treatment of osteoarthrosis. *Rheumatol Rehabil* 1974;13(4):198-203.

Emanuelli A, Sacchetti G. Indoprofen in the treatment of osteoarthritis. Results of a phase IV multiclinic study in 1629 patients. *Eur J Rheumatol Inflamm* 1981;4(1):113-117.

Emery CF, Keefe FJ, France CR, Affleck G, Waters S, Fondow MD, McKee DC, France JL, Hackshaw KV, Caldwell DS, Stainbrook D. Effects of a brief coping skills training intervention on nociceptive flexion reflex threshold in patients having osteoarthritic knee pain: a preliminary laboratory study of sex differences. *J Pain Symptom Manage* 2006;31(3):262-269.

Endres S. High-flexion versus conventional total knee arthroplasty: a 5-year study. *J Orthop Surg (Hong Kong)* 2011 Aug;19(2):226-229.

Englund M, Guermazi A, Roemer FW, Aliabadi P, Yang M, Lewis CE, Torner J, Nevitt MC, Sack B, Felson DT. Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: The Multicenter Osteoarthritis Study. *Arthritis Rheum* 2009;60(3):831-839.

Englund M, Lohmander LS. Patellofemoral osteoarthritis coexistent with tibiofemoral osteoarthritis in a meniscectomy population. *Ann Rheum Dis* 2005;64(12):1721-1726.

Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. *Arthritis Rheum* 2004;50(9):2811-2819.

Englund M, Roos EM, Lohmander LS. Impact of type of meniscal tear on radiographic and symptomatic knee osteoarthritis: a sixteen-year followup of meniscectomy with matched controls. *Arthritis Rheum* 2003;48(8):2178-2187.

Englund M,Roos EM,Roos HP,Lohmander LS. Patient-relevant outcomes fourteen years after meniscectomy: influence of type of meniscal tear and size of resection. *Rheumatology (Oxford)* 2001;40(6):631-639.

Erak S,Naudie D,MacDonald SJ,McCalden RW,Rorabeck CH,Bourne RB. Total knee arthroplasty following medial opening wedge tibial osteotomy Technical issues early clinical radiological results. *Knee* 2010 Dec 6;.

Erdmann GH. Oxyphenbutazone and flufenamic acid in the treatment of osteo-arthritis of the knee. A double-blind trial comparison. *S Afr Med J* 1974;48(22):947-948.

Ergun H,Kulcu D,Kutlay S,Bodur H,Tulunay FC. Efficacy and safety of topical nimesulide in the treatment of knee osteoarthritis. *J Clin Rheumatol* 2007;13(5):251-255.

Erhart JC,Mundermann A,Elspas B,Giori NJ,Andriacchi TP. A variable-stiffness shoe lowers the knee adduction moment in subjects with symptoms of medial compartment knee osteoarthritis. *J Biomech* 2008;41(12):2720-2725.

Erhart JC,Mundermann A,Elspas B,Giori NJ,Andriacchi TP. Changes in knee adduction moment, pain, and functionality with a variable-stiffness walking shoe after 6 months. *J Orthop Res* 2010;.

Erhart-Hledik JC,Elspas B,Giori NJ,Andriacchi TP. Effect of variable-stiffness walking shoes on knee adduction moment, pain, and function in subjects with medial compartment knee osteoarthritis after 1 year. *J Orthop Res* 2011 Sep 23;.

Erhart-Hledik JC,Elspas B,Giori NJ,Andriacchi TP. Effect of variable-stiffness walking shoes on knee adduction moment, pain, and function in subjects with medial compartment knee osteoarthritis after 1 year. *J Orthop Res* 2012 Apr;30(4):514-521.

Ericsson YB,Roos EM,Dahlberg L. Muscle strength, functional performance, and self-reported outcomes four years after arthroscopic partial meniscectomy in middle-aged patients. *Arthritis Rheum* 2006;55(6):946-952.

Erturk H,Celiker R,Aydin M. Comparison of efficacy and tolerability of acemetacin and Acetaminophen in the treatment of knee osteoarthritis. [Turkish]. *Journal* 1998;9:157-161.

Escalante TFJ. Comparative clinical trial of tiaprofenic acid against Naproxen in osteoarthritis of the knee. <ORIGINAL> ENSAYO CLINICO COMPARATIVO DEL ACIDO TIAPROFENICO VS NAPROXEN EN PACIENTES CON GONARTROSIS. *INVEST MED INT* 1981;8:218-236.

Escalante Y,Garcia-Hermoso A,Saavedra JM. Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: A systematic review. *J Sci Med Sport* 2010 Nov 24;.

Escalante Y,Saavedra JM,Garcia-Hermoso A,Silva AJ,Barbosa TM. Physical exercise and reduction of pain in adults with lower limb osteoarthritis: a systematic review. *J Back Musculoskelet Rehabil* 2010 Jan;23(4):175-186.

Esenkaya I,Elmali N. Proximal tibia medial open-wedge osteotomy using plates with wedges: early results in 58 cases. *Knee Surg Sports Traumatol Arthrosc* 2006;14(10):955-961.

Eti E,Kouakou HB,Daboiko JC,Ouali B,Ouattara B,Gabla KA,Kouakou MN. Epidemiology and features of knee osteoarthritis in the Ivory Coast. *Rev Rhum Engl Ed* 1998;65(12):766-770.

Ettinger WH,Davis MA,Neuhaus JM,Mallon KP. Long-term physical functioning in persons with knee osteoarthritis from NHANES. I: Effects of comorbid medical conditions. *J Clin Epidemiol* 1994;47(7):809-815.

Eungpinichpong W. The efficacy of physical exercise programmes for patients with osteoarthritis of the knee as determined by clinical and gait parameters. *New Zealand Journal Physiotherapy* 1998;26:5.

Evarts CM,DeHaven K,Nelson CL. Proximal tibial osteotomy for degenerative arthritis of the knee. *Orthop Clin North Am* 1971;2(1):231-243.

Evcik D,Kavuncu V,Yeter A,Yigit I. The efficacy of balneotherapy and mud-pack therapy in patients with knee osteoarthritis. *Joint Bone Spine* 2007;74(1):60-65.

Evcik D,Sonel B. Effectiveness of a home-based exercise therapy and walking program on osteoarthritis of the knee. *Rheumatol Int* 2002;22(3):103-106.

Fabricant PD,Rosenberger PH,Jokl P,Ickovics JR. Predictors of short-term recovery differ from those of long-term outcome after arthroscopic partial meniscectomy. *Arthroscopy* 2008;24(7):769-778.

Faik A,Benbouazza K,Amine B,Maaroufi H,Bahiri R,Lazrak N,Aboukal R,Hajjaj-Hassouni N. Translation and validation of Moroccan Western Ontario and McMaster Universities (WOMAC) osteoarthritis index in knee osteoarthritis. *Rheumatol Int* 2008;28(7):677-683.

Falagas ME,Zarkadoulia E,Rafailidis PI. The therapeutic effect of balneotherapy: Evaluation of the evidence from randomised controlled trials. *Int J Clin Pract* 2009;63(7):1068-1084.

Falconer J,Hayes KW,Chang RW. Effect of ultrasound on mobility in osteoarthritis of the knee. A randomized clinical trial. *Arthritis Care Res* 1992;5(1):29-35.

Fan J,Shi D,Dai J,Zhu L,Qin J,Shao Z,Qiu X,Xu Z,Chen D,Jiang Q. Genetic polymorphism of PITX1 in susceptibility to knee osteoarthritis in a Chinese Han population: a case-control study. *Rheumatol Int* 2010;.

Fargas-Babjak A,Rooney P,Gerecz E. Randomized trial of Codetron for pain control in osteoarthritis of the hip/knee. *Clin J Pain* 1989;5(2):137-141.

Farid R,Mirfeizi Z,Mirheidari M,Rezaieyazdi Z,Mansouri H,Esmaili H,Zibadi S,Rohdewald P,Watson RR. Pycnogenol supplementation reduces pain and stiffness and improves physical function in adults with knee osteoarthritis. *Nutrition Research* 2007;27(11):692-697.

Farr J,Mont MA,Garland D,Caldwell JR,Zizic TM. Pulsed electrical stimulation in patients with osteoarthritis of the knee: follow-up in 288 patients who had failed non-operative therapy. *Surg Technol Int* 2006;15:227-233.

Farr JN,Going SB,Lohman TG,Rankin L,Kasle S,Cornett M,Cussler E. Physical activity levels in patients with early knee osteoarthritis measured by accelerometry. *Arthritis Rheum* 2008;59(9):1229-1236.

Farr JN,Going SB,McKnight PE,Kasle S,Cussler EC,Cornett M. Progressive resistance training improves overall physical activity levels in patients with early osteoarthritis of the knee: a randomized controlled trial. *Phys Ther* 2010;90(3):356-366.

Faucher M,Poiraudeau S,Lefevre-Colau MM,Rannou F,Fermanian J,Revel M. Algo-functional assessment of knee osteoarthritis: Comparison of the test-retest reliability and construct validity of the WOMAC and Lequesne indexes. *Osteoarthritis and Cartilage* 2002;10(8):602-610.

Faucher M,Poiraudeau S,Lefevre-Colau MM,Rannou F,Fermanian J,Revel M. Assessment of the test-retest reliability and construct validity of a modified Lequesne index in knee osteoarthritis. *Joint Bone Spine* 2003;70(6):521-525.

Faucher M,Poiraudeau S,Lefevre-Colau MM,Rannou F,Fermanian J,Revel M. Assessment of the test-retest reliability and construct validity of a modified WOMAC index in knee osteoarthritis. *Joint Bone Spine* 2004;71(2):121-127.

Fauno P,Nielsen AB. Arthroscopic partial meniscectomy: A long-term follow-up. *Arthroscopy* 1992;8(3):345-349.

Fawthrop F,Yaqub R,Belcher C,Bayliss M,Ledingham J,Doherty M. Chondroitin and keratan sulphate epitopes, glycosaminoglycans, and hyaluronan in progressive versus non-progressive osteoarthritis. *Ann Rheum Dis* 1997;56(2):119-122.

Fedder M,Stroehmann I. Efficacy and safety of nabumetone in 5,421 patients with osteoarthritis of the hip and/or knee joints. A subgroup evaluation of an outpatient study involving 18,047 patients. *Drugs* 1990;40 Suppl 5:75-77.

Felson DT,Anderson JJ,Naimark A,Walker AM,Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med* 1988;109(1):18-24.

Felson DT,Goggins J,Niu J,Zhang Y,Hunter DJ. The effect of body weight on progression of knee osteoarthritis is dependent on alignment. *Arthritis Rheum* 2004;50(12):3904-3909.

Felson DT,Niu J,Clancy M,Aliabadi P,Sack B,Guermazi A,Hunter DJ,Amin S,Rogers G,Booth SL. Low levels of vitamin D and worsening of knee osteoarthritis: results of two longitudinal studies. *Arthritis Rheum* 2007;56(1):129-136.

Felson DT,Niu J,Clancy M,Sack B,Aliabadi P,Zhang Y. Effect of recreational physical activities on the development of knee osteoarthritis in older adults of different weights: the Framingham Study. *Arthritis Rheum* 2007;57(1):6-12.

Felson DT,Zhang Y,Anthony JM,Naimark A,Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. *Ann Intern Med* 1992;116(7):535-539.

Felson DT. Clinical practice. Osteoarthritis of the knee. *N Engl J Med* 2006;354(8):841-848.

Felson DT. Obesity and osteoarthritis of the knee. *Bull Rheum Dis* 1992;41(2):6-7.

Felson DT. Osteoarthritis of the knee. *N Engl J Med* 2006;354(8):841-848.

- Felts E, Parratte S, Pauly V, Aubaniac JM, Argenson JN. Function and quality of life following medial unicompartmental knee arthroplasty in patients 60 years of age or younger. *Orthop Traumatol Surg Res* 2010 Dec;96(8):861-867.
- Fernandes FA, Pucinelli ML, da Silva NP, Feldman D. Serum cartilage oligomeric matrix protein (COMP) levels in knee osteoarthritis in a Brazilian population: clinical and radiological correlation. *Scand J Rheumatol* 2007;36(3):211-215.
- Fernandez-Lopez JC, Laffon A, Blanco FJ, Carmona L. Prevalence, risk factors, and impact of knee pain suggesting osteoarthritis in Spain. *Clin Exp Rheumatol* 2008;26(2):324-332.
- Figgie HE, Goldberg VM, Heiple KG, Moller HS, Gordon NH. The influence of tibial-patellofemoral location on function of the knee in patients with the posterior stabilized condylar knee prosthesis. *J Bone Joint Surg Am* 1986;68(7):1035-1040.
- Filardo G, Kon E, Buda R, Timoncini A, Di MA, Cenacchi A, Fornasari PM, Giannini S, Marcacci M. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2011 Apr;19(4):528-535.
- Filardo G, Kon E, Pereira Ruiz MT, Vaccaro F, Guitaldi R, Di MA, Cenacchi A, Fornasari PM, Marcacci M. Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. *Knee Surg Sports Traumatol Arthrosc* 2011 Dec 28.
- Finch E, Kennedy D. The lower extremity activity profile: a health status instrument for measuring lower extremity disability. *Physiother Can* 1995;47(4):239-246.
- Finkelstein JA, Gross AE, Davis A. Varus osteotomy of the distal part of the femur. A survivorship analysis. *J Bone Joint Surg Am* 1996;78(9):1348-1352.
- Fioravanti A, Bellisai B, Iacoponi F, Manica P, Galeazzi M. Phytothermotherapy in osteoarthritis: A randomized controlled clinical trial. *J Altern Complement Med* 2011 May 1;17(5):407-412.
- Fioravanti A, Cantarini L, Bacarelli MR, de LA, Ceccatelli L, Blardi P. Effects of Spa therapy on serum leptin and adiponectin levels in patients with knee osteoarthritis. *Rheumatol Int* 2010;.
- Fioravanti A, Iacoponi F, Bellisai B, Cantarini L, Galeazzi M. Short- and long-term effects of spa therapy in knee osteoarthritis. ;89(2):125-132.
- Fioravanti A, Storri L, Di MS, Bisogno S, Oldani V, Scotti A, Marcolongo R. A randomized, double-blind, multicenter trial of nimesulide-beta-cyclodextrin versus Naproxen in patients with osteoarthritis. *Clin Ther* 2002;24(4):504-519.
- Fioravanti A. Short- and long-term effects of spa therapy in knee osteoarthritis. 2010.
- Fischer G, Pelka RB, Barovic J. [Adjuvant treatment of osteoarthritis of the knee with weak pulsing magnetic fields - Results of a prospective, placebo controlled trial]. *Aktuelle Rheumatologie* 2006;31:226-233.
- Fisher DE. Proximal tibial osteotomy 1970-1995. *Iowa Orthop J* 1998;18:54-63.

- Fisher NM, Gresham G, Pendergast DR. Effects of a quantitative progressive rehabilitation program applied unilaterally to the osteoarthritic knee. *Arch Phys Med Rehabil* 1993;74(12):1319-1326.
- Fisher NM, Gresham GE, Abrams M, Hicks J, Horrigan D, Pendergast DR. Quantitative effects of physical therapy on muscular and functional performance in subjects with osteoarthritis of the knees. *Arch Phys Med Rehabil* 1993;74(8):840-847.
- Fisher NM, Pendergast DR. Reduced muscle function in patients with osteoarthritis. *Scand J Rehabil Med* 1997;29(4):213-221.
- Fisher NM, White SC, Yack HJ, Smolinski RJ, Pendergast DR. Muscle function and gait in patients with knee osteoarthritis before and after muscle rehabilitation. *Disabil Rehabil* 1997;19(2):47-55.
- Fitzgerald GK, Piva SR, Irrgang JJ, Bouzubar F, Starz TW. Quadriceps activation failure as a moderator of the relationship between quadriceps strength and physical function in individuals with knee osteoarthritis. *Arthritis Rheum* 2004;51(1):40-48.
- Fitzgerald GK. Agility and perturbation training techniques in exercise therapy for reducing pain and improving function in people with knee osteoarthritis: a randomized clinical trial. 2011.
- Flecher X, Parratte S, Aubaniac JM, Argenson JN. A 12-28-year followup study of closing wedge high tibial osteotomy. *Clin Orthop Relat Res* 2006;452:91-96.
- Fleischmann R, Tannenbaum H, Patel NP, Notter M, Sallstig P, Reginster JY. Long-term retention on treatment with Lumiracoxib 100mg once or twice daily compared with Celecoxib 200mg once daily: a randomised controlled trial in patients with osteoarthritis. *BMC Musculoskelet Disord* 2008;9:32.
- Flierl S, Sabo D, Hornig K, Perlick L. Open wedge high tibial osteotomy using fractioned drill osteotomy: a surgical modification that lowers the complication rate. *Knee Surg Sports Traumatol Arthrosc* 1996;4(3):149-153.
- Florete OG, Xiang J, Vorsanger GJ. Effects of extended-release Tramadol on pain-related sleep parameters in patients with osteoarthritis. *Expert Opin Pharmacother* 2008;9(11):1817-1827.
- Flusser D, Abu-Shakra M, Friger M, Codish S, Sukenik S. Therapy with mud compresses for knee osteoarthritis: Comparison of natural mud preparations with mineral-depleted mud. *Journal of Clinical Rheumatology* 2002;8(4):197-203.
- Focht BC, Ewing V, Gauvin L, Rejeski WJ. The unique and transient impact of acute exercise on pain perception in older, overweight, or obese adults with knee osteoarthritis. *Ann Behav Med* 2002;24(3):201-210.
- Focht BC, Garver MJ, Devor ST, Dials J, Rose M, Lucas AR, Emery CF, Hackshaw K, Rejeski WJ. Improving maintenance of physical activity in older, knee osteoarthritis patients trial-pilot (IMPACT-P): Design and methods. *Contemp Clin Trials* 2012 May 1.
- Foley A, Halbert J, Hewitt T, Crotty M. Does hydrotherapy improve strength and physical function in patients with osteoarthritis--a randomised controlled trial comparing a gym based and a hydrotherapy based strengthening programme. *Ann Rheum Dis* 2003;62(12):1162-1167.

- Fond J, Rodin D, Ahmad S, Nirschl RP. Arthroscopic debridement for the treatment of osteoarthritis of the knee: 2- and 5-year results. *Arthroscopy* 2002;18(8):829-834.
- Forestier R. Magnitude and duration of the effects of two spa therapy courses on knee and hip osteoarthritis: an open prospective study in 51 consecutive patients. *Joint Bone Spine* 2000;67(4):296-304.
- Formiguera SS, Esteve de MR. Intra-articular hyaluronic acid in the treatment osteoarthritis of the knee: A short term study. *Eur J Rheumatol Inflamm* 1995;15(1):33-38.
- Forster MC, Straw R. A prospective randomised trial comparing intra-articular Hyalgan injection and arthroscopic washout for knee osteoarthritis. *Knee* 2003;10(3):291-293.
- Foster NA, Segal NA, Clearfield JS, Lewis CE, Keysor J, Nevitt MC, Torner JC. Central versus lower body obesity distribution and the association with lower limb physical function and disability. *PM R* 2010 Dec;2(12):1119-1126.
- Foster NE, Thomas E, Barlas P, Hill JC, Young J, Mason E, Hay EM. Acupuncture as an adjunct to exercise based physiotherapy for osteoarthritis of the knee: randomised controlled trial. *BMJ* 2007;335(7617):436.
- Foster NE, Thomas E, Hill JC, Hay EM. The relationship between patient and practitioner expectations and preferences and clinical outcomes in a trial of exercise and acupuncture for knee osteoarthritis. *Eur J Pain* 2010;14(4):402-409.
- Fotopoulos VC, Tzinia A, Tzurbakis M, Kalfakakou V, Levidiotou-Stefanou S, Georgoulis A. Expression levels of matrix metalloproteinase (MMP)-9 and its specific inhibitor TIMP-1, in septic and aseptic arthritis of the knee. *Knee Surg Sports Traumatol Arthrosc* 2011 Sep 24;.
- Fox BA, Schmitz ED, Wallace R. Glucosamine and chondroitin for osteoarthritis. *Am Fam Physician* 2006;73(7):1245-1248.
- Foy CG, Lewis CE, Hairston KG, Miller GD, Lang W, Jakicic JM, Rejeski WJ, Ribisl PM, Walkup MP, Wagenknecht LE. Intensive lifestyle intervention improves physical function among obese adults with knee pain: findings from the Look AHEAD trial. *Obesity (Silver Spring)* 2011 Jan;19(1):83-93.
- Foy CG, Penninx BW, Shumaker SA, Messier SP, Pahor M. Long-term exercise therapy resolves ethnic differences in baseline health status in older adults with knee osteoarthritis. *J Am Geriatr Soc* 2005;53(9):1469-1475.
- Fraenkel L, Fried T. If You Want Patients with Knee Osteoarthritis (OA) to Exercise: Tell them about NSAIDS. *Patient* 2008;1(1):21-26.
- Frampton JE. Hylan G-F 20 single-injection formulation. *Drugs Aging* 2010;27(1):77-85.
- Franchi R, Liverta C, Pollini C, Pontiroli AE. Parenteral administration of Ketoprofen in osteoarthritis: a double-blind trial versus the N-methyl-d-glucamine salt of indomethacin. *Scand J Rheumatol Suppl* 1979;(26):1-7.
- Franchimont P. A double blind study to compare a once daily dose of 1600 mg sustained release ibuprofen with standard 400 mg ibuprofen tablets given four times daily in patients with osteoarthritis of the knee. *Scand J Rheumatol Suppl* 1990;85:61.

Francis GS. Ask Dr. Francis. I am taking a medication called Rofecoxib for knee arthritis, and it works well. But I've heard reports that this type of medication may be dangerous for people with heart disease. Should I be worried?. *Heart Advis* 2002;5(7):8.

Fransen M,Margiotta E,Crosbie J,Edmonds J. A revised group exercise program for osteoarthritis of the knee. *Physiother Res Int* 1997;2(1):30-41.

Fransen M,Margiotta E,Heussler J,Edmonds J. Group exercise for subjects with osteoarthritis of the knee. *Australian Journal of Physiotherapy* 1995;41(4):255-260.

Fransen M,McConnell S,Hernandez-Molina G,Reichenbach S. Exercise for osteoarthritis of the hip (Cochrane review) [with consumer summary]. *Cochrane Database of Systematic Reviews* 2009;Issue 3\ \:.

Fransen M,McConnell S. Land-based exercise for osteoarthritis of the knee: a metaanalysis of randomized controlled trials (Brief record). *J Rheumatol* 2009;36:1109-1117.

Fransen M,Nairn L,Winstanley J,Lam P,Edmonds J. Physical activity for osteoarthritis management: a randomized controlled clinical trial evaluating hydrotherapy or Tai Chi classes. *Arthritis Rheum* 2007;57(3):407-414.

Freitas GG. A double-blind comparison of etodolac and Piroxicam in the treatment of osteoarthritis. *Curr Med Res Opin* 1990;12(4):255-262.

French HP,Brennan A,White B,Cusack T. Manual therapy for osteoarthritis of the hip or knee - a systematic review. *Man Ther* 2011 Apr;16(2):109-117.

Frestedt JL,Kuskowski MA,Zenk JL. A natural seaweed derived mineral supplement (Aquamin F) for knee osteoarthritis: a randomised, placebo controlled pilot study. *Nutr J* 2009;8:7.

Frestedt JL,Walsh M,Kuskowski MA,Zenk JL. A natural mineral supplement provides relief from knee osteoarthritis symptoms: a randomized controlled pilot trial. *Nutr J* 2008;7:9.

Frias G,Caracuel MA,Escudero A,Rumbao J,Perez-Gujo V,del Carmen CM,Font P,Gonzalez J,Collantes E. Assessment of the efficacy of joint lavage versus joint lavage plus corticoids in patients with osteoarthritis of the knee. *Curr Med Res Opin* 2004;20(6):861-867.

Frias G,Font P,Munoz GE,Caracuel MA,Escudero A,Castro MC,Collantes EE. [Assessing the efficacy of non-arthroscopic joint lavage in patients with osteoarthritis of the knee]. *Reumatologia Clinica* 2009;5:189-193.

Friedmann N,Klutzaritz V,Webster L. Efficacy and safety of an extended-release oxycodone (Remoxy) formulation in patients with moderate to severe osteoarthritic pain. *J Opioid Manag* 2011 May;7(3):193-202.

Fries JF,Carey C,MCS Shane DJ. Patient education in arthritis: randomized controlled trial of a mail-delivered program. *J Rheumatol* 1997;24(7):1378-1383.

Frizziero L,Pasquali R. Intra-articular treatment of osteoarthritis of the knee: An arthroscopic and clinical comparison between sodium hyaluronate (500-730 kDa) and methylprednisolone acetate. *Journal of Orthopaedics and Traumatology* 2002;3(2):89-96.

- Fu MY,Zhang ZL. [Knee osteoarthritis treated with acupuncture at the points selected according to syndrome differentiation: a randomized controlled trial]. *Zhongguo zhen jiu = Chinese acupuncture & moxibustion* 2011;31:1062-1066.
- Fujisawa Y,Masuhara K,Shiomi S. The effect of high tibial osteotomy on osteoarthritis of the knee. An arthroscopic study of 54 knee joints. *Orthop Clin North Am* 1979;10(3):585-608.
- Fujita T,Fujii Y,Okada SF,Miyauchi A,Takagi Y. Analgesic effect of etidronate on degenerative joint disease. *J Bone Miner Metab* 2001;19(4):251-256.
- Fujita T,Ohue M,Fujii Y,Miyauchi A,Takagi Y. Analgesic and chondroprotective effects of risedronate in osteoarthritis assessed by electroalgometry and measurement of collagen type II fragments in urine. *J Int Med Res* 2008;36(5):932-941.
- Fujita T,Ohue M,Fujii Y,Miyauchi A,Takagi Y. Comparison of the analgesic effects of bisphosphonates: etidronate, alendronate and risedronate by electroalgometry utilizing the fall of skin impedance. *J Bone Miner Metab* 2009;27(2):234-239.
- Fukuda TY,Ovanessian V,Cunha RAD,Filho ZJ,Cazarini C,Rienzo FA,Centini AA. Pulsed short wave effect in pain and function in patients with knee osteoarthritis. *Journal of Applied Research* 2008;8(3):189-198.
- Fulga C,Fulga IG,Predescu M. Clinical study of the effect of laser therapy in rheumatic degenerative diseases. *Rom J Intern Med* 1994;32(3):227-233.
- Fullerton BD,Reeves KD. Ultrasonography in regenerative injection (prolotherapy) using dextrose, platelet-rich plasma, and other injectants. *Phys Med Rehabil Clin N Am* 2010 Aug;21(3):585-605.
- Furuzawa-Carballeda J,Munoz-Chable OA,Macias-Hernandez SI,Agualimpia-Janning A. Effect of polymerized-type I collagen in knee osteoarthritis. II. In vivo study. *Eur J Clin Invest* 2009;39(7):598-606.
- Gaal J,Varga J,Szekanecz Z,Kurko J,Ficzere A,Bodolay E,Bender T. Balneotherapy in elderly patients: effect on pain from degenerative knee and spine conditions and on quality of life. *Isr Med Assoc J* 2008;10(5):365-369.
- Gaasbeek RDA,Nicolaas L,Rijnberg WJ,Van Loon CJM,van KA. Correction accuracy and collateral laxity in open versus closed wedge high tibial osteotomy. A one-year randomised controlled study. *Int Orthop* 2010;34(2 SPECIAL ISSUE):201-207.
- Gaines JM,Metter EJ,Talbot LA. The effect of neuromuscular electrical stimulation on arthritis knee pain in older adults with osteoarthritis of the knee. *Appl Nurs Res* 2004;17(3):201-206.
- Gaines JM,Talbot LA,Metter EJ. The relationship of arthritis self-efficacy to functional performance in older men and women with osteoarthritis of the knee. *Geriatr Nurs* 2002;23(3):167-170.
- Galantino ML,Sowers K,Kelly M,Mao J,LaRiccia P,Farrar J. Acupuncture as an adjuvant modality with physical therapy for patients with knee osteoarthritis. *Medical Acupuncture* 2009;21(3):157-166.

Gallacchi G,Hodinka L. [Randomized, double blind, multicentre, parallel group study to compare efficacy and safety of acetaminophen and indometacin in patients with activated osteoarthritis of the knee]. 2009;98:635-642.

Gana TJ,Pascual ML,Fleming RR,Schein JR,Janagap CC,Xiang J,Vorsanger GJ. Extended-release Tramadol in the treatment of osteoarthritis: a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Curr Med Res Opin* 2006;22(7):1391-1401.

Garland D,Holt P,Harrington JT,Caldwell J,Zizic T,Cholewczynski J. A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthritis and Cartilage* 2007;15(6):630-637.

Garrett J. Evaluation and treatment of the arthritic knee. *Journal of Bone and Joint Surgery - Series A* 2003;85(1):156-157.

Garrett WE,Kaeding CC,ElAttrache NS,Xerogeanes JW,Hewitt MS,Skrepnik NV,Papilion JD,O'Donnell JB,Fox DL,Ruvuna F,Whitaker JS,Demopoulos GA. Novel drug OMS103HP reduces pain and improves joint motion and function for 90 days after arthroscopic meniscectomy. *Arthroscopy* 2011 Aug;27(8):1060-1070.

Gay MC,Philippot P,Luminet O. Differential effectiveness of psychological interventions for reducing osteoarthritis pain: a comparison of Erickson [correction of Erickson] hypnosis and Jacobson relaxation. *Eur J Pain* 2002;6(1):1-16.

Gazi MB,Sakata RK,Issy AM. Intra-articular morphine versus bupivacaine for knee motion among patients with osteoarthritis: randomized double-blind clinical trial. *Sao Paulo Med J* 2008;126(6):309-313.

Geba GP,Weaver AL,Polis AB,Dixon ME,Schnitzer TJ. Efficacy of Rofecoxib , Celecoxib , and Acetaminophen in osteoarthritis of the knee: a randomized trial. *JAMA* 2002;287(1):64-71.

Gebhard F,Krettek C,Hufner T,Grutzner PA,Stockle U,Imhoff AB,Lorenz S,Ljungqvist J,Keppler P. Reliability of computer-assisted surgery as an intraoperative ruler in navigated high tibial osteotomy. *Arch Orthop Trauma Surg* 2011 Mar;131(3):297-302.

Geier KA. The UniSpacer for knee osteoarthritis. *Orthop Nurs* 2003;22(5):369-370.

Geiger F,Schneider U,Lukoschek M,Ewerbeck V. External fixation in proximal tibial osteotomy: a comparison of three methods. *Int Orthop* 1999;23(3):160-163.

Gemmell HA,Jacobson BH,Hayes BM. Effect of a topical herbal cream on osteoarthritis of the hand and knee: a pilot study. *J Manipulative Physiol Ther* 2003;26(5):e15.

Gentile-Bonassies S,Le CP,Meziers M,Ayral X,Dougados M. Comparison of the responsiveness of symptomatic outcome measures in knee osteoarthritis. *Arthritis Care Res* 2000;13(5):280-285.

George E. Intra-articular hyaluronan treatment for osteoarthritis. *Ann Rheum Dis* 1998;57(11):637-640.

George RC,Chrisman OD. The role of cartilage polysaccharides in osteoarthritis. *Clin Orthop Relat Res* 1968;57:259-265.

Ghosh P,Edelman J,March L,Smith M. Effects of pentosan polysulfate in osteoarthritis of the knee: A randomized, double-blind, placebo-controlled pilot study. *Current Therapeutic Research - Clinical and Experimental* 2005;66(6):552-571.

Ghosh S,Paul S,Das N,Bhattacharyya TK. A study on the effects of Diclofenac sodium and Etoricoxib in the treatment of osteoarthritis. *J Indian Med Assoc* 2007;105(5):260-262.

Giagounidis EM,Sell S. High tibial osteotomy: factors influencing the duration of satisfactory function. *Arch Orthop Trauma Surg* 1999;119(7-8):445-449.

Gibson JN,White MD,Chapman VM,Strachan RK. Arthroscopic lavage and debridement for osteoarthritis of the knee. *J Bone Joint Surg Br* 1992;74(4):534-537.

Gibson T,Winter PJ,Grahame R. Radiotherapy in the treatment of osteoarthrosis of the knee. *Rheumatol Rehabil* 1973;12(1):42-46.

Gibson TJ,Winter PJ,Grahame R. Radiotherapy in the treatment of osteoarthrosis of the knee. *Ann Rheum Dis* 1972;31(5):423-424.

Gidwani S,Fairbank A. The orthopaedic approach to managing osteoarthritis of the knee. *BMJ* 2004;329(7476):1220-1224.

Giggins OM,Fullen BM,Coughlan GF. Neuromuscular electrical stimulation in the treatment of knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil* 2012 Feb 9.

Gijzen BJ. [Efficacy and safety of nabumetone in the treatment of knee osteoarthritis: a comparative clinical trial versus Aceclofenac. Study Group of Nabumetone for Osteoarthritis of the Knee]. *Medicina clinica* 1997;109:130-134.

Gill AM,Cousins A,Nunn AJ,Choonara IA. Opiate-induced respiratory depression in pediatric patients. *Ann Pharmacother* 1996 Feb;30(2):125-129.

Gillespie WJ. The results of tibial osteotomy for osteoarthritis of the knee. *J R Coll Surg Edinb* 1974;19(4):222-227.

Gillquist J,Oretorp N. Arthroscopic partial meniscectomy. Technique and long-term results. *Clin Orthop Relat Res* 1982;(167):29-33.

Giori NJ. Load-shifting brace treatment for osteoarthritis of the knee: a minimum 2 1/2-year follow-up study. *J Rehabil Res Dev* 2004;41(2):187-194.

Glorioso S,Todesco S,Mazzi A,Marcolongo R,Giordano M,Colombo B,Cherie-Ligniere G,Mattara L,Leardini G,Passeri M,... Double-blind multicentre study of the activity of S-adenosylmethionine in hip and knee osteoarthritis. *Int J Clin Pharmacol Res* 1985;5(1):39-49.

Goei The HS,Lund B,Distel MR,Bluhmki E. A double-blind, randomized trial to compare meloxicam 15mg with Diclofenac 100mg in the treatment of osteoarthritis of the knee. *Osteoarthritis Cartilage* 1997;5(4):283-288.

Goekoop RJ,Kloppenburger M,Kroon HM,Dirkse LE,Huizinga TW,Westendorp RG,Gussekloo J. Determinants of absence of osteoarthritis in old age. *Scand J Rheumatol* 2011 Jan;40(1):68-73.

Goel TC. Injection treatment for pain in osteo-arthritis of knee joint. *J Indian Med Assoc* 1977;69(2):33-34.

Golden HE, Moskowitz RW, Minic M. Analgesic efficacy and safety of nonprescription doses of Naproxen sodium compared with Acetaminophen in the treatment of osteoarthritis of the knee. *Am J Ther* 2004;11(2):85-94.

Goldie I, Wetterqvist H. Pletysmographic and intramedullary pressure measurements before and after tibial osteotomy for osteoarthritis of the knee. *Acta Orthop Belg* 1974;40(3):285-293.

Goldman RT, Scuderi GR, Kelly MA. Arthroscopic treatment of the degenerative knee in older athletes. *Clin Sports Med* 1997;16(1):51-68.

Gomes WF, Lacerda AC, Mendonca VA, Arriero AN, Fonseca SF, Amorim MR, Rocha-Vieira E, Teixeira AL, Teixeira MM, Miranda AS, Coimbra CC, Brito-Melo GE. Effect of aerobic training on plasma cytokines and soluble receptors in elderly women with knee osteoarthritis, in response to acute exercise. *Clin Rheumatol* 2012 May;31(5):759-766.

Gomoll AH, Farr J, Gillogly SD, Kercher J, Minas T. Surgical management of articular cartilage defects of the knee. *Journal of Bone and Joint Surgery - Series A* 2010;92(14):2470-2490.

Gomoll AH. High tibial osteotomy for the treatment of unicompartmental knee osteoarthritis: a review of the literature, indications, and technique. *Phys Sportsmed* 2011 Oct;39(3):45-54.

Goncalves RS, Cabri J, Pinheiro JP, Ferreira PL, Gil J. Reliability, validity and responsiveness of the Portuguese version of the Knee injury and Osteoarthritis Outcome Score--Physical Function Short-form (KOOS-PS). *Osteoarthritis Cartilage* 2010;18(3):372-376.

Goorman SD, Watanabe TK, Miller EH, Perry C. Functional outcome in knee osteoarthritis after treatment with hylan G-F 20: a prospective study. *Arch Phys Med Rehabil* 2000;81(4):479-483.

Gordon A, Merenstein JH, D'Amico F, Hudgens D. The effects of therapeutic touch on patients with osteoarthritis of the knee. *J Fam Pract* 1998;47(4):271-277.

Gosal HS, Jackson AM, Bickerstaff DR. Intra-articular steroids after arthroscopy for osteoarthritis of the knee. *J Bone Joint Surg Br* 1999;81(6):952-954.

Gotte S, Homma W, Vallee P, Wittenborg A. Treatment of arthritis with controlled-release anti-inflammatory drugs. *Fortschr Med* 1986;104:567-570.

Gottesdiener K, Schnitzer T, Fisher C, Bockow B, Markenson J, Ko A, DeTora L, Curtis S, Geissler L, Gertz BJ. Results of a randomized, dose-ranging trial of Etoricoxib in patients with osteoarthritis. *Rheumatology (Oxford)* 2002;41(9):1052-1061.

Goulton J, Baker PG, Wilkinson MA. A multicentre hospital study of Orudis in osteoarthritis of the hip and knee. *Br J Clin Pract* 1979;33(1):26-28.

Goutallier D, Van DS, Manicom O, Soriali E, Bernageau J, Radier C. Influence of lower-limb torsion on long-term outcomes of tibial valgus osteotomy for medial compartment knee osteoarthritis. *J Bone Joint Surg Am* 2006;88(11):2439-2447.

Grace D,Rogers J,Skeith K,Anderson K. Topical Diclofenac versus placebo: a double blind, randomized clinical trial in patients with osteoarthritis of the knee. *J Rheumatol* 1999;26(12):2659-2663.

Graf J,Neusel E,Schneider E,Niethard FU. Intra-articular treatment with hyaluronic acid in osteoarthritis of the knee joint: a controlled clinical trial versus mucopolysaccharide polysulfuric acid ester. *Clin Exp Rheumatol* 1993;11(4):367-372.

Gramajo RJ,Cutroneo EJ,Fernandez DE,Gibson JL,Caceres Maldonado JC,Romero FL,Houssay RH. A single-blind, placebo-controlled study of glycosaminoglycan-peptide complex ('Rumalon') in patients with osteoarthritis of the hip or knee. *Curr Med Res Opin* 1989;11(6):366-373.

Grayson MF. A clinical trial of diflunisal against aspirin in osteoarthritis. *Rheumatol Rehabil* 1978;17(4):265-269.

Gremion G,Gaillard D,Leyvraz PF,Jolles BM. Effect of biomagnetic therapy versus physiotherapy for treatment of knee osteoarthritis: a randomized controlled trial. *J Rehabil Med* 2009;41(13):1090-1095.

Gremion G,Gaillard D,Leyvraz PF,Jolles BM. Effect of biomagnetic therapy versus physiotherapy for treatment of knee osteoarthritis: a randomized controlled trial (Provisional abstract). *Journal of Rehabilitation Medicine* 2009;41:1090-1095.

Grimmer K. A controlled double blind study comparing the effects of strong burst mode. *Australian Journal of Physiotherapy* 1992;38(1):49-56.

Grimmer K. A controlled double blind study comparing the effects of strong burst mode TENS and High Rate TENS on painful osteoarthritic knees. *Australian Journal of Physiotherapy* 1992;38:49-56.

Grindrod KA,Marra CA,Colley L,Cibere J,Tsuyuki RT,Esdaile JM,Gastonguay L,Kopec J. After patients are diagnosed with knee osteoarthritis, what do they do?. *Arthritis Care Res (Hoboken)* 2010;62(4):510-515.

Grisanti AM,Vaz AA,Samara AM. Comparison of etodolac and Diclofenac in osteoarthritis of the knee. *Clin Ther* 1992;14(6):791-800.

Grober JS,Thethi AK. Osteoarthritis: When are alternative therapies a good alternative?. *Consultant* 2003;43(2):197-202.

Gross DE,Brenner SL,Esformes I,Gross ML. Arthroscopic treatment of degenerative joint disease of the knee. *Orthopedics* 1991;14(12):1317-1321.

Gross KD. Device use: walking AIDS, braces, and orthoses for symptomatic knee osteoarthritis. *Clin Geriatr Med* 2010 Aug;26(3):479-502.

Gross MT. Shoe wear recommendations for the older adult. *Clinical Geriatrics* 2010 May;18(5):26-33.

Grotle M,Hagen KB,Natvig B,Dahl FA,Kvien TK. Prevalence and burden of osteoarthritis: results from a population survey in Norway. *J Rheumatol* 2008;35(4):677-684.

Grube B,Grunwald J,Krug L,Staiger C. Efficacy of a comfrey root (*Symphyti offic. radix*) extract ointment in the treatment of patients with painful osteoarthritis of the knee: results of a double-blind, randomised, bicenter, placebo-controlled trial. 2007;14(1):2-10.

Gruenwald J, Petzold E, Busch R, Petzold HP, Graubaum HJ. Effect of glucosamine sulfate with or without omega-3 fatty acids in patients with osteoarthritis. *Adv Ther* 2009;26(9):858-871.

Gstoettner M, Raschner C, Dirnberger E, Leimser H, Krismer M. Preoperative proprioceptive training in patients with total knee arthroplasty. *Knee* 2010 Aug 26;.

Gstottner M, Pedross F, Liebensteiner M, Bach C. Long-term outcome after high tibial osteotomy. *Arch Orthop Trauma Surg* 2008;128(1):111-115.

Gudbergesen H, Boesen M, Christensen R, Astrup A, Bliddal H. Radiographs and low field MRI (0.2T) as predictors of efficacy in a weight loss trial in obese women with knee osteoarthritis. *BMC Musculoskeletal Disorders* 2011;12 Article Number(56. Date of Publication):.

Gudbergesen H, Boesen M, Lohmander LS, Christensen R, Henriksen M, Bartels EM, Christensen P, Rindel L, Aaboe J, Danneskiold-Samsøe B, Riecke BF, Bliddal H. Weight loss is effective for symptomatic relief in obese subjects with knee osteoarthritis independently of joint damage severity assessed by high-field MRI and radiography. *Osteoarthritis Cartilage* 2012 Jun;20(6):495-502.

Guermazi A, Hayashi D, Roemer FW, Felson DT, Wang K, Lynch J, Amin S, Torner JC, Lewis CE, Nevitt M. Longitudinal changes of MRI-detected osteoarthritis features in kellgren-lawrence grade 4 knees. Data from the most study. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S179-S180.

Guermazi A, Roemer FW, Hayashi D, Crema MD, Niu J, Zhang Y, Marra MD, Katur A, Lynch JA, El-Khoury GY, Baker K, Hughes LB, Nevitt MC, Felson DT. Assessment of synovitis with contrast-enhanced MRI using a whole-joint semiquantitative scoring system in people with, or at high risk of, knee osteoarthritis: The MOST study. *Annals of the Rheumatic Diseases* 2011;70(5):805-811.

Guermazi M, Poiraudéau S, Yahia M, Mezganni M, Fermanian J, Elleuch MH, Revel M. Translation, adaptation and validation of the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) for an Arab population: The Sfax modified WOMAC. *Osteoarthritis and Cartilage* 2004;12(6):459-468.

Gumpel JM. Radioactive colloids in the treatment of arthritis. Review of published and personal results. Criteria for selection of patients. *Ann Rheum Dis* 1973;32 Suppl 6:Suppl-33.

Gumpel JM. The role of radiocolloids in the treatment of arthritis. *Rheumatol Rehabil* 1974;13(1):1-9.

Gundog M, Atamaz F, Kanyilmaz S, Kirazli Y, Celepoglu G. Interferential current therapy in patients with knee osteoarthritis: comparison of the effectiveness of different amplitude-modulated frequencies. *Am J Phys Med Rehabil* 2012 Feb;91(2):107-113.

Gunn AL. Results of treatment of painful deformed knee by upper tibial osteotomy. *Guys Hosp Rep* 1969;118(2):293-306.

Haaz S, Bartlett SJ. Yoga for Arthritis: A Scoping Review. *Rheumatic Disease Clinics of North America* 2011;37(1):33-46.

Habata T, Uematsu K, Hattori K, Kasanami R, Takakura Y, Fujisawa Y. High tibial osteotomy that does not cause recurrence of varus deformity for medial gonarthrosis. *Knee Surg Sports Traumatol Arthrosc* 2006;14(10):962-967.

- Habib GS. Systemic effects of intra-articular corticosteroids. *Clin Rheumatol* 2009;28(7):749-756.
- Ha'eri GB,Wiley AM. High tibial osteotomy combined with joint debridement: a long-term study of results. *Clin Orthop Relat Res* 1980;(151):153-159.
- Haflah NH,Jaarin K,Abdullah S,Omar M. Palm vitamin E and glucosamine sulphate in the treatment of osteoarthritis of the knee. *Saudi Med J* 2009;30(11):1432-1438.
- Hair PI,Curran MP,Keam SJ. Tramadol extended-release tablets. *Drugs* 2006;66(15):2017-2027.
- Hakshur K,Benhar I,Bar-Ziv Y,Halperin N,Segal D,Eliaz N. The effect of hyaluronan injections into human knees on the number of bone and cartilage wear particles captured by bio-ferrography. *Acta Biomater* 2011 Feb;7(2):848-857.
- Halbert J,Crotty M,Weller D,Ahern M,Silagy C. Primary care-based physical activity programs: effectiveness in sedentary older patients with osteoarthritis symptoms. *Arthritis Rheum* 2001;45(3):228-234.
- Hallock RH,Fell BM. Unicompartmental tibial hemiarthroplasty: early results of the UniSpacer knee. *Clin Orthop Relat Res* 2003;(416):154-163.
- Han CD,Kim NH,Kang HJ. Clinical evaluation of sodium hyaluronate (ARTZ(registered trademark)) on osteoarthritis of the knee. *Journal of the Western Pacific Orthopaedic Association* 1992;29(SPEC. ISS.):35-39.
- Han CD,Lee DH,Yang IH. Intra-synovial ropivacaine and morphine for pain relief after total knee arthroplasty: a prospective, randomized, double blind study. *Yonsei Med J* 2007;48(2):295-300.
- Hara R,Yasuda K,Aoki Y,Ohno K,Ohkoshi Y,Miyagi N,Tanabe Y. High tibial osteotomy for medial osteoarthritic knee - Long term follow-up. *Hokkaido Journal of Orthopedic and Traumatic Surgery* 1990;33(2):9-15.
- Harden RN,Gagnon CM,Graciosa J,Gould EM. Negligible analgesic tolerance seen with extended release oxymorphone: a post hoc analysis of open-label longitudinal data. *Pain Med* 2010 Aug;11(8):1198-1208.
- Harmer AR. Land-based versus water-based rehabilitation following total knee replacement: a randomized, single-blind trial. 2009.
- Harris WR,Kostuik JP. High tibial osteotomy for osteo-arthritis of the knee. *J Bone Joint Surg Am* 1970;52(2):330-336.
- Harrison MM,Morrell J,Hopman WM. Influence of obesity on outcome after knee arthroscopy. *Arthroscopy* 2004;20(7):691-695.
- Harrison MM,Waddell JP. A comparison of plate versus staple-and-cast fixation in maintaining femoral tibial alignment after valgus tibial osteotomy. *Can J Surg* 2005;48(1):33-38.
- Harth M,Bondy DC. Indomethacin and acetylsalicylic acid in the treatment of osteoarthritis of the hips and knees. *Can Med Assoc J* 1969;101(6):311-316.
- Hartman CA. Effects of Tai Chi training on function and quality of life indicators in older adults with osteoarthritis. 2000.

- Harvey WF, Hunter DJ. Pharmacologic intervention for osteoarthritis in older adults. *Clin Geriatr Med* 2010 Aug;26(3):503-515.
- Harwin SF. Arthroscopic debridement for osteoarthritis of the knee: predictors of patient satisfaction. *Arthroscopy* 1999;15(2):142-146.
- Hashemi SM, Madadi F, Razavi S, Nikooseresht M, Kiyabi FH, Nasiripour S. Intra-articular hyaluronic acid injections Vs. dextrose prolotherapy in the treatment of osteoarthritic knee pain. *Tehran University Medical Journal* 2012;70(2):119-125.
- Hassan BS, Doherty SA, Mockett S, Doherty M. Effect of pain reduction on postural sway, proprioception, and quadriceps strength in subjects with knee osteoarthritis. *Ann Rheum Dis* 2002;61(5):422-428.
- Hassan BS, Mockett S, Doherty M. Influence of elastic bandage on knee pain, proprioception, and postural sway in subjects with knee osteoarthritis. *Ann Rheum Dis* 2002;61(1):24-28.
- Hassan BS, Mockett S, Doherty M. Static postural sway, proprioception, and maximal voluntary quadriceps contraction in patients with knee osteoarthritis and normal control subjects. *Annals of the Rheumatic Diseases* 2001;60(6):612-618.
- Hatori M, Sakurai M, Kokubun S, Rijal KP. Piroxicam suppositories in the treatment of osteoarthritis of the knee joint. *Clin Ther* 1990;12(3):227-229.
- Hay EM, Foster NE, Thomas E, Peat G, Phelan M, Yates HE, Blenkinsopp A, Sim J. Effectiveness of community physiotherapy and enhanced pharmacy review for knee pain in people aged over 55 presenting to primary care: pragmatic randomised trial. *BMJ* 2006;333(7576):995.
- Hay EM. Effectiveness of community physiotherapy and enhanced pharmacy review for knee pain in people aged over 55 presenting to primary care: pragmatic randomised trial [with consumer summary]. 2006.
- Hede A, Larsen E, Sandberg H. Partial versus total meniscectomy: A prospective, randomised study with long-term follow-up. *Journal of Bone and Joint Surgery - Series B* 1992;74(1):118-121.
- Hee HT, Low CK, Seow KH, Tan SK. Comparing staple fixation to buttress plate fixation in high tibial osteotomy. *Ann Acad Med Singapore* 1996;25(2):233-235.
- Hegedus B, Viharos L, Gervain M, Galfi M. The effect of low-level laser in knee osteoarthritis: a double-blind, randomized, placebo-controlled trial. *Photomed Laser Surg* 2009;27(4):577-584.
- Heidari B, Heidari P, Hajian-Tilaki K. Association between serum vitamin D deficiency and knee osteoarthritis. *Int Orthop* 2010 Dec 30;.
- Heidari B, Heidari P, Hajian-Tilaki K. Association between serum vitamin D deficiency and knee osteoarthritis. *Int Orthop* 2011 Nov;35(11):1627-1631.
- Heim N, Snijder MB, Heymans MW, Deeg DJ, Seidell JC, Visser M. Optimal cutoff values for high-risk waist circumference in older adults based on related health outcomes. *Am J Epidemiol* 2011 Aug 15;174(4):479-489.

Helfet AJ,Manley MT,Vaughan CL. The helicoid knee brace: a lightweight but effective support for the damaged knee. *Injury* 1983;15(3):189-192.

Hellio Le Graverand MP,Brandt KD,Mazzuca SA,Katz BP,Buck R,Lane KA,Pickering E,Nemirovskiy OV,Sunyer T,Welsch DJ. Association between concentrations of urinary type II collagen neoepitope (uTIINE) and joint space narrowing in patients with knee osteoarthritis. *Osteoarthritis Cartilage* 2006;14(11):1189-1195.

Hellio Le Graverand MP,Buck RJ,Wyman BT,Vignon E,Mazzuca SA,Brandt KD,Piperno M,Charles HC,Hudelmaier M,Hunter DJ,Jackson C,Kraus VB,Link TM,Majumdar S,Prasad PV,Schnitzer TJ,Vaz A,Wirth W,Eckstein F. Subregional femorotibial cartilage morphology in women--comparison between healthy controls and participants with different grades of radiographic knee osteoarthritis. *Osteoarthritis Cartilage* 2009;17(9):1177-1185.

Hempfling H. Intra-articular hyaluronic acid after knee arthroscopy: a two-year study. *Knee Surg Sports Traumatol Arthrosc* 2007;15(5):537-546.

Henderson CJ. Dietary outcomes in osteoarthritis disease management. *Bull Rheum Dis* 2003;52(12. Date of Publication):.

Henderson EB,Smith EC,Pegley F,Blake DR. Intra-articular injections of 750 kD hyaluronan in the treatment of osteoarthritis: a randomised single centre double-blind placebo-controlled trial of 91 patients demonstrating lack of efficacy. *Ann Rheum Dis* 1994;53(8):529-534.

Hepper CT,Halvorson JJ,Duncan ST,Gregory AJ,Dunn WR,Spindler KP. The efficacy and duration of intra-articular corticosteroid injection for knee osteoarthritis: a systematic review of level I studies (Provisional abstract). *J Am Acad Orthop Surg* 2009;:638-646.

Hernigou P,Medevielle D,Debeyre J,Goutallier D. Proximal tibial osteotomy for osteoarthritis with varus deformity. A ten to thirteen-year follow-up study. *J Bone Joint Surg Am* 1987;69(3):332-354.

Herrera JA,Gonzalez M. Comparative evaluation of the effectiveness and tolerability of nimesulide versus Rofecoxib taken once a day in the treatment of patients with knee osteoarthritis. *Am J Ther* 2003;10(6):468-472.

Herrero-Beaumont G,Ivorra JA,Del Carmen TM,Blanco FJ,Benito P,Martin-Mola E,Paulino J,Marenco JL,Porto A,Laffon A,Araujo D,Figueroa M,Branco J. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: a randomized, double-blind, placebo-controlled study using Acetaminophen as a side comparator. *Arthritis Rheum* 2007;56(2):555-567.

Herrmann G,Steegeer D,Klasser M,Wirbitzky J,Furst M,Venbrocks R,Rohde H,Jungmichel D,Hildebrandt HD,Parnham MJ,Gimbel W,Dirschedl H. Oxaceprol is a well-tolerated therapy for osteoarthritis with efficacy equivalent to Diclofenac. *Clin Rheumatol* 2000;19(2):99-104.

Hesslink R,Armstrong D,Nagendran MV,Sreevatsan S,Barathur R. Cetylated fatty acids improve knee function in patients with osteoarthritis. *J Rheumatol* 2002;29(8):1708-1712.

Hetland ML, Ostergaard M, Ejbjerg B, Jacobsen S, Stengaard-Pedersen K, Junker P, Lottenburger T, Hansen I, Andersen LS, Tarp U, Svendsen A, Pedersen JK, Skjodt H, Ellingsen T, Lindegaard H, Podenphant J, Horslev-Petersen K, Jensen SH, Lorenzen T, Bendtsen H, Faarvang KL, Han. Short- and long-term efficacy of intra-articular injections with betamethasone as part of a treat-to-target strategy in early rheumatoid arthritis: Impact of joint area, repeated injections, MRI findings, anti-CCP, IgM-RF and CRP. *Annals of the Rheumatic Diseases* 2012;71(6):851-856.

Heuts PH, de BR, Drieteelaar M, Aretz K, Hopman-Rock M, Bastiaenen CH, Metsemakers JF, van WC, van SO. Self-management in osteoarthritis of hip or knee: a randomized clinical trial in a primary healthcare setting. *J Rheumatol* 2005;32(3):543-549.

Highton J, Grahame R. Benoxaprofen in the treatment of osteoarthritis--a comparison with ibuprofen. *J Rheumatol Suppl* 1980;6:125-131.

Higuchi H, Kimura M, Shirakura K, Terauchi M, Takagishi K. Factors affecting long-term results after arthroscopic partial meniscectomy. *Clin Orthop Relat Res* 2000;(377):161-168.

Hill CL, Hunter DJ, Niu J, Clancy M, Guermazi A, Genant H, Gale D, Grainger A, Conaghan P, Felson DT. Synovitis detected on magnetic resonance imaging and its relation to pain and cartilage loss in knee osteoarthritis. *Ann Rheum Dis* 2007;66(12):1599-1603.

Hill J, Bird HA. Failure of Selenium-ACE to improve osteoarthritis. *Br J Rheumatol* 1990;29(3):211-213.

Hilliquin P, Le DP, Menkes CJ. Comparison of the efficacy of nonsurgical synovectomy (synoviorthesis) and joint lavage in knee osteoarthritis with effusions. *Rev Rhum Engl Ed* 1996;63(2):93-102.

Hingorani K. A comparative study of azapropazone and ibuprofen in the treatment of osteoarthrosis of the knee. *Curr Med Res Opin* 1976;4(1):57-64.

Hinman MR, Ford J, Heyl H. Effects of static magnets on chronic knee pain and physical function: a double-blind study. *Altern Ther Health Med* 2002;8(4):50-55.

Hinman RS, Bennell KL, Crossley KM, McConnell J. Immediate effects of adhesive tape on pain and disability in individuals with knee osteoarthritis. *Rheumatology (Oxford)* 2003;42(7):865-869.

Hinman RS, Bowles KA, Payne C, Bennell KL. Effect of length on laterally-wedged insoles in knee osteoarthritis. *Arthritis Rheum* 2008;59(1):144-147.

Hinman RS, Crossley KM, McConnell J, Bennell KL. Efficacy of knee tape in the management of osteoarthritis of the knee: blinded randomised controlled trial. *BMJ* 2003;327(7407):135.

Hinman RS, Crossley KM, McConnell J, Hunter D, Felson D. Therapeutic knee taping improved pain and disability in osteoarthritis of the knee. *Evidence-Based Medicine* 2004;9(1):18.

Hinman RS, Heywood SE, Day AR. Aquatic physical therapy for hip and knee osteoarthritis: results of a single-blind randomized controlled trial. *Phys Ther* 2007;87(1):32-43.

Hinman RS, Payne C, Metcalf BR, Wrigley TV, Bennell KL. Lateral wedges in knee osteoarthritis: what are their immediate clinical and biomechanical effects and can these predict a three-month clinical outcome?. *Arthritis Rheum* 2008;59(3):408-415.

- Hinman RS. Lateral wedge insoles for medial knee osteoarthritis: effects on lower limb frontal plane biomechanics. 2012.
- Hitzeman N,Masley C. Arthroscopic surgery for knee osteoarthritis. *Am Fam Physician* 2008;78(3):331-332.
- Hochberg MC,Clegg DO. Potential effects of chondroitin sulfate on joint swelling: a GAIT report. *Osteoarthritis Cartilage* 2008;16 Suppl 3:S22-S24.
- Hochberg MC,Lethbridge-Cejku M,Scott WW,Reichle R,Plato CC,Tobin JD. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: data from the Baltimore Longitudinal Study of Aging. *J Rheumatol* 1995;22(3):488-493.
- Hoell S,Suttmoeller J,Stoll V,Fuchs S,Gosheger G. The high tibial osteotomy, open versus closed wedge, a comparison of methods in 108 patients. *Arch Orthop Trauma Surg* 2005;125(9):638-643.
- Hofmann AA,Wyatt RWB,Beck SW. High tibial osteotomy: The use of an osteotomy jig, rigid fixation, and early motion. *Techniques in Orthopaedics* 1989;4(1):41-46.
- Holden DL,James SL,Larson RL,Slocum DB. Proximal tibial osteotomy in patients who are fifty years old or less. A long-term follow-up study. *J Bone Joint Surg Am* 1988;70(7):977-982.
- Holla JFM,Steultjens MPM,Roorda LD,Heymans MW,Ten WS,Dekker J. Prognostic factors for the two-year course of activity limitations in early osteoarthritis of the hip and/or knee. *Arthritis Care and Research* 2010 Oct;62(10):1415-1425.
- Holliday KL,McWilliams DF,Maciewicz RA,Muir KR,Zhang W,Doherty M. Lifetime body mass index, other anthropometric measures of obesity and risk of knee or hip osteoarthritis in the GOAL case-control study. *Osteoarthritis Cartilage* 2011 Jan;19(1):37-43.
- Holt HL,Katz JN,Reichmann WM,Gerlovin H,Wright EA,Hunter DJ,Jordan JM,Kessler CL,Losina E. Forecasting the burden of advanced knee osteoarthritis over a 10-year period in a cohort of 60-64 year-old US adults. *Osteoarthritis Cartilage* 2011 Jan;19(1):44-50.
- Hooper G,Leslie H,Burn J,Schouten R,Beci I. Oblique upper tibial opening wedge osteotomy for genu varum. *Operative Orthopadie und Traumatologie* 2005;17(6):662-673.
- Hopman-Rock M,Westhoff MH. The effects of a health educational and exercise program for older adults with osteoarthritis for the hip or knee. *J Rheumatol* 2000;27(8):1947-1954.
- Horlick SG,Loomer RL. Valgus knee bracing for medial gonarthrosis. *Clin J Sport Med* 1993;3(4):251-255.
- Hosie J,Distel M,Bluhmki E. Efficacy and tolerability of meloxicam versus Piroxicam in patients with osteoarthritis of the hip or knee. A six-month double-blind study. *Clinical Drug Investigation* 1997;13(4):175-184.
- Hosie J,Distel M,Bluhmki E. Meloxicam in osteoarthritis: a 6-month, double-blind comparison with Diclofenac sodium. *Br J Rheumatol* 1996;35 Suppl 1:39-43.

- Haupt JB,McMillan R,Paget DD,Russell A,Gahunia HK. Effect of Glucosamine Hydrochloride in the Treatment of Pain of Osteoarthritis of the Knee. *Unpublished* 1998.
- Howarth D,Inman D,Lingard E,McCaskie A,Gerrand C. Barriers to weight loss in obese patients with knee osteoarthritis. *Ann R Coll Surg Engl* 2010.
- Howe TE,Rafferty D. Quadriceps activity and physical activity profiles over long durations in patients with osteoarthritis of the knee and controls. *J Electromyogr Kinesiol* 2009;19(2):e78-e83.
- Howell SM. The role of arthroscopy in treating osteoarthritis of the knee in the older patient. *Orthopedics* 2010 Sep;33(9):652.
- Hoyeraal HM,Fagertun H,Ingemann-Hansen T,Ersmark H,Ronn O. Characterization of responders and nonresponders to tiaprofenic acid and Naproxen in the treatment of patients with osteoarthritis. *J Rheumatol* 1993;20(10):1747-1752.
- Hsieh S,Lai J,Chen P,Chen C,Chen H,Wang J. Is Duhuo Jisheng Tang containing Xixin safe? A four-week safety study. *Chinese Medicine* 2010;5 Article Number(6. Date of Publication):.
- Hsieh YS,Yang SF,Chu SC,Chen PN,Chou MC,Hsu MC,Lu KH. Expression changes of gelatinases in human osteoarthritic knees and arthroscopic debridement. *Arthroscopy* 2004;20(5):482-488.
- Hu DY,Xiao P,Fu SC,Zhong WJ,Feng W,Zhang FH. [Jingusu glucosamine hydrochloride functional food for improving knee joint function in patients with knee osteoarthritis: a human intake trial]. *Zhongguo Linchuang Kangfu* 2005;9:8-9.
- Huang MH,Lin YS,Lee CL,Yang RC. Use of ultrasound to increase effectiveness of isokinetic exercise for knee osteoarthritis. *Arch Phys Med Rehabil* 2005;86(8):1545-1551.
- Huang TL,Wu HT,Liu JC,Chen WM,Chen TH. Do we get a 'real' alignment of knee in the preoperative planning of high tibia osteotomy: a prospective study of reproducibility. *J Chin Med Assoc* 2004;67(4):185-188.
- Huang W,Bliwise DL,Carnevale CV,Kutner NG. Acupuncture for pain and sleep in knee osteoarthritis. *J Am Geriatr Soc* 2010;58:1218-1220.
- Hubbard MJ. Articular debridement versus washout for degeneration of the medial femoral condyle. A five-year study. *J Bone Joint Surg Br* 1996;78(2):217-219.
- Huber R,Prestel U,Bloss I,Meyer U,Ludtke R. Effectiveness of subcutaneous injections of a cartilage preparation in osteoarthritis of the knee--a randomized, placebo controlled phase II study. *Complement Ther Med* 2010 Jun;18(3-4):113-118.
- Huetink K,Nelissen RG,Watt I,van Erkel AR,Bloem JL. Localized development of knee osteoarthritis can be predicted from MR imaging findings a decade earlier. *Radiology* 2010 Aug;256(2):536-546.
- Hughes SL. Long-term impact of fit and strong! On older adults with osteoarthritis. 2006.
- Hui C,Salmon LJ,Kok A,Williams HA,Hockers N,van der Tempel WM,Chana R,Pinczewski LA. Long-term survival of high tibial osteotomy for medial compartment osteoarthritis of the knee. *Am J Sports Med* 2011 Jan;39(1):64-70.

Hultin J,Hamberg P,Stenstrom A. Knee arthroscopy using local anesthesia. *Arthroscopy* 1992;8(2):239-241.

Hunt MA,Birmingham TB,Bryant D,Jones I,Giffin JR,Jenkyn TR,Vandervoort AA. Lateral trunk lean explains variation in dynamic knee joint load in patients with medial compartment knee osteoarthritis. *Osteoarthritis Cartilage* 2008;16(5):591-599.

Hunt MA,Wrigley TV,Hinman RS,Bennell KL. Individuals with severe knee osteoarthritis (OA) exhibit altered proximal walking mechanics compared with individuals with less severe OA and those without knee pain. *Arthritis Care Res (Hoboken)* 2010 Oct;62(10):1426-1432.

Hunter D,Gross KD,McCree P,Li L,Hirko K,Harvey WF. Realignment treatment for medial tibiofemoral osteoarthritis: randomised trial. *Ann Rheum Dis* 2012 Feb 29.

Hunter DJ,Lo GH,Gale D,Grainger AJ,Guermazi A,Conaghan PG. The reliability of a new scoring system for knee osteoarthritis MRI and the validity of bone marrow lesion assessment: BLOKS (Boston Leeds Osteoarthritis Knee Score). *Ann Rheum Dis* 2008;67(2):206-211.

Hunter DJ,Wise B. Review: Diacerein is more effective than placebo and is as effective as. *Evidence-Based Medicine* 2007;12(3):74.

Hurley M,Walsh N,Mitchell H,Nicholas J,Patel A. Long term outcomes and costs of ESCAPE-knee pain: An integrated rehabilitation programme for chronic knee pain. *Arthritis Care Res (Hoboken)* 2011 Sep 27;.

Hurley MV,Scott DL. Improvements in quadriceps sensorimotor function and disability of patients with knee osteoarthritis following a clinically practicable exercise regime. *Br J Rheumatol* 1998;37(11):1181-1187.

Hurley MV,Walsh NE,Mitchell H,Nicholas J,Patel A. Long-term outcomes and costs of an integrated rehabilitation program for chronic knee pain: a pragmatic, cluster randomized, controlled trial. *Arthritis Care Res (Hoboken)* 2012 Feb;64(2):238-247.

Hurley MV,Walsh NE,Mitchell HL,Pimm TJ,Williamson E,Jones RH,Reeves BC,Dieppe PA,Patel A. Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain. *Arthritis Rheum* 2007;57(7):1220-1229.

Hurley MV. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster randomized trial. 2007.

Hurley MV. Muscle dysfunction and effective rehabilitation of knee osteoarthritis: what we know and what we need to find out. *Arthritis Rheum* 2003;49(3):444-452.

Hurwitz DE,Ryals AR,Block JA,Sharma L,Schnitzer TJ,Andriacchi TP. Knee pain and joint loading in subjects with osteoarthritis of the knee. *J Orthop Res* 2000;18(4):572-579.

Huskin JP,Vandekerckhove B,Delince P,Verdonk R,Dubuc JE,Willems S,Hardy P,Blanco FJ,Charrois O,Handelberg F. Multicentre, prospective, open study to evaluate the safety and efficacy of hylan G-F 20 in knee osteoarthritis subjects presenting with pain following arthroscopic meniscectomy. *Knee Surg Sports Traumatol Arthrosc* 2008;16(8):747-752.

- Huskiesson E,Donnelly S. Is hyaluronic acid effective in patients with osteoarthritis of the knee?. *West J Med* 2000;173(4):252.
- Huskiesson EC,Berry H,Gishen P,Jubb RW,Whitehead J. Effects of antiinflammatory drugs on the progression of osteoarthritis of the knee. LINK Study Group. Longitudinal Investigation of Nonsteroidal Antiinflammatory Drugs in Knee Osteoarthritis. *J Rheumatol* 1995;22(10):1941-1946.
- Huskiesson EC,Donnelly S. Hyaluronic acid in the treatment of osteoarthritis of the knee. *Rheumatology (Oxford)* 1999;38(7):602-607.
- Huskiesson EC,Doyle DV,Lanham JG. Drug treatment of osteoarthritis. *Clin Rheum Dis* 1985;11(2):421-431.
- Huskiesson EC,Macciocchi A,Rahlf s VW,Bernstein RM,Bremner AD,Doyle DV,Molloy mg,Burton AE. Nimesulide versus Diclofenac in the treatment of osteoarthritis of the hip or knee: An active controlled equivalence study. *Current Therapeutic Research, Clinical & Experimental* 1999;60:253-265.
- Huskiesson EC,Scott J. Orgotein in osteoarthritis of the knee joint. *Eur J Rheumatol Inflamm* 1981;4(2):212-218.
- Hussain SA,Jassim NA,Numan IT,Al-Khalifa II,Abdullah TA. Anti-inflammatory activity of silymarin in patients with knee osteoarthritis. A comparative study with Piroxicam and meloxicam. *Saudi Med J* 2009;30(1):98-103.
- Hyaluronic acid minimally effective for knee osteoarthritis. *J Fam Pract* 2004;53(4):265.
- Ichiba A,Kishimoto I. Effects of articular cartilage and meniscus injuries at the time of surgery on osteoarthritic changes after anterior cruciate ligament reconstruction in patients under 40 years old. *Arch Orthop Trauma Surg* 2009;129(3):409-415.
- Ike RW,Arnold WJ,Rothschild EW,Shaw HL. Tidal irrigation versus conservative medical management in patients with osteoarthritis of the knee: a prospective randomized study. Tidal Irrigation Cooperating Group. *J Rheumatol* 1992;19(5):772-779.
- Ilahi OA,Stein JD,Ho DM,Bocell JR,Lindsey RW. Arthroscopic findings in knees undergoing proximal tibial osteotomy. *J Knee Surg* 2008;21(1):63-67.
- Ilic KV,Sefik-Bukilica M,Jankovic S,Vujasinovic-Stupar N. Efficacy and safety of two generic copies of nimesulide in patients with low back pain or knee osteoarthritis. 2009;61(1):27-33.
- Illingworth KD,Musahl V,Lorenz SGF,Fu FH. Use of fibrin clot in the Knee. *Operative Techniques in Orthopaedics* 2010;20(2):90-97.
- Im SH,Lee SC,Park YB,Cho SR,Kim JC. Feasibility of sonography for intra-articular injections in the knee through a medial patellar portal. *J Ultrasound Med* 2009;28(11):1465-1470.
- IMAZUMI-Tsukasa ea. Clinical Evaluation of the Analgesic Floctafenine in Osteoarthritis of the Knee: A Double-Blind Controlled Study with Aspirin. *Yakuri to Chiryō* 1981;9:555-565.
- Imeokparia RL,Barrett JP,Arrieta MI,Leaverton PE,Wilson AA,Hall BJ,Marlowe SM. Physical activity as a risk factor for osteoarthritis of the knee. *Ann Epidemiol* 1994;4(3):221-230.

Ingram F,Anderson MBC. Intramuscular artemparon in osteoarthrosis of the knee - A double blind trial. *Aktuelle Rheumatologie* 1982;7(Spec. Iss. 3):164-166.

Inoue R,Ishibashi Y,Tsuda E,Yamamoto Y,Matsuzaka M,Takahashi I,Danjo K,Umeda T,Nakaji S,Toh S. Knee osteoarthritis, knee joint pain and aging in relation to increasing serum hyaluronan level in the Japanese population. *Osteoarthritis Cartilage* 2011 Jan;19(1):51-57.

Insall J,Shoji H,Mayer V. High tibial osteotomy. A five-year evaluation. *J Bone Joint Surg Am* 1974;56(7):1397-1405.

Insall JN. High tibial osteotomy in the treatment of osteoarthritis of the knee. *Surg Annu* 1975;7:347-359.

Intra-articular injections for osteoarthritis of the knee. *Med Lett Drugs Ther* 2006;48(1231):25-27.

Ioannidou D,Krasagakis K,Stefanidou M,Tosca A. Erythema annulare centrifugum and osteoarthritis treated with hyaluronic acid. *Clin Exp Dermatol* 2002;27(8):720-722.

Iorio R,Healy WL. Unicompartmental arthritis of the knee. *J Bone Joint Surg Am* 2003;85-A(7):1351-1364.

Irrgang JJ,Snyder-Mackler L,Wainner RS,Fu FH,Harner CD. Development of a patient-reported measure of function of the knee. *Journal of Bone and Joint Surgery - Series A* 1998;80(8):1132-1145.

Is acupuncture more effective than conventional therapy in improving pain and functionality for osteoarthritis of the knee?. *Manag Care Interface* 2006;19(12):69.

Isolaure J,Lapinsuo M,Aho H,Tervo T,Rokkanen P. Proximal osteotomy of the tibia in the treatment of osteoarthritis of the knee. *Arch Orthop Trauma Surg* 1983;102(2):107-110.

Itoh K,Hirota S,Katsumi Y,Ochi H,Kitakoji H. A pilot study on using acupuncture and transcutaneous electrical nerve stimulation (TENS) to treat knee osteoarthritis (OA). *Chin Med* 2008;3:2.

Itoh K,Hirota S,Katsumi Y,Ochi H,Kitakoji H. Trigger point acupuncture for treatment of knee osteoarthritis--a preliminary RCT for a pragmatic trial. *Acupunct Med* 2008;26(1):17-26.

Iveson JM,Longton EB,Wright V. Comparative study of tibial (single) and tibiofemoral (double) osteotomy for osteoarthrosis and rheumatoid arthritis. *Ann Rheum Dis* 1977;36(4):319-326.

Iwata H. Pharmacologic and clinical aspects of intraarticular injection of hyaluronate. *Clin Orthop* 1993;(289):285-291.

Iwegbu CG,Patel RJ,McLeod P,Helal B. A double-blind comparison of Piroxicam mane with Piroxicam nocte in patients awaiting hip and/or knee joint replacement. *Eur J Rheumatol Inflamm* 1981;4(3):342-347.

Jørgensen A,Stengaard PK,Simonsen O,Pfeiffer JM,Eriksen C,Bliddal H,Pedersen NW,Bødtker S,Hørsløv PK,Snerum L†,Egund N,Frimer LH. Intra-articular hyaluronan is without clinical effect in knee osteoarthritis: a multicentre, randomised, placebo-controlled, double-blind study of 337 patients followed for 1 year. *Annals of the Rheumatic Diseases* 2010;69:1097-1102.

Jackson JP,Waugh W,Green JP. High tibial osteotomy for osteoarthritis of the knee. *J Bone Joint Surg Br* 1969;51(1):88-94.

- Jackson JP, Waugh W. The technique and complications of upper tibial osteotomy. A review of 226 operations. *J Bone Joint Surg Br* 1974;56(2):236-245.
- Jackson RW, Dieterichs C. The results of arthroscopic lavage and debridement of osteoarthritic knees based on the severity of degeneration: a 4- to 6-year symptomatic follow-up. *Arthroscopy* 2003;19(1):13-20.
- Jackson RW, Gilbert JE, Sharkey PF. Arthroscopic debridement versus arthroplasty in the osteoarthritic knee. *J Arthroplasty* 1997;12(4):465-469.
- Jackson RW. The role of arthroscopy in the management of the arthritic knee. *Clin Orthop Relat Res* 1974;(101):28-35.
- Jacobson JJ, Gorman R, Yamanashi WS, Saxena BB, Clayton L. Low-amplitude, extremely low frequency magnetic fields for the treatment of osteoarthritic knees: a double-blind clinical study. *Altern Ther Health Med* 2001;7:54-59.
- Jacquet A, Girodet P, Pariente A, Forest K, Mallet L, Moore N. Phytalgic((registered trademark)), a food supplement, versus placebo in patients with osteoarthritis of the knee or hip: A randomised double-blind placebo-controlled clinical trial. *Arthritis Research and Therapy* 2009;11(6 Article Number):.
- Jacquet A, Girodet PO, Pariente A, Forest K, Mallet L, Moore N. Phytalgic, a food supplement, versus placebo in patients with osteoarthritis of the knee or hip: a randomised double-blind placebo-controlled clinical trial. *Arthritis Res Ther* 2009;11(6):R192.
- Jagtap SA, Lahoti S, Anwaruddin K, Ram S, Ballary C, Desai A. Evaluation of efficacy, safety and tolerability of Valdecoxib in osteo-arthritis patients--an Indian study. *J Indian Med Assoc* 2002;100(11):673-674.
- Jahangier ZN, Jacobs JW, Swen WA, Moolenburgh JD, Bruyn GA, Griep EN, Bijlsma JW. Can simple ultrasonography predict the clinical effect of intra-articular injection therapy of the knee joint?. *Clin Rheumatol* 2010 Nov 16;.
- James IG, O'Brien CM, McDonald CJ. A randomized, double-blind, double-dummy comparison of the efficacy and tolerability of low-dose transdermal buprenorphine (BuTrans seven-day patches) with buprenorphine sublingual tablets (Temgesic) in patients with osteoarthritis pain. *J Pain Symptom Manage* 2010 Aug;40(2):266-278.
- Jamtvedt G, Dahm KT, Holm I, Flottorp S. Measuring physiotherapy performance in patients with osteoarthritis of the knee: a prospective study. *BMC Health Serv Res* 2008;8:145.
- Jamtvedt G, Rosenbaum S, Dahm KT, Flottorp S. Chocolate bar as an incentive did not increase response rate among physiotherapists: a randomised controlled trial. *BMC Res Notes* 2008;1:34.
- Jan MH, Chai HM, Wang CL, Lin YF, Tsai LY. Effects of repetitive shortwave diathermy for reducing synovitis in patients with knee osteoarthritis: an ultrasonographic study. *Phys Ther* 2006;86(2):236-244.
- Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. *J Formos Med Assoc* 1991;90(10):1008-1013.

- Jan MH,Tang PF,Lin JJ,Tseng SC,Lin YF,Lin DH. Efficacy of a target-matching foot-stepping exercise on proprioception and function in patients with knee osteoarthritis. *J Orthop Sports Phys Ther* 2008;38(1):19-25.
- Janke PG,Diggins JB,Currie WJ,Dasgupta PK,Glick EN,Sheikh NA,Shujja UD. A multi-centre study of sulindac versus Naproxen in the treatment of elderly osteoarthritic patients. *Pharmatherapeutica* 1984;3(10):663-667.
- Jansen MJ,Hendriks EJ,Oostendorp RA,Dekker J,de Bie RA. Quality indicators indicate good adherence to the clinical practice guideline on 'Osteoarthritis of the hip and knee' and few prognostic factors influence outcome indicators: a prospective cohort study. *Eur J Phys Rehabil Med* 2010;.
- Jarvenpaa J,Kettunen J,Kroger H,Miettinen H. Obesity may impair the early outcome of total knee arthroplasty. *Scand J Surg* 2010;99(4):45-49.
- Jarvholm B,From C,Lewold S,Malchau H,Vingard E. Incidence of surgically treated osteoarthritis in the hip and knee in male construction workers. *Occup Environ Med* 2008;65(4):275-278.
- Jenkinson CM,Doherty M,Avery AJ,Read A,Taylor MA,Sach TH,Silcocks P,Muir KR. Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. *BMJ* 2009;339:b3170.
- Jensen EM,Andersen RB,Fossgreen J,et a. A randomized, double-blind long-term trial comparing tenoxicam and Piroxicam in osteoarthritis of the hip or knee. A 12-month interim report. *CURR THER RES , CLIN EXP* 1986;39:365-377.
- Jensen EM,Ginsberg F. Tramadol versus dextropropoxyphene in the treatment of osteoarthritis: A short term double-blind study. *Drug Investigation* 1994;8(4):211-218.
- Jensen H,Zesler R,Christensen T. Transcutaneous electrical nerve stimulation (TNS) for painful osteoarthrosis of the knee. *Int J Rehabil Res* 1991;14(4):356-358.
- Jevtic T,Mejdi Z,Vukomanovic J,Milovanovic D,Jevtic M. Application of methylprednisolone suspension by iontophoresis in patients with arthrosis of the knee. *Serbian Journal of Experimental and Clinical Research* 2008;9(1):13-17.
- Jia J,Mao GL,Hu SH,Dong XC. [Acupuncture combined with function exercise for the elder patients with knee osteoarthritis]. *Zhongguo Linchuang Kangfu* 2005;9:18-19.
- Jiang A,Zhang L,Zhao C,Yang F. Clinical effect of acupuncture treatment in 109 cases of knee osteoarthritis. *J Tradit Chin Med* 2001;21(4):282-285.
- Jitpraphai C,Cheamvaraporn K. Conservative management of degenerative knee: an experience with 508 cases at Ramathibodi Hospital. *J Med Assoc Thai* 1992;75(1):35-38.
- Johnson DP. The effect of continuous passive motion on wound-healing and joint mobility after knee arthroplasty. *J Bone Joint Surg Am* 1990;72(3):421-426.
- Johnson JE. Patient education and self-advocacy. Managing pain in osteoarthritis. *J Pain Palliat Care Pharmacother* 2009;23(2):171-173.

Johnson SR, Archibald A, Davis AM, Badley E, Wright JG, Hawker GA. Is self-reported improvement in osteoarthritis pain and disability reflected in objective measures?. *J Rheumatol* 2007;34(1):159-164.

Jokic A, Sremcevic N, Karagulle Z, Pekmezovic T, Davidovic V. Oxidative stress, hemoglobin content, superoxide dismutase and catalase activity influenced by sulphur baths and mud packs in patients with osteoarthritis. *Vojnosanit Pregl* 2010 Jul;67(7):573-578.

Jokio PJ, Lindholm TS, Vankka E. Medical and lateral gonarthrosis treated with high tibial osteotomy. A prospective study. *Arch Orthop Trauma Surg* 1985;104(3):135-144.

Jokio PJ, Ragni P, Lindholm TS. Management of the fibula in high tibial osteotomy for arthritis of the knee. Union times and complications. *Ital J Orthop Traumatol* 1986;12(1):41-52.

Jones AC, Patrick M, Doherty S, Doherty M. Intra-articular hyaluronic acid compared to intra-articular triamcinolone hexacetonide in inflammatory knee osteoarthritis. *Osteoarthritis Cartilage* 1995;3(4):269-273.

Jordan KM, Arden NK, Doherty M, Dougados M, Hunter DJ. Review: Evidence exists for 33 different treatment options for osteoarthritis of the knee. *Evidence-Based Medicine* 2004;9(3):81.

Jorge LL, Feres CC, Teles VEP. Topical preparations for pain relief: Efficacy and patient adherence. *Journal of Pain Research* 2011;4:11-24.

Joubert PH, Kushlick AR, McNeill WG, Sheard ES, Muller FO. South African multicentre trial with Voltaren in osteo-arthritis of the knee. *S Afr Med J* 1974;48(47):1973-1978.

Jubb RW, Piva S, Beinat L, Dacre J, Gishen P. A one-year, randomised, placebo (saline) controlled clinical trial of 500-730 kDa sodium hyaluronate (Hyalgan) on the radiological change in osteoarthritis of the knee. *Int J Clin Pract* 2003;57(6):467-474.

Jubb RW, Tukmachi ES, Jones PW, Dempsey E, Waterhouse L, Brailsford S. A blinded randomised trial of acupuncture (manual and electroacupuncture) compared with a non-penetrating sham for the symptoms of osteoarthritis of the knee. *Acupunct Med* 2008;26(2):69-78.

Jung YB, Roh KJ, Jung JA, Jung K, Yoo H, Cho YB, Kwak WJ, Kim DK, Kim KH, Han CK. Effect of SKI 306X, a new herbal anti-arthritic agent, in patients with osteoarthritis of the knee: a double-blind placebo controlled study. *Am J Chin Med* 2001;29(3-4):485-491.

Juvin E. A pragmatic trial of oxaceprol 200mg in the long-term treatment of lower limb osteoarthritis: <ORIGINAL> ESSAI PRAGMATIQUE DE L'OXACEPROL 200mg DANS LE TRAITEMENT AU LONG COURS DE L'ARTHROSE DES MEMBRES INFERIEURS. *Semaine Des Hopitaux* 1998;74:47-54.

KAGEYAMA T, SUGANO T, YAMAMOTO M, MIYOSHI K, ABE M, SUGAWARA S, KUSUMOTO T, KURIMURA H, KAWAI K, NIHEI R, NOZUE Y, HOSOKAWA M, KOIDE S, TANAKA M, MUROTA K, TSUYAMA N, AZUMA A, IGARASHI M, KABATA K, NAGANO M, MITANI S, OMORI S, NISHIMURA T, IWATA S, MORI Y, et al. Clinical Evaluation of Diflunisal in the Treatment of Osteoarthritis of the Knee -A Double-Blind Comparative Study. *Rinsho Hyoka* 1983;11:461-487.

Kageyama T. Clinical evaluation of Naproxen in the treatment of osteoarthritis--double-blind, cross-over trial. *Scand J Rheumatol* 1973;.

- Kahan A, Le PC, Llew PL, Maurel F, Salin L. A nine-month cost-effectiveness analysis of two therapeutic strategies in patients with knee osteoarthritis. *Journal D'Economie Medicale* 2002;20:92-104.
- Kahan A, Llew PL, Salin L. Prospective randomized study comparing the medicoeconomic benefits of Hyal G-F 20 versus conventional treatment in knee osteoarthritis. *Joint Bone Spine* 2003;70(4):276-281.
- Kahler M, Hillstrom HJ, McGuire J, Whitney K, Schumacher HR. Immediate effects of foot orthoses on gait parameters in subjects with medial type knee osteoarthritis. *Gait Posture* 1998;7(2):177.
- Kalman DS, Heimer M, Valdeon A, Schwartz H, Sheldon E. Effect of a natural extract of chicken combs with a high content of hyaluronic acid (Hyal-Joint) on pain relief and quality of life in subjects with knee osteoarthritis: a pilot randomized double-blind placebo-controlled trial. *Nutr J* 2008;7:3.
- Kamath CC, Kremers HM, Vanness DJ, O'Fallon WM, Cabanela RL, Gabriel SE. The cost-effectiveness of Acetaminophen, NSAIDs, and selective COX-2 inhibitors in the treatment of symptomatic knee osteoarthritis. *Value Health* 2003;6(2):144-157.
- Kanamiya T, Naito M, Hara M, Yoshimura I. The influences of biomechanical factors on cartilage regeneration after high tibial osteotomy for knees with medial compartment osteoarthritis: clinical and arthroscopic observations. *Arthroscopy* 2002;18(7):725-729.
- Kang JG, Wang ML, Zhang XN. [Treatment of knee osteoarthritis with arthroscopic debridement and intra-articular sodium hyaluronate injection]. *Jilin Daxue Xuebao Yixue Ban* 2005;31:802-805.
- Kang RW, Lewis PB, Kramer A, Hayden JK, Cole BJ. Prospective randomized single-blinded controlled clinical trial of percutaneous neuromodulation pain therapy device versus sham for the osteoarthritic knee: a pilot study. *Orthopedics* 2007;30(6):439-445.
- Kao MJ, Wu MP, Tsai MW, Chang WW, Wu SF. The effectiveness of a self-management program on quality of life for knee osteoarthritis (OA) patients. *Arch Gerontol Geriatr* 2011 Jul 2;.
- Karakaya M. A double-blind comparison of a new anti-inflammatory substance, proquazone, with indomethacin and placebo in osteoarthritis of the knee joint. *Current Therapeutic Research Clinical and Experimental* 1977;22:127.
- Karaoglan B, Erten A, Ayhan F, Dumlu S, Oguz A, Erdem R. The effects of etodolac on the clinical course and gastric mucosal PGE of knee osteoarthritis. *Gazi Medical Journal* 1995;6:169-172.
- Karatay S, Kiziltunc A, Yildirim K, Karanfil RC, Senel K. Effects of different hyaluronic acid products on synovial fluid levels of intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 in knee osteoarthritis. *Ann Clin Lab Sci* 2004;34(3):330-335.
- Karatay S, Kiziltunc A, Yildirim K, Karanfil RC, Senel K. Effects of different hyaluronic acid products on synovial fluid NO levels in knee osteoarthritis. *Clin Rheumatol* 2005;24(5):497-501.
- Karatosun V, Unver B, Gocen Z, Sen A, Gunal I. Intra-articular hyaluronic acid compared with progressive knee exercises in osteoarthritis of the knee: a prospective randomized trial with long-term follow-up. *Rheumatol Int* 2006;26(4):277-284.

- Karatosun V, Unver B, Gocen Z, Sen A. Comparison of two hyaluronan drugs in patients with advanced osteoarthritis of the knee. A prospective, randomized, double-blind study with long term follow-up. *Clin Exp Rheumatol* 2005;23(2):213-218.
- Karel P, Coste P, Geher P, Krejci G. Efficacy and safety of piascledine 300 versus chondroitin sulfate in a 6 months treatment plus 2 months observation in patients with osteoarthritis of the knee. *Clin Rheumatol* 2010 Jun;29(6):659-670.
- Karlsson J, Pivodic A, Aguirre D, Schnitzer TJ. Efficacy, safety, and tolerability of the cyclooxygenase-inhibiting nitric oxide donator Naproxen in treating osteoarthritis of the hip or knee. *J Rheumatol* 2009;36(6):1290-1297.
- Karlsson M, Berggren AC. Efficacy and safety of low-dose transdermal buprenorphine patches (5, 10, and 20 microg/h) versus prolonged-release Tramadol tablets (75, 100, 150, and 200mg) in patients with chronic osteoarthritis pain: a 12-week, randomized, open-label, controlled, pa. *Clin Ther* 2009;31(3):503-513.
- Karlsson MK, Josefsson PO, Nordkvist A, Akesson K, Seeman E, Obrant KJ. Bone loss following tibial osteotomy: a model for evaluating post-traumatic osteopenia. *Osteoporos Int* 2000;11(3):261-264.
- Katsuragawa Y, Fukui N, Nakamura K. Change of bone mineral density with valgus knee bracing. *Int Orthop* 1999;23(3):164-167.
- Katz JN, Harris TM, Larson mg, Krushell RJ, Brown CH, Fossel AH, Liang MH. Predictors of functional outcomes after arthroscopic partial meniscectomy. *J Rheumatol* 1992;19(12):1938-1942.
- Katz JN, Meredith DS, Lang P, Creel AH, Yoshioka H, Neumann G, Fossel AH, De PP, Losina E. Associations among preoperative MRI features and functional status following arthroscopic partial meniscectomy. *Osteoarthritis Cartilage* 2006;14(5):418-422.
- Katz N, Hale M, Morris D, Stauffer J. Morphine sulfate and naltrexone hydrochloride extended release capsules in patients with chronic osteoarthritis pain. *Postgrad Med* 2010 Jul;122(4):112-128.
- Katz N, Sun S, Johnson F, Stauffer J. ALO-01 (morphine sulfate and naltrexone hydrochloride) extended-release capsules in the treatment of chronic pain of osteoarthritis of the hip or knee: pharmacokinetics, efficacy, and safety. *The journal of pain : official journal of the American Pain Society* 2010;11:303-311.
- Kaufman KR, Hughes C, Morrey BF, Morrey M, An KN. Gait characteristics of patients with knee osteoarthritis. *J Biomech* 2001;34(7):907-915.
- Kauppila AM, Kyllonen E, Mikkonen P, Ohtonen P, Laine V, Siira P, Niinimäki J, Arokoski JP. Disability in end-stage knee osteoarthritis. *Disabil Rehabil* 2009;31(5):370-380.
- Kawabata M, Igarashi M, Mikami R, Ninomiya S, Oda H, Hoshino Y, Yamamoto S, Kurokawa T, Ogawa N. [Clinical Evaluation of SLM-10 (Sodium Hyaluronate Injection) in Patients with Osteoarthritis of the Knee: A Multi-Center Comparative Trial with ARTZ as Control Drug]. *Yakuri to Chiryō* 1993;21:257-283.
- Kawaguchi H. Approach for therapeutic targets of osteoarthritis. *Folia Pharmacologica Japonica* 2011;138(1):22-25.

Kawasaki T,Kurosawa H,Ikeda H,Kim SG,Osawa A,Takazawa Y,Kubota M,Ishijima M. Additive effects of glucosamine or risedronate for the treatment of osteoarthritis of the knee combined with home exercise: a prospective randomized 18-month trial. *J Bone Miner Metab* 2008;26(3):279-287.

Kawasaki T,Kurosawa H,Ikeda H,Takazawa Y,Ishijima M,Kubota M,Kajihara H,Maruyama Y,Kim SG,Kanazawa H,Doi T. Therapeutic home exercise versus intraarticular hyaluronate injection for osteoarthritis of the knee: 6-month prospective randomized open-labeled trial. *J Orthop Sci* 2009;14(2):182-191.

Kean WF,Bouchard S,Roderich GE. Women with pain due to osteoarthritis: the efficacy and safety of a once-daily formulation of tramadol. *Pain Med* 2009;10(6):1001-1011.

Keating EM,Faris PM,Ritter MA,Kane J. Use of lateral heel and sole wedges in the treatment of medial osteoarthritis of the knee. *Orthop Rev* 1993;22(8):921-924.

Keefe FJ,Blumenthal J,Baucom D,Affleck G,Waugh R,Caldwell DS,Beaupre P,Kashikar-Zuck S,Wright K,Egert J,Lefebvre J. Effects of spouse-assisted coping skills training and exercise training in patients with osteoarthritic knee pain: a randomized controlled study. *Pain* 2004;110(3):539-549.

Keefe FJ,Caldwell DS,Queen K,Gil KM,Martinez S,Crisson JE,Ogden W,Nunley J. Osteoarthritic knee pain: a behavioral analysis. *Pain* 1987;28(3):309-321.

Keefe FJ,Caldwell DS,Williams DA,Gil KM,et a. Pain coping skills training in the management of osteoarthritic knee pain: A comparative study. *Behav Ther* 1990;21:49-62.

Keene GCR,Paterson RS,Teague DC. Advances in arthroscopic surgery. *Clin Orthop* 1987;(224):64-70.

Keene JS,Dyreby JR. High tibial osteotomy in the treatment of osteoarthritis of the knee. The role of preoperative arthroscopy. *J Bone Joint Surg Am* 1983;65(1):36-42.

Keene JS,Monson DK,Roberts JM,Dyreby JR. Evaluation of patients for high tibial osteotomy. *Clin Orthop Relat Res* 1989;(243):157-165.

Keet JG. A comparative clinical trial of diflunisal and ibuprofen in the control of pain in osteoarthritis. *J Int Med Res* 1979;7(4):272-276.

Keim HA. Upper tibial osteotomy for osteoarthritis of knee. *N Y State J Med* 1971;71(12):1514-1517.

Kelley MT. Nonsurgical management of osteoarthritis of the knee. *JAAPA* 2006;19(1):26-32.

Kelly MA,Backstein D. The new arthritic patient and nonarthroplasty treatment options: Femoral osteotomy: Indications, technique, and outcomes. *Journal of Bone and Joint Surgery - Series A* 2009;91(SUPPL. 5):41-42.

Kemper F,Gebhardt U,Meng T,Murray C. Tolerability and short-term effectiveness of hylan G-F 20 in 4253 patients with osteoarthritis of the knee in clinical practice. *Curr Med Res Opin* 2005;21(8):1261-1269.

- Kennedy AC,Mullen BJ,Roth SH,Germain BF,Bonebrake RA,Wei N,Willkens RF,Lawson JG,Appelrouth DJ,White RE. A double-blind comparison of the efficacy and safety of Ketoprofen extended-release (200mg once daily) and Diclofenac (75mg twice daily) for treatment of osteoarthritis. *Current Therapeutic Research - Clinical and Experimental* 1994;55(2):119-132.
- Kenwright J,Duthie RB. Surgical management of arthritis of the knee. *Semin Arthritis Rheum* 1971;1(1):58-86.
- Kersten P,White PJ,Tennant A. The Visual Analogue WOMAC 3.0 scale - internal validity and responsiveness of the VAS version. *BMC Musculoskelet Disord* 2010;11(1):80.
- Kerzberg EM,Roldan EJ,Castelli G,Huberman ED. Combination of glycosaminoglycans and acetylsalicylic acid in knee osteoarthritis. *Scand J Rheumatol* 1987;16(5):377-380.
- Keysor JJ,Heislein DM. Physical activity considerations among people with knee and hip osteoarthritis. *International Journal of Clinical Rheumatology* 2010;5(6):659-667.
- Khalil SA,El Zahaar MS. Hoffman external fixation in high tibial osteotomy. *Journal of Neurological and Orthopaedic Medicine and Surgery* 1991;12(1):12-16.
- Khan FM,Williams PI. Double-blind comparison of etodolac SR and Diclofenac SR in the treatment of patients with degenerative joint disease of the knee. *Curr Med Res Opin* 1992;13(1):1-12.
- Khan MT,Matthews JG. High tibial osteotomy without internal fixation for medial unicompartmental osteoarthritis. *Orthopedics* 2000;23(10):1045-1048.
- Kidd B,Frenzel W. A multicenter, randomized, double blind study comparing Lornoxicam with Diclofenac in osteoarthritis. *J Rheumatol* 1996;23(9):1605-1611.
- Kilcoglu O,Donmez A,Karagulle Z,Erdogan N,Akalan E,Temelli Y. Effect of balneotherapy on temporospatial gait characteristics of patients with osteoarthritis of the knee. *Rheumatol Int* 2010;30(6):739-747.
- Kim EJ,Jang MK,Yoon EH,Jung CY,Nam DW,Lee SD,Kim KS. Efficacy of pharmacopuncture using root bark of *Ulmus davidiana* Planch in patients with knee osteoarthritis: a double-blind randomized controlled trial. *J Acupunct Meridian Stud* 2010 Mar;3(1):16-23.
- Kim J,Lee EY,Koh EM,Cha HS,Yoo B,Lee CK,Lee YJ,Ryu H,Lee KH,Song YW. Comparative clinical trial of S-adenosylmethionine versus nabumetone for the treatment of knee osteoarthritis: an 8-week, multicenter, randomized, double-blind, double-dummy, Phase IV study in Korean patients. *Clin Ther* 2009;31(12):2860-2872.
- Kim LS,Axelrod LJ,Howard P,Buratovich N,Waters RF. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. *Osteoarthritis Cartilage* 2006;14(3):286-294.
- Kim SJ,Koh YG,Chun YM,Kim YC,Park YS,Sung CH. Medial opening wedge high-tibial osteotomy using a kinematic navigation system versus a conventional method: a 1-year retrospective, comparative study. *Knee Surg Sports Traumatol Arthrosc* 2009;17(2):128-134.
- Kimmatkar N,Thawani V,Hingorani L,Khiyani R. Efficacy and tolerability of *Boswellia serrata* extract in treatment of osteoarthritis of knee--a randomized double blind placebo controlled trial. 2003;10(1):3-7.

Kirchheiner B,Holm P,Jensen EM,et a. A new long-acting anti-inflammatory agent, tenoxicam (Tilcotil (Reg.trademark)): In osteoarthritis of the knee and the hip: A randomized comparison with indomethacin. *CURR THER RES , CLIN EXP* 1982;32:627-632.

Kirchner M,Marshall D. A double-blind randomized controlled trial comparing alternate forms of high molecular weight hyaluronan for the treatment of osteoarthritis of the knee. *Osteoarthritis Cartilage* 2006;14(2):154-162.

Kirkley A,Rampersaud R,Griffin S,Amendola A,Litchfield R,Fowler P. Tourniquet versus no tourniquet use in routine knee arthroscopy: a prospective, double-blind, randomized clinical trial. *Arthroscopy* 2000;16(2):121-126.

Kirkness CS,Yu J,Asche CV. The effect on comorbidity and pain in patients with osteoarthritis. *Journal of Pain and Palliative Care Pharmacotherapy* 2008;22(4):336-348.

Kitay GS,Koren MJ,Helfet DL,Parides MK,Markenson JA. Efficacy of combined local mechanical vibrations, continuous passive motion and thermotherapy in the management of osteoarthritis of the knee. *Osteoarthritis Cartilage* 2009;17(10):1269-1274.

Kiviluoto O,Salenius P,Santavirta S. Proximal tibial osteotomy in the treatment of osteoarthritis of the knee. *Arch Orthop Trauma Surg* 1984;103(1):57-61.

Kivitz A,Fairfax M,Sheldon EA,Xiang Q,Jones BA,Gammaitoni AR,Gould EM. Comparison of the effectiveness and tolerability of lidocaine patch 5% versus Celecoxib for osteoarthritis-related knee pain: post hoc analysis of a 12 week, prospective, randomized, active-controlled, open-label, parallel-group trial in adults. *Clin Ther* 2008;30(12):2366-2377.

Kivitz A,Ma C,Ahdieh H,Galer BS. A 2-week, multicenter, randomized, double-blind, placebo-controlled, dose-ranging, phase III trial comparing the efficacy of oxymorphone extended release and placebo in adults with pain associated with osteoarthritis of the hip or knee. *Clin Ther* 2006;28(3):352-364.

Kivitz AJ,Makarowski WS,Fiechtner JJ,Recker DP. A flexible daily dosage regimen of oxaprozin potassium in patients with acute knee pain associated with osteoarthritis: 24-Hour analgesic durability and safety. *Clinical Drug Investigation* 2001;21:745-753.

Klaber Moffett JA,Richardson PH,Frost H,Osborn A. A placebo controlled double blind trial to evaluate the effectiveness of pulsed short wave therapy for osteoarthritic hip and knee pain. *Pain* 1996;67(1):121-127.

Klein G,Kulich W. Short-term treatment of painful osteoarthritis of the knee with oral enzymes. A randomised, double-blind study versus Diclofenac. *Clinical Drug Investigation* 2000;19:15-23.

Kneer W,Rother I,Rother M,Seidel E. A multiple-dose, open-label, safety, compliance, and usage evaluation study of epicutaneously applied Diractin (Ketoprofen in Transfersome) in joint/musculoskeletal pain or soft tissue inflammation. *Curr Drug Saf* 2009;4(1):5-10.

Knoop J,van der Leeden M,Thorstensson CA,Roorda LD,Lems WF,Knol DL,Steuertjens MP,Dekker J. Identification of phenotypes with different clinical outcomes in knee osteoarthritis: Data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken)* 2011 Nov;63(11):1535-1542.

- Knuesel O, Weber M, Suter A. Arnica montana gel in osteoarthritis of the knee: an open, multicenter clinical trial. *Adv Ther* 2002;19(5):209-218.
- Ko S, Ling SM, Schreiber C, Nesbitt M, Ferrucci L. Gait patterns during different walking conditions in older adults with and without knee osteoarthritis-Results from the Baltimore Longitudinal Study of Aging. *Gait Posture* 2011 Feb;33(2):205-210.
- Koca B, Oz B, Olmez N, Memis A. Effect of lateral-wedge shoe insoles on pain and function in patients with knee osteoarthritis. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi* 2009;55(4):158-162.
- Kocaman O, Koyuncu H, Dinc A, Toros H, Karamehmetoglu SS. The comparison of the effects of electrical stimulation and exercise in the treatment of knee osteoarthritis. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi* 2008;54(2):54-58.
- Kocher MS, Steadman JR, Briggs KK, Sterett WI, Hawkins RJ. Reliability, validity, and responsiveness of the Lysholm knee scale for various chondral disorders of the knee. *Journal of Bone and Joint Surgery - Series A* 2004;86(6):1139-1145.
- Koeck FX, Perlick L, Luring C, Handel M, Beckmann J, Linhardt O, Grifka J. Leg axis correction with ConforMIS iForma (interpositional device) in unicompartmental arthritis of the knee. *Int Orthop* 2009;33(4):955-960.
- Koehler BE, Urowitz MB, Killinger DW. The systemic effects of intra-articular corticosteroid. *J Rheumatol* 1974;1(1):117-125.
- Koenen NJ, Haag RF, Bias P, Rose P. Percutaneous therapy of activated osteoarthritis of the knee - Comparison between DMSO and Diclofenac. *Munchener Medizinische Wochenschrift* 1996;138:534-538.
- Kogstad O. Double blind crossover trial of Piroxicam and Naproxen in the treatment of osteoarthritis of hip and knee. *Br J Clin Pract* 1981;35(1):45-50.
- Kohatsu ND, Schurman DJ. Risk factors for the development of osteoarthrosis of the knee. *Clin Orthop Relat Res* 1990;(261):242-246.
- Kolarz G, Kotz R, Broll H, Dunky A, Landsiedl F, Mayrhofer F, Rainer F, Ramach W, Singer F, Metz M. Hyaluronic acid in the treatment of osteoarthritis of the knee joint: Interim results of a comparative clinical study. *Eur J Rheumatol Inflamm* 1995;15(1):39-45.
- Kolarz G, Kotz R, Hochmayer I. Long-term benefits and repeated treatment cycles of intra-articular sodium hyaluronate (Hyalgan) in patients with osteoarthritis of the knee. *Semin Arthritis Rheum* 2003;32(5):310-319.
- Kolasinski SL, Garfinkel M, Tsai AG, Matz W, Van DA, Schumacher HR. Iyengar yoga for treating symptoms of osteoarthritis of the knees: a pilot study. *J Altern Complement Med* 2005;11(4):689-693.
- Kolb W, Guhlmann H, Windisch C, Kolb K, Koller H, Grutzner P. Opening-wedge high tibial osteotomy with a locked low-profile plate. *J Bone Joint Surg Am* 2009;91(11):2581-2588.

Kolb W, Guhlmann H, Windisch C, Koller H, Grutzner P, Kolb K. Opening-wedge high tibial osteotomy with a locked low-profile plate: surgical technique. *J Bone Joint Surg Am* 2010 Sep;92 Suppl 1 Pt 2:197-207.

Kolen AF, de Nijs RN, Wagemakers FM, Meier AJ, Johnson MI. Effects of spatially targeted transcutaneous electrical nerve stimulation using an electrode array that measures skin resistance on pain and mobility in patients with osteoarthritis in the knee: a randomized controlled trial. *Pain* 2012 Feb;153(2):373-381.

Kon E, Mandelbaum B, Buda R, Filardo G, Delcogliano M, Timoncini A, Fornasari PM, Giannini S, Marcacci M. Platelet-rich plasma intra-articular injection versus hyaluronic Acid viscosupplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. *Arthroscopy* 2011 Nov;27(11):1490-1501.

Konig B. A long-term (two years) clinical trial with S-adenosylmethionine for the treatment of osteoarthritis. *Am J Med* 1987;83(5A):89-94.

Konstari S, Paananen M, Heliovaara M, Knekt P, Marniemi J, Impivaara O, Arokoski J, Karppinen J. Association of 25-hydroxyvitamin D with the incidence of knee and hip osteoarthritis: a 22-year follow-up study. *Scand J Rheumatol* 2011 Nov 1;.

Korn MW. A new approach to dome high tibial osteotomy. *Am J Knee Surg* 1996;9(1):12-21.

Kornaat PR, Ceulemans RYT, Kroon HM, Riyazi N, Kloppenburg M, Carter WO, Woodworth TG, Bloem JL. MRI assessment of knee osteoarthritis: Knee Osteoarthritis Scoring System (KOSS) - Inter-observer and intra-observer reproducibility of a compartment-based scoring system. *Skeletal Radiol* 2005;34(2):95-102.

Kornasoff D, Frerick H, Bowdler J, Montull E. Aceclofenac is a well-tolerated alternative to Naproxen in the treatment of osteoarthritis. *Clin Rheumatol* 1997;16(1):32-38.

Koshino T, Machida J. Grading system of articular cartilage degeneration in osteoarthritis of the knee. *Bull Hosp Jt Dis* 1993;53(3):41-46.

Koshino T, Morii T, Wada J, Saito H, Ozawa N, Noyori K. High tibial osteotomy with fixation by a blade plate for medial compartment osteoarthritis of the knee. *Orthop Clin North Am* 1989;20(2):227-243.

Koshino T, Murase T, Saito T. Medial opening-wedge high tibial osteotomy with use of porous hydroxyapatite to treat medial compartment osteoarthritis of the knee. *J Bone Joint Surg Am* 2003;85-A(1):78-85.

Koshino T, Ranawat NS. Healing process of osteoarthritis in the knee after high tibial osteotomy. Through observation of strontium-85 scintimetry. *Clin Orthop Relat Res* 1972;82:149-156.

Koshino T, Saito T, Orito K, Mitsuhashi S, Takeuchi R, Kurosaka T. Increase in range of knee motion to obtain floor sitting after high tibial osteotomy for osteoarthritis. *Knee* 2002;9(3):189-196.

Koshino T, Tsuchiya K. The effect of high tibial osteotomy on osteoarthritis of the knee. Clinical and histological observations. *Int Orthop* 1979;3(1):37-45.

- Koshino T, Wada S, Ara Y, Saito T. Regeneration of degenerated articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis of the knee. *Knee* 2003;10(3):229-236.
- Koshino T, Yoshida T, Ara Y, Saito I, Saito T. Fifteen to twenty-eight years' follow-up results of high tibial valgus osteotomy for osteoarthritic knee. *Knee* 2004;11(6):439-444.
- Koshino T. Classification of stage of regenerated articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis of the knee. *Techniques in Knee Surgery* 2010 Jun;9(2):101-106.
- Koshino T. High tibial osteotomy with blade plate fixation for osteoarthritis of Japanese knee. *Journal of the Western Pacific Orthopaedic Association* 1989;26(2):59-69.
- Kostopoulos D. Comparative effects of aquatic recreational and aquatic exercise programs on mobility, pain perception, and treatment satisfaction among elderly persons with osteoarthritis of the knee. 2000;.
- Kosuwon W, Sirichatiwapee W, Wisanuyotin T, Jeeravipoolvarn P, Laupattarakasem W. Efficacy of symptomatic control of knee osteoarthritis with 0.0125% of capsaicin versus placebo. *J Med Assoc Thai* 2010 Oct;93(10):1188-1195.
- Kotevoglou N, Iyibozkurt PC, Hiz O, Toktas H, Kuran B. A prospective randomised controlled clinical trial comparing the efficacy of different molecular weight hyaluronan solutions in the treatment of knee osteoarthritis. *Rheumatol Int* 2006;26(4):325-330.
- Kotz R, Kolarz G. Intra-articular hyaluronic acid: duration of effect and results of repeated treatment cycles. *Am J Orthop (Belle Mead NJ)* 1999;28(11 Suppl):5-7.
- Kovacs I, Bender T. The therapeutic effects of Cserkeszolo thermal water in osteoarthritis of the knee: a double blind, controlled, follow-up study. *Rheumatol Int* 2002;21(6):218-221.
- Kozanoglu E, Basaran S, Guzel R, Guler-Uysal F. Short term efficacy of ibuprofen phonophoresis versus continuous ultrasound therapy in knee osteoarthritis. *Swiss Med Wkly* 2003;133(23-24):333-338.
- Kraemer WJ, Ratamess NA, Anderson JM, Maresh CM, Tiberio DP, Joyce ME, Messinger BN, French DN, Rubin MR, Gomez AL, Volek JS, Hesslink R. Effect of a cetylated fatty acid topical cream on functional mobility and quality of life of patients with osteoarthritis. *J Rheumatol* 2004;31(4):767-774.
- Kraemer WJ, Ratamess NA, Maresh CM, Anderson JA, Volek JS, Tiberio DP, Joyce ME, Messinger BN, French DN, Sharman MJ, Rubin MR, Gomez AL, Silvestre R, Hesslink RL. A cetylated fatty acid topical cream with menthol reduces pain and improves functional performance in individuals with arthritis. *J Strength Cond Res* 2005;19(2):475-480.
- Kreindler H, Lewis CB, Rush S, Schaefer K. Effects of three exercise protocols on strength of persons with osteoarthritis of the knee. *Topics in Geriatric Rehabilitation* 1989;4(3):32-39.
- Kriegel W, Korff KJ, Ehrlich JC, Lehnhardt K, Macciocchi A, Moresino C, Pawlowski C. Double-blind study comparing the long-term efficacy of the COX-2 inhibitor nimesulide and Naproxen in patients with osteoarthritis. *Int J Clin Pract* 2001;55(8):510-514.

Kruger H, Garche U. The use of isokinetic systems at osteoarthritis during in-patient rehabilitation, part II - Isokinetic training. <ORIGINAL> EINSATZ ISOKINETISCHER SYSTEME BEI GONARTHROSEN WAHREND STATIONÄRER REHABILITATION: TEIL II - ISOKINETISCHES TRAINING. *Pravention Und Rehabilitation* 1997;9:161-165.

Kruger K, Klasser M, Mossinger J, Becker U. Oxaceprol--a randomised, placebo-controlled clinical study in osteoarthritis with a non-conventional non-steroidal anti-inflammatory drug. *Clin Exp Rheumatol* 2007;25(1):29-34.

Kruger-Franke M, Siebert CH, Kugler A, Trouillier HH, Rosemeyer B. Late results after arthroscopic partial medial meniscectomy. *Knee Surg Sports Traumatol Arthrosc* 1999;7(2):81-84.

Krystallis CT, Kirkos JM, Papavasiliou KA, Konstantinides PA, Kyrkos MJ, Kapetanios GA. Arthroscopic debridement of the osteoarthritic knee under local anaesthesia. *Acta Orthop Belg* 2004;70(3):260-267.

Krzeski P, Buckland-Wright C, Balint G, Cline GA, Stoner K, Lyon R, Beary J, Aronstein WS, Spector TD. Development of musculoskeletal toxicity without clear benefit after administration of PG-116800, a matrix metalloproteinase inhibitor, to patients with knee osteoarthritis: a randomized, 12-month, double-blind, placebo-controlled study. *Arthritis Res Ther* 2007;9(5):R109.

Kujawa J, Talar J, Gworys K, Gworys P, Pieszynski I, Janiszewski M. The analgesic effectiveness of laser therapy in patients with gonarthrosis: an evaluation. *Ortop Traumatol Rehabil* 2004;6(3):356-366.

Kukuk P, Lungenhausen M, Molsberger A, Endres HG. Long-term improvement in pain coping for cLBP and gonarthrosis patients following body needle acupuncture: a prospective cohort study. *Eur J Med Res* 2005;10(6):263-272.

Kulcu DG, Gulsen G, Altunok EC. Short-term efficacy of pulsed electromagnetic field therapy on pain and functional level in knee osteoarthritis: A randomized controlled study. *Turkish Journal of Rheumatology* 2009;24(3):144-148.

Kulich WC, Niksic F, Klein G. Effect of nimesulide on metalloproteinases and matrix degradation in osteoarthritis: a pilot clinical study. *Int J Clin Pract Suppl* 2002;(128):24-29.

Kul-Panza E, Berker N. Is hyaluronate sodium effective in the management of knee osteoarthritis? A placebo-controlled double-blind study. *Minerva Med* 2010;101(2):63-72.

Kumar AM, Wen XL. Acupuncture treatment for osteoarthritic pain and inflammation of the knee. *Altern Ther Health Med* 2002;8(6):128, 126.

Kumar PJ, McPherson EJ, Dorr LD, Wan Z, Baldwin K. Rehabilitation after total knee arthroplasty: a comparison of 2 rehabilitation techniques. *Clin Orthop Relat Res* 1996;(331):93-101.

Kumm J, Tamm A, Lintrop M, Tamm A. Association between ultrasonographic findings and bone/cartilage biomarkers in patients with early-stage knee osteoarthritis. *Calcif Tissue Int* 2009;85(6):514-522.

Kuntz D, Lermusiaux JL, Teyssedou JP, Ryckewaert A. A double-blind study of the analgesic action of benorylate suspension in osteoarthritis of the hip and knee. *Scand J Rheumatol Suppl* 1975;(13):25-28.

- Kuptniratsaikul V, Pinthong T, Bunjob M, Thanakhumtorn S, Chinswangwatanakul P, Thamlikitkul V. Efficacy and safety of *Derris scandens* benth extracts in patients with knee osteoarthritis. *J Altern Complement Med* 2011 Feb 1;17(2):147-153.
- Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V. Efficacy and safety of *Curcuma domestica* extracts in patients with knee osteoarthritis. *J Altern Complement Med* 2009;15(8):891-897.
- Kuptniratsaikul V, Tosayanonda O, Nilganuwong S, Thamalikitkul V. The efficacy of a muscle exercise program to improve functional performance of the knee in patients with osteoarthritis. *J Med Assoc Thai* 2002;85(1):33-40.
- Kuremsky MA, Schaller TM, Hall CC, Roehr BA, Masonis JL. Comparison of autograft versus allograft in opening-wedge high tibial osteotomy. *J Arthroplasty* 2010 Sep;25(6):951-957.
- Kuzmanova SI. Treatment of knee osteoarthritis by arthroscopic synovectomy and debridement of cartilage lesions--late results. *Folia Med (Plovdiv)* 2003;45(3):66-72.
- Kvien TK, Brors O, Staff PH, Rognstad S, Nordby J. Improved cost-effectiveness ratio with a patient self-adjusted Naproxen dosing regimen in osteoarthritis treatment. *Scand J Rheumatol* 1991;20(4):280-287.
- Kwon YB, Kim JH, Yoon JH, Lee JD, Han HJ, Mar WC, Beitz AJ, Lee JH. The analgesic efficacy of bee venom acupuncture for knee osteoarthritis: a comparative study with needle acupuncture. *Am J Chin Med* 2001;29(2):187-199.
- Kyne PJ. Proximal tibial osteotomy for compartmental tibiofemoral osteoarthritis. *N Y State J Med* 1970;70(9):1059-1063.
- la Mantia K, Marks R. The efficacy of aerobic exercises for treating osteoarthritis of the knee. *New Zealand Journal of Physiotherapy* 1995;23(2):23-30.
- Laberge MA, Baum T, Virayavanich W, Nardo L, Nevitt MC, Lynch J, McCulloch CE, Link TM. Obesity increases the prevalence and severity of focal knee abnormalities diagnosed using 3T MRI in middle-aged subjects--data from the Osteoarthritis Initiative. *Skeletal Radiol* 2011 Sep 2;.
- Lador R, Segal G, Kosashvili Y, Drexler M, Chechik O, Haim A, Salai M, Debi R, Elbaz A. Patients with knee osteoarthritis demonstrate improved gait and clinical symptoms following a non-invasive biomechanical therapy. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S225.
- Lai JN, Chen HJ, Chen CC, Lin JH, Hwang JS, Wang JD. Duhuo jisheng tang for treating osteoarthritis of the knee: a prospective clinical observation. *Chin Med* 2007;2:4.
- Laine L, White WB, Rostom A, Hochberg M. COX-2 Selective Inhibitors in the Treatment of Osteoarthritis. *Seminars in Arthritis and Rheumatism* 2008;38(3):165-187.
- Lamb SE, Toye F, Barker KL. Chronic disease management programme in people with severe knee osteoarthritis: efficacy and moderators of response. *Clin Rehabil* 2008;22(2):169-178.
- Lanas A, Tornero J, Zamorano JL. Assessment of gastrointestinal and cardiovascular risk in patients with osteoarthritis who require NSAIDs: The LOGICA study. *Annals of the Rheumatic Diseases* 2010;69(8):1453-1458.

Landry SC,McKean KA,Hubley-Kozey CL,Stanish WD,Deluzio KJ. Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed. *J Biomech* 2007;40(8):1754-1761.

Lange AK,Fiatarone Singh MA,Smith RM,Foroughi N,Baker MK,Shnier R,Vanwanseele B. Degenerative meniscus tears and mobility impairment in women with knee osteoarthritis. *Osteoarthritis Cartilage* 2007;15(6):701-708.

Lange AK, Vanwanseele B,Fiatarone-Singh MA. Strength training for treatment of osteoarthritis of the knee: a systematic review (Structured abstract). *Arthritis and Rheumatism* 2008;59:1488-1494.

Lange AK, Vanwanseele B,Foroughi N,Baker MK,Shnier R,Smith RM,Singh MA. Resistive Exercise for Arthritic Cartilage Health (REACH): a randomized double-blind, sham-exercise controlled trial. *BMC Geriatr* 2009;9:1.

Lange B,Kuperwasser B,Okamoto A,Steup A,Haufel T,Ashworth J,Etropolski M. Efficacy and safety of tapentadol prolonged release for chronic osteoarthritis pain and low back pain. *Adv Ther* 2010 Jun;27(6):381-399.

Langford R,McKenna F,Ratcliffe S,Vojtassak J,Richarz U. Transdermal fentanyl for improvement of pain and functioning in osteoarthritis: a randomized, placebo-controlled trial. *Arthritis Rheum* 2006;54(6):1829-1837.

Langworthy MJ,Saad A,Langworthy NM. Conservative treatment modalities and outcomes for osteoarthritis: the concomitant pyramid of treatment. *Phys Sportsmed* 2010 Jun;38(2):133-145.

Lansdown H,Howard K,Brealey S,MacPherson H. Acupuncture for pain and osteoarthritis of the knee: a pilot study for an open parallel-arm randomised controlled trial. *BMC Musculoskelet Disord* 2009;10:130.

LaPrade RF,Spiridonov SI,Nystrom LM,Jansson KS. Prospective outcomes of young and middle-aged adults with medial compartment osteoarthritis treated with a proximal tibial opening wedge osteotomy. *Arthroscopy* 2012 Mar;28(3):354-364.

Larsson SE,Ahlgren O. Reconstruction with endoprosthesis in gonarthrosis: a report of 111 consecutive cases operated upon from 1973 through 1977. *Clin Orthop Relat Res* 1979;(145):126-135.

Lattermann C,Jakob RP. High tibial osteotomy alone or combined with ligament reconstruction in anterior cruciate ligament-deficient knees. *Knee Surg Sports Traumatol Arthrosc* 1996;4(1):32-38.

Lau CS,Chiu PKY,Chu EMY,Cheng IYW,Tang WM,Man RYK,Halpern GM. Treatment of knee osteoarthritis with Lyprinol(registered trademark), lipid extract of the green-lipped mussel - A double-blind placebo-controlled study. *Progress in Nutrition* 2004;6(1):17-31.

Lau CS,Chiu PKY,Chu EMY,Cheng IYW,Tang WM,Man RYK,Halpern GM. Treatment of knee osteoarthritis with Lyprinol, lipid extract of the green-lipped mussel - a double-blind placebo-controlled study. *Progress in Nutrition* 2004;6:17-31.

Lau F,Bagch D,Raychaudhuri S. Undenatured type II collagen (UC-II) in the treatment of osteoarthritis. *Clin Immunol* 2010;135 SUPPL. 1:S99.

Laufer Y,Zilberman R,Porat R,Nahir AM. Effect of pulsed short-wave diathermy on pain and function of subjects with osteoarthritis of the knee: a placebo-controlled double-blind clinical trial. *Clin Rehabil* 2005;19(3):255-263.

Law PP,Cheing GL,Tsui AY. Does Transcutaneous Electrical Nerve Stimulation Improve the Physical Performance of People With Knee Osteoarthritis?. *J Clin Rheumatol* 2004;10(6):295-299.

Law PP,Cheing GL. Optimal stimulation frequency of transcutaneous electrical nerve stimulation on people with knee osteoarthritis. *J Rehabil Med* 2004;36(5):220-225.

Le L,Pavelka K,Richarz U. Transdermal fentanyl for the treatment of pain caused by osteoarthritis of the knee or hip: an open, multicentre study. *BMC Musculoskelet Disord* 2005;6:31.

Leach RE,Baumgard S,Broom J. Obesity: its relationship to osteoarthritis of the knee. *Clin Orthop Relat Res* 1973;(93):271-273.

Leardini G,Franceschini M,Mattara L,Bruno R,Perbellini A. Intra-articular sodium hyaluronate (Hyalgan(registered trademark)) in gonarthrosis. A controlled study comparing methylprednisolone acetate. *Clin Trials J* 1987;24(4):341-350.

Leardini G,Mattara L,Franceschini M,Perbellini A. Intra-articular treatment of knee osteoarthritis. A comparative study between hyaluronic acid and 6-methyl prednisolone acetate. *Clin Exp Rheumatol* 1991;9(4):375-381.

Leblan D,Chantre P,Fournie B. Harpagophytum procumbens in the treatment of knee and hip osteoarthritis. Four-month results of a prospective, multicenter, double-blind trial versus diacerhein. *Joint Bone Spine* 2000;67(5):462-467.

Lee HJ,Park HJ,Chae Y,Kim SY,Kim SN,Kim ST,Kim JH,Yin CS,Lee H. Tai Chi Qigong for the quality of life of patients with knee osteoarthritis: a pilot, randomized, waiting list controlled trial. *Clin Rehabil* 2009;23(6):504-511.

Lee S,Park D,Chmell SJ. Viscosupplementation with hylan G-F 20 (Synvisc): pain and mobility observations from 74 consecutive patients. *J Knee Surg* 2004;17(2):73-77.

Lee SC,Jung KA,Nam CH,Jung SH,Hwang SH. The Short-term Follow-up Results of Open Wedge High Tibial Osteotomy with Using an Aescula Open Wedge Plate and an Allogenic Bone Graft: The Minimum 1-Year Follow-up Results. *Clin Orthop Surg* 2010;2(1):47-54.

Leeb BF,Bucsi L,Keszthelyi B,Báhmova J,Valesova M,Hawel R,Mayrhofer F,Singer F,Aglas F,Br÷ll H. [Treatment of osteoarthritis of the knee joint. Efficacy and tolerance to acemetacin slow release in comparison to Celecoxib]. *Der OrthopΣde* 2004;33:1032-1041.

Leffler CT,Philippi AF,Leffler SG,Mosure JC,Kim PD. Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double-blind, placebo-controlled pilot study. *Mil Med* 1999;164(2):85-91.

Lehn OF,Jensen ON,Andersen LA,Christensen KA,Solheim L,Barslev J,Mjølstad W,Wiig G,Ibøfelt HH,Kjonnixsen T,... Enteric-coated and plain Naproxen tablets in osteoarthritis; tolerability and efficacy. *Eur J Rheumatol Inflamm* 1992;12(2):31-36.

- Leigh Brown AP,Kennedy ADM,Grant AM,Campbell J,MacNicol MF,Torgerson DJ. The development and validation of the Edinburgh Knee Function Scale: A simple tool for outcome measurement in non-surgical patients. *Knee* 1999;6(2):115-123.
- Lenz D,Smid Z. Closing-Wedge Valgus High Tibial Osteotomy. *Acta Chir Orthop Traumatol Cech* 2012;79(1):59-64.
- Leopold SS,Redd BB,Warme WJ,Wehrle PA,Pettis PD,Shott S. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee. A prospective, randomized trial. *J Bone Joint Surg Am* 2003;85-A(7):1197-1203.
- Lesaffre E. Use and misuse of the p-value. *Bull NYU Hosp Jt Dis* 2008;66(2):146-149.
- Lessard LA,Scudds RA,Amendola A,Vaz MD. The efficacy of cryotherapy following arthroscopic knee surgery. *J Orthop Sports Phys Ther* 1997;26(1):14-22.
- Lester DK,Zhang K. Gait Analysis of Knee Arthritis Treated With Hyaluronic Acid. *J Arthroplasty* 2009;.
- Lester DK,Zhang K. Gait Analysis of Knee Arthritis Treated With Hyaluronic Acid. *J Arthroplasty* 2010 Dec;25(8):1290-1294.
- Leung A,Liew D,Lim J,Page C,Boukris-Sayag V,Mundae M,Wong M,Choong P,Dowsey M,Clemens L,Lim K. The effect of joint aspiration and corticosteroid injections in osteoarthritis of the knee. *Int J Rheum Dis* 2011 Oct;14(4):384-389.
- Leung AT,Malmstrom K,Gallacher AE,Sarembok B,Poor G,Beaulieu A,Castro R,Sanchez M,Detora LM,Ng J. Efficacy and tolerability profile of Etoricoxib in patients with osteoarthritis: A randomized, double-blind, placebo and active-comparator controlled 12-week efficacy trial. *Curr Med Res Opin* 2002;18(2):49-58.
- Leutloff D,Tobian F,Perka C. High tibial osteotomy for valgus and varus deformities of the knee. *Int Orthop* 2001;25(2):93-96.
- Levenstein JH. Isoxicam and indomethacin in acute osteo-arthritis. A GP multicentre double-blind comparison. *S Afr Med J* 1985;67(17):676-679.
- Levi F,Le LC,Reinberg A. Timing optimizes sustained-release indomethacin treatment of osteoarthritis. *Clin Pharmacol Ther* 1985;37(1):77-84.
- Levy M,Pauker M,Lotem M,Seelenfreund M,Fried A. High tibial osteotomy: a follow-up study and description of a modified technic. *Clin Orthop Relat Res* 1973;(93):274-277.
- Levy R,Khokhlov A,Kopenkin S,Bart B,Ermolova T,Kantemirova R,Mazurov V,Bell M,Caldron P,Pillai L,Burnett B. Efficacy and safety of flavocoxid compared with Naproxen in subjects with osteoarthritis of the knee- a subset analysis. *Adv Ther* 2010 Dec;27(12):953-962.
- Levy RM,Saikovsky R,Shmidt E,Khokhlov A,Burnett BP. Flavocoxid is as effective as Naproxen for managing the signs and symptoms of osteoarthritis of the knee in humans: a short-term randomized, double-blind pilot study. *Nutr Res* 2009;29(5):298-304.

- Lewis B, Lewis D, Cumming G. The comparative analgesic efficacy of transcutaneous electrical nerve stimulation and a non-steroidal anti-inflammatory drug for painful osteoarthritis. *Br J Rheumatol* 1994;33(5):455-460.
- Li J, Li Q, Zhong G, Li Q, Li Z, Cao C, Chen S. Technique of arthroscopic meniscus repair with autograft tendon fibers. *Techniques in Knee Surgery* 2008;7(2):89-96.
- Li RT, Lorenz S, Xu Y, Harner CD, Fu FH, Irrgang JJ. Predictors of Radiographic Knee Osteoarthritis After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2011 Oct 21;.
- Li X, Shah A, Franklin P, Merolli R, Bradley J, Busconi B. Arthroscopic debridement of the osteoarthritic knee combined with hyaluronic acid (Orthovisc(R)) treatment: A case series and review of the literature. *J Orthop Surg Res* 2008;3:43.
- li ZC. Mixture Use of Meloxicam and Sodium Hyaluronate in the Treatment of Osteoarthritis. *Current Medical Journal* 2001;7:72-73.
- Liikavainio T, Lyytinen T, Tyrvaenen E, Sipila S, Arokoski JP. Physical function and properties of quadriceps femoris muscle in men with knee osteoarthritis. *Arch Phys Med Rehabil* 2008;89(11):2185-2194.
- Likar R, Schafer M, Paulak F, Sittl R, Pipam W, Schalk H, Geissler D, Bernatzky G. Intraarticular morphine analgesia in chronic pain patients with osteoarthritis. *Anesth Analg* 1997;84(6):1313-1317.
- Lim BW, Hinman RS, Wrigley TV, Bennell KL. Varus malalignment and its association with impairments and functional limitations in medial knee osteoarthritis. *Arthritis Rheum* 2008;59(7):935-942.
- Lim BW, Hinman RS, Wrigley TV, Sharma L, Bennell KL. Does knee malalignment mediate the effects of quadriceps strengthening on knee adduction moment, pain, and function in medial knee osteoarthritis? A randomized controlled trial. *Arthritis Rheum* 2008;59(7):943-951.
- Lim BW, Kemp G, Metcalf B, Wrigley TV, Bennell KL, Crossley KM, Hinman RS. The association of quadriceps strength with the knee adduction moment in medial knee osteoarthritis. *Arthritis Rheum* 2009;61(4):451-458.
- Lim BW. A comparative study of open and closed kinetic chain exercise regimes in patients with knee osteoarthritis. *Physiotherapy Singapore* 2002;5(2):34-40.
- Lin DH, Lin YF, Chai HM, Han YC, Jan MH. Comparison of proprioceptive functions between computerized proprioception facilitation exercise and closed kinetic chain exercise in patients with knee osteoarthritis. *Clin Rheumatol* 2007;26(4):520-528.
- Lin J, Li R, Kang X, Li H. Risk factors for radiographic tibiofemoral knee osteoarthritis: the wuchuan osteoarthritis study. *Int J Rheumatol* 2010;2010:385826.
- Lin SY, Davey RC, Cochrane T. Community rehabilitation for older adults with osteoarthritis of the lower limb: a controlled clinical trial. *Clin Rehabil* 2004;18(1):92-101.
- Lindblad S, Hedfors E, Malmborg A. Rifamycin SV in local treatment of synovitis. A clinical, arthroscopic and pharmacologic evaluation. *J Rheumatol* 1985;12(5):900-903.

- Linde K, Weidenhammer W, Streng A, Hoppe A, Melchart D. Acupuncture for osteoarthritic pain: an observational study in routine care. *Rheumatology (Oxford)* 2006;45(2):222-227.
- Linde K, Witt CM, Streng A, Weidenhammer W, Wagenpfeil S, Brinkhaus B, Willich SN, Melchart D. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. *Pain* 2007;128(3):264-271.
- Linke RD, Ulmer M, Imhoff AB. [Replacement of the meniscus with a collagen implant (CMI)]. *Oper Orthop Traumatol* 2006;18(5-6):453-462.
- Linschoten NJ, Johnson CA. Arthroscopic debridement of knee joint arthritis: effect of advancing articular degeneration. *J South Orthop Assoc* 1997;6(1):25-36.
- Lisowski LA, van den Bekerom MP, Pilot P, van Dijk CN, Lisowski AE. Oxford Phase 3 unicompartmental knee arthroplasty: medium-term results of a minimally invasive surgical procedure. *Knee Surg Sports Traumatol Arthrosc* 2011 Feb;19(2):277-284.
- Lisse J, Espinoza L, Zhao SZ, Dedhiya SD, Osterhaus JT. Functional status and health-related quality of life of elderly osteoarthritic patients treated with Celecoxib. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M167-M175.
- Listrat V, Ayral X, Patarnello F, Bonvarlet JP, Simonnet J, Amor B, Dougados M. Arthroscopic evaluation of potential structure modifying activity of hyaluronan (Hyalgan) in osteoarthritis of the knee. *Osteoarthritis Cartilage* 1997;5(3):153-160.
- Liu WC, Liu Y, Zhang J. Effect of electromagnetic field on treating knee osteoarthritis. *Proceeding of Clinical Medicine* 2004;13:281-282.
- Liu Y, Guo L, Ma S. Treatment of 256 cases of osteoarthritis of knee joint with Guo Jianhua's four-step therapy. *J Tradit Chin Med* 2008;28(2):114-117.
- Lloyd ME, Hart DJ, Nandra D, McAlindon TE, Wheeler M, Doyle DV, Spector TD. Relation between insulin-like growth factor-I concentrations, osteoarthritis, bone density, and fractures in the general population: the Chingford study. *Ann Rheum Dis* 1996;55(12):870-874.
- Loew L, Brosseau L, Wells GA, Tugwell P, Kenny GP, Reid R, Maetzel A, Huijbregts M, McCullough C, De AG, Coyle D, Egan M, Dubouloz CJ, King J, Casimiro L, Brooks-Lineker S, Bell M, Finestone HM, Laferriere L, Haines-Wangda A, Russell-Doreleyers M, Welch VA, Milne S, Levesque L. Ottawa Panel Evidence-Based Clinical Practice Guidelines for Aerobic Walking Programs in the Management of Osteoarthritis. *Arch Phys Med Rehabil* 2012 Mar 12.
- Lohmander LS, Gerhardsson d, Rollof J, Nilsson PM, Engstrom G. Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass: a population-based prospective cohort study. *Ann Rheum Dis* 2009;68(4):490-496.
- Lohmander LS, Roos EM. Clinical update: treating osteoarthritis. *Lancet* 2007;370(9605):2082-2084.
- Lomen PL, Lamborn KR, Porter GH, Turner LF, Brinn EL. Treatment of osteoarthritis of the knee. A comparison of flurbiprofen and aspirin. *Am J Med* 1986;80(3A):97-102.

- Lone AR,Wafai ZA,Buth BA,Wani TA,Koul PA,Khan SH. Analgesic efficacy of transcutaneous electrical nerve stimulation compared with Diclofenac sodium in osteo-arthritis of the knee. *Physiotherapy* 2003;89(8):478-485.
- Longyhore DS,Seaton TL. Glucosamine and chondroitin effective for knee osteoarthritis. *J Fam Pract* 2003;52(12):919-920.
- Lord J. Therapeutic knee taping decreases pain from knee osteoarthritis. *J Fam Pract* 2003;52(12):920-923.
- Loyola SA,Richardson J,MacIntyre NJ. Efficacy of ultrasound therapy for the management of knee osteoarthritis: a systematic review with meta-analysis (Provisional abstract). *Osteoarthritis and Cartilage* 2010;18:1117-1126.
- Lu Y,He Z. Rehabilitative treatment for knee osteoarthritis in 28 hemiplegic patients after stroke. *Neural Regeneration Research* 2007;2(11):702-704.
- Luepongsak N,Amin S,Krebs DE,McGibbon CA,Felson D. The contribution of type of daily activity to loading across the hip and knee joints in the elderly. *Osteoarthritis Cartilage* 2002;10(5):353-359.
- Luites JW,Brinkman JM,Wymenga AB,van Heerwaarden RJ. Fixation stability of opening- versus closing-wedge high tibial osteotomy: a randomised clinical trial using radiostereometry. *J Bone Joint Surg Br* 2009;91(11):1459-1465.
- Lund B,Andersen RB,Fossgreen J,Holm P,Jensen EM,Kirchheiner B,Kryger J,Pichard J. A long-term randomised trial on tenoxicam and Piroxicam in osteoarthritis of the hip or knee: a 24-month interim report focusing on the 12-24 month interval. *Eur J Rheumatol Inflamm* 1987;9(2):58-67.
- Lund B,Distel M,Bluhmki E. A double-blind, randomized, placebo-controlled study of efficacy and tolerance of meloxicam treatment in patients with osteoarthritis of the knee. *Scand J Rheumatol* 1998;27(1):32-37.
- Lund H,Weile U,Christensen R,Rostock B,Downey A,Bartels EM,Danneskiold-Samsøe B,Bliddal H. A randomized controlled trial of aquatic and land-based exercise in patients with knee osteoarthritis. *J Rehabil Med* 2008;40(2):137-144.
- Lund OK,Menander Huber KB. Intra-articular orgotein therapy in osteoarthritis of the knee. A double-blind, placebo-controlled trial. *Arzneimittel-Forschung/Drug Research* 1983;33(8):1199-1203.
- Lund-Olesen K,Menander KB. Orgotein: a new anti-inflammatory metalloprotein drug: preliminary evaluation of clinical efficacy and safety in degenerative joint disease. *Curr Ther Res Clin Exp* 1974;16(7):706-717.
- Lund-Olesen K,Menander-Huber KB. Intra-articular orgotein therapy in osteoarthritis of the knee. A double-blind, placebo-controlled trial. *Arzneimittelforschung* 1983;33(8):1199-1203.
- Lung YB,Seong SC,Lee MC,Shin YU,Kim DH,Kim JM,Jung YK,Ahn JH,Seo JG,Park YS,Lee CS,Roh KJ,Han CK,Cho YB,Chang DY,Kwak WJ,Jung KO,Park BJ. A four-week, randomized, double-blind trial of the efficacy and safety of SKI306X: a herbal anti-arthritis agent versus Diclofenac in osteoarthritis of the knee. *Am J Chin Med* 2004;32(2):291-301.

Luo F,Xu C,Wang E. Combination of intraarticular injection of hyaluronate and pain-point injection of betamethasone for improving the pain symptom in patients with osseous gonarthritis. *Chinese Journal of Clinical Rehabilitation* 2005;9(46):184-185.

Lussier A,Bellamy N. Viscosupplementation as a treatment option in the management of osteoarthritis. *Journal of Clinical Rheumatology* 1999;5(6 SUPPL.):S1.

Lussier A,Elie R,Gareau J. A placebo-controlled trial of floctafenine (idarac) against enteric-coated acetylsalicylic acid in osteoarthritic patients. *Rheumatol Rehabil* 1980;19(1):52-59.

Müller I,Pérez M,Monfort J,Benito P,Cuevas J,Perna C,Domènech G,Herrero M,Montell E,Vergés J. Effectiveness of chondroitin sulphate in patients with concomitant knee osteoarthritis and psoriasis: a randomized, double-blind, placebo-controlled study. *Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society* 2010;18 Suppl 1:S32-S40.

Mabrey JD,McCollum DE. High tibial osteotomy: a retrospective review of 72 cases. *South Med J* 1987;80(8):975-980.

Maccagno A,Di Giorgio EE,Caston OL,Sagasta CL. Double-blind controlled clinical trial of oral S-adenosylmethionine versus Piroxicam in knee osteoarthritis. *Am J Med* 1987;83(5A):72-77.

Maccagno A,Sebastian O,Di GE. Comparative double-blind study of tiaprofenic acid versus Piroxicam in the treatment of osteoarthritis of the knee. *Drugs* 1988;35 Suppl 1:64-67.

Maciel SB,Scheinberg MA. Serum chondrex values in knee osteoarthritis (OA). The effect of arthroscopy. *Clin Rheumatol* 2000;19(1):76-77.

Madadi F,Eajazi A,Madadi F,Besheli LD,Rokni R,Abbasian MR,Bigdeli MR. Clinical results of reversed V-shaped high tibial corticotomy with minimally invasive surgery without internal fixation devices. *Orthopedics* 2010 Jun;33(6):388.

Madan S,Ranjith RK,Fiddian NJ. Intermediate follow-up of high tibial osteotomy: a comparison of two techniques. *Bull Hosp Jt Dis* 2002;61(1-2):11-16.

Madan S,Rushforth GF. Clinical effectiveness of high tibial osteotomy for osteoarthritis of the knee. *Bull Hosp Jt Dis* 2002;61(1-2):45-48.

Madenci E,-Gursoy-S. The comparison of the applying of iontophoresis and phonophoresis methods and their impact on the quality of life in patients with knee osteoarthritis. [Turkish]. *Journal* 2002;13:98-101.

Magilavy D,Polisson R,Parenti D. Re: Karlsson et al. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. *Rheumatology (Oxford)* 2003;42:1262-1263.

Magill CD. Non-surgical aid for the degenerated knee. *Rocky Mt Med J* 1968;65(11):45-48.

Magyar G,Ahl TL,Vibe P,Toksvig-Larsen S,Lindstrand A. Open-wedge osteotomy by hemicallotaxis or the closed-wedge technique for osteoarthritis of the knee. A randomised study of 50 operations. *J Bone Joint Surg Br* 1999;81(3):444-448.

Magyar G,Toksvig-Larsen S,Lindstrand A. Hemicallotasis open-wedge osteotomy for osteoarthritis of the knee. Complications in 308 operations. *J Bone Joint Surg Br* 1999;81(3):449-451.

Magyar G,Toksvig-Larsen S,Lindstrand A. Open wedge tibial osteotomy by callus distraction in gonarthrosis. Operative technique and early results in 36 patients. *Acta Orthop Scand* 1998;69(2):147-151.

Maheu E,Mazieres B,Valat JP,Loyau G,Le L,Bourgeois P,Grouin JM,Rozenberg S. Symptomatic efficacy of avocado/soybean unsaponifiables in the treatment of osteoarthritis of the knee and hip: a prospective, randomized, double-blind, placebo-controlled, multicenter clinical trial with a six-month treatment period and a two-month follow. *Arthritis Rheum* 1998;41(1):81-91.

Maheu E. Hyaluronan in knee osteoarthritis: A review of the clinical trials with Hyalgan((registered trademark)). *Eur J Rheumatol Inflamm* 1995;15(1):17-24.

Mahowald ML,Krug HE,Singh JA,Dykstra D. Intra-articular Botulinum Toxin Type A: a new approach to treat arthritis joint pain. *Toxicon* 2009;54(5):658-667.

Maiko OY. Homoeopathic therapy of gonarthrosis with Zeel T. *Biologische Medizin* 2002;31:68-74.

Maimoona A,Naeem I,Saddiqe Z,Jameel K. A review on biological, nutraceutical and clinical aspects of French maritime pine bark extract. *J Ethnopharmacol* 2011 Jan 27;133(2):261-277.

Majani G,Giardini A,Scotti A. Subjective impact of osteoarthritis flare-ups on patients' quality of life. *Health Qual Life Outcomes* 2005;3:14.

Majima T,Yasuda K,Aoki Y,Minami A. Impact of patellofemoral osteoarthritis on long-term outcome of high tibial osteotomy and effects of ventralization of tibial tubercle. *J Orthop Sci* 2008;13(3):192-197.

Majima T,Yasuda K,Katsuragi R,Kaneda K. Progression of joint arthrosis 10 to 15 years after high tibial osteotomy. *Clin Orthop Relat Res* 2000;(381):177-184.

Makarowski W,Weaver A,Rubin B,Caldwell J,McMahon FG,Noveck RJ,Lee D,Offenberg H,Sack M,Sikes D,Trapp R,Rush S,Kuss M,Ganju J,Bocanegra TS,Ratliff JM. The efficacy, tolerability, and safety of 1200mg/d of oxaprozin and 1500mg/d of nabumetone in the treatment of patients with osteoarthritis of the knee. *Clin Ther* 1996;18(1):114-124.

Maletius W,Messner K. The effect of partial meniscectomy on the long-term prognosis of knees with localized, severe chondral damage. A twelve- to fifteen-year followup. *Am J Sports Med* 1996;24(3):258-262.

Malladi AS,Gratton SB,Stone D,Scalapino KJ,Charles JF. Recurrent adverse psychiatric effects following intra-articular corticosteroid injection. *Journal of Clinical Rheumatology* 2011;17(5):284-285.

Mallen CD,Peat G,Thomas E,Lacey R,Croft P. Predicting poor functional outcome in community-dwelling older adults with knee pain: prognostic value of generic indicators. *Ann Rheum Dis* 2007;66(11):1456-1461.

Malonne H,Coffiner M,Fontaine D,Sonet B,Sereno A,Peretz A,Vanderbist F. Long-term tolerability of Tramadol LP, a new once-daily formulation, in patients with osteoarthritis or low back pain. *J Clin Pharm Ther* 2005;30(2):113-120.

- Malonne H, Coffiner M, Sonet B, Sereno A, Vanderbist F. Efficacy and tolerability of sustained-release Tramadol in the treatment of symptomatic osteoarthritis of the hip or knee: a multicenter, randomized, double-blind, placebo-controlled study. *Clin Ther* 2004;26(11):1774-1782.
- Malvankar SM, Khan WS. An overview of the different approaches used in the development of meniscal tissue engineering. *Curr Stem Cell Res Ther* 2012 Mar;7(2):157-163.
- Maly MR, Costigan PA, Olney SJ. Contribution of psychosocial and mechanical variables to physical performance measures in knee osteoarthritis. *Phys Ther* 2005;85(12):1318-1328.
- Maly MR, Costigan PA, Olney SJ. Self-efficacy mediates walking performance in older adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci* 2007;62(10):1142-1146.
- Mandal BB, Park SH, Gil ES, Kaplan DL. Multilayered silk scaffolds for meniscus tissue engineering. *Biomaterials* 2011 Jan;32(2):639-651.
- Mangione KK, McCully K, Gloviak A, Lefebvre I, Hofmann M, Craik R. The effects of high-intensity and low-intensity cycle ergometry in older adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci* 1999;54(4):M184-M190.
- Manicourt DH, Azria M, Mindeholm L, Thonar EJ, Devogelaer JP. Oral salmon calcitonin reduces Lequesne's algofunctional index scores and decreases urinary and serum levels of biomarkers of joint metabolism in knee osteoarthritis. *Arthritis Rheum* 2006;54(10):3205-3211.
- Maniscalco P. High tibial osteotomy with external fixator in the varus gonarthritic knee. *Acta Biomed* 2003;74(2):76-80.
- Manninen P, Riihimäki H, Heliovaara M, Makela P. Overweight, gender and knee osteoarthritis. *Int J Obes Relat Metab Disord* 1996;20(6):595-597.
- Manninen P, Riihimäki H, Heliovaara M, Suomalainen O. Weight changes and the risk of knee osteoarthritis requiring arthroplasty. *Ann Rheum Dis* 2004;63(11):1434-1437.
- Maquet P. Valgus osteotomy for osteoarthritis of the knee. *Clin Orthop Relat Res* 1976;(120):143-148.
- Marcu F, Lazar L, Mutiu G. The impact of balneo-physical-kinetic therapy in bearing joints osteoarthritis. *Archives of the Balkan Medical Union* 2009;44(4):315-320.
- Marengo JL, Perez M, Navarro FJ, Martinez FG, Beltran J, Salvatierra D, Alonso A, Ballarin M, Eguidazu I, Zapata A, Horas M, Torres F, Artigas R, Mauleon D. A multicentre, randomised, double-blind study to compare the efficacy and tolerability of dexKetoprofen trometamol versus Diclofenac in the symptomatic treatment of knee osteoarthritis. *Clinical Drug Investigation* 2000;19(4):247-256.
- Markou P, Chatzopoulos D. Yttrium-90 silicate radiosynovectomy treatment of painful synovitis in knee osteoarthritis. Results after 6 months. *Hellenic Journal of Nuclear Medicine* 2009;12(1):33-36.
- Markow MJ, Secor ER. Acupuncture for the pain management of osteoarthritis of the knee. *Techniques in Orthopaedics* 2003;18(1):33-36.
- Marks R, Allegrante JP. Chronic osteoarthritis and adherence to exercise: a review of the literature. *Journal of Aging and Physical Activity* 2005;13(4):434-460.

- Marks R, de Palma F. Clinical efficacy of low power laser therapy in osteoarthritis. *Physiother Res Int* 1999;4(2):141-157.
- Marks R, Ghanagaraja S, Ghassemi M. Ultrasound for osteo-arthritis of the knee: A systematic review. *Physiotherapy* 2000;86(9):452-463.
- Marks R, Ghassemi M, Duarte R, Van Nguyen JP. A review of the literature on shortwave diathermy as applied to osteo-arthritis of the knee. *Physiotherapy* 1999;85(6):304-316.
- Marks R, Ungar M, Ghasemmi M. Electrical muscle stimulation for osteoarthritis of the knee: biological basis and systematic review. *New Zealand Journal of Physiotherapy* 2000;28(3):6-20.
- Marks R, van NJ. Pulsed electromagnetic field therapy and osteoarthritis of the knee: synthesis of the literature (Structured abstract). *International Journal of Therapy and Rehabilitation* 2005;12:347-354.
- Marks R. Obesity profiles with knee osteoarthritis: correlation with pain, disability, disease progression. *Obesity (Silver Spring)* 2007;15(7):1867-1874.
- Marks R. Reliability and validity of self-paced walking time measures for knee osteoarthritis. *Arthritis Care Res* 1994;7(1):50-53.
- Marmor L. Osteoarthritis of the knee. *JAMA* 1971;218(2):213-215.
- Marshall D, Pericak D, Grootendorst P, Gooch K, Faris P, Frank C, Bellamy N, Torrance G, Feeny D. Validation of a prediction model to estimate health utilities index Mark 3 utility scores from WOMAC index scores in patients with osteoarthritis of the hip. *Value Health* 2008;11(3):470-477.
- Marshall DA, Strauss ME, Pericak D, Buitendyk M, Coddling C, Torrance GW. Economic evaluation of controlled-release oxycodone versus oxycodone-Acetaminophen for osteoarthritis pain of the hip or knee. *Am J Manag Care* 2006;12(4):205-214.
- Martel-Pelletier J, Kwan TS, Pelletier J. Effects of chondroitin sulfate in the pathophysiology of the osteoarthritic joint: a narrative review. *Osteoarthritis and Cartilage* 2010;18(SUPPL. 1):S7-S11.
- Martens M. Piroxicam treatment for postoperative pain of orthopedic surgery: A double-blind comparative study. *Curr Ther Res Clin Exp* 1991;49:750-763.
- Marti RK, Verhagen RA, Kerkhoffs GM, Moojen TM. Proximal tibial varus osteotomy. Indications, technique, and five to twenty-one-year results. *J Bone Joint Surg Am* 2001;83-A(2):164-170.
- Martin JG, Rodriguez LPR, Mora CD, Torres RR, Gomez FP, Pellico LG. Liquid nitrogen cryotherapy effect on gait and pain in subjects with osteoarthritis of the knee. *Europa Medicophysica* 1998;34(1):17-24.
- Martin K, Fontaine KR, Nicklas BJ, Dennis KE, Goldberg AP, Hochberg MC. Weight loss and exercise walking reduce pain and improve physical functioning in overweight postmenopausal women with knee osteoarthritis. *J Clin Rheumatol* 2001;7(4):219-223.
- Martinez LM. Naproxen, indomethacin, and aspirin in the treatment of osteoarthritis: A comparison using a modification of the double-blind crossover design. *Clin Ther* 1991;13:16-19.
- Mathews J, Cobb AG, Richardson S, Bentley G. Distal femoral osteotomy for lateral compartment osteoarthritis of the knee. *Orthopedics* 1998;21(4):437-440.

- Matsui N,Moriya H,Kitahara H. The use of arthroscopy for follow-up in knee joint surgery. *Orthop Clin North Am* 1979;10(3):697-708.
- Matsuno H,Nakamura H,Katayama K,Hayashi S,Kano S,Yudoh K,Kiso Y. Effects of an oral administration of glucosamine-chondroitin-quercetin glucoside on the synovial fluid properties in patients with osteoarthritis and rheumatoid arthritis. *Biosci Biotechnol Biochem* 2009;73(2):288-292.
- Matthews LS,Goldstein SA,Malvitz TA,Katz BP,Kaufer H. Proximal tibial osteotomy. Factors that influence the duration of satisfactory function. *Clin Orthop Relat Res* 1988;(229):193-200.
- Mattsson E,Weidenhielm L. Improvement after surgery in patients with osteoarthrosis of the knee. *Scand J Caring Sci* 1995;9(1):47-54.
- Maurer F,Wassmer G. High tibial osteotomy: does navigation improve results?. *Orthopedics* 2006;29(10 Suppl):S130-S132.
- Mazieres B,Bard H,Ligier M,Bru I,d'Orsay GG,Le PC. Medicoeconomic evaluation of hyaluronic acid for knee osteoarthritis in everyday practice: the MESSAGE study. *Joint Bone Spine* 2007;74(5):453-460.
- Mazieres B,Loyau G,Menkes CJ,Valat JP,Dreiser RL,Charlot J,Masounabe PA. Chondroitin sulfate for the treatment of coxarthrosis and gonarthrosis. A prospective, multicenter, placebo-controlled, double-blind trial with five months follow-up. <ORIGINAL> LE CHONDROITINE SULFATE DANS LE TRAITEMENT DE LA GONARTHROSE ET DE LA COXARTH. *REV RHUM MAL OSTEO ARTICULAIRES* 1992;59:466-472.
- Mazieres B,Masquelier AM,Capron MH. A French controlled multicenter study of intraarticular orpotein versus intraarticular corticosteroids in the treatment of knee osteoarthritis: a one-year followup. *J Rheumatol Suppl* 1991;27:134-137.
- Mazières B,Loyau G,Menkes CJ,Valat JP,Dreiser RL,Charlot J,Masounabe PA. [Chondroitin sulfate in the treatment of gonarthrosis and coxarthrosis. 5-months result of a multicenter double-blind controlled prospective study using placebo]. *Revue du rhumatisme et des maladies ostéo articulaires* 1992;59:466-472.
- Mazzuca SA,Brandt KD,Chakr R,Lane KA. Varus malalignment negates the structure-modifying benefits of doxycycline in obese women with knee osteoarthritis. *Osteoarthritis Cartilage* 2010 Aug;18(8):1008-1011.
- Mazzuca SA,Brandt KD,Katz BP,Chambers M,Byrd D,Hanna M. Effects of self-care education on the health status of inner-city patients with osteoarthritis of the knee. *Arthritis Rheum* 1997;40(8):1466-1474.
- Mazzuca SA,Brandt KD,Katz BP,Lane KA,Buckwalter KA. Comparison of quantitative and semiquantitative indicators of joint space narrowing in subjects with knee osteoarthritis. *Ann Rheum Dis* 2006;65(1):64-68.
- Mazzuca SA,Brandt KD,Katz BP,Ragozzino LR,G'sell PM. Can a Nurse-Directed Intervention Reduce the Exposure of Patients With Knee Osteoarthritis to Nonsteroidal Antiinflammatory Drugs?. *J Clin Rheumatol* 2004;10(6):315-322.

Mazzuca SA,Brandt KD,Schauwecker DS,Katz BP,Meyer JM,Lane KA,Bradley JD,Hugenberg ST,Wolfe F,Moreland LW,Heck LW,Yocum DE,Schnitzer TJ,Sharma L,Manzi S,Oddis CV. Severity of joint pain and Kellgren-Lawrence grade at baseline are better predictors of joint space narrowing than bone scintigraphy in obese women with knee osteoarthritis. *J Rheumatol* 2005;32(8):1540-1546.

Mazzuca SA,Page MC,Meldrum RD,Brandt KD,Petty-Saphon S. Pilot study of the effects of a heat-retaining knee sleeve on joint pain, stiffness, and function in patients with knee osteoarthritis. *Arthritis Rheum* 2004;51(5):716-721.

McAlindon T,Formica M,Schmid CH,Fletcher J. Changes in Barometric Pressure and Ambient Temperature Influence Osteoarthritis Pain. *Am J Med* 2007;120(5):429-434.

McAlindon TE,Felson DT,Zhang Y,Hannan MT,Aliabadi P,Weissman B,Rush D,Wilson PW,Jacques P. Relation of dietary intake and serum levels of vitamin D to progression of osteoarthritis of the knee among participants in the Framingham Study. *Ann Intern Med* 1996;125(5):353-359.

McAlindon TE,Jacques P,Zhang Y,Hannan MT,Aliabadi P,Weissman B,Rush D,Levy D,Felson DT. Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis?. *Arthritis Rheum* 1996;39(4):648-656.

McAuley Ra. Soft laser: A treatment for osteoarthritis of the knee?. *Archives Physical Medicine Rehabilitation* 1985;66:553-554.

McBride GG,Constance RM,Hofmann AA,Carson RW. Arthroscopic partial medial meniscectomy in the older patient. *J Bone Joint Surg Am* 1984;66(4):547-551.

McCarberg BH,Argoff CE. Topical Diclofenac epolamine patch 1.3% for treatment of acute pain caused by soft tissue injury. *Int J Clin Pract* 2010;64(11):1546-1553.

McCarthy CJ,Callaghan MJ,Oldham JA. The reliability of isometric strength and fatigue measures in patients with knee osteoarthritis. *Man Ther* 2008;13(2):159-164.

McCarthy CJ,Mills PM,Pullen R,Richardson G,Hawkins N,Roberts CR,Silman AJ,Oldham JA. Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis of the knees: a randomised controlled trial and health economic analysis. *Health Technol Assess* 2004;8(46):iii-61.

McCarthy CJ,Oldham JA. The effectiveness of exercise in the treatment of osteoarthritic knees: a critical review. *Physical Therapy Reviews* 1999;4(4):241-250.

McCarthy CJ,Oldham JA. The reliability, validity and responsiveness of an aggregated locomotor function (ALF) score in patients with osteoarthritis of the knee. *Rheumatology (Oxford)* 2004;43(4):514-517.

McCormack R. Prevention of disability in daily activities in older persons with knee osteoarthritis. *Clin J Sport Med* 2002;12(6):405.

McDonald C,Hantel S,Strohmeier M. A randomised, controlled study to compare the performance and safety of two sources of sodium hyaluronate given as a viscosupplement by intra-articular injection to patients with osteoarthritis of the knee. *Journal of Clinical Research* 2000;3(41-50):41-50.

McGinley BJ,Cushner FD,Scott WN. Debridement arthroscopy. 10-year followup. *Clin Orthop Relat Res* 1999;(367):190-194.

McGinty JB. Arthroscopic removal of loose bodies. *Orthop Clin North Am* 1982;13(2):313-328.

McKnight PE,Kasle S,Going S,Villanueva I,Cornett M,Farr J,Wright J,Streeter C,Zautra A. A comparison of strength training, self-management, and the combination for early osteoarthritis of the knee. *Arthritis Care Res (Hoboken)* 2010;62(1):45-53.

McLeod MM,Gribble P,Pfister KR,Pietrosimone BG. Effects of Arthroscopic Partial Meniscectomy on Quadriceps Strength: A Systematic Review. *J Sport Rehabil* 2011 Dec 30.

McNicholas MJ,Rowley DI,McGurty D,Adalberth T,Abdon P,Lindstrand A,Lohmander LS. Total meniscectomy in adolescence. A thirty-year follow-up. *J Bone Joint Surg Br* 2000;82(2):217-221.

Medhi B,Kishore K,Singh U,Seth SD. Comparative clinical trial of castor oil and Diclofenac sodium in patients with osteoarthritis. *Phytother Res* 2009;23(10):1469-1473.

Meenagh G,Filippucci E,Delle SA,Iagnocco A,Scire CA,Riente L,Montecucco C,Valesini G,Bombardieri S,Grassi W. Ultrasound imaging for the rheumatologist XXX. Sonographic assessment of the painful knee. *Clin Exp Rheumatol* 2010 Nov;28(6):803-805.

Megied WSA,Mahran MA,Thakeb MF,Abouelela AAKH,Elbatrawy Y. The new 'dual osteotomy': Combined open wedge and tibial tuberosity anteriorisation osteotomies. *Int Orthop* 2010;34(2 SPECIAL ISSUE):231-237.

Melo Gomes JA,Roth SH,Zeeh J,Bruyn GA,Woods EM,Geis GS. Double-blind comparison of efficacy and gastroduodenal safety of Diclofenac/misoprostol, Piroxicam, and Naproxen in the treatment of osteoarthritis. *Ann Rheum Dis* 1993;52(12):881-885.

Melton JW,Lussier A,Ward JR,Neustadt D,Multz C. Naproxen versus aspirin in osteoarthritis of the hip and knee. *J Rheumatol* 1978;5(3):338-346.

Menkes CJ. Intraarticular treatment of osteoarthritis and guidelines to its assessment. *J Rheumatol Suppl* 1994;41:74-76.

Mensitieri M,Ambrosio L,Iannace S,Nicolais L,Perbellini A. Viscoelastic evaluation of different knee osteoarthritis therapies. *Journal of Materials Science* 1995;6(3):130-137.

Merchan EC,Galindo E. Arthroscope-guided surgery versus nonoperative treatment for limited degenerative osteoarthritis of the femorotibial joint in patients over 50 years of age: a prospective comparative study. *Arthroscopy* 1993;9(6):663-667.

Merchan ECR,De la Corte H. The role of rehabilitation after high tibial osteotomy in patients with medial gonarthrosis. *Journal of Orthopaedic Rheumatology* 1993;6(4):151-153.

Meredith DS,Losina E,Mahomed NN,Wright J,Katz JN. Factors predicting functional and radiographic outcomes after arthroscopic partial meniscectomy: a review of the literature. *Arthroscopy* 2005;21(2):211-223.

Merle-Vincent F, Couris CM, Schott AM, Conrozier T, Piperno M, Mathieu P, Vignon E. Factors predicting patient satisfaction 2 years after total knee arthroplasty for osteoarthritis. *Joint Bone Spine* 2010 Dec 31;.

Messier SP, Glasser JL, Ettinger WH, Craven TE, Miller ME. Declines in strength and balance in older adults with chronic knee pain: a 30-month longitudinal, observational study. *Arthritis Rheum* 2002;47(2):141-148.

Messier SP, Gutekunst DJ, Davis C, DeVita P. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum* 2005;52(7):2026-2032.

Messier SP, Legault C, Loeser RF, Van Arsdale SJ, Davis C, Ettinger WH, DeVita P. Does high weight loss in older adults with knee osteoarthritis affect bone-on-bone joint loads and muscle forces during walking?. *Osteoarthritis Cartilage* 2011 Mar;19(3):272-280.

Messier SP, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, Ettinger WH, Pahor M, Williamson JD. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum* 2004;50(5):1501-1510.

Messier SP, Loeser RF, Mitchell MN, Valle G, Morgan TP, Rejeski WJ, Ettinger WH. Exercise and weight loss in obese older adults with knee osteoarthritis: a preliminary study. *J Am Geriatr Soc* 2000;48(9):1062-1072.

Messier SP, Mihalko S, Loeser RF, Legault C, Jolla J, Pfruender J, Prosser B, Adrian A, Williamson JD. Glucosamine/chondroitin combined with exercise for the treatment of knee osteoarthritis: a preliminary study. *Osteoarthritis Cartilage* 2007;15(11):1256-1266.

Messier SP, Thompson CD, Ettinger J. Effects of long-term aerobic or weight training regimens on gait in an older, osteoarthritic population. *Journal of Applied Biomechanics* 1997;13(2):205-225.

Messier SP. Diet and exercise for obese adults with knee osteoarthritis. *Clin Geriatr Med* 2010 Aug;26(3):461-477.

Messier SP. Physical activity and weight loss interventions in older adults with knee osteoarthritis. *N C Med J* 2007;68(6):436-438.

Meurice J. Treatment of osteoarthritis: a 3-month comparison between tiaprofenic acid and indomethacin. *Curr Med Res Opin* 1983;8(5):295-301.

Meyerhoff J. Rofecoxib , 25mg/d, was more effective than Rofecoxib , 12.5mg/d, Celecoxib , or Acetaminophen in osteoarthritis of the knee. *ACP J Club* 2002;137(1):26.

Michaela G, Florian P, Michael L, Christian B. Long-term outcome after high tibial osteotomy. *Archives of Orthopaedic and Trauma Surgery* 2008;128(1):111-115.

Michalsen A, Klotz S, Ludtke R, Moebus S, Spahn G, Dobos GJ. Effectiveness of leech therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 2003;139(9):724-730.

Michel BA, Stucki G, Frey D, De VF, Vignon E, Bruehlmann P, Uebelhart D. Chondroitins 4 and 6 sulfate in osteoarthritis of the knee: a randomized, controlled trial. *Arthritis Rheum* 2005;52(3):779-786.

Migliore A, Giovannangeli F, Granata M, Lagana B. Hylan g-f 20: review of its safety and efficacy in the management of joint pain in osteoarthritis. *Clin Med Insights Arthritis Musculoskelet Disord* 2010;3:55-68.

Mihalko WM, Krackow KA. Preoperative planning for lower extremity osteotomies: an analysis using 4 different methods and 3 different osteotomy techniques. *J Arthroplasty* 2001;16(3):322-329.

Mikesky AE, Mazzuca SA, Brandt KD, Perkins SM, Damush T, Lane KA. Effects of strength training on the incidence and progression of knee osteoarthritis. *Arthritis Rheum* 2006;55(5):690-699.

Miller BS, Downie B, McDonough EB, Wojtys EM. Complications after medial opening wedge high tibial osteotomy. *Arthroscopy* 2009;25(6):639-646.

Miller BS, Joseph TA, Barry EM, Rich VJ, Sterett WI. Patient satisfaction after medial opening high tibial osteotomy and microfracture. *J Knee Surg* 2007;20(2):129-133.

Miller GD, Nicklas BJ, Davis CC, Ambrosius WT, Loeser RF, Messier SP. Is serum leptin related to physical function and is it modifiable through weight loss and exercise in older adults with knee osteoarthritis?. *Int J Obes Relat Metab Disord* 2004;28(11):1383-1390.

Miller GD, Nicklas BJ, Loeser RF. Inflammatory biomarkers and physical function in older, obese adults with knee pain and self-reported osteoarthritis after intensive weight-loss therapy. *J Am Geriatr Soc* 2008;56(4):644-651.

Miller KL, Clegg DO. Glucosamine and Chondroitin Sulfate. *Rheumatic Disease Clinics of North America* 2011;37(1):103-118.

Miller MJS, Mehta K, Kunte S, Raut V, Gala J, Dhumale R, Shukla A, Tupalli H, Parikh H, Bobrowski P, Chaudhary J. Early relief of osteoarthritis symptoms with a natural mineral supplement and a herbomineral combination: a randomized controlled trial [ISRCTN38432711]. *J Inflamm* 2005;2:11.

Miltner O, Schneider U, Siebert CH, Niedhart C, Niethard FU. Efficacy of intraarticular hyaluronic acid in patients with osteoarthritis—a prospective clinical trial. *Osteoarthritis Cartilage* 2002;10(9):680-686.

Miniaci A, Ballmer FT, Ballmer PM, Jakob RP. Proximal tibial osteotomy. A new fixation device. *Clin Orthop Relat Res* 1989;(246):250-259.

Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum* 1989;32(11):1396-1405.

Minor MA. Impact of Exercise on Osteoarthritis Outcomes. *J Rheumatol* 2004;31(SUPPL. 70):81-86.

Misra NP. A comparative study of flurbiprofen and Piroxicam in osteoarthritis. *J Postgrad Med* 1992;38(4):164-166.

Miura H, Takasugi S, Kawano T, Manabe T, Iwamoto Y. Varus-valgus laxity correlates with pain in osteoarthritis of the knee. *Knee* 2009;16(1):30-32.

Mody S, Jolly M, Kwasny MJ, Block JA. Patient reported outcomes and analgesia use in osteoarthritis of the knee. *Osteoarthritis Cartilage* 2008;16(11):1294-1299.

- Mohomed NN. Manual physical therapy and exercise improved function in osteoarthritis of the knee. *J Bone Joint Surg Am* 2000;82(9):1324.
- Moisio K, Chang A, Eckstein F, Chmiel JS, Wirth W, Almagor O, Prasad P, Cahue S, Kothari A, Sharma L. Varus-valgus alignment reduced risk of subsequent cartilage loss in the less loaded compartment. *Arthritis and Rheumatism* 2011 Apr;63(4):1002-1009.
- Monfort J, Benito P, Sierpowska J, Blanco L, Contreras O, Lopez M, Pujol J. Objective assesment of the effects of chondroitin sulfate in knee osteoarthritis pain by functional MRI: A randomized, double-blind, placebo controlled clinical trial. *Basic and Clinical Pharmacology and Toxicology* 2011 Oct;109 SUPPL. 3:49-50.
- Moreland LW. New therapeutic options for treating knee osteoarthritis. *P and T* 1999;24(5):238-245.
- Moretti B, Vitale E, Esposito A, Colella A, Cassano M, Notarnicola A. Comparison of pain perception between open and minimally invasive surgery in total knee arthroplasty. *Int J Gen Med* 2010;3:297-304.
- Moretti M. Effectiveness of treatment with oxygen-ozone and hyaluronic acid in osteoarthritis of the knee. *International Journal of Ozone Therapy* 2010;9(1):25-29.
- Morgan SL, Baggott JE, Moreland L, Desmond R, Kendrach AC. The safety of flavocoxid, a medical food, in the dietary management of knee osteoarthritis. *J Med Food* 2009;12(5):1143-1148.
- Moriya H, Sasho T, Sano S, Wada Y. Arthroscopic posteromedial release for osteoarthritic knees with flexion contracture. *Arthroscopy* 2004;20(10):1030-1039.
- Morreale P, Manopulo R, Galati M, Boccanera L, Saponati G, Bocchi L. Comparison of the antiinflammatory efficacy of chondroitin sulfate and Diclofenac sodium in patients with knee osteoarthritis. *J Rheumatol* 1996;23(8):1385-1391.
- Morrey BF. Upper tibial osteotomy for secondary osteoarthritis of the knee. *J Bone Joint Surg Br* 1989;71(4):554-559.
- Moseley JB, O'Malley K, Petersen NJ, Wray NP, Gillespie WJ. Arthroscopic surgery was not effective for relieving pain or improving function in osteoarthritis of the knee: Commentary. *Evidence-Based Medicine* 2003;8(2):56.
- Moseley JB, Wray NP, Kuykendall D, Willis K, Landon G. Arthroscopic treatment of osteoarthritis of the knee: a prospective, randomized, placebo-controlled trial. Results of a pilot study. *Am J Sports Med* 1996;24(1):28-34.
- Moser C, Baltzer AW. Treatment of knee osteoarthritis with autologous conditioned serum (ACS): a prospective, randomized, placebo-controlled, patient- and observer-blind, parallel-design trial. Therapeutic study, level I (randomized controlled trial- RCT, ISRCTN: 71311752). *The Journal of Bone and Joint Surgery* 2009;91-B:157-15a.
- Moskowitz RW, Sunshine A, Brugger A, Lefkowitz JB, Zhao WW, Geis GS. American pain society pain questionnaire and other pain measures in the assessment of osteoarthritis pain: a pooled analysis of three Celecoxib pivotal studies. *Am J Ther* 2003;10(1):12-20.

- Moskowitz RW, Sunshine A, Hooper M, Olson NZ, Cawtkwell GD. An analgesic model for assessment of acute pain response in osteoarthritis of the knee. *Osteoarthritis Cartilage* 2006;14(11):1111-1118.
- Moss P, Sluka K, Wright A. The initial effects of knee joint mobilization on osteoarthritic hyperalgesia. *Man Ther* 2007;12(2):109-118.
- Motycka T, Eggerth G, Landsiedl F. The incidence of thrombosis in high tibial osteotomies with and without the use of a tourniquet. *Arch Orthop Trauma Surg* 2000;120(3-4):157-159.
- Mounach A, Nouijai A, Ghazlani I, Ghazi M, Achemlal L, Bezza A, El MA. Risk factors for knee osteoarthritis in Morocco. A case control study. *Clin Rheumatol* 2008;27(3):323-326.
- Moyer RF, Birmingham TB, Chesworth BM, Kean CO, Giffin JR. Alignment, body mass and their interaction on dynamic knee joint load in patients with knee osteoarthritis. *Osteoarthritis and Cartilage* 2010 Jul;18(7):888-893.
- Muller FO, Gosling JA, Erdmann GH. A comparison of tolmetin with aspirin in the treatment of osteoarthritis of the knee. *S Afr Med J* 1977;51(22):794-796.
- Muller M, Strecker W. Arthroscopy prior to osteotomy around the knee?. *Arch Orthop Trauma Surg* 2008;128(11):1217-1221.
- Muller-Fassbender H, Bach GL, Haase W, Rovati LC, Setnikar I. Glucosamine sulfate compared to ibuprofen in osteoarthritis of the knee. *Osteoarthritis Cartilage* 1994;2(1):61-69.
- Muncie HL. Medical aspects of the multidisciplinary assessment and management of osteoarthritis. *Clin Ther* 1986;9 Suppl B:4-13.
- Mundermann A, Dyrby CO, Hurwitz DE, Sharma L, Andriacchi TP. Potential strategies to reduce medial compartment loading in patients with knee osteoarthritis of varying severity: reduced walking speed. *Arthritis Rheum* 2004;50(4):1172-1178.
- Munera C, Drehobl M, Sessler NE, Landau C. A randomized, placebo-controlled, double-blinded, parallel-group, 5-week study of buprenorphine transdermal system in adults with osteoarthritis. *J Opioid Manag* 2010 May;6(3):193-202.
- Muraki S, Dennison E, Jameson K, Boucher BJ, Akune T, Yoshimura N, Judge A, Arden NK, Javaid K, Cooper C. Association of vitamin D status with knee pain and radiographic knee osteoarthritis. *Osteoarthritis Cartilage* 2011 Nov;19(11):1301-1306.
- Murphy SL, Strasburg DM, Lyden AK, Smith DM, Koliba JF, Dadabhoy DP, Wallis SM. Effects of activity strategy training on pain and physical activity in older adults with knee or hip osteoarthritis: a pilot study. *Arthritis Rheum* 2008;59(10):1480-1487.
- Myllykangas LR, Lu HS, Chen SL, Choon D, Amante C, Chow CT, Pasero G, Genti G, Sarembok B, Zerbini CA, Vrijens F, Moan A, Rodgers DB, De TL, Laurenzi M, -OF-study-group-. Comparison of low-dose Rofecoxib versus 1000 mg Naproxen in patients with osteoarthritis. Results of two randomized treatment trials of six weeks duration. *Scand J Rheumatol* 2002;31:337-344.

Myllykangas-Luosujarvi R, Lu HS, Chen SL, Choon D, Amante C, Chow CT, Pasero G, Genti G, Sarembok B, Zerbini CA, Vrijens F, Moan A, Rodgers DB, De TL, Laurenzi M. Comparison of low-dose Rofecoxib versus 1000 mg Naproxen in patients with osteoarthritis. Results of two randomized treatment trials of six weeks duration. *Scand J Rheumatol* 2002;31(6):337-344.

Myrer JW, Feland JB, Fellingham GW. The effects of a topical analgesic and placebo in treatment of chronic knee pain. *J Aging Phys Act* 2004;12(2):199-213.

Myrner R. Clinical results with the SAAB jig in high tibial osteotomy for medial gonarthrosis. *Acta Orthop Scand* 1980;51(3):565-567.

Myrner R. High tibial osteotomy with overcorrection of varus malalignment in medial gonarthrosis. *Acta Orthop Scand* 1980;51(3):557-560.

Nadaud MC, Komistek RD, Mahfouz MR, Dennis DA, Anderle MR. In vivo three-dimensional determination of the effectiveness of the osteoarthritic knee brace: a multiple brace analysis. *J Bone Joint Surg Am* 2005;87 Suppl 2:114-119.

Nagashima H, Suzuki M, Araki S, Yamabe T, Muto C. Preliminary assessment of the safety and efficacy of tanezumab in Japanese patients with moderate to severe osteoarthritis of the knee: a randomized, double-blind, dose-escalation, placebo-controlled study. *Osteoarthritis Cartilage* 2011 Oct 5;.

Nahabedian MY, Orlando JC, Delanois RE, Mont MA, Hungerford DS. Salvage procedures for complex soft tissue defects of the knee. *Clin Orthop Relat Res* 1998;(356):119-124.

Nahlaer G, Metelmann H, Sperber H. Treating osteoarthritis of the knee with a homeopathic preparation: results of a randomized, controlled, clinical trial in comparison th hyaluronic acid. *Biomed Ther* 1998;16:186-191.

Najm WI, Reinsch S, Hoehler F, Tobis JS, Harvey PW. S-adenosyl methionine (SAME) versus Celecoxib for the treatment of osteoarthritis symptoms: a double-blind cross-over trial. [ISRCTN36233495]. *BMC Musculoskelet Disord* 2004;5:6.

Nakamura E, Mizuta H, Kudo S, Takagi K, Sakamoto K. Open-wedge osteotomy of the proximal tibia hemicallotasis. *J Bone Joint Surg Br* 2001;83(8):1111-1115.

Namiki O, Toyoshima H, Morisaki N. Therapeutic effect of intra-articular injection of high molecular weight hyaluronic acid on osteoarthritis of the knee. *Int J Clin Pharmacol Ther Toxicol* 1982;20(11):501-507.

Naudie D, Bourne RB, Rorabeck CH, Bourne TJ. The Install Award. Survivorship of the high tibial valgus osteotomy. A 10- to -22-year followup study. *Clin Orthop Relat Res* 1999;(367):18-27.

Navarro SF, Coronel P, Collantes E, Navarro FJ, de la Serna AR, Naranjo A, Gimeno M, Herrero BG, -AMELIA-study-group. A 40-month multicentre, randomised placebo-controlled study to assess the efficacy and carry-over effect of repeated intra-articular injections of hyaluronic acid in knee osteoarthritis: the AMELIA project. *Annals of the Rheumatic Diseases* 2011;70:1957-1962.

Nejrup K, Olivarius NF, Jacobsen JL, Siersma V. Randomised controlled trial of extraarticular gold bead implantation for treatment of knee osteoarthritis: a pilot study. *Clin Rheumatol* 2008;27(11):1363-1369.

Nelissen EM, van Langelaan EJ, Nelissen RGHH. Stability of medial opening wedge high tibial osteotomy: A failure analysis. *Int Orthop* 2010;34(2 SPECIAL ISSUE):217-223.

Nelson AE, Golightly YM, Kraus VB, Stabler T, Renner JB, Helmick CG, Jordan JM. Serum transforming growth factor-beta 1 is not a robust biomarker of incident and progressive radiographic osteoarthritis at the hip and knee: the Johnston County Osteoarthritis Project. *Osteoarthritis Cartilage* 2010;18(6):825-829.

Neogi T, Nevitt MC, Yang M, Curtis JR, Torner J, Felson DT. Consistency of knee pain: correlates and association with function. *Osteoarthritis Cartilage* 2010 Oct;18(10):1250-1255.

Nestorova R, Rashkov R, Reshkova V, Kapandjieva N. Efficiency of collagen injections nullGuna MDsnull in patients with gonarthrosis, assessed clinically and by ultrasound. *Osteoporos Int* 2012 Mar;23 SUPPL. 2:S143.

Neustadt D, Caldwell J, Bell M, Wade J, Gimbel J. Clinical effects of intraarticular injection of high molecular weight hyaluronan (Orthovisc) in osteoarthritis of the knee: a randomized, controlled, multicenter trial. *J Rheumatol* 2005;32(10):1928-1936.

Neustadt DH. Intra-articular injections for osteoarthritis of the knee. *Cleve Clin J Med* 2006;73(10):897-4, 906.

Neustadt DH. Long-term efficacy and safety of intra-articular sodium hyaluronate (Hyalgan) in patients with osteoarthritis of the knee. *Clin Exp Rheumatol* 2003;21(3):307-311.

Nevitt MC, Zhang Y, Javaid MK, Neogi T, Curtis JR, Niu J, McCulloch CE, Segal NA, Felson DT. High systemic bone mineral density increases the risk of incident knee OA and joint space narrowing, but not radiographic progression of existing knee OA: the MOST study. *Ann Rheum Dis* 2010;69(1):163-168.

Ng NT, Heesch KC, Brown WJ. Efficacy of a progressive walking program and glucosamine sulphate supplementation on osteoarthritic symptoms of the hip and knee: a feasibility trial. *Arthritis Res Ther* 2010;12(1):R25.

Nguyen C, Rudan J, Simurda MA, Cooke TD. High tibial osteotomy compared with high tibial and Maquet procedures in medial and patellofemoral compartment osteoarthritis. *Clin Orthop Relat Res* 1989;(245):179-187.

Nguyen M, Revel M, Dougados M. Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized controlled trial. *Br J Rheumatol* 1997;36(1):77-81.

Nicholls AS, Kiran A, Javaid MK, Hart DJ, Spector TD, Carr AJ, Arden NK. Change in body mass index during middle age affects risk of total knee arthroplasty due to osteoarthritis: A 19-year prospective study of 1003 women. *Knee* 2011 Jul 20;.

Nicklas BJ, Ambrosius W, Messier SP, Miller GD, Penninx BW, Loeser RF, Palla S, Bleecker E, Pahor M. Diet-induced weight loss, exercise, and chronic inflammation in older, obese adults: a randomized controlled clinical trial. *Am J Clin Nutr* 2004;79(4):544-551.

Nicklas BJ, Mychaleckyj J, Kritchevsky S, Palla S, Lange LA, Lange EM, Messier SP, Bowden D, Pahor M. Physical function and its response to exercise: associations with cytokine gene variation in older adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci* 2005;60(10):1292-1298.

Nicol WJ, Sarkin TL. Indications for intra-articular steroid in osteo-arthritis of the knee. *S Afr Med J* 1972;46(13):379.

Nicolakis P, Kollmitzer J, Crevenna R, Bittner C, Erdogmus CB, Nicolakis J. Pulsed magnetic field therapy for osteoarthritis of the knee--a double-blind sham-controlled trial. *Wien Klin Wochenschr* 2002;114(15-16):678-684.

Niemeyer P, Koestler W, Kaehny C, Kreuz PC, Brooks CJ, Strohm PC, Helwig P, Suedkamp NP. Two-year results of open-wedge high tibial osteotomy with fixation by medial plate fixator for medial compartment arthritis with varus malalignment of the knee. *Arthroscopy* 2008;24(7):796-804.

Niethard FU, Gold MS, Solomon GS, Liu JM, Unkauf M, Albrecht HH, Elkik F. Efficacy of topical Diclofenac diethylamine gel in osteoarthritis of the knee. *J Rheumatol* 2005;32(12):2384-2392.

Niethard FU. Hyaluronic acid in the therapy of osteoarthritis: A comparison of different experiences. 1990;42(SPEC. ISS. 1):182-183.

Nishimura A, Hasegawa M, Kato K, Yamada T, Uchida A, Sudo A. Risk factors for the incidence and progression of radiographic osteoarthritis of the knee among Japanese. *Int Orthop* 2010 Jun 18;.

Nishimura A, Hasegawa M, Kato K, Yamada T, Uchida A, Sudo A. Risk factors for the incidence and progression of radiographic osteoarthritis of the knee among Japanese. *Int Orthop* 2011 Jun;35(6):839-843.

Niu J, Zhang YQ, Torner J, Nevitt M, Lewis CE, Aliabadi P, Sack B, Clancy M, Sharma L, Felson DT. Is obesity a risk factor for progressive radiographic knee osteoarthritis?. *Arthritis Rheum* 2009;61(3):329-335.

N^{es}esch E, Rutjes-Anne WS, Trelle S, Reichenbach S, Jⁿi P. Doxycycline for osteoarthritis of the knee or hip. N^{es}esch Eveline , Rutjes Anne WS, Trelle Sven , Reichenbach Stephan , Jⁿi Peter Doxycycline for osteoarthritis of the knee or hip *Cochrane Database of Systematic Reviews: Reviews 2009 Issue 4 John Wiley & Sons , Ltd Chichester, UK DOI : 10 1002 /1465185* 2009;.

Nobi G, Azad AK, Ahmed B, Rashid I, Islam T, Shakoob M. Effects of activities of daily living (ADL) instructions on patient with osteoarthritis of the knee. *J Med* 2012;13(1):27-31.

Norimatsu T, Osaki M, Tomita M, Ye Z, Abe Y, Honda S, Kanagae M, Mizukami S, Takamura N, Kusano Y, Shindo H, Aoyagi K. Factors predicting health-related quality of life in knee osteoarthritis among community-dwelling women in Japan: The Hizen-Oshima Study. *Orthopedics* 2011 Sep;34(9):e535-e540.

Northmore-Ball MD, Dandy DJ, Jackson RW. Arthroscopic, open partial, and total meniscectomy. A comparative study. *J Bone Joint Surg Br* 1983;65(4):400-404.

Northmore-Ball MD, Dandy DJ. Long-term results of arthroscopic partial meniscectomy. *Clin Orthop Relat Res* 1982;(167):34-42.

- Notarnicola A, Tafuri S, Fusaro L, Moretti L, Pesce V, Moretti B. The 'MESACA' study: Methylsulfonylmethane and boswellic acids in the treatment of gonarthrosis. *Adv Ther* 2011 Oct;28(10):894-906.
- Notarnicola A, Tafuri S, Fusaro L, Moretti L, Pesce V, Moretti B. The 'MESACA' study: Methylsulfonylmethane and boswellic acids in the treatment of gonarthrosis. *Adv Ther* 2011;;1-13.
- Nourbakhsh M, Motifard M, Shemshaki H, Etemadifar M, Zarezade A, Farajzadegan Z, Mazoochian F. Efficacy of tibial proximal osteotomy in correction of lower limb alignment indexes in patients with osteoarthritis in medial compartment of knee. *Med Arh* 2012;66(1):58-60.
- Noyes FR, Barber SD, Simon R. High tibial osteotomy and ligament reconstruction in varus angulated, anterior cruciate ligament-deficient knees. A two- to seven-year follow-up study. *Am J Sports Med* 1993;21(1):2-12.
- Nuesch E, Rutjes AWS, Husni E, Welch V, Juni P. Oral or transdermal opioids for osteoarthritis of the knee or hip. *Cochrane Database of Systematic Reviews* 2008;3 Article Number.
- Nunes CP, De Oliveira PC, De Oliveira JM, Mibielli MA, Cohen JC, Nunes FP, Ribeiro mg, Geller M. A double-blind, comparative, placebo-controlled study in two arms of the safety and efficacy of the anti-inflammatory and analgesic action of the association of cyanocobalamin, pyridoxine chlorhydrate, thiamine mononitrate and Diclofenac sodium in tablet. *Rev Bras Med* 2005;62(11):486-491.
- Nunez M, Lozano L, Nunez E, Sastre S, Luis d, Suso S. Good Quality of Life in Severely Obese Total Knee Replacement Patients: A Case-Control Study. *Obes Surg* 2010 Jun 6;.
- Nunez M, Lozano L, Nunez E, Segur JM, Sastre S. Factors influencing health-related quality of life after TKA in patients who are obese. *Clin Orthop Relat Res* 2011 Apr;469(4):1148-1153.
- Oben J, Enonchong E, Kothari S, Chambliss W, Garrison R, Dolnick D. Phellodendron and Citrus extracts benefit joint health in osteoarthritis patients: a pilot, double-blind, placebo-controlled study. *Nutr J* 2009;8:38.
- Oberg U, Oberg T. Functional outcome after high tibial osteotomy: a study using individual goal achievement as the primary outcome variable. *J Rehabil Res Dev* 2000;37(5):501-510.
- O'Connor MI. Osteoarthritis of the Hip and Knee: Sex and Gender Differences. *Orthopedic Clinics of North America* 2006;37(4):559-568.
- Odabasi E, Turan M, Erdem H, Pay S, Gulec M, Karagulle MZ. The effect of mud pack treatment in knee osteoarthritis. *Turkish Journal of Rheumatology* 2009;24(2):72-76.
- Odabasi E, Turan M, Erdem H, Tekbas F. Does mud pack treatment have any chemical effect? A randomized controlled clinical study. *J Altern Complement Med* 2008;14(5):559-565.
- Odenbring S, Egund N, Hagstedt B, Larsson J, Lindstrand A, Toksvig-Larsen S. Ten-year results of tibial osteotomy for medial gonarthrosis. The influence of overcorrection. *Arch Orthop Trauma Surg* 1991;110(2):103-108.
- Odenbring S, Egund N, Knutson K, Lindstrand A, Larsen ST. Revision after osteotomy for gonarthrosis. A 10-19-year follow-up of 314 cases. *Acta Orthop Scand* 1990;61(2):128-130.

- Odole AC,Akinpelu AO,Bamgboye EA. Validity and internal consistency of a Yoruba version of the Ibadan knee/hip osteoarthritis outcome measure (Yoruba IKHOAM). *Afr J Med Med Sci* 2006;35(3):349-357.
- Odole AC,Akinpelu AO. Validity and internal consistency of a Hausa version of the Ibadan Knee/Hip Osteoarthritis Outcome Measure. *Health and Quality of Life Outcomes* 2008;6:86.
- Ogata K,Yasunaga M,Nomiyama H. The effect of wedged insoles on the thrust of osteoarthritic knees. *Int Orthop* 1997;21(5):308-312.
- Ogilvie-Harris DJ,Fitsialos DP. Arthroscopic management of the degenerative knee. *Arthroscopy* 1991;7(2):151-157.
- Ohno K,Oguma T,Matsuno S. High tibial osteotomy by hemicallotasis in medial osteoarthritic knees. *Hokkaido Journal of Orthopedic and Traumatic Surgery* 1993;37(1):1-7.
- Ohsawa S,Hukuda K,Inamori Y,Yasui N. High tibial osteotomy for osteoarthritis of the knee with varus deformity utilizing the hemicallotasis method. *Arch Orthop Trauma Surg* 2006;126(9):588-593.
- Oida Y,Morozumi K,Nakamura N,Kitabatake Y,Shiozawa S,Sato S,Miura K,Nishi A,Itakura M. [Effectiveness of a community health service program using exercise intervention for elderly people with osteoarthritis of the knees: a randomized controlled trial]. [*Nihon k &#333 ;sh&#363 ; eisei zasshi*] *Japanese journal of public health* 2008;55:228-237.
- Okahashi K,Fujisawa Y,Sugimoto K,Tanaka Y. Cartilage regeneration of knee OA after high tibial osteotomy. *Techniques in Knee Surgery* 2010 Jun;9(2):95-100.
- O'Keeffe M,Moran CJ,Cawley D,Shannon FJ. An evaluation of the use of opening-wedge osteotomy about the knee. *Ir J Med Sci* 2011;180 SUPPL. 8:S261.
- Oldham JA,Howe TE,Patterson T,Smith GP,Tallis RC. Electrotherapeutic rehabilitation of the quadriceps in elderly osteoarthritic patients: A double blind assessment of patterned neuromuscular stimulation. *Clin Rehabil* 1995;9(1):10-20.
- Olejarova M,Svobodova R,Jarsova H,Votavova M,Istvankova E,Losterova M,Pavelka K. [Efficacy evaluation of nonpharmacological treatment (regular exercise), pharmacotherapy (glucosamine sulphate, GS Condro Forte) and the combination of both methods in symptomatic osteoarthritis of the knee. Results of open, randomized, controlled study]. *Ceska Revmatologie* 2008;16:153-160.
- Oliveria SA,Felson DT,Cirillo PA,Reed JI,Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology* 1999;10(2):161-166.
- Omololu B,Alonge TO,Ogunlade SO,Aduroja OO. Double blind clinical trial comparing the safety and efficacy of nimesulide 100mg and Diclofenac in osteoarthrosis of the hip and knee joints. *West Afr J Med* 2005;24(2):128-133.
- Omori G,Koga Y,Miyao M,Takemae T,Sato T,Yamagiwa H. High tibial osteotomy using two threaded pins and figure-of-eight wiring fixation for medial knee osteoarthritis: 14 to 24 years follow-up results. *J Orthop Sci* 2008;13(1):39-45.

- Onel E,Kolsun K,Kauffman JI. Post-Hoc analysis of a head-to-head hyaluronic acid comparison in knee osteoarthritis using the 2004 OMERACT-OARSI responder criteria. *Clin Drug Investig* 2008;28(1):37-45.
- Ones K,Tetik S,Tetik C,Ones N. The effects of heat on osteoarthritis of the knee. *Pain Clinic* 2006;18(1):67-75.
- O'Reilly S. The treatment of osteoarthritis. *CPD Rheumatology* 2001;2(1):14-16.
- O'Reilly SC,Jones A,Muir KR,Doherty M. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. *Ann Rheum Dis* 1998;57(10):588-594.
- Ormrod D,Wellington K,Wagstaff AJ. Valdecocixib. *Drugs* 2002;62(14):2059-2071.
- Ornetti P,Perruccio AV,Roos EM,Lohmander LS,Davis AM,Maillefert JF. Psychometric properties of the French translation of the reduced KOOS and HOOS (KOOS-PS and HOOS-PS). *Osteoarthritis Cartilage* 2009;17(12):1604-1608.
- Orozco-Alcala JJ,Barrera-Tenorio EF. A long-term, double-blind, comparative study of tenoxicam (Ro 12-0068) and Piroxicam in gonarthrosis and coxarthrosis. *Eur J Rheumatol Inflamm* 1987;9(2):109-113.
- Ortolani M,Meneghini A,Polonio D,Gerardi A,Piran D,-CognolatoF.. Treatment of the osteoarthritis of the knee with paraffin and NSAID: a comparative study. *Giornale Italiano Medicina Riabilitativa* 1991;3:56-61.
- Osborne RH,Buchbinder R,Ackerman IN. Can a disease-specific education program augment self-management skills and improve Health-Related Quality of Life in people with hip or knee osteoarthritis?. *BMC Musculoskelet Disord* 2006;7:90.
- Ou ZX,Jin JC,Huang D. [Comparative study on effects of combined massage-smouldering-washing therapy and mini-invasive surgery in treating knee osteoarthritis]. *Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi = Chinese journal of integrated traditional and Western medicine / Zhongguo Zhong xi yi jie he xue hui , Zhongguo Zhong yi yan jiu yuan zhu ban* 2008;28:925-928.
- Ozao-Choy J,Tammaro Y,Fradis M,Weber K,Divino CM. Clopidogrel and bleeding after general surgery procedures. *Am Surg* 2008 Aug;74(8):721-725.
- Ozdinler AR,Yeldan I,Kinali P. The effects of closed kinetic chain exercise on pain and functional performance of patients with knee osteoarthritis. *Pain Clinic* 2005;17(1):107-115.
- Ozgönenel L,Aytekin E,oglu G. A double-blind trial of clinical effects of therapeutic ultrasound in knee osteoarthritis. *Ultrasound in medicine & biology* 2009;35:44-49.
- Ozgonenel L,Aytekin E,Durmusoglu G. A double-blind trial of clinical effects of therapeutic ultrasound in knee osteoarthritis. *Ultrasound Med Biol* 2009;35(1):44-49.
- Ozguclu E,Cetin A,Cetin M,Calp E. Additional effect of pulsed electromagnetic field therapy on knee osteoarthritis treatment: a randomized, placebo-controlled study. ;29(8):927-931.

Ozoran K,Caner N,Seckin GU,Ucan H,Yucel M. Diflunisal (Dolphin (R)) treatment in knee osteoarthritis: Double blind, placebo controlled study. <ORIGINAL> DIZ OSTEOARTRITINDE DIFLUNISAL (DOLPHIN(R)) TEDAVISI: PLASEBO KONTROLLU CIFT KOR CALISMA. *Journal of Rheumatology and Medical Rehabilitation* 1996;7:89-93.

Ozturk C,Atamaz F,Hepguler S,Argin M,Arkun R. The safety and efficacy of intraarticular hyaluronan with/without corticosteroid in knee osteoarthritis: 1-year, single-blind, randomized study. *Rheumatol Int* 2006;26(4):314-319.

Paccola CA,Fogagnolo F. Double-plating nonunions of high tibial osteotomies. *J Knee Surg* 2003;16(1):38-41.

Paker N,Tekdos D,Kesiktas N,Soy D. Comparison of the therapeutic efficacy of TENS versus intra-articular hyaluronic acid injection in patients with knee osteoarthritis: a prospective randomized study. *Adv Ther* 2006;23(2):342-353.

Pallu S,Francin PJ,Guillaume C,Gegout-Pottie P,Netter P,Mainard D,Terlain B,Presle N. Obesity affects the chondrocyte responsiveness to leptin in patients with osteoarthritis. *Arthritis Res Ther* 2010;12(3):R112.

Palmieri-Smith RM,Thomas AC,Karvonen-Gutierrez C,Sowers MF. Isometric Quadriceps Strength in Women with Mild, Moderate, and Severe Knee Osteoarthritis. *Am J Phys Med Rehabil* 2010;.

Papachristou G,Plessas S,Sourlas J,Levidiotis C,Chronopoulos E,Papachristou C. Deterioration of long-term results following high tibial osteotomy in patients under 60 years of age. *Int Orthop* 2006;30(5):403-408.

Papp M,Szabo L,Lazar I,Takacs I,Karolyi Z,Nagy GG,Vereb G. Combined High Tibial Osteotomy Decreases Biomechanical Changes Radiologically Detectable in the Sagittal Plane Compared With Closing-Wedge Osteotomy. *Arthroscopy - Journal of Arthroscopic and Related Surgery* 2009;25(4):355-364.

Paradowski PT,Englund M,Lohmander LS,Roos EM. The effect of patient characteristics on variability in pain and function over two years in early knee osteoarthritis. *Health Qual Life Outcomes* 2005;3:59.

Paradowski PT,Englund M,Roos EM,Lohmander LS. Similar group mean scores, but large individual variations, in patient-relevant outcomes over 2 years in meniscectomized subjects with and without radiographic knee osteoarthritis. *Health Qual Life Outcomes* 2004;2:38.

Pareek A,Chandurkar N,Gupta A,Sirsikar A,Dalal B,Jesalpura B,Mehrotra A,Mukherjee A. Efficacy and safety of Aceclofenac-cr and Aceclofenac in the treatment of knee osteoarthritis: a 6-week, comparative, randomized, multicentric, double-blind study. *The journal of pain : official journal of the American Pain Society* 2011;12:546-553.

Pareek A,Gupta AK,Chandurkar NB,Sirsikar AD,Ambade RE,Jesalpura BH,Swamy AP. Zaltoprofen, a noninferior alternative to Diclofenac for the treatment of primary knee osteoarthritis -- a comparative evaluation of efficacy and safety in a 4-week, multicentric, randomized, double-blind, double-dummy trial. *Expert Opinion on Pharmacotherapy* 2011;12:1007-1015.

Paresce E,Carabba M,Angelini M,Perbellini A,Franchini S,Colombo S. Intra-articular hyaluronic acid in osteoarthritis of the knee. Middle-term study versus orgotein. *Scand J Rheumatol Suppl* 1990;85:38.

Paresce E, Carrabba M, Angelini M, Nicolais L, Perbellini A. The treatment of knee osteoarthritis with hyaluronic acid. An evaluation of clinical and rheological effects. *Scand J Rheumatol Suppl* 1992;93:40.

Park KS, Choi JJ, Kim WU, Min JK, Park SH, Cho CS. The efficacy of tramadol/Acetaminophen combination tablets (Ultracet(R)) as add-on and maintenance therapy in knee osteoarthritis pain inadequately controlled by nonsteroidal anti-inflammatory drug (NSAID). *Clin Rheumatol* 2011 Aug 3;.

Park KS, Choi JJ, Kim WU, Min JK, Park SH, Cho CS. The efficacy of tramadol/Acetaminophen combination tablets (Ultracet(R)) as add-on and maintenance therapy in knee osteoarthritis pain inadequately controlled by nonsteroidal anti-inflammatory drug (NSAID). *Clin Rheumatol* 2012 Feb;31(2):317-323.

Park S, Kim S, Shin I, Kim H, Choe J. Effect of AIF on knee osteoarthritis patients: Double-blind, randomized placebo-controlled study. *Korean Journal of Physiology and Pharmacology* 2009;13(1):33-37.

Parment S, Lynn C, Glass RM. Osteoarthritis of the Knee. *Journal of the American Medical Association* 2003;289(8):1068.

Parmigiani L, Furtado RN, Lopes RV, Ribeiro LH, Natour J. Joint lavage associated with triamcinolone hexacetonide injection in knee osteoarthritis: a randomized double-blind controlled study. *Clin Rheumatol* 2010 Nov;29(11):1311-1315.

Pasquali R, Guerra D, Taparelli F, Boraldi F, Bergamini G, Mori G, Zizzi F, Frizziero L. Morphological analysis of knee synovial membrane biopsies from a randomized controlled clinical study comparing the effects of sodium hyaluronate (Hyalgan) and methylprednisolone acetate (Depomedrol) in osteoarthritis. *Rheumatology (Oxford)* 2001;40(2):158-169.

Patel A, Buszewicz M, Beecham J, Griffin M, Rait G, Nazareth I, Atkinson A, Barlow J, Haines A. Economic evaluation of arthritis self-management in primary care. *BMJ* 2009;339:b3532.

Patel S, Hossain FS, Paton B, Haddad FS. The effects of a non-operative multimodal programme on osteoarthritis of the knee. *Ann R Coll Surg Engl* 2010 Sep;92(6):467-471.

Pathy MS. Acute monoarticular presentation of osteoarthrosis of the knee. *J Int Med Res* 1978;6(5):365-368.

Pathy MS. Osteoarthritis and non-steroidal and anti-inflammatory drugs: a multi-centre comparative study. *Curr Med Res Opin* 1982;7(Suppl 1):41-52.

Pavelka JK, Peliskova Z, Stehlikova H, Repas C. Comparison of the effectiveness of Tramadol and Diclofenac in the symptomatic treatment of osteoarthritis. *Ceska Revmatologie* 1995;3:171-176.

Pavelka K, Bruyere O, Rovati LC, Olejarova M, Giacovelli G, Reginster JY. Relief in mild-to-moderate pain is not a confounder in joint space narrowing assessment of full extension knee radiographs in recent osteoarthritis structure-modifying drug trials. *Osteoarthritis Cartilage* 2003;11(10):730-737.

Pavelka K, Forejtova S, Olejarova M, Gatterova J, Senolt L, Spacek P, Braun M, Hulejova M, Stovickova J, Pavelkova A. Hyaluronic acid levels may have predictive value for the progression of knee osteoarthritis. *Osteoarthritis Cartilage* 2004;12(4):277-283.

Pavelka K, Gatterova J, Gollerova V, Urbanova Z, Sedlackova M, Altman RD. A 5-year randomized controlled, double-blind study of glycosaminoglycan polysulphuric acid complex (Rumalon) as a structure modifying therapy in osteoarthritis of the hip and knee. *Osteoarthritis Cartilage* 2000;8(5):335-342.

Pavelka K, Le L, Bjorneboe O, Herrero-Beaumont G, Richarz U. Benefits of transdermal fentanyl in patients with rheumatoid arthritis or with osteoarthritis of the knee or hip: an open-label study to assess pain control. *Curr Med Res Opin* 2004;20(12):1967-1977.

Pavelka K, Peliskova Z, Stehlikova H, Ratcliffe S, Repas C. Intraindividual differences in pain relief and functional improvement in osteoarthritis with Diclofenac or tramadol. *Clin Drug Investig* 1998;16(6):421-429.

Pavelka KS, Pavelka KJ, Trnavsky K. Double blind comparison of lonazolac and indomethacin administered combined orally and per rectum in patients with osteoarthritis. *Fysiatr Revmatol Vestn* 1989;67:223-229.

Pelletier JP, Beaulieu A, Bessette L, Morin F, Raynauld JP, Fernandes A, Martel-Pelletier J. Twenty-four-month clinical trial on the effects of chondroitin sulfate on structural changes in knee osteoarthritis patients as assessed by MRI. *Basic and Clinical Pharmacology and Toxicology* 2011 Oct;109 SUPPL. 3:48-49.

Pelletier JP, Raynauld JP, Berthiaume MJ, Abram F, Choquette D, Haraoui B, Beary JF, Cline GA, Meyer JM, Martel-Pelletier J. Risk factors associated with the loss of cartilage volume on weight-bearing areas in knee osteoarthritis patients assessed by quantitative magnetic resonance imaging: a longitudinal study. *Arthritis Res Ther* 2007;9(4):R74.

Pelletier JP, Raynauld JP, Caron J, Mineau F, Abram F, Dorais M, Haraoui B, Choquette D, Martel-Pelletier J. Decrease in serum level of matrix metalloproteinases is predictive of the disease-modifying effect of osteoarthritis drugs assessed by quantitative MRI in patients with knee osteoarthritis. *Ann Rheum Dis* 2010 Dec;69(12):2095-2101.

Pelletier JP, Yaron M, Haraoui B, Cohen P, Nahir MA, Choquette D, Wigler I, Rosner IA, Beaulieu AD. Efficacy and safety of Diacerein in osteoarthritis of the knee: a double-blind, placebo-controlled trial. The Diacerein Study Group. *Arthritis Rheum* 2000;43(10):2339-2348.

Pells JJ, Shelby RA, Keefe FJ, Dixon KE, Blumenthal JA, Lacaille L, Tucker JM, Schmitt D, Caldwell DS, Kraus VB. Arthritis self-efficacy and self-efficacy for resisting eating: relationships to pain, disability, and eating behavior in overweight and obese individuals with osteoarthritic knee pain. *Pain* 2008;136(3):340-347.

Peloquin L, Bravo G, Gauthier P, Lacombe G, Billiard JS. Effects of a Cross-Training Exercise Program in Persons with Osteoarthritis of the Knee A Randomized Controlled Trial. *J Clin Rheumatol* 1999;5(3):126-136.

Peloso PM, Bellamy N, Bensen W, Thomson GT, Harsanyi Z, Babul N, Darke AC. Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee. *J Rheumatol* 2000;27(3):764-771.

Penninx BW,Rejeski WJ,Pandya J,Miller ME,Di BM,Applegate WB,Pahor M. Exercise and depressive symptoms: a comparison of aerobic and resistance exercise effects on emotional and physical function in older persons with high and low depressive symptomatology. *J Gerontol B Psychol Sci Soc Sci* 2002;57(2):124-132.

Peregoy J,Wilder FV. The effects of vitamin C supplementation on incident and progressive knee osteoarthritis: a longitudinal study. *Public Health Nutr* 2011 Apr;14(4):709-715.

Perez BM,Calero E,Rodriguez M,Castellon AP,Bermudez A,Linares LF,Mesa J,Fernandez CC,Garcia C,Garcia LA,Valenzuela A,Povedano A,Garcia PS,Lopez MA,Caliz R,Garcia VF,Cano M,Gines MF,Gonzalez J,Caracuel MA,Roldan R,Guzman UM,Gonzalez A,Marengo de la Fuente. Comparison of Aceclofenac with Piroxicam in the treatment of osteoarthritis. *Clin Rheumatol* 1997;16(2):154-159.

Perlman AI,Ali A,Njike VY,Hom D,Davidi A,Gould-Fogerite S,Milak C,Katz DL. Massage therapy for osteoarthritis of the knee: A randomized dose-finding trial. *PLoS One* 2012 Feb 8;7(2 Article Number):.

Perpignano G,Bogliolo A,Puccetti L. Double-blind comparison of the efficacy and safety of etodolac SR 600 mg u.i.d. and of tenoxicam 20mg u.i.d. in elderly patients with osteoarthritis of the hip and of the knee. *Int J Clin Pharmacol Res* 1994;14(5-6):203-216.

Perrot S,Poiraudeau S,Kabir M,Bertin P,Sichere P,Serrie A,Rannou F. Active or passive pain coping strategies in hip and knee osteoarthritis? Results of a national survey of 4,719 patients in a primary care setting. *Arthritis Rheum* 2008;59(11):1555-1562.

Perrot S,Ravaud P,Bertin P. Patient acceptable symptomatic state thresholds and minimal clinically important improvement for pain at rest and on movement in osteoarthritis. *European Journal of Pain Supplements* 2011 Sep;5(1):79.

Petera P,Tausch G,Eberl R. Double blind trial comparing tiaprofenic acid and ibuprofen in patients with osteoarthritis of the hips and the knees. *Wien Med Wochenschr* 1983;133:409-412.

Petera P,Tausch G,Ebner W,Eberl R. Randomized study with orgotein versus a corticosteroid in activated osteoarthritis of the knee. *THERAPIEWOCHE* 1985;35:3429-3434.

Petersen B,Rovati S. Diclofenac epolamine (Flector) patch: evidence for topical activity. *Clin Drug Investig* 2009;29(1):1-9.

Petersen SG,Saxne T,Heinegard D,Hansen M,Holm L,Koskinen S,Stordal C,Christensen H,Aagaard P,Kjaer M. Glucosamine but not ibuprofen alters cartilage turnover in osteoarthritis patients in response to physical training. *Osteoarthritis Cartilage* 2010;18(1):34-40.

Peterson mg,Kovar-Toledano PA,Otis JC,Allegrante JP,MacKenzie CR,Gutin B,Kroll MA. Effect of a walking program on gait characteristics in patients with osteoarthritis. *Arthritis Care Res* 1993;6(1):11-16.

Petrella RJ,Bartha C. Home-based exercise therapy for older patients with knee osteoarthritis: a randomized clinical trial. *J Rheumatol* 2000;27(9):2215-2221.

Petrella RJ,Cogliano A,Decaria J. Combining two hyaluronic acids in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Clin Rheumatol* 2008;27(8):975-981.

Petrella RJ,Decaria J,Petrella MJ. Long term efficacy and safety of a combined low and high molecular weight hyaluronic acid in the treatment of osteoarthritis of the knee. *Rheumatology Reports* 2011;3(1):16-21.

Petrella RJ,DiSilvestro MD,Hildebrand C. Effects of hyaluronate sodium on pain and physical functioning in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled clinical trial. *Arch Intern Med* 2002;162(3):292-298.

Petrella RJ. Hyaluronic acid for the treatment of knee osteoarthritis: long-term outcomes from a naturalistic primary care experience. *Am J Phys Med Rehabil* 2005;84(4):278-283.

Petterson SC,Mizner RL,Stevens JE,Raisis L,Bodenstab A,Newcomb W,Snyder-Mackler L. Improved function from progressive strengthening interventions after total knee arthroplasty: a randomized clinical trial with an imbedded prospective cohort. *Arthritis Rheum* 2009 Feb 15;61(2):174-183.

Petty CA,Lubowitz JH. Does arthroscopic partial meniscectomy always cause arthritis?. *Sports Med Arthrosc* 2012 Jun;20(2):58-61.

Petty CA,Lubowitz JH. Does arthroscopic partial meniscectomy result in knee osteoarthritis? A systematic review with a minimum of 8 years' follow-up. *Arthroscopy* 2011 Mar;27(3):419-424.

Pfahler M,Lutz C,Anetzberger H,Maier M,Hausdorf J,Pellengahr C,Refior HJ. Long-term results of high tibial osteotomy for medial osteoarthritis of the knee. *Acta Chir Belg* 2003;103(6):603-606.

Pham T,Le HA,Ravaud P,Dieppe P,Paolozzi L,Dougados M. Evaluation of the symptomatic and structural efficacy of a new hyaluronic acid compound, NRD101, in comparison with Diacerein and placebo in a 1 year randomised controlled study in symptomatic knee osteoarthritis. *Ann Rheum Dis* 2004;63(12):1611-1617.

Phillips RS,Cullen CH. Surgical treatment of osteoarthritis. *Geriatrics* 1968;23(11):161-178.

Phiphobmongkol V,Sudhasaneya V. The effectiveness and safety of intra-articular injection of sodium hyaluronate (500-730 kDa) in the treatment of patients with painful knee osteoarthritis. *J Med Assoc Thai* 2009;92(10):1287-1294.

Pietrogrande V,Melanotte PL,D'Agnolo B,Ulivi M,Benigni GA,Turchetto L,Pierfederici P,Perbellini A. Hyaluronic acid versus methylprednisolone intra-articularly injected for treatment of osteoarthritis of the knee. *Current Therapeutic Research - Clinical and Experimental* 1991;50(5):691-701.

Pietrosimone BG,Hart JM,Saliba SA,Hertel J,Ingersoll CD. Immediate effects of transcutaneous electrical nerve stimulation and focal knee joint cooling on quadriceps activation. *Med Sci Sports Exerc* 2009;41(6):1175-1181.

Pietrosimone BG,Hertel J,Ingersoll CD,Hart JM,Saliba SA. Voluntary Quadriceps Activation Deficits in Patients with Tibiofemoral Osteoarthritis: A Meta-Analysis. *PM and R* 2011 Feb;3(2):153-162.

Pietrosimone BG,Saliba SA,Hart JM,Hertel J,Ingersoll CD. Contralateral effects of disinhibitory tens on quadriceps function in people with knee osteoarthritis following unilateral treatment. *N Am J Sports Phys Ther* 2010 Sep;5(3):111-121.

Pincus T,Koch G,Lei H,Mangal B,Sokka T,Moskowitz R,Wolfe F,Gibofsky A,Simon L,Zlotnick S,Fort JG. Patient Preference for Placebo, Acetaminophen (Paracetamol) or Celecoxib Efficacy Studies (PACES): two randomised, double blind, placebo controlled, crossover clinical trials in patients with knee or hip osteoarthritis. *Ann Rheum Dis* 2004;63(8):931-939.

Pincus T,Koch GG,Sokka T,Lefkowitz J,Wolfe F,Jordan JM,Luta G,Callahan LF,Wang X,Schwartz T,Abramson SB,Caldwell JR,Harrell RA,Kremer JM,Lautzenheiser RL,Markenson JA,Schnitzer TJ,Weaver A,Cummins P,Wilson A,Morant S,Fort J. A randomized, double-blind, crossover clinical trial of Diclofenac plus misoprostol versus Acetaminophen in patients with osteoarthritis of the hip or knee. *Arthritis Rheum* 2001;44(7):1587-1598.

Pincus T,Wang X,Chung C,Sokka T,Koch GG. Patient preference in a crossover clinical trial of patients with osteoarthritis of the knee or hip: face validity of self-report questionnaire ratings. *J Rheumatol* 2005;32(3):533-539.

Pinheiro GC,Rachid A,Brito AS,Buoniconiti A,Atra E,de Freitas GG,Chahade WH,Sobrinho PS. Open multicentre clinical trial of diflunisal in osteoarthritis. *Curr Med Res Opin* 1976;4(6):402-410.

Pipitone N,Scott DL. Magnetic pulse treatment for knee osteoarthritis: a randomised, double-blind, placebo-controlled study. *Curr Med Res Opin* 2001;17(3):190-196.

Piscosa J,Rodriguez Z,Bustamante SA,Okuhama NN,Miller MJ,Sandoval M. Efficacy and safety of freeze-dried cat's claw in osteoarthritis of the knee: mechanisms of action of the species *Uncaria guianensis*. *Inflamm Res* 2001;50(9):442-448.

Pisters MF,Veenhof C,de Bakker DH,Schellevis FG,Dekker J. Behavioural graded activity results in better exercise adherence and more physical activity than usual care in people with osteoarthritis: a cluster-randomised trial. *Aust J Physiother* 2010;56(1):41-47.

Pisters MF,Veenhof C,Schellevis FG,de Bakker DH,Dekker J. Long-term effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized controlled trial comparing two different physical therapy interventions. *Osteoarthritis Cartilage* 2010 Aug;18(8):1019-1026.

Pisters MF,Veenhof C,Schellevis FG,Twisk JW,Dekker J,de Bakker DH. Exercise adherence improves long-term patient outcome in patients with osteoarthritis of the hip and/or knee. *Arthritis Care Res (Hoboken)* 2010;.

Poitras S,Avouac J,Rossignol M,Avouac B,Cedraschi C,Nordin M,Rousseaux C,Rozenberg S,Savarieau B,Thoumie P,Valat JP,Vignon E,Hilliquin P. A critical appraisal of guidelines for the management of knee osteoarthritis using Appraisal of Guidelines Research and Evaluation criteria. *Arthritis Res Ther* 2007;9(6):R126.

Pollard H,Ward G,Hoskins W,Hardy K. The effect of a manual therapy knee protocol on osteoarthritic knee pain: a randomised controlled trial. *J Can Chiropr Assoc* 2008;52(4):229-242.

Pollo FE. Bracing and heel wedging for unicompartmental osteoarthritis of the knee. *Am J Knee Surg* 1998;11(1):47-50.

Polyzois D,Stavlas P,Polyzois V,Zacharakis N. The oblique high tibial osteotomy technique without bone removal and with rigid blade plate fixation for the treatment of medial osteoarthritis of the varus knee: medium and long-term results. *Knee Surg Sports Traumatol Arthrosc* 2006;14(10):940-947.

Pope JE, Prashker M, Anderson J. The efficacy and cost effectiveness of N of 1 studies with Diclofenac compared to standard treatment with nonsteroidal antiinflammatory drugs in osteoarthritis. *J Rheumatol* 2004;31(1):140-149.

Potter HG, Jain SK, Ma Y, Black BR, Fung S, Lyman S. Cartilage injury after acute, isolated anterior cruciate ligament tear: immediate and longitudinal effect with clinical/MRI follow-up. *Am J Sports Med* 2012 Feb;40(2):276-285.

Potter TA. Correction of angular deformities in the arthritic knee by osteotomy or soft tissue release. *Surg Clin North Am* 1969;49(4):929-937.

Povoroznyuk V, Grygorieva N, Unusova S, Palamarchuk A. Effectiveness of exercise therapy in combination with glucosamine and chondroitin treatment in postmenopausal women with knee osteoarthritis. *European Journal of Pain Supplements* 2011 Sep;5(1):185.

Power JD, Cott CA, Badley EM, Hawker GA. Physical therapy services for older adults with at least moderately severe hip or knee arthritis in 2 Ontario counties. *J Rheumatol* 2005;32(1):123-129.

Prasad M, Culham E, Rudan J. The biomechanics of foot orthotics in people with medial compartment knee osteoarthritis. *Arch Physiol Biochem* 2000;108(1-2):74.

Pritchard CH, Sripada P, Bankes PF, Smith DG, Schneider D. A retrospective comparison of the efficacy and tolerability of sodium hyaluronate and hylan G-F 20 in the treatment of osteoarthritis of the knee. *Journal of Musculoskeletal Research* 2002;6(3-4):197-205.

Prouse PJ, Bevis PJ, Bluhmki E, Distel M. Evaluation of the safety, tolerability, and efficacy of meloxicam tablets in patients with osteoarthritis. *Clin Ther* 1996;18(3):429-439.

Pua YH, Liang Z, Ong PH, Bryant AL, Lo NN, Clark RA. Associations of knee extensor strength and standing balance with physical function in knee osteoarthritis. *Arthritis Care Res (Hoboken)* 2011 Dec;63(12):1706-1714.

Puhl W, Biehl G, Koelbel R, Hofer H. Results of a multicenter trial of orgotein in osteoarthritis of the knee. <ORIGINAL> ERGEBNIS EINER MULTIZENTRISCHEN ORGOTEIN-PRUFUNG BEI GONARTHROSE. *EUR J RHEUMATOL INFLAM* 1981;4:264-270.

Punzi L. Intra-articular sodium hyaluronate reduces pain and improves function in osteoarthritis of knee. *Clin Exp Rheumatol* 2001;19(1):9-10.

Putnam MD, Mears DC, Fu FH. Combined Maquet and proximal tibial valgus osteotomy. *Clin Orthop Relat Res* 1985;(197):217-223.

Pybus PK. Osteoarthritis. A new neurological method of pain control. *Med Hypotheses* 1984;14(4):413-422.

Pyne D, Ioannou Y, Mootoo R, Bhanji A. Intra-articular steroids in knee osteoarthritis: a comparative study of triamcinolone hexacetonide and methylprednisolone acetate. *Clin Rheumatol* 2004;23(2):116-120.

Qiu GX, Gao SN, Giacobelli G, Rovati L, Setnikar I. Efficacy and safety of glucosamine sulfate versus ibuprofen in patients with knee osteoarthritis. *Arzneimittelforschung* 1998;48(5):469-474.

- Qiu GX,Weng XS,Zhang K,Zhou YX,Lou SQ,Wang YP,Li W,Zhang H,Liu Y. [A multi-central, randomized, controlled clinical trial of glucosamine hydrochloride/sulfate in the treatment of knee osteoarthritis]. *Zhonghua yi xue za zhi* 2005;85:3067-3070.
- Quilty B,Tucker M,Campbell R,Dieppe P. Physiotherapy, including quadriceps exercises and patellar taping, for knee osteoarthritis with predominant patello-femoral joint involvement: randomized controlled trial. *J Rheumatol* 2003;30(6):1311-1317.
- Quirk AS,Newman RJ,Newman KJ. An evaluation of interferential therapy, shortwave diathermy and exercise in the treatment of osteoarthrosis of the knee. *Physiotherapy* 1985;71(2):55-57.
- Rabago D,Zgierska A,Fortney L,Kijowski R,Mundt M,Ryan M,Grettie J,Patterson JJ. Hypertonic dextrose injections (prolotherapy) for knee osteoarthritis: results of a single-arm uncontrolled study with 1-year follow-up. *J Altern Complement Med* 2012 Apr;18(4):408-414.
- Rand JA. Arthroscopic management of degenerative meniscus tears in patients with degenerative arthritis. *Arthroscopy* 1985;1(4):253-258.
- Rand JA. Role of arthroscopy in osteoarthritis of the knee. *Arthroscopy* 1991;7(4):358-363.
- Randall C,Dickens A,White A,Sanders H,Fox M,Campbell J. Nettle sting for chronic knee pain: A randomised controlled pilot study. *Complement Ther Med* 2008;16(2):66-72.
- Ranieri L,Traina GC,Maci C. High tibial osteotomy in osteoarthrosis of the knee (a long term clinical study of 187 knees). *Ital J Orthop Traumatol* 1977;3(3):289-300.
- Rastogi S,Sharma VK,Chandra R,Sivaraman ST. Open label multicentre trial on safety and efficacy of intra-articular hyaluronic acid in the treatment of osteoarthritis of the knee - A prospective study. *Journal, Indian Academy of Clinical Medicine* 2005;6(3):232-235.
- Rat A,Baumann C,Guillemin F. National, multicentre, prospective study of quality of life in patients with osteoarthritis of the knee treated with hylane G-F 20. *Clin Rheumatol* 2011 Oct;30(10):1285-1293.
- Rattanachaiyanont M,Kuptniratsaikul V. No additional benefit of shortwave diathermy over exercise program for knee osteoarthritis in peri-/post-menopausal women: an equivalence trial. *Osteoarthritis Cartilage* 2008;16(7):823-828.
- Rau R,Lobsiger M,Gross D. Tolmetin treatment in patients with osteoarthritis of the hip and the knee. *Scand J Rheumatol Suppl* 1975;;S10-S12.
- Ravaud P,Auleley GR,Ayral X,Marre JP,Amor B. Piroxicam therapy: a double blind, randomized, multicenter study comparing 2 versus 4 week treatment in patients with painful knee osteoarthritis with effusion. *J Rheumatol* 1998;25(12):2425-2431.
- Ravaud P,Giraudeau B,Logeart I,Larguier JS,Rolland D,Treves R,Euller-Ziegler L,Bannwarth B,Dougados M. Management of osteoarthritis (OA) with an unsupervised home-based exercise programme and/or patient administered assessment tools. A cluster randomised controlled trial with a 2x2 factorial design. *Ann Rheum Dis* 2004;63(6):703-708.

Ravaud P, Moulinier L, Giraudeau B, Ayral X, Guerin C, Noel E, Thomas P, Fautrel B, Mazieres B, Dougados M. Effects of joint lavage and steroid injection in patients with osteoarthritis of the knee: results of a multicenter, randomized, controlled trial. *Arthritis Rheum* 1999;42(3):475-482.

Raynauld JP, Goldsmith CH, Bellamy N, Torrance GW, Polisson R, Belovich D, Pericak D, Tugwell P. Effectiveness and safety of repeat courses of hylan G-F 20 in patients with knee osteoarthritis. *Osteoarthritis Cartilage* 2005;13(2):111-119.

Raynauld JP, Martel-Pelletier J, Beaulieu A, Bessette L, Morin F, Choquette D, Haraoui B, Abram F, Pelletier JP. An Open-Label Pilot Study Evaluating by Magnetic Resonance Imaging the Potential for a Disease-Modifying Effect of Celecoxib Compared to a Modelized Historical Control Cohort in the Treatment of Knee Osteoarthritis. *Semin Arthritis Rheum* 2010;.

Raynauld JP, Martel-Pelletier J, Berthiaume MJ, Beaudoin G, Choquette D, Haraoui B, Tannenbaum H, Meyer JM, Beary JF, Cline GA, Pelletier JP. Long term evaluation of disease progression through the quantitative magnetic resonance imaging of symptomatic knee osteoarthritis patients: correlation with clinical symptoms and radiographic changes. *Arthritis Res Ther* 2006;8(1):R21.

Raynauld JP, Torrance GW, Band PA, Goldsmith CH, Tugwell P, Walker V, Schultz M, Bellamy N. A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part 1 of 2): clinical results. *Osteoarthritis Cartilage* 2002;10(7):506-517.

Raynauld JP. Clinical trials: impact of intraarticular steroid injections on the progression of knee osteoarthritis. *Osteoarthritis Cartilage* 1999;7(3):348-349.

Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. *Altern Ther Health Med* 2000;6(2):68-80.

Reginster J, Tajana E. Single oral dose of (1200mg) sachet of chondroitin 4&6 sulfate (CS4&6-chondrosulf(registered trademark)) relieves pain and improves function. Results of a double blind study, versus placebo and an active treatment in knee OA patients. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S226-S227.

Reginster JY, Malmstrom K, Mehta A, Bergman G, Ko AT, Curtis SP, Reicin AS. Evaluation of the efficacy and safety of Etoricoxib compared with Naproxen in two, 138-week randomised studies of patients with osteoarthritis. *Ann Rheum Dis* 2007;66(7):945-951.

Reichenbach S, Dieppe PA, Nuesch E, Williams S, Villiger PM, Juni P. Association of bone attrition with knee pain, stiffness and disability: A cross-sectional study. *Annals of the Rheumatic Diseases* 2011;70(2):293-298.

Reichenbach S, Rutjes AWS, Nuesch E, Trelle S, Juni P. Arthroscopic lavage for osteoarthritis of the knee. *Cochrane Database of Systematic Reviews* 2008;(3 Article Number).

Reid DA, McNair PJ. Effects of an acute hamstring stretch in people with and without osteoarthritis of the knee. *Physiotherapy* 2010;96(1):14-21.

- Reijman M, Bierma-Zeinstra SM, Pols HA, Koes BW, Stricker BH, Hazes JM. Is there an association between the use of different types of nonsteroidal antiinflammatory drugs and radiologic progression of osteoarthritis? The Rotterdam Study. *Arthritis Rheum* 2005;52(10):3137-3142.
- Reinhold T, Witt CM, Jena S, Brinkhaus B, Willich SN. Quality of life and cost-effectiveness of acupuncture treatment in patients with osteoarthritis pain. *Eur J Health Econ* 2008;9(3):209-219.
- Reischl N, Wahl P, Jacobi M, Clerc S, Gautier E, Jakob RP. Infections after high tibial open wedge osteotomy: a case control study. *Arch Orthop Trauma Surg* 2009;129(11):1483-1487.
- Rejeski WJ, Ettinger WH, Martin K, Morgan T. Treating disability in knee osteoarthritis with exercise therapy: a central role for self-efficacy and pain. *Arthritis Care Res* 1998;11(2):94-101.
- Rejholec V. Long-term studies of antiosteoarthritic drugs: An assessment. *Seminars in Arthritis and Rheumatism* 1987;17(2 SUPPL. 2):35-53.
- Rene J, Weinberger M, Mazzuca SA, Brandt KD, Katz BP. Reduction of joint pain in patients with knee osteoarthritis who have received monthly telephone calls from lay personnel and whose medical treatment regimens have remained stable. *Arthritis Rheum* 1992;35(5):511-515.
- Rezende MU, Campos GC, Pailo AF, Frucchi R, Pasqualim T. Evaluation of the effect of adding corticosteroid to viscosupplementation: A prospective and randomized study. *Osteoporos Int* 2012;23 SUPPL. 2:S132-S133.
- Richardson G, Hawkins N, McCarthy CJ, Mills PM, Pullen R, Roberts C, Silman A, Oldham JA. Cost-effectiveness of a supplementary class-based exercise program in the treatment of knee osteoarthritis. *Int J Technol Assess Health Care* 2006;22(1):84-89.
- Richette P, Poitou C, Garnerio P, Vicaut E, Bouillot JL, Lacorte JM, Basdevant A, Clement K, Bardin T, Chevalier X. Benefits of massive weight loss on symptoms, systemic inflammation and cartilage turnover in obese patients with knee osteoarthritis. *Ann Rheum Dis* 2011 Jan;70(1):139-144.
- Riecke BF, Christensen R, Christensen P, Leeds AR, Boesen M, Lohmander LS, Astrup A, Bliddal H. Comparing two low-energy diets for the treatment of knee osteoarthritis symptoms in obese patients: a pragmatic randomized clinical trial. *Osteoarthritis Cartilage* 2010;18(6):746-754.
- Riskowski J, Dufour AB, Hannan MT. Arthritis, foot pain and shoe wear: Current musculoskeletal research on feet. *Current Opinion in Rheumatology* 2011 Mar;23(2):148-155.
- Riva-Sanseverino E. Oxygen-ozone therapy in knee-joint disorders. 1990;42(SPEC. ISS. 1):165.
- Rivera D, Ortiz J, Colon C, Colon J, Magraner M, Bredy R. Correlation between body mass index and need for total knee replacement in a group of Latin patients with knee osteoarthritis. *Bol Asoc Med P R* 2011 Apr;103(2):17-20.
- Rockborn P, Gillquist J. Long term results after arthroscopic meniscectomy. The role of preexisting cartilage fibrillation in a 13 year follow-up of 60 patients. *Int J Sports Med* 1996;17(8):608-613.
- Rodrigues PT, Ferreira AF, Pereira RM, Bonfa E, Borba EF, Fuller R. Effectiveness of medial-wedge insole treatment for valgus knee osteoarthritis. *Arthritis Rheum* 2008;59(5):603-608.

Rogers LQ, Macera CA, Hootman JM, Ainsworth BE, Blairi SN. The association between joint stress from physical activity and self-reported osteoarthritis: an analysis of the Cooper Clinic data. *Osteoarthritis Cartilage* 2002;10(8):617-622.

Rogers MW, Wilder FV. The association of BMI and knee pain among persons with radiographic knee osteoarthritis: a cross-sectional study. *BMC Musculoskelet Disord* 2008;9:163.

Rolf CG, Engstrom B, Ohrvik J, Valentin A, Lilja B, Levine DW. A comparative study of the efficacy and safety of hyaluronan viscosupplements and placebo in patients with symptomatic and arthroscopy-verified cartilage pathology. *Journal of Clinical Research* 2005;8:15-32.

Rondier J, Cayla J, Menkes CJ. A controlled trial of Ketoprofen (administered rectally) in arthritis of the hip and knee. *Rheumatol Rehabil* 1976;Suppl:71-74.

Roos EM, Bremander AB, Englund M, Lohmander LS. Change in self-reported outcomes and objective physical function over 7 years in middle-aged subjects with or at high risk of knee osteoarthritis. *Ann Rheum Dis* 2008;67(4):505-510.

Roos EM, Herzog W, Block JA, Bennell KL. Muscle weakness, afferent sensory dysfunction and exercise in knee osteoarthritis. *Nat Rev Rheumatol* 2011 Jan;7(1):57-63.

Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64.

Roos EM, Ostenberg A, Roos H, Ekdahl C, Lohmander LS. Long-term outcome of meniscectomy: symptoms, function, and performance tests in patients with or without radiographic osteoarthritis compared to matched controls. *Osteoarthritis Cartilage* 2001;9(4):316-324.

Roos H, Lauren M, Adalberth T, Roos EM, Jonsson K, Lohmander LS. Knee osteoarthritis after meniscectomy: prevalence of radiographic changes after twenty-one years, compared with matched controls. *Arthritis Rheum* 1998;41(4):687-693.

Rosemann T, Joos S, Koerner T, Szecsenyi J, Laux G. Comparison of AIMS2-SF, WOMAC, x-ray and a global physician assessment in order to approach quality of life in patients suffering from osteoarthritis. *BMC Musculoskeletal Disorders* 2006;7 Article Number(6. Date of Publication):.

Rosemann T, Kuehlein T, Laux G, Szecsenyi J. Osteoarthritis of the knee and hip: a comparison of factors associated with physical activity. *Clin Rheumatol* 2007;26(11):1811-1817.

Rosenberger PH, Dhabhar FS, Epel E, Jokl P, Ickovics JR. Sex differences in factors influencing recovery from arthroscopic knee surgery. *Clin Orthop Relat Res* 2010 Dec;468(12):3399-3405.

Rosenthal M, Moore P, Groves E, Iwan T, Schlosser LG, Dziewanowska Z, Negro-Vilar A. Sleep improves when patients with chronic OA pain are managed with morning dosing of once a day extended-release morphine sulfate (AVINZA): findings from a pilot study. *J Opioid Manag* 2007;3(3):145-154.

Roskos SE. Intra-articular corticosteroid for treating osteoarthritis of the knee. *Am Fam Physician* 2005;72(7):1222-1223.

- Rossini M, Viapiana O, Ramonda R, Bianchi G, Olivieri I, Lapadula G, Adami S. Intra-articular clodronate for the treatment of knee osteoarthritis: dose ranging study versus hyaluronic acid. *Rheumatology (Oxford)* 2009;48(7):773-778.
- Roth R, Kipshoven C. Efficacy of an intra-articular treatment of osteoarthritis of the knee with hyaluronan (GO-ON(registered trademark)). *Osteoporos Int* 2012;23 SUPPL. 2:S180-S181.
- Rovati LC, Pavelka K, Giacobelli G, Reginster JY. Assessment of joint space narrowing with conventional standing antero-posterior radiographs: relief in mild-to-moderate pain is not a confounder in recent osteoarthritis structure-modifying drug trials. *Osteoarthritis Cartilage* 2006;14 Suppl A:A14-A18.
- Rovensky J, Micekova D, Gubzova Z, Fimmers R, Lenhard G, Vogtle-Junkert U, Schreyer F. Treatment of knee osteoarthritis with a topical non-steroidal antiinflammatory drug. Results of a randomized, double-blind, placebo-controlled study on the efficacy and safety of a 5% ibuprofen cream. *Drugs Exp Clin Res* 2001;27(5-6):209-221.
- Roy V, Gupta U, Sharma S, Dhaon BK, Singh NP, Gulati P. Comparative efficacy and tolerability of nimesulide and Piroxicam in osteoarthritis with specific reference to chondroprotection: a double blind randomised study. *J Indian Med Assoc* 1999;97(10):442-445.
- Rozkydal Z, Kura V, Ondrusek S. The arthroscopic debridement in the management of osteoarthritis of the knee joint by high tibial osteotomy. *Bratisl Lek Listy* 2003;104(11):362-366.
- Rubin R, Menz HB. Use of laterally wedged custom foot orthoses to reduce pain associated with medial knee osteoarthritis: a preliminary investigation. *J Am Podiatr Med Assoc* 2005;95(4):347-352.
- Rubinstein J, Sidi A. Long-term study with tenoxicam (Ro 12-0068) in the treatment of gonarthrosis and coxarthrosis. *Eur J Rheumatol Inflamm* 1987;9(2):126-128.
- Rudan J, Harrison M, Simurda MA. Optimizing femorotibial alignment in high tibial osteotomy. *Can J Surg* 1999;42(5):366-370.
- Rudy AC, Bradley JD, Ryan SI, Kalasinski LA, Xiaotao Q, Hall SD. Variability in the disposition of ibuprofen enantiomers in osteoarthritis patients. *Ther Drug Monit* 1992;14(6):464-470.
- Ruff KJ, Winkler A, Jackson RW, DeVore DP, Ritz BW. Eggshell membrane in the treatment of pain and stiffness from osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled clinical study. *Clin Rheumatol* 2009;28(8):907-914.
- Rutherford DJ, Hubley-Kozey CL, Stanish WD. Maximal voluntary isometric contraction exercises: A methodological investigation in moderate knee osteoarthritis. *J Electromyogr Kinesiol* 2011;21(1):154-160.
- Ryang WS, Koog YH, Jeong KI, Wi H. Effects of pulsed electromagnetic field on knee osteoarthritis: a systematic review. *Rheumatology (Oxford)* 2012 Apr 13.
- Rybka V. Effect of high tibial and double osteotomy on osteoarthritic and rheumatoid deformity of the knee. *Acta Univ Carol Med Monogr* 1979;91:1-149.

Saag K, van der Heijde D, Fisher C, Samara A, DeTora L, Bolognese J, Sperling R, Daniels B. Rofecoxib, a new cyclooxygenase 2 inhibitor, shows sustained efficacy, comparable with other nonsteroidal anti-inflammatory drugs: a 6-week and a 1-year trial in patients with osteoarthritis. Osteoarthritis Studies Group. *Arch Fam Med* 2000;9(10):1124-1134.

Sacchetti G, Di MR, Mandelli V, Gallico S. Clinical testing of indoprofen in osteoarthritis: A controlled trial using a balanced incomplete block design. *CURR THER RES, CLIN EXP* 1978;24:274-283.

Sach TH, Barton GR, Doherty M, Muir KR, Jenkinson C, Avery AJ. The relationship between body mass index and health-related quality of life: comparing the EQ-5D, EuroQol VAS and SF-6D. *Int J Obes (Lond)* 2007;31(1):189-196.

Sacks S. Diclophenac sodium in rheumatoid arthritis and osteo-arthritis. *S Afr Med J* 1974;48(6):213-215.

Sadreddini S, Noshad H, Molaeeefard M, Moloudi R, Ardalan MR, Ghojzadeh M. A double blind, randomized, placebo controlled study to evaluate the efficacy of erythromycin in patients with knee effusion due to osteoarthritis. *Int J Rheum Dis* 2009;12(1):44-51.

Saito T, Takeuchi R, Ara Y, Yoshida T, Koshino T. High tibial osteotomy with anterior advancement of distal fragment for medial and patellofemoral compartmental osteoarthritis of the knee. *Knee* 2002;9(2):127-132.

Sakaguchi M. Anti-inflammatory effects of water-soluble dexamethasone-phosphate and -sulfate given by intra-articular injections. *Kumamoto Med J* 1982;35(3):109-113.

Salaffi F, Carotti M, Grassi W. Health-related quality of life in patients with hip or knee osteoarthritis: comparison of generic and disease-specific instruments. *Clin Rheumatol* 2005;24(1):29-37.

Salaffi F, Carotti M, Stancati A, Grassi W. Health-related quality of life in older adults with symptomatic hip and knee osteoarthritis: a comparison with matched healthy controls. *Aging Clin Exp Res* 2005;17(4):255-263.

Salaffi F, Piva S, Barreca C, Cacace E, Ciancio G, Leardini G, Mannoni A, Minari C, Occhi P, Pianon M, Punzi L, Re KA, Scarpa R, Sulli A, Troise-Rioda W. Validation of an Italian version of the Arthritis Impact Measurement Scales 2 (ITALIAN-AIMS2) for patients with osteoarthritis of the knee. *Rheumatology (Oxford)* 2000;39(7):720-727.

Salavati M, Mazaheri M, Negahban H, Sohani SM, Ebrahimian MR, Ebrahimi I, Kazemnejad A, Salavati M. Validation of a Persian-version of Knee injury and Osteoarthritis Outcome Score (KOOS) in Iranians with knee injuries. *Osteoarthritis and Cartilage* 2008;16(10):1178-1182.

Salim M. Transcutaneous electrical nerve stimulation (TENS) in chronic pain. *Alternative Therapies in Clinical Practice* 1996;3:33-35.

Salim M. Transcutaneous electrical nerve stimulation (TENS) in chronic pain 1254 3168. *Alternative Therapies in Clinical Practice* 1996 Jul Aug ; 3: 33 5 1996;:33-35.

Salisbury RB, Nottage WM, Gardner V. The effect of alignment on results in arthroscopic debridement of the degenerative knee. *Clin Orthop Relat Res* 1985;(198):268-272.

Salk RS,Chang TJ,D'Costa WF,Soomekh DJ,Grogan KA. Sodium hyaluronate in the treatment of osteoarthritis of the ankle: a controlled, randomized, double-blind pilot study. *J Bone Joint Surg Am* 2006;88(2):295-302.

Salter A,Bagg SD,Creasy JL,Romano C,Romano D,Richmond FJR,Loeb GE. First Clinical Experience with BION Implants for Therapeutic Electrical Stimulation. *Neuromodulation* 2004;7(1):38-47.

Sanga P,Katz N,Polverejan E,Wang S,Kelly K,Oh C,Thippawong J. Efficacy, safety, and tolerability of fulranumab, an anti-nerve growth factor antibody, in treatment of patients with moderate-to-severe osteoarthritis pain. *Journal of Pain* 2011 Apr;12(4 SUPPL. 1):53.

Sanghi D,Srivastava RN,Agarwal S,Natu SM,Singh A,Avasthi S. Role of vitamin D in osteoarthritis knee: A six month double blind, randomized, placebo control trial. *Osteoarthritis and Cartilage* 2011 Sep;19 SUPPL. 1:S36.

Sangwan SS,Siwach RC,Singh Z,Duhan S. Unicompartmental osteoarthritis of the knee: an innovative osteotomy. *Int Orthop* 2000;24(3):148-150.

Santic V,Tudor A,Sestan B,Legovic D,Sirola L,Rakovac I. Bone allograft provides bone healing in the medial opening high tibial osteotomy. *Int Orthop* 2010;34(2 SPECIAL ISSUE):225-229.

Santos MLAS,Gomes WF,Pereira DS,Oliveira Dmg,Dias JMD,Ferrioli E,Pereira LSM. Muscle strength, muscle balance, physical function and plasma interleukin-6 (IL-6) levels in elderly women with knee osteoarthritis (OA). *Arch Gerontol Geriatr* 2011;52(3):322-326.

Sarkin TL. Indications for intra-articular steroid in osteo-arthritis of the knee. *S Afr Med J* 1972;46(7):157-159.

Sasaki S. Multi-centered clinical evaluation of oxepinac against peripheral arthropathy particularly osteoarthritis. *Arzneimittelforschung* 1978;28(3):462-468.

Sasaki T,Yagi T,Monji J,Yasuda K,Tsuge H. High tibial osteotomy combined with anterior displacement of the tibial tubercle for osteoarthritis of the knee. *Int Orthop* 1986;10(1):31-40.

Sasaki T,Yasuda K. Clinical evaluation of the treatment of osteoarthritic knees using a newly designed wedged insole. *Clin Orthop Relat Res* 1987;(221):181-187.

Sawitzke AD,Shi H,Finco MF,Dunlop DD,Bingham CO,Harris CL,Singer NG,Bradley JD,Silver D,Jackson CG,Lane NE,Oddis CV,Wolfe F,Lisse J,Furst DE,Reda DJ,Moskowitz RW,Williams HJ,Clegg DO. The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. *Arthritis Rheum* 2008;58(10):3183-3191.

Sawitzke AD,Shi H,Finco MF,Dunlop DD,Harris CL,Singer NG,Bradley JD,Silver D,Jackson CG,Lane NE,Oddis CV,Wolfe F,Lisse J,Furst DE,Bingham CO,Reda DJ,Moskowitz RW,Williams HJ,Clegg DO. Clinical efficacy and safety of glucosamine, chondroitin sulphate, their combination, Celecoxib or placebo taken to treat osteoarthritis of the knee: 2-year results from GAIT. *Ann Rheum Dis* 2010 Aug;69(8):1459-1464.

Scale D,Wobig M,Wolpert W. Viscosupplementation of osteoarthritic knees with hylan: A treatment schedule study. *Current Therapeutic Research - Clinical and Experimental* 1994;55(3):220-232.

- Scali JJ. Intra-articular hyaluronic acid in the treatment of osteoarthritis of the knee: A long term study. *Eur J Rheumatol Inflamm* 1995;15(1):57-62.
- Scarpellini M,Lurati A,Vignati G,Marrazza mg,Telese F,Re K,Bellistri A. Biomarkers, type II collagen, glucosamine and chondroitin sulfate in osteoarthritis follow-up: the 'Magenta osteoarthritis study'. *J Orthop Traumatol* 2008;9(2):81-87.
- Schallberger A,Jacobi M,Wahl P,Maestretti G,Jakob RP. High tibial valgus osteotomy in unicompartamental medial osteoarthritis of the knee: a retrospective follow-up study over 13-21 years. *Knee Surg Sports Traumatol Arthrosc* 2011 Jan;19(1):122-127.
- Schank JA,Herdman SJ,Bloyer RG. Physical therapy in the multidisciplinary assessment and management of osteoarthritis. *Clin Ther* 1986;9 Suppl B:14-23.
- Scharf HP,Mansmann U,Streitberger K,Witte S,Kramer J,Maier C,Trampisch HJ,Victor N. Acupuncture and knee osteoarthritis: a three-armed randomized trial. *Ann Intern Med* 2006;145(1):12-20.
- Scharf HP,Mansmann U,Streitberger K,Witte S,Kramer J,Maier C,Trampisch HJ,Victor N,Bachmann J. [Acupuncture and knee osteoarthritis: a three-armed randomized trial]. *Revista Internacional de Acupuntura* 2007;1:41-2TN.
- Scharf Y,Nahir M,Schapira D,Lorber M. A comparative study of Naproxen with Diclofenac sodium in osteoarthritis of the knees. *Rheumatol Rehabil* 1982;21(3):167-170.
- Schein JR,Kosinski MR,Janagap-Benson C,Gajria K,Lin P,Freedman JD. Functionality and health-status benefits associated with reduction of osteoarthritis pain. *Curr Med Res Opin* 2008;24(5):1255-1265.
- Scherak O,Kolarz G,Schodl C,Blankenhorn G. Therapy with high doses of vitamin E in patients with osteoarthritis. *Z Rheumatol* 1990;49:369-373.
- Schiff M,Minic M. Comparison of the analgesic efficacy and safety of nonprescription doses of Naproxen sodium and Ibuprofen in the treatment of osteoarthritis of the knee. *J Rheumatol* 2004;31(7):1373-1383.
- Schiff MH. A comparison of Naprelan and Naprosyn in the treatment of osteoarthritis of the knee. *Am J Orthop (Belle Mead NJ)* 1996;25(9 Suppl):14-20.
- Schindler OS,Scott WN,Scuderi GR. The practice of unicompartamental knee arthroplasty in the United Kingdom. *J Orthop Surg (Hong Kong)* 2010 Dec;18(3):312-319.
- Schmalz T,Blumentritt S,Drewitz H,Freslier M. The influence of sole wedges on frontal plane knee kinetics, in isolation and in combination with representative rigid and semi-rigid ankle-foot-orthoses. *Clin Biomech (Bristol , Avon)* 2006;21(6):631-639.
- Schmid B,Ludtke R,Selbmann HK,Kotter I,Tschirdewahn B,Schaffner W,Heide L. Efficacy and tolerability of a standardized willow bark extract in patients with osteoarthritis: randomized placebo-controlled, double blind clinical trial. *Phytother Res* 2001;15(4):344-350.
- Schmid F. The Maquet procedure in the treatment of patellofemoral osteoarthritis. Long-term results. *Clin Orthop Relat Res* 1993;(294):254-258.
- Schmidt S,Stoy K. Fasting therapy in osteoarthritis. *Rheumatology (Oxford)* 2012 Feb;51 SUPPL. 1:i29.

Schnitzer TJ,Ballard IM,Constantine G,McDonald P. Double-blind, placebo-controlled comparison of the safety and efficacy of orally administered etodolac and nabumetone in patients with active osteoarthritis of the knee. *Clin Ther* 1995;17(4):602-612.

Schnitzer TJ,Beier J,Geusens P,Hasler P,Patel SK,Senftleber I,Gitton X,Moore A,Sloan VS,Poor G. Efficacy and safety of four doses of Lumiracoxib versus Diclofenac in patients with knee or hip primary osteoarthritis: a phase II, four-week, multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2004;51(4):549-557.

Scholtissen S,Bruyere O,Neuprez A,Severens JL,Herrero-Beaumont G,Rovati L,Hiligsmann M,Reginster JY. Glucosamine sulphate in the treatment of knee osteoarthritis: cost-effectiveness comparison with Paracetamol . *Int J Clin Pract* 2010 May;64(6):756-762.

Schoo AMM,Morris ME,Bui QM. The effects of mode of exercise instruction on compliance with a home exercise program in older adults with osteoarthritis. *Physiotherapy* 2005;91(2):79-86.

Schultz W,Gobel D. Articular cartilage regeneration of the knee joint after proximal tibial valgus osteotomy: a prospective study of different intra- and extra-articular operative techniques. *Knee Surg Sports Traumatol Arthrosc* 1999;7(1):29-36.

Schultz W,Gobel D. The influence of high tibial osteotomy on the patello-femoral joint: An arthroscopic study. *Knee* 1998;5(1):43-47.

Schumacher HR,Paul C,Hitchon CA,El-Gabalawy H,Zonay L,Clayburne G,Sieck M,Schwab E. Hyaluronate effects on synovium and synovial fluid. A prospective blinded study in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage* 2006;14(5):501-503.

Scott D,Smith C,Lohmander S,Chard J. Osteoarthritis. *Clin Evid* 2003;(10):1402-1430.

Scott DL,Berry H,Capell H,Coppock J,Daymond T,Doyle DV,Fernandes L,Hazleman B,Hunter J,Huskinson EC,Jawad A,Jubb R,Kennedy T,McGill P,Nichol F,Palit J,Webley M,Woolf A,Wotjulewski J. The long-term effects of non-steroidal anti-inflammatory drugs in osteoarthritis of the knee: a randomized placebo-controlled trial. *Rheumatology (Oxford)* 2000;39(10):1095-1101.

Scott WN. Arthroscopic debridement: tunnel vision?. *Orthopedics* 1999;22(9):867-868.

Seal PV,Chan RN. Tibial osteotomy for osteoarthrosis of the knee. *Acta Orthop Scand* 1975;46(1):141-151.

Seckin U,Gunduz S,Borman P,Akyuz M. Evaluation of the compliance to exercise therapy in patients with knee osteoarthritis. *Journal of Back and Musculoskeletal Rehabilitation* 2000;14(3):133-137.

Seed SM,Dunican KC,Lynch AM. Osteoarthritis: a review of treatment options. *Geriatrics* 2009 Oct;64(10):20-29.

Segal NA. Bracing and Orthoses: A Review of Efficacy and Mechanical Effects for Tibiofemoral Osteoarthritis. *PM and R* 2012 May;4(5 SUPPL.):S89-S96.

Seki T,Hasegawa Y,Yamaguchi J,Kanoh T,Ishiguro N,Tsuboi M,Ito Y,Hamajima N,Suzuki K. Association of serum carotenoids, retinol, and tocopherols with radiographic knee osteoarthritis: possible risk factors in rural Japanese inhabitants. *J Orthop Sci* 2010 Jul;15(4):477-484.

Selfe TK, Bourguignon C, Taylor AG. Effects of noninvasive interactive neurostimulation on symptoms of osteoarthritis of the knee: A randomized, sham-controlled pilot study. *J Altern Complement Med* 2008;14(9):1075-1081.

Selfe TK, Innes KE. Mind-body therapies and osteoarthritis of the knee. *Current Rheumatology Reviews* 2009;5(4):204-211.

Selfe TK, Taylor AG. Acupuncture and osteoarthritis of the knee: a review of randomized controlled trials (Structured abstract). *Fam Community Health* 2008;31:247-254.

Selvan T, Rajiah K, Nainar MS, Mathew EM. A Clinical Study on Glucosamine Sulfate versus Combination of Glucosamine Sulfate and NSAIDs in Mild to Moderate Knee Osteoarthritis. *ScientificWorldJournal* 2012;2012:902676.

Sen A, Gocen Z, Unver B, Karatosun V, Gunal I. The frequency of visits by the physiotherapist of patients receiving home-based exercise therapy for knee osteoarthritis. *Knee* 2004;11(2):151-153.

Sengupta K, Alluri KV, Satish AR, Mishra S, Golakoti T, Sarma KV, Dey D, Raychaudhuri SP. A double blind, randomized, placebo controlled study of the efficacy and safety of 5-Loxin for treatment of osteoarthritis of the knee. *Arthritis Res Ther* 2008;10(4):R85.

Seror R, Tubach F, Baron G, Falissard B, Logeart I, Dougados M, Ravaud P. Individualising the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) function subscale: incorporating patient priorities for improvement to measure functional impairment in hip or knee osteoarthritis. *Ann Rheum Dis* 2008;67(4):494-499.

Serry MM. A low-dosage Ketoprofen preparation in the management of osteoarthrosis of the knee joint. *J Int Med Res* 1980;8(6):388-390.

Serry MM. Proquazone ('Biarison') in osteoarthritis of the knee: a double-blind, dose comparison trial. *Pharmatherapeutica* 1980;2(5):323-329.

Seto H, Ikeda H, Hisaoka H, Kurosawa H. Effect of heat- and steam-generating sheet on daily activities of living in patients with osteoarthritis of the knee: randomized prospective study. *J Orthop Sci* 2008;13(3):187-191.

Sevick MA, Bradham DD, Muender M, Chen GJ, Enarson C, Dailey M, Ettinger WH. Cost-effectiveness of aerobic and resistance exercise in seniors with knee osteoarthritis. *Med Sci Sports Exerc* 2000;32(9):1534-1540.

Sevick MA, Miller GD, Loeser RF, Williamson JD, Messier SP. Cost-effectiveness of exercise and diet in overweight and obese adults with knee osteoarthritis. *Med Sci Sports Exerc* 2009;41(6):1167-1174.

Sevick MA, Miller GD, Loeser RF, Williamson JD, Messier SP. Cost-effectiveness of exercise and diet in overweight and obese adults with knee osteoarthritis (Provisional abstract). *Med Sci Sports Exerc* 2009;41:1167-1174.

Shackel NA, Day RO, Kellett B, Brooks PM. Copper-salicylate gel for pain relief in osteoarthritis: a randomised controlled trial. *Med J Aust* 1997;167(3):134-136.

Shafshak TS,el-Sheshai AM,Soltan HE. Personality traits in the mechanisms of interferential therapy for osteoarthritic knee pain. *Arch Phys Med Rehabil* 1991;72(8):579-581.

Shafshak TS. Electroacupuncture and exercise in body weight reduction and their application in rehabilitating patients with knee osteoarthritis. *Am J Chin Med* 1995;23(1):15-25.

Shah KD,Wright V. Intra-articular hydrocortisone in osteo-arthritis. *Ann Rheum Dis* 1967;26(4):316-318.

Shaikh KA,Ali M,Sharafatullah T. Comparative study of Diclofenac sodium and flurbiprofen in osteoarthritis. *J Pak Med Assoc* 1996;46(12):270-272.

Shainhouse JZ,Grierson LM,Naseer Z. A Long-Term, Open-Label Study to Confirm the Safety of Topical Diclofenac Solution Containing Dimethyl Sulfoxide in the Treatment of the Osteoarthritic Knee. *Am J Ther* 2010;.

Shakoor MA,Taslim MA,Hossain MS. Effects of activity modification on the patients with osteoarthritis of the knee. *Bangladesh Med Res Counc Bull* 2007;33(2):55-59.

Shakoor N,Furmanov S,Nelson DE,Li Y,Block JA. Pain and its relationship with muscle strength and proprioception in knee OA: results of an 8-week home exercise pilot study. *J Musculoskelet Neuronal Interact* 2008;8(1):35-42.

Shakoor N,Sengupta M,Foucher KC,Wimmer MA,Fogg LF,Block JA. The effects of common footwear on joint loading in osteoarthritis of the knee. *Arthritis Care Res (Hoboken)* 2010;.

Shamim SA,Kumar R,Halanaik D,Kumar A,Shandal V,Shukla J,Kumar A,Trikha V,Chandra P,Bandopadhyaya G,Malhotra A. Role of rhenium-188 tin colloid radiosynovectomy in patients with inflammatory knee joint conditions refractory to conventional therapy. *Nucl Med Commun* 2010 Sep;31(9):814-820.

Shannon FJ,Devitt AT,Poynton AR,Fitzpatrick P,Walsh mg. Short-term benefit of arthroscopic washout in degenerative arthritis of the knee. *Int Orthop* 2001;25(4):242-245.

Sharma A,Rathod R,Baliga VP. An open prospective study on postmarketing evaluation of the efficacy and tolerability of Diacerein in osteo-arthritis of the knee (DOK). *J Indian Med Assoc* 2008;106(1):54-6, 58.

Sharma B. Efficacy of lateral wedged insole with subtalar strapping on the functional status of medial compartment 3rd grade osteoarthritis of the knee. 2010;:3.

Sharma L,Dunlop DD,Cahue S,Song J,Hayes KW. Quadriceps strength and osteoarthritis progression in malaligned and lax knees. *Ann Intern Med* 2003;138(8):613-619.

Sharma L,Hayes KW,Felson DT,Buchanan TS,Kirwan-Mellis G,Lou C,Pai YC,Dunlop DD. Does laxity alter the relationship between strength and physical function in knee osteoarthritis?. *Arthritis Rheum* 1999;42(1):25-32.

Shea JD. Osteoarthritis of the knee: diagnosis and complications of treatment by high tibial osteotomy. *South Med J* 1973;66(9):1030-1034.

Shea MK,Houston DK,Nicklas BJ,Messier SP,Davis CC,Miller ME,Harris TB,Kitzman DW,Kennedy K,Kritchevsky SB. The effect of randomization to weight loss on total mortality in older overweight and obese adults: the ADAPT Study. *J Gerontol A Biol Sci Med Sci* 2010;65(5):519-525.

Shelbourne KD,Stube KC,Patel DV. Conservative treatment of degenerative joint disease of the knee using cold compression therapy. *Sports Exercise and Injury* 1996;2(4):176-180.

Shelbourne KD,Wilckens JH. Intraarticular anterior cruciate ligament reconstruction in the symptomatic arthritic knee. *Am J Sports Med* 1993;21(5):685-688.

Sheldon E,Beaulieu A,Paster Z,Dutta D,Yu S,Sloan VS. Efficacy and tolerability of Lumiracoxib in the treatment of osteoarthritis of the knee: a 13-week, randomized, double-blind comparison with Celecoxib and placebo. *Clin Ther* 2005;27(1):64-77.

Sheldon EA,Beaulieu A,Paster Z,Yu S,Rebuli R. Long-term efficacy and safety of Lumiracoxib 100mg: an open-label extension of a 13-week randomized controlled trial in patients with primary osteoarthritis of the knee. *Clin Exp Rheumatol* 2008;26(4):611-619.

Shen CL,James CR,Chyu MC,Bixby WR,Brismee JM,Zumwalt MA,Poklikuha G. Effects of Tai Chi on gait kinematics, physical function, and pain in elderly with knee osteoarthritis--a pilot study. *Am J Chin Med* 2008;36(2):219-232.

Shen H,Sprott H,Aeschlimann A,Gay RE,Michel BA,Gay S,Sprott H. Analgesic action of Acetaminophen in symptomatic osteoarthritis of the knee. *Rheumatology (Oxford)* 2006;45(6):765-770.

Shen X,Zhao L,Ding G,Tan M,Gao J,Wang L,Lao L. Effect of combined laser acupuncture on knee osteoarthritis: a pilot study. *Lasers Med Sci* 2009;24(2):129-136.

Shen Y,Liu F,Cao H,Ma A. Clinical manifestation and influence factors in patients with knee osteoarthritis. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2011 Feb;15(9):1643-1646.

Shephard NW,Steele CE. Comparison of tolmetin sodium with indomethacin in osteoarthritis. *Practitioner* 1981;225(1361):1696-1697.

Sherman AL,Ojeda-Correal G,Mena J. Use of Glucosamine and Chondroitin in Persons With Osteoarthritis. *PM and R* 2012 May;4(5 SUPPL.):S110-S116.

Sherman G,Zeller L,Avriel A,Friger M,Harari M,Sukenik S. Intermittent balneotherapy at the Dead Sea area for patients with knee osteoarthritis. *Isr Med Assoc J* 2009;11(2):88-93.

Shifman AC. The clinical response of 328 private patients to acupuncture therapy. *Am J Chin Med (Gard City N Y)* 1975;3(2):165-179.

Shimada S,Kobayashi S,Wada M,Uchida K,Sasaki S,Kawahara H,Yayama T,Kitade I,Kamei K,Kubota M,Baba H. Effects of disease severity on response to lateral wedged shoe insole for medial compartment knee osteoarthritis. *Arch Phys Med Rehabil* 2006;87(11):1436-1441.

Shimizu M,Higuchi H,Takagishi K,Shinozaki T,Kobayashi T. Clinical and biochemical characteristics after intra-articular injection for the treatment of osteoarthritis of the knee: prospective randomized study of sodium hyaluronate and corticosteroid. *J Orthop Sci* 2010;15(1):51-56.

Shoji H, Insall J. High tibial osteotomy for osteoarthritis of the knee with valgus deformity. *J Bone Joint Surg Am* 1973;55(5):963-973.

Sibbitt WL, Band PA, Kettwich LG, Chavez-Chiang NR, DeLea SL, Bankhurst AD. A randomized controlled trial evaluating the cost-effectiveness of sonographic guidance for intra-articular injection of the osteoarthritic knee. *J Clin Rheumatol* 2011 Dec;17(8):409-415.

Siclari A, Mascaro G, Gentili C, Cancedda R, Boux E. A Cell-free Scaffold-based Cartilage Repair Provides Improved Function Hyaline-like Repair at One year. *Clin Orthop Relat Res* 2011 Oct 1;.

Silva A, Serrao PR, Driusso P, Mattiello SM. The effects of therapeutic exercise on the balance of women with knee osteoarthritis: a systematic review. *Rev Bras Fisioter* 2012 Jan;16(1):1-9.

Simeoni E, Bauman A, Stenmark J, O'Brien J. Evaluation of a community arthritis program in Australia: dissemination of a developed program. *Arthritis Care Res* 1995;8(2):102-107.

Singer F, Oberleitner H. Osteoarthritis of the knee - Effectiveness of enzymes versus Diclofenac in acute phase of osteoarthritis of the knee - A randomized, double blind controlled study. *Wiener Medizinische Wochenschrift* 1996;146:55-58.

Singer F, Singer C, Oberleitner H. Phlogenzym(registered trademark) versus Diclofenac in the treatment of activated osteoarthritis of the knee. A double-blind prospective randomized study. *International Journal of Immunotherapy* 2001;17(2-4):135-141.

Singh BB, Berman BM, Hadhazy V, Bareta J, Lao L, Zarow FM, Hochberg M. Clinical decisions in the use of acupuncture as an adjunctive therapy for osteoarthritis of the knee. *Altern Ther Health Med* 2001;7(4):58-65.

Singh BB, Mishra L, Aquilina N, Kohlbeck F. Usefulness of guggul (*Commiphora mukul*) for osteoarthritis of the knee: An experimental case study. *Altern Ther Health Med* 2001;7(2):120, 112-120, 114.

Singh BB, Mishra LC, Vinjamury SP, Aquilina N, Singh VJ, Shepard N. The effectiveness of *Commiphora mukul* for osteoarthritis of the knee: an outcomes study. *Altern Ther Health Med* 2003;9(3):74-79.

Sirbu AB. Osteotomy of the lower extremity for degenerative arthritis and deformity. *J La State Med Soc* 1971;123(4):119-127.

Skwara A, Peterlein CD, Tibesku CO, Rosenbaum D, Fuchs-Winkelmann S. Changes of gait patterns and muscle activity after intraarticular treatment of patients with osteoarthritis of the knee: a prospective, randomised, doubleblind study. *Knee* 2009;16(6):466-472.

Sled EA, Khoja L, Deluzio KJ, Olney SJ, Culham EG. Effect of a Home Program of Hip Abductor Exercises on Knee Joint Loading, Strength, Function, and Pain in People With Knee Osteoarthritis: A Clinical Trial. *Phys Ther* 2010;.

Smith EM, Juvinall RC, Corell EB, Nyboer VJ. Bracing the unstable arthritic knee. *Arch Phys Med Rehabil* 1970;51(1):22-28.

Smith TO, Sexton D, Mitchell P, Hing CB. Opening- or closing-wedged high tibial osteotomy: A meta-analysis of clinical and radiological outcomes. *Knee* 2010 Oct 28;.

Smolen JS, Weinblatt ME. When patients with rheumatoid arthritis fail tumour necrosis factor inhibitors: what is the next step?. *Ann Rheum Dis* 2008 Nov;67(11):1497-1498.

Smugar SS, Schnitzer TJ, Weaver AL, Rubin BR, Polis AB, Tershakovec AM. Rofecoxib 12.5mg, Rofecoxib 25mg, and Celecoxib 200mg in the treatment of symptomatic osteoarthritis: results of two similarly designed studies. *Curr Med Res Opin* 2006;22(7):1353-1367.

Snijders GF, van den Ende CH, van den Bemt BJ, van Riel PL, van den Hoogen FH, den Broeder AA. Treatment outcomes of a Numeric Rating Scale (NRS)-guided pharmacological pain management strategy in symptomatic knee and hip osteoarthritis in daily clinical practice. *Clin Exp Rheumatol* 2012 Mar;30(2):164-170.

Soleimanpour H, Ghahramani K, Mehdizadeh ER. Successful low level laser therapy for knee osteoarthritis: A prospective descriptive study. *Pain Practice* 2012 Feb;12 SUPPL. 1:67-68.

Soles GR, Cabri J, Pascoa PJ. Cross-cultural adaptation and validation of the Portuguese version of the Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS). *Clin Rheumatol* 2008;27(11):1445-1449.

Solomon DH, Avorn J, Warsi A, Brown CH, Martin S, Martin TL, Wright J, Burgener M, Katz JN. Which patients with knee problems are likely to benefit from nonarthroplasty surgery? Development of a clinical prediction rule. *Arch Intern Med* 2004;164(5):509-513.

Solomon L, Abrams G. Orudis in the management of osteo-arthritis of the knee. A double-blind trial. *S Afr Med J* 1974;48(36):1526-1529.

Soltanian AR, Faghihzadeh S, Mehdibarzi D, Gerami A, Nasery M, Cheng J. Assessment of Marhame-Mafasel pomade effect on knee osteoarthritis with non-compliance. *Journal of Research in Health Sciences* 2009;9(2):19-24.

Somers TJ, Blumenthal JA, Guilak F, Kraus VB, Schmitt DO, Babyak MA, Craighead LW, Caldwell DS, Rice JR, McKee DC, Shelby RA, Campbell LC, Pells JJ, Sims EL, Queen R, Carson JW, Connelly M, Dixon KE, Lacaille LJ, Huebner JL, Rejeski WJ, Keefe FJ. Pain coping skills training and lifestyle behavioral weight management in patients with knee osteoarthritis: A randomized controlled study. *Pain* 2012 Jun;153(6):1199-1209.

Somers TJ, Keefe FJ, Carson JW, Pells JJ, Lacaille L. Pain catastrophizing in borderline morbidly obese and morbidly obese individuals with osteoarthritic knee pain. *Pain Res Manag* 2008;13(5):401-406.

Sommerlath KG. Results of meniscal repair and partial meniscectomy in stable knees. *Int Orthop* 1991;15(4):347-350.

Song EK, Seon JK, Park SJ, Jeong MS. The complications of high tibial osteotomy: closing- versus opening-wedge methods. *J Bone Joint Surg Br* 2010 Sep;92(9):1245-1252.

Song IH, Althoff CE, Hermann KG, Scheel AK, Knetsch T, Burmester GR, Backhaus M. Contrast-enhanced ultrasound in monitoring the efficacy of a bradykinin receptor 2 antagonist in painful knee osteoarthritis compared with MRI. *Ann Rheum Dis* 2009;68(1):75-83.

- Song R, Lee EO, Lam P, Bae SC. Effects of tai chi exercise on pain, balance, muscle strength, and perceived difficulties in physical functioning in older women with osteoarthritis: a randomized clinical trial. *J Rheumatol* 2003;30(9):2039-2044.
- Song R, Roberts BL, Lee EO, Lam P, Bae SC. A randomized study of the effects of t'ai chi on muscle strength, bone mineral density, and fear of falling in women with osteoarthritis. *J Altern Complement Med* 2010;16(3):227-233.
- Song WG, Wu T, Liu M. Clinical analysis of knee osteoarthritis treated mainly by acupuncture. *J Acu Tuina Sci* 2004;2:26.
- Sontakke S, Thawani V, Pimpalkhute S, Kabra P, Babhulkar S, Hingorani L. Open, randomized, controlled clinical trial of Boswellia serrata extract as compared to Valdecoxib in osteoarthritis of knee. *Indian Journal of Pharmacology* 2007;39(1):27-29.
- Sorensen TJ, Langberg H, Aaboe J, Bandholm T, Bliddal H, Henriksen M. The association between submaximal quadriceps force steadiness and the knee adduction moment during walking in patients with knee osteoarthritis. *J Orthop Sports Phys Ther* 2011 Aug;41(8):592-599.
- Soto-Molina H, Rizzoli-Cordoba A, Pizarro-Castellanos M, Delgado-Ginebra I, Tellez-Giron G. Cost utility analysis of chondroitin sulphate (CS) in the treatment of osteoarthritis (OA) of the knee in Mexican patients. *Value in Health* 2011 May;14(3):A129.
- Sowers M, Jannausch ML, Gross M, Karvonen-Gutierrez CA, Palmieri RM, Crutchfield M, Richards-McCullough K. Performance-based physical functioning in African-American and Caucasian women at midlife: considering body composition, quadriceps strength, and knee osteoarthritis. *Am J Epidemiol* 2006;163(10):950-958.
- Sowers M, Karvonen-Gutierrez CA, Jacobson JA, Jiang Y, Yosef M. Associations of anatomical measures from MRI with radiographically defined knee osteoarthritis score, pain, and physical functioning. *Journal of Bone and Joint Surgery - Series A* 2011;93(3):241-251.
- Sowers M, Karvonen-Gutierrez CA, Palmieri-Smith R, Jacobson JA, Jiang Y, Ashton-Miller JA. Knee osteoarthritis in obese women with cardiometabolic clustering. *Arthritis Rheum* 2009;61(10):1328-1336.
- Spahn G, Kirschbaum S, Kahl E. Factors that influence high tibial osteotomy results in patients with medial gonarthrosis: a score to predict the results. *Osteoarthritis Cartilage* 2006;14(2):190-195.
- Spahn G, Klinger HM, Muckley T, Hofmann GO. Four-year results from a randomized controlled study of knee chondroplasty with concomitant medial meniscectomy: mechanical debridement versus radiofrequency chondroplasty. *Arthroscopy* 2010 Sep;26(9 Suppl):S73-S80.
- Spahn G, Muckley T, Kahl E, Hofmann GO. Factors affecting the outcome of arthroscopy in medial-compartment osteoarthritis of the knee. *Arthroscopy* 2006;22(11):1233-1240.
- Spahn G, Muckley T, Klinger HM, Hofmann GO. Whole-Organ Arthroscopic Knee Score (WOAKS). *BMC Musculoskelet Disord* 2008;9:155.
- Spahn G. Complications in high tibial (medial opening wedge) osteotomy. *Arch Orthop Trauma Surg* 2004;124(10):649-653.

- Spector TD, Conaghan PG, Buckland-Wright JC, Garnero P, Cline GA, Beary JF, Valent DJ, Meyer JM. Effect of risedronate on joint structure and symptoms of knee osteoarthritis: results of the BRISK randomized, controlled trial [ISRCTN01928173]. *Arthritis Res Ther* 2005;7(3):R625-R633.
- Spector TD, Hart DJ, Byrne J, Harris PA, Dacre JE, Doyle DV. Definition of osteoarthritis of the knee for epidemiological studies. *Ann Rheum Dis* 1993;52(11):790-794.
- Sprague NF. Arthroscopic debridement for degenerative knee joint disease. *Clin Orthop Relat Res* 1981;(160):118-123.
- Stannus O, Jones G, Cicuttini F, Parameswaran V, Quinn S, Burgess J, Ding C. Circulating levels of IL-6 and TNF-(alpha) are associated with knee radiographic osteoarthritis and knee cartilage loss in older adults. *Osteoarthritis and Cartilage* 2010 Nov;18(11):1441-1447.
- Stanos SP. Topical Agents for the Management of Musculoskeletal Pain. *J Pain Symptom Manage* 2007;33(3):342-355.
- Staubli AE, De SC, Babst R, Lobenhoffer P. TomoFix: a new LCP-concept for open wedge osteotomy of the medial proximal tibia--early results in 92 cases. *Injury* 2003;34 Suppl 2:B55-B62.
- Steadman JR, Ramappa AJ, Maxwell RB, Briggs KK. An arthroscopic treatment regimen for osteoarthritis of the knee. *Arthroscopy* 2007;23(9):948-955.
- Stein T, Mehling AP, Welsch F, von Eisenhart-Rothe R, Jager A. Long-term outcome after arthroscopic meniscal repair versus arthroscopic partial meniscectomy for traumatic meniscal tears. *Am J Sports Med* 2010 Aug;38(8):1542-1548.
- Stengaard-Pedersen K, Ekesbo R, Karvonen AL, Lyster M. Celecoxib 200mg q.d. is efficacious in the management of osteoarthritis of the knee or hip regardless of the time of dosing. *Rheumatology (Oxford)* 2004;43(5):592-595.
- Sterett WI, Steadman JR, Huang MJ, Matheny LM, Briggs KK. Chondral Resurfacing and High Tibial Osteotomy in the Varus Knee: Survivorship Analysis. *Am J Sports Med* 2010;.
- Sterett WI, Steadman JR. Chondral resurfacing and high tibial osteotomy in the varus knee. *Am J Sports Med* 2004;32(5):1243-1249.
- Sternheim A, Garbedian S, Backstein D. Distal femoral varus osteotomy: unloading the lateral compartment: long-term follow-up of 45 medial closing wedge osteotomies. *Orthopedics* 2011 Sep;34(9):e488-e490.
- Steultjens MP, Dekker J, van Baar ME, Oostendorp RA, Bijlsma JW. Muscle strength, pain and disability in patients with osteoarthritis. *Clin Rehabil* 2001;15(3):331-341.
- Stiglic-Rogoznica N, Stamenkovic D, Frlan-Vrgoc L, Avancini-Dobrovic V, Vrbanic TS. Analgesic effect of high intensity laser therapy in knee osteoarthritis. *Coll Antropol* 2011 Sep;35 Suppl 2:183-185.
- Stitik TP, Altschuler E, Foye PM. Pharmacotherapy of osteoarthritis. *Am J Phys Med Rehabil* 2006;85(11):.

- Stitik TP,Blacksin MF,Stiskal DM,Kim JH,Foye PM,Schoenherr L,Choi ES,Chen B,Saunders HJ,Nadler SF. Efficacy and safety of hyaluronan treatment in combination therapy with home exercise for knee osteoarthritis pain. *Arch Phys Med Rehabil* 2007;88(2):135-141.
- Stitik TP,Kumar A,Foye PM. Corticosteroid injections for osteoarthritis. *Am J Phys Med Rehabil* 2006;85(11):.
- Stitik TP,Levy JA. Viscosupplementation (biosupplementation) for osteoarthritis. *Am J Phys Med Rehabil* 2006;85(11):.
- Stitik TP,Yonclas P,Foye PM,Schoenherr L. Osteoarthritis of the knee and hip: Practical nondrug steps to successful therapy. *Consultant* 2005;45(12):1248-1258.
- Stoneman PD. Effect of manual therapy and exercise on pain, stiffness and function in persons with knee osteoarthritis [dissertation]. 2001;.
- Strand LI,Ljunggren AE,Bogen B,Ask T,Johnsen TB. The Short-Form McGill Pain Questionnaire as an outcome measure: test-retest reliability and responsiveness to change. *Eur J Pain* 2008;12(7):917-925.
- Strand V,Baraf HS,Lavin PT,Lim S,Hosokawa H. A multicenter, randomized controlled trial comparing a single intra-articular injection of Gel-200, a new cross-linked formulation of hyaluronic acid, to phosphate buffered saline for treatment of osteoarthritis of the knee. *Osteoarthritis Cartilage* 2012 May;20(5):350-356.
- Strand V,Simon LS,Dougados M,Sands GH,Bhadra P,Breazna A,Immitt J. Treatment of Osteoarthritis with Continuous Versus Intermittent Celecoxib . *J Rheumatol* 2011 Nov 1;.
- Stratford PW,Kennedy DM,Woodhouse LJ. Performance measures provide assessments of pain and function in people with advanced osteoarthritis of the hip or knee. *Phys Ther* 2006;86(11):1489-1496.
- Stuart MJ,Grace JN,Ilstrup DM,Kelly CM,Adams RA,Morrey BF. Late recurrence of varus deformity after proximal tibial osteotomy. *Clin Orthop Relat Res* 1990;(260):61-65.
- Stucki G,Bozzzone P,Treuer E,Wassmer P,Felder M. Efficacy and safety of radiation synovectomy with yttrium-90: A retrospective long-term analysis of 164 applications in 82 patients. *Br J Rheumatol* 1993;32(5):383-386.
- Sturmer T,Gunther KP,Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study. *J Clin Epidemiol* 2000;53(3):307-313.
- Sturnieks DL,Besier TF,Hamer PW,Ackland TR,Mills PM,Stachowiak GW,Podsiadlo P,Lloyd DG. Knee strength and knee adduction moments following arthroscopic partial meniscectomy. *Med Sci Sports Exerc* 2008;40(6):991-997.
- Sturnieks DL,Besier TF,Lloyd DG. Muscle activations to stabilize the knee following arthroscopic partial meniscectomy. *Clin Biomech (Bristol , Avon)* 2011 Mar;26(3):292-297.
- Su JY,Chang JK,Lu YM,Lin SY. Arthroscopic debridement for osteoarthritis of the knee: a seven years follow-up study. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1995;11(12):667-672.

Suarez-Almazor ME. Is treatment with pulsed electromagnetic fields effective in patients with knee osteoarthritis?. *Nat Clin Pract Rheumatol* 2006;2(1):14-15.

Sugimoto H,Yamada H,Terada N,Kanaji A,Kato S,Date H,Ichinose H,Miyazaki K. Intraarticular injection of high molecular weight hyaluronan for osteoarthritis of the knee - prediction of effectiveness with biological markers. *J Rheumatol* 2006;33(12):2527.

Sun SF,Hsu CW,Hwang CW,Hsu PT,Wang JL,Tsai SL,Chou YJ,Hsu YW,Huang CM,Wang YL. Hyaluronate improves pain, physical function and balance in the geriatric osteoarthritic knee: a 6-month follow-up study using clinical tests. *Osteoarthritis Cartilage* 2006;14(7):696-701.

Sundermann HH,Rechziegler H,Dullenkopf B. Double-blind study of acemetacine and Naproxen in patients with osteoarthrosis. *Medizinische Welt* 1995;46:101-105.

Superio-Cabuslay E,Ward MM,Lorig KR. Patient education interventions in osteoarthritis and rheumatoid arthritis: a meta-analytic comparison with nonsteroidal antiinflammatory drug treatment. *Arthritis Care Res* 1996;9(4):292-301.

Surin V,Markhede G,Sundholm K. Factors influencing results of high tibial osteotomy in gonarthrosis. *Acta Orthop Scand* 1975;46(6):996-1007.

Sutbeyaz ST,Sezer N,Koseoglu BF,Ibrahimoglu F,Tekin D. Influence of knee osteoarthritis on exercise capacity and quality of life in obese adults. *Obesity (Silver Spring)* 2007;15(8):2071-2076.

Sutipornpalangkul W,Pichaisak W. Comparison of arthroscopic and open arthrotomy treatment of septic arthritis of the knee in Thai patients. *Osteoporos Int* 2012;23 SUPPL. 2:S112-S113.

Sutton AJ,Muir KR,Mockett S,Fentem P. A case-control study to investigate the relation between low and moderate levels of physical activity and osteoarthritis of the knee using data collected as part of the Allied Dunbar National Fitness Survey. *Ann Rheum Dis* 2001;60(8):756-764.

Svarcova J,Trnavsky K,Zvarova J. The influence of ultrasound, galvanic currents and shortwave diathermy on pain intensity in patients with osteoarthritis. *Scand J Rheumatol Suppl* 1987;67:83-85.

Svensson O,Malmenas M,Fajutrao L,Roos EM,Lohmander LS. Greater reduction of knee than hip pain in osteoarthritis treated with Naproxen, as evaluated by WOMAC and SF-36. *Ann Rheum Dis* 2006;65(6):781-784.

Swank AM. Prehabilitation before total knee arthroplasty increases strength and function in older adults with severe osteoarthritis. 2011.

Szanto E. Long-term follow-up of 90Yttrium-treated knee-joint arthritis. *Scand J Rheumatol* 1977;6(4):209-212.

Szucs L,Ratko I,Lesko T,Szoor I,Genti G,Balint G. Double-blind trial on the effectiveness of the Puspokladany thermal water on arthrosis of the knee-joints. *J R Soc Health* 1989;109(1):7-9.

Tagesson S,Oberg B,Good L,Kvist J. A comprehensive rehabilitation program with quadriceps strengthening in closed versus open kinetic chain exercise in patients with anterior cruciate ligament deficiency: a randomized clinical trial evaluating dynamic tibial translation and muscle function. *Am J Sports Med* 2008;36(2):298-307.

Takahashi S, Tomihisa K, Saito T. Decrease of osteosclerosis in subchondral bone of medial compartmental osteoarthritic knee seven to nineteen years after high tibial valgus osteotomy. *Bull Hosp Jt Dis* 2002;61(1-2):58-62.

Takahashi T, Wada Y, Tanaka M, Iwagawa M, Ikeuchi M, Hirose D, Yamamoto H. Dome-shaped proximal tibial osteotomy using percutaneous drilling for osteoarthritis of the knee. *Arch Orthop Trauma Surg* 2000;120(1-2):32-37.

Takeda W, Wessel J. Acupuncture for the treatment of pain of osteoarthritic knees. *Arthritis Care Res* 1994;7(3):118-122.

Takeuchi R, Ishikawa H, Aratake M, Bito H, Saito I, Kumagai K, Akamatsu Y, Saito T. Medial opening wedge high tibial osteotomy with early full weight bearing. *Arthroscopy* 2009;25(1):46-53.

Takeuchi R, Ishikawa H, Kumagai K, Yamaguchi Y, Chiba N, Akamatsu Y, Saito T. Fractures Around the Lateral Cortical Hinge After a Medial Opening-Wedge High Tibial Osteotomy: A New Classification of Lateral Hinge Fracture. *Arthroscopy* 2011 Oct 7;.

Talbot LA, Gaines JM, Huynh TN, Metter EJ. A home-based pedometer-driven walking program to increase physical activity in older adults with osteoarthritis of the knee: a preliminary study. *J Am Geriatr Soc* 2003;51(3):387-392.

Talbot LA, Gaines JM, Ling SM, Metter EJ. A home-based protocol of electrical muscle stimulation for quadriceps muscle strength in older adults with osteoarthritis of the knee. *J Rheumatol* 2003;30(7):1571-1578.

Tamir E, Robinson D, Koren R, Agar G, Halperin N. Intra-articular hyaluronan injections for the treatment of osteoarthritis of the knee: a randomized, double blind, placebo controlled study. *Clin Exp Rheumatol* 2001;19(3):265-270.

Tan J, Balci N, Sepici V, Gener FA. Isokinetic and isometric strength in osteoarthrosis of the knee. A comparative study with healthy women. *Am J Phys Med Rehabil* 1995;74(5):364-369.

Tan PH, Buerkle H, Cheng JT, Shih HC, Chou WY, Yang LC. Double-blind parallel comparison of multiple doses of apraclonidine, clonidine, and placebo administered intra-articularly to patients undergoing arthroscopic knee surgery. *Clin J Pain* 2004;20(4):256-260.

Tanaka S, Ito T, Mori E, Muroga T, Nakajima A. Double-blind study of Naproxen in osteoarthritis of the knee joint. *J Rheumatol* 1976;3(1):27-36.

Tanamas SK, Wluka AE, Davies-Tuck M, Wang Y, Strauss BJ, Proietto J, Dixon JB, Jones G, Cicuttini FM. Weight gain is associated with worse knee symptoms in community-based men and women: A longitudinal study. *Obesity Research and Clinical Practice* 2011;5 SUPPL. 1:S50.

Tander B, Canturk F, Cengiz K, Durmus D, Akyol Y. Are the physical therapeutic modalities really safe?. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi* 2005;51(4):131-133.

Tang WC, Henderson IJ. High tibial osteotomy: long term survival analysis and patients' perspective. *Knee* 2005;12(6):410-413.

- Tangtrakulwanich B, Chongsuvivatwong V, Geater AF. Associations between floor activities and knee osteoarthritis in Thai Buddhist monks: the Songkhla study. *J Med Assoc Thai* 2006;89(11):1902-1908.
- Tangtrakulwanich B, Chongsuvivatwong V, Geater AF. Habitual floor activities increase risk of knee osteoarthritis. *Clin Orthop* 2007;(454):147-154.
- Tanner SM, Dainty KN, Marx RG, Kirkley A. Knee-specific quality-of-life instruments: Which ones measure symptoms and disabilities most important to patients?. *Am J Sports Med* 2007;35(9):1450-1458.
- Tarigan TJ, Kasjmir YI, Atmakusuma D, Lydia A, Bashiruddin J, Kusumawijaya K, Prihartono J. The degree of radiographic abnormalities and postural instability in patients with knee osteoarthritis. *Acta Med Indones* 2009;41(1):15-19.
- Tascioglu F, Armagan O, Tabak Y, Corapci I, Oner C. Low power laser treatment in patients with knee osteoarthritis. *Swiss Med Wkly* 2004;134(17-18):254-258.
- Tasciotaoglu F, Oner C. Efficacy of intra-articular sodium hyaluronate in the treatment of knee osteoarthritis. *Clin Rheumatol* 2003;22(2):112-117.
- Teekachunhatean S, Kunanusorn P, Rojanasthien N, Sananpanich K, Pojchamarnwiputh S, Lhieochaiphunt S, Pruksakorn S. Chinese herbal recipe versus Diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial [ISRCTN70292892]. *BMC Complement Altern Med* 2004;4:19.
- Teixeira F, Porto A, Moura J. Efficacy of a single daily dose of a nonsteroidal anti-inflammatory drug with an intermediate plasma half-life: A double-blind, comparative trial of acemetacin and Piroxicam. *Current Therapeutic Research, Clinical & Experimental* 1993;53:103-112.
- Telhag H, Bach-Andersen R, Persson B. A double-blind comparative evaluation of tolmetin versus Naproxen in osteoarthritis. *Curr Med Res Opin* 1981;7(6):392-400.
- Telhag H. Niflumic acid in osteoarthrosis. A comparative study of niflumic acid and indomethacin in osteoarthrosis of the knee. *Scand J Rheumatol* 1973;(1):Suppl-5.
- Telhag H. Niflumic acid in osteoarthrosis. Long term tolerance. *Scand J Rheumatol* 1973;(1):Suppl-9.
- Temple AR, Benson GD, Zinsenheim JR, Schweinle JE. Multicenter, randomized, double-blind, active-controlled, parallel-group trial of the long-term (6-12 months) safety of Acetaminophen in adult patients with osteoarthritis. *Clin Ther* 2006;28(2):222-235.
- Terry GC, Cimino PM. Distal femoral osteotomy for valgus deformity of the knee. *Orthopedics* 1992;15(11):1283-1289.
- Tetik S, Ones K, Tetik C. Efficacy of intra-articular Hylan G-F 20 on osteoarthritis of the knee. *Pain Clinic* 2003;15(4):459-466.
- Teule M. Double-blind comparative multicenter study of the efficacy and safety of a slow-release tablet of 200-mg Ketoprofen once daily and a 50-mg Ketoprofen capsule four times daily. *CURR THER RES, CLIN EXP* 1986;40:1129-1146.

Thamsborg G,Florescu A,Oturai P,Fallentin E,Tritsaris K,Dissing S. Treatment of knee osteoarthritis with pulsed electromagnetic fields: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage* 2005;13(7):575-581.

Theiler R,Bischoff HA,Good M,Uebelhart D. Rofecoxib improves quality of life in patients with hip or knee osteoarthritis. *Swiss Med Wkly* 2002;132(39-40):566-573.

Theiler R,Bischoff-Ferrari HA,Good M,Bellamy N. Responsiveness of the electronic touch screen WOMAC 3.1 OA Index in a short term clinical trial with Rofecoxib . *Osteoarthritis Cartilage* 2004;12(11):912-916.

Theiler R,Bruhlmann P. Overall tolerability and analgesic activity of intra-articular sodium hyaluronate in the treatment of knee osteoarthritis. *Curr Med Res Opin* 2005;21(11):1727-1733.

Thein R,Haviv B,Kidron A,Bronak S. Intra-articular injection of hyaluronic acid following arthroscopic partial meniscectomy of the knee. *Orthopedics* 2010 Oct;33(10):724.

Theodosakis J. A randomized, double blind, placebo controlled trial of a topical cream containing glucosamine sulfate, chondroitin sulfate, and camphor for osteoarthritis of the knee. *The Journal of rheumatology* 2004;31:826-827.

Thiengwittayaporn S,Wetpityakul P,Foosakun Y,Ngamsom T,Vathanavit P,Pintongtun J. Comparison of the accuracy of quadriceps isometric exercise between using quadriceps education device (QED) and not using QED for osteoarthritic knee patients: a randomized controlled trial. *J Med Assoc Thai* 2009;92 Suppl 6:S33-S38.

Thomas KS,Miller P,Doherty M,Muir KR,Jones AC,O'Reilly SC. Cost effectiveness of a two-year home exercise program for the treatment of knee pain. *Arthritis Rheum* 2005;53(3):388-394.

Thomas KS,Muir KR,Doherty M,Jones AC,O'Reilly SC,Bassey EJ. Home-based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial. *BMJ* 2002;325(7367):752.

Thomas SG,Pagura SM,Kennedy D. Physical activity and its relationship to physical performance in patients with end stage knee osteoarthritis. *J Orthop Sports Phys Ther* 2003;33(12):745-754.

Thompson LR,Boudreau R,Newman AB,Hannon MJ,Chu CR,Nevitt MC,Kent KC. The association of osteoarthritis risk factors with localized, regional and diffuse knee pain. *Osteoarthritis Cartilage* 2010 Oct;18(10):1244-1249.

Thorlund JB,Aagaard P,Roos EM. Thigh muscle strength, functional capacity, and self-reported function in patients at high risk of knee osteoarthritis compared with controls. *Arthritis Care Res (Hoboken)* 2010 Sep;62(9):1244-1251.

Thorpe P. Intra-articular triamcinolone acetonide and methylprednisolone acetate in arthritis. *Current Therapeutic Research - Clinical and Experimental* 1985;38(3):513-518.

Thorstensson CA,Henriksson M,von PA,Sjodahl C,Roos EM. The effect of eight weeks of exercise on knee adduction moment in early knee osteoarthritis--a pilot study. *Osteoarthritis Cartilage* 2007;15(10):1163-1170.

- Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858]. *BMC Musculoskelet Disord* 2005;6:27.
- Tiew GK. Open wedge high tibial osteotomy using allo and autogeneous bone graft. *Journal of the Western Pacific Orthopaedic Association* 1992;29(2):93-98.
- Tiffreau V, Mulleman D, Coudeyre E, Lefevre-Colau MM, Revel M, Rannou F. The value of individual or collective group exercise programs for knee or hip osteoarthritis. Clinical practice recommendations. *Ann Readapt Med Phys* 2007;50(9):741-40.
- Tiffreau V, Mulleman D, Coudeyre E, Lefevre-Colau MM, Revel M, Rannou F. The value of individual or collective group exercise programs for knee or hip osteoarthritis. Elaboration of French clinical practice guidelines. *Annales de Readaptation et de Medecine Physique* 2007;50(9):741-746.
- Tigani D, Ferrari D, Trentani P, Barbanti-Brodano G, Trentani F. Patellar height after high tibial osteotomy. *Int Orthop* 2001;24(6):331-334.
- Tigani D, Trentani F, Trentani P, Fravisini M. Closing-wedge tibial osteotomy with a compression-dynamic fixation system. *Techniques in Knee Surgery* 2007;6(1):42-50.
- Tillu A, Tillu S, Vowler S. Effect of acupuncture on knee function in advanced osteoarthritis of the knee: a prospective, non-randomised controlled study. *Acupunct Med* 2002;20(1):19-21.
- Tilwe GH, Beria S, Turakhia NH, Daftary GV, Schiess W. Efficacy and tolerability of oral enzyme therapy as compared to Diclofenac in active osteoarthrosis of knee joint: an open randomized controlled clinical trial. *J Assoc Physicians India* 2001;49:617-621.
- Timoney JM, Kneisl JS, Barrack RL, Alexander AH. Arthroscopy in the osteoarthritic knee: Long-term follow-up. *Orthop Rev* 1990;19(4):371-382.
- Timoney JM, Kneisl JS, Barrack RL, Alexander AH. Arthroscopy update #6. Arthroscopy in the osteoarthritic knee. Long-term follow-up. *Orthop Rev* 1990;19(4):371-379.
- Tishler M, Rosenberg O, Levy O, Elias I, Amit-Vazina M. The effect of balneotherapy on osteoarthritis. Is an intermittent regimen effective?. *Eur J Intern Med* 2004;15(2):93-96.
- Tive L, Schnitzer TJ, Katz N, Evans R, Shelton D. Tanezumab, a humanized anti-nerve growth factor antibody in the treatment of three chronic pain types. *Pain Medicine* 2010;Conference: 26th Annual Meeting of the American Ac:.
- Tjornstrand B, Egund N, Hagstedt B, Lindstrand A. Tibial osteotomy in medial gonarthrosis. The importance of over-correction of varus deformity. *Arch Orthop Trauma Surg* 1981;99(2):83-89.
- Tjornstrand B, Hagstedt B, Persson BM. Results of surgical treatment for non-union after high tibial osteotomy in osteoarthritis of the knee. *J Bone Joint Surg Am* 1978;60(7):973-977.
- Tjornstrand B, Svensson K, Thorngren KG. Prediction of long-term outcome of tibial osteotomy in medial gonarthrosis. *Arch Orthop Trauma Surg* 1985;103(6):396-401.

Tjornstrand BA, Egund N, Hagstedt BV. High tibial osteotomy: a seven-year clinical and radiographic follow-up. *Clin Orthop Relat Res* 1981;(160):124-136.

Toda Y, Kato A, Tsukimura N. Dynamic effect of an elastically strapped lateral wedged insole on the subtalar joint in convenient foot print analysis using facsimile paper. *Modern Rheumatology* 2003;13(3):215-219.

Toda Y, Segal N, Kato A, Yamamoto S, Irie M. Correlation between body composition and efficacy of lateral wedged insoles for medial compartment osteoarthritis of the knee. *J Rheumatol* 2002;29(3):541-545.

Toda Y, Segal N, Kato A, Yamamoto S, Irie M. Effect of a novel insole on the subtalar joint of patients with medial compartment osteoarthritis of the knee. *J Rheumatol* 2001;28(12):2705-2710.

Toda Y, Segal N. Usefulness of an insole with subtalar strapping for analgesia in patients with medial compartment osteoarthritis of the knee. *Arthritis Rheum* 2002;47(5):468-473.

Toda Y, Tsukimura N, Kato A. The effects of different elevations of laterally wedged insoles with subtalar strapping on medial compartment osteoarthritis of the knee. *Arch Phys Med Rehabil* 2004;85(4):673-677.

Toda Y, Tsukimura N, Segal N. An optimal duration of daily wear for an insole with subtalar strapping in patients with varus deformity osteoarthritis of the knee. *Osteoarthritis Cartilage* 2005;13(4):353-360.

Toft B, Christophersen J, Christensen N, Hesselsoe G, Mikkelsen S, Aaboe T, Mose K, Thorsager T, Jakobsen G. A double-blind, crossover study of a sustained-release tablet of Ketoprofen and normal Ketoprofen capsules in the treatment of patients with osteoarthritis. *Curr Med Res Opin* 1985;9(10):708-712.

Toh EM, Prasad PS, Teanby D. Correlating the efficacy of knee viscosupplementation with osteoarthritic changes on roentgenological examination. *Knee* 2002;9(4):321-330.

Tohyama H, Yasuda K, Kaneda K. Treatment of osteoarthritis of the knee with heel wedges. *Int Orthop* 1991;15(1):31-33.

Torgerson WR, Kettelkamp DB, Igou RA, Leach RE. Tibial osteotomy for the treatment of degenerative arthritis of the knee. *Clin Orthop Relat Res* 1974;(101):46-52.

Touma Z, Chen L, Arayssi T. Topical nonsteroidal anti-inflammatory drugs in the treatment of osteoarthritis. *Future Rheumatology* 2007;2(2):163-175.

Towheed T, Maxwell L, Anastassiades TP, Shea B, Houpt JB, Welch V, Hochberg MC, Wells GA. Glucosamine therapy for treating osteoarthritis. *Cochrane Database of Systematic Reviews* 2009;(4 Article Number):.

Townsend RR, Bakris GL, Erdy G, Hazan L, Hall CE, Longlade P, Fleming R. A 12-week, double-blind, randomized, forced-titration, parallel group study to assess the effects of Naproxen versus Naproxen on arterial blood pressure as measured by ambulatory blood pressure monitoring in osteoarthritis patients with controlled essential hypertension. *Journal* 2009;11:A136.

Trans T, Aaboe J, Henriksen M, Christensen R, Bliddal H, Lund H. Effect of whole body vibration exercise on muscle strength and proprioception in females with knee osteoarthritis. *Knee* 2009;16(4):256-261.

- Trelles MA, Rigau J, Sala P, Calderhead G, Ohshiro T. Infrared diode laser in low reactive-level laser therapy (LLLT) for knee osteoarthritis. *Laser Therapy* 1991;3(4):149-153.
- Trnavsky K, Fischer M, Vogtle-Junkert U, Schreyger F. Efficacy and safety of 5% ibuprofen cream treatment in knee osteoarthritis. Results of a randomized, double-blind, placebo-controlled study. *J Rheumatol* 2004;31(3):565-572.
- Trock DH, Bollet AJ, Markoll R. The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee and cervical spine. Report of randomized, double blind, placebo controlled trials. *J Rheumatol* 1994;21(10):1903-1911.
- Trombini-Souza F, Yokota M, Matias A, Goldenstein-Schainberg C, Fuller R, Sacco ICN. Benefic effect of the use of flexible and minimalist footwear on knee osteoarthritis. *Osteoporos Int* 2012;23 SUPPL. 2:S355-S356.
- Tsai PF, Beck C, Chang JY, Hagen J, Kuo YF, Roberson PK, Rosengren K, Beuscher L, Doan CL, Anand KJ. The effect of tai chi on knee osteoarthritis pain in cognitively impaired elders: pilot study. *Geriatr Nurs* 2009;30(2):132-139.
- Tsai PF, Beck C, Richards KC, Phillips L, Roberson PK, Evans J. The Pain Behaviors for Osteoarthritis Instrument for Cognitively Impaired Elders (PBOICIE). *Res Gerontol Nurs* 2008;1(2):116-122.
- Tsauo JY, Cheng PF, Yang RS. The effects of sensorimotor training on knee proprioception and function for patients with knee osteoarthritis: a preliminary report. *Clin Rehabil* 2008;22(5):448-457.
- Tsuchida T, Yasuda K, Aoki Y, Ohzeki S, Hiraoka M, Hara R. Change of alignment of lower extremity through ten years after high tibial osteomy in medial osteoarthritic knees. *Hokkaido Journal of Orthopedic and Traumatic Surgery* 1990;33(2):17-23.
- TSUYAMA N, KUROKAWA T, NAGANO A, NIHEI R, TACHIBANA N, HANAOKA K. Clinical Evaluation of L-141 Ointment on Arthritis Deformans of Knee. *Rinsho Iyaku* 1985;1:697-729.
- Tubach F, Dougados M, Falissard B, Baron G, Logeart I, Ravaud P. Feeling good rather than feeling better matters more to patients. *Arthritis Rheum* 2006;55(4):526-530.
- Tubach F, Giraudeau B, Ravaud P. The variability in minimal clinically important difference and patient acceptable symptomatic state values did not have an impact on treatment effect estimates. *J Clin Epidemiol* 2009;62(7):725-728.
- Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, Bombardier C, Felson D, Hochberg M, van der Heijde D, Dougados M. Evaluation of clinically relevant states in patient reported outcomes in knee and hip osteoarthritis: the patient acceptable symptom state. *Ann Rheum Dis* 2005;64(1):34-37.
- Tugwell PS, Wells GA, Shainhouse JZ. Equivalence study of a topical Diclofenac solution (pennsaid) compared with oral Diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *J Rheumatol* 2004;31(10):2002-2012.
- Tukker A, Visscher TL, Picavet HS. Overweight and health problems of the lower extremities: osteoarthritis, pain and disability. *Public Health Nutr* 2009;12(3):359-368.

- Tukmachi E, Jubb R, Dempsey E, Jones P. The effect of acupuncture on the symptoms of knee osteoarthritis--an open randomised controlled study. *Acupunct Med* 2004;22(1):14-22.
- Turajane T, Tanavaree A, Labpiboonpong V, Maungsiri S. Outcomes of intra-articular injection of sodium hyaluronate for the treatment of osteoarthritis of the knee. *J Med Assoc Thai* 2007;90(9):1845-1852.
- Turajane T, Wongbunnak R, Patcharatrakul T, Ratansumawong K, Poigampetch Y, Songpatanasilp T. Gastrointestinal and cardiovascular risk of non-selective NSAIDs and COX-2 inhibitors in elderly patients with knee osteoarthritis. *J Med Assoc Thai* 2009;92 Suppl 6:S19-S26.
- Turi G, Boscaro C, De BG. Double-blind comparative study of isoxicam and Naproxen in the treatment of patients with osteoarthritis. *CURR THER RES, CLIN EXP* 1983;33:83-88.
- Tuzun EH, Aytar A, Eker L, Daskapan A. Effectiveness of two different physical therapy programmes in the treatment of knee osteoarthritis. *Pain Clinic* 2004;16(4):379-387.
- Tuzun EH, Otman S, Kirdi N. Comparison of different methods of pulsed shortwave diathermy in knee osteoarthritis. *Pain Clinic* 2003;15(4):421-427.
- Uebelhart D, Knols R, de Bruin ED, Verbruggen G. Treatment of knee osteoarthritis with oral chondroitin sulfate. *Adv Pharmacol* 2006;53:523-539.
- Uebelhart D, Knussel O, Theiler R. Efficacy and tolerability of oral avian chondroitin sulfate in painful knee osteoarthritis. *Schweizerische Medizinische Wochenschrift* 1999;129:1174.
- Uebelhart D, Thonar EJ, Delmas PD, Chantaine A, Vignon E. Effects of oral chondroitin sulfate on the progression of knee osteoarthritis: a pilot study. *Osteoarthritis Cartilage* 1998;6 Suppl A:39-46.
- Underwood M, Ashby D, Cross P, Hennessy E, Letley L, Martin J, Mt-Isa S, Parsons S, Vickers M, Whyte K. Advice to use topical or oral ibuprofen for chronic knee pain in older people: randomised controlled trial and patient preference study. *BMJ* 2008;336(7636):138-142.
- Unlu Z, Ay K. Intra-articular injection of tenoxicam in the treatment of osteoarthritis of the knee. *Journal of Musculoskeletal Pain* 2006;14(4):37-47.
- Unsal S, Caglar YH, Kaya K, Sahin OS, Ozel S. [Comparison of effectiveness of intraarticular sodium hyaluronat and physical therapy applications in patients with knee osteoarthritis: randomized prospective study]. *Journal of Rheumatology and Medical Rehabilitation* 2008;19:16-22.
- Usha PR, Naidu MU. Randomised, Double-Blind, Parallel, Placebo-Controlled Study of Oral Glucosamine, Methylsulfonylmethane and their Combination in Osteoarthritis. *Clin Drug Investig* 2004;24(6):353-363.
- Usha PR, Naidu MUR. Clinical evaluation of eazmov plus in patients of osteoarthritis. *Phytomedica* 2006;7:21-30.
- Vaht M, Birkenfeldt R, Ubner M. An evaluation of the effect of differing lengths of spa therapy upon patients with osteoarthritis (OA). *Complement Ther Clin Pract* 2008;14(1):60-64.
- Vainionpaa S, Laike E, Kirves P, Tiusanen P. Tibial osteotomy for osteoarthritis of the knee. A five to ten-year follow-up study. *J Bone Joint Surg Am* 1981;63(6):938-946.

- Vajaradul Y. Double-blind clinical evaluation of intra-articular glucosamine in outpatients with gonarthrosis. *Clin Ther* 1981;3(5):336-343.
- Vajranetra P. Clinical trial of glucosamine compounds for osteoarthritis of knee joints. *J Med Assoc Thai* 1984;67(7):409-418.
- Valenti JR, Calvo R, Lopez R, Canadell J. Long term evaluation of high tibial valgus osteotomy. *Int Orthop* 1990;14(4):347-349.
- Vallow S, Sanga P, Polverejan E, Wang S, Kelly K, Thipphawong J. Impact of pain relief with fulranumab in the treatment of patients with moderate to severe osteoarthritis pain. *Journal of Pain* 2011 Apr;12(4 SUPPL. 1):54.
- Valtonen EJ, Alaranta H. Comparative clinical study of the effect of short-wave and long-wave diathermy on osteo-arthritis of the knee and hip. *Scand J Rehabil Med* 1971;3(3):109-112.
- Valtonen EJ. Clinical comparison of fenbufen and aspirin in osteoarthritis. *Scand J Rheumatol Suppl* 1979;(27):1-7.
- Valtonen J. Clinical comparison of triamcinolonehexacetonide and betamethasone in the treatment of osteoarthritis of the knee-joint. *Scand J Rheumatol* 1981;10(Suppl. 41):3-7.
- van Baar ME, Assendelft WJ, Dekker J. Review: Exercise therapy may reduce pain and disability in osteoarthritis of the hip or knee. *Evidence-Based Medicine* 2000;5(2):53.
- van Baar ME, Dekker J, Oostendorp RA, Bijl D, Voorn TB, Bijlsma JW. Effectiveness of exercise in patients with osteoarthritis of hip or knee: nine months' follow-up. *Ann Rheum Dis* 2001;60(12):1123-1130.
- van Baar ME, Dekker J, Oostendorp RA, Bijl D, Voorn TB, Lemmens JA, Bijlsma JW. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. *J Rheumatol* 1998;25(12):2432-2439.
- van den Bekerom MP, Patt TW, Kleinhout MY, van der Vis HM, Albers GH. Early complications after high tibial osteotomy: a comparison of two techniques. *J Knee Surg* 2008;21(1):68-74.
- van den Ende E. Taping reduces pain and disability in patients with knee osteoarthritis. *Aust J Physiother* 2004;50(3):186.
- van der Esch M, Steultjens M, Harlaar J, Wolterbeek N, Knol D, Dekker J. Varus-valgus motion and functional ability in patients with knee osteoarthritis. *Ann Rheum Dis* 2008;67(4):471-477.
- van der Goes MC, Straub RH, Wenting MJG, Capellino S, Jacobs JWG, Jahangier ZN, Rauch L, Bijlsma JWJ, Lافeber FPJG. Intra-articular glucocorticoid injections decrease the number of steroid hormone receptor positive cells in synovial tissue of patients with persistent knee arthritis. *Annals of the Rheumatic Diseases* 2012;. Date of Publication(13 Apr 2012):.
- van Dijk GM, Veenhof C, Spreeuwenberg P, Coene N, Burger BJ, van SD, van den Ende CH, Lankhorst GJ, Dekker J. Prognosis of limitations in activities in osteoarthritis of the hip or knee: a 3-year cohort study. *Arch Phys Med Rehabil* 2010;91(1):58-66.

van Es PP,Luijsterburg PA,Dekker J,Koopmanschap MA,Bohnen AM,Verhaar JA,Koes BW,Bierma-Zeinstra SM. Cost-effectiveness of exercise therapy versus general practitioner care for osteoarthritis of the hip: design of a randomised clinical trial. *BMC Musculoskelet Disord* 2011;12:232.

van Gool CH,Penninx BW,Kempen GI,Miller GD,van Eijk JT,Pahor M,Messier SP. Determinants of high and low attendance to diet and exercise interventions among overweight and obese older adults. Results from the arthritis, diet, and activity promotion trial. *Contemp Clin Trials* 2006;27(3):227-237.

van Gool CH,Penninx BW,Kempen GI,Rejeski WJ,Miller GD,van Eijk JT,Pahor M,Messier SP. Effects of exercise adherence on physical function among overweight older adults with knee osteoarthritis. *Arthritis Rheum* 2005;53(1):24-32.

van Haselen RA,Fisher PA. A randomized controlled trial comparing topical Piroxicam gel with a homeopathic gel in osteoarthritis of the knee. *Rheumatology (Oxford)* 2000;39(7):714-719.

van OM,Sont JK,Bajema IM,Breedveld FC,van Laar JM. Comparison of efficacy of arthroscopic lavage plus administration of corticosteroids, arthroscopic lavage plus administration of placebo, and joint aspiration plus administration of corticosteroids in arthritis of the knee: A randomized controlled trial. *Arthritis Rheum* 2006;55(6):964-970.

van Raaij TM,Reijman M,Brouwer RW,Bierma-Zeinstra SM,Verhaar JA. Medial Knee Osteoarthritis Treated by Insoles or Braces: A Randomized Trial. *Clin Orthop Relat Res* 2010;.

van RT,Reijman M,Brouwer RW,Jakma TS,Verhaar JN. Survival of closing-wedge high tibial osteotomy: good outcome in men with low-grade osteoarthritis after 10-16 years. *Acta Orthop* 2008;79(2):230-234.

Vanelli R,Costa P,Rossi SM,Benazzo F. Efficacy of intra-articular polynucleotides in the treatment of knee osteoarthritis: a randomized, double-blind clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2010;.

Vangsness CT,Spiker W,Erickson J. A review of evidence-based medicine for glucosamine and chondroitin sulfate use in knee osteoarthritis. *Arthroscopy* 2009;25(1):86-94.

Vas J,Perea-Milla E,Mendez C. Acupuncture and moxibustion as an adjunctive treatment for osteoarthritis of the knee--a large case series. *Acupunct Med* 2004;22(1):23-28.

Vasishta VG. Long-term efficacy of sequentially programmed magnetic field (SPMF) therapy in patients with osteoarthritis of the knee. *Osteoarthritis and Cartilage* 2011;19 SUPPL. 1:S147.

Vecka M,Prokes L,Tvrzicka E,Karpas K,Pernicky A,Pfleger R,Votruba M. Anti-inflammatory effect of flavonoids from Comfort-G and the changes in arachidonic acid metabolism. *Klinicka Biochemie a Metabolismus* 2008;16(1):27-32.

Veenhof C,Koke AJ,Dekker J,Oostendorp RA,Bijlsma JW,van Tulder MW,van den Ende CH. Effectiveness of behavioral graded activity in patients with osteoarthritis of the hip and/or knee: A randomized clinical trial. *Arthritis Rheum* 2006;55(6):925-934.

Verhagen A,Bierma-Zeinstra S,Lambeck J,Cardoso JR,de Bie R,Boers M,de Vet HC. Balneotherapy for osteoarthritis. A cochrane review. *The Journal of rheumatology* 2008;35(6):1118-1123.

Verhaven E,Casteleyn PP,Haentjens P,Handelberg F,De BH, Van BF,Opdecam P. Dome osteotomy of the tibia for osteoarthritis of the knee. *Acta Orthop Belg* 1989;55(4):547-555.

Verkleij SP,Luijsterburg PA,Koes BW,Bohnen AM,Bierma-Zeinstra SM. Effectiveness of Diclofenac versus Acetaminophen in primary care patients with knee osteoarthritis: [NTR1485], DIPA-trial: design of a randomized clinical trial. *BMC Musculoskelet Disord* 2010;11:7.

Veth RPH. Clinical significance of knee joint changes after meniscectomy. *Clin Orthop* 1985;NO. 198:56-60.

Victor CR,Ross F,Axford J. Capturing lay perspectives in a randomized control trial of a health promotion intervention for people with osteoarthritis of the knee. *J Eval Clin Pract* 2004;10:63-70.

Villanueva I,del Mar GM,Javier TF,Ariza-Ariza R,Navarro F. Relative efficiency and validity properties of a visual analogue versus a categorical scaled version of the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index: Spanish versions. *Osteoarthritis Cartilage* 2004;12(3):225-231.

Vinje O,Fagertun HE,Laerum E,Lund H,Larsen S. Ketoprofen controlled release (CR) in the treatment of osteoarthritis; a double blind, randomized multicentre study of single morning versus evening dose. Norwegian Study Group of General Practitioners. *Scand J Prim Health Care* 1993;11(2):91-97.

Virkkunen M,Krusius FE,Heiskanen T. Experiences of intra-articular administration of radioactive gold. *Acta Rheumatol Scand* 1967;13(2):81-91.

Vishal AA,Mishra A,Raychaudhuri SP. A double blind, randomized, placebo controlled clinical study evaluates the early efficacy of aflapin in subjects with osteoarthritis of knee. *Int J Med Sci* 2011;8(7):615-622.

Vogels E,Hendriks HJM,van Baar ME,Dekker J,Hopman-Rock M,Oostendorp RAB,Hullegie W,Bloo H,Hilberdink W,Munneke M,Verhoef J. KNGF guidelines: Clinical practice guidelines for physical therapy in patients with osteoarthritis of the hip or knee [methodology of a clinical practice guideline for clinicians]. 2003;.

Vojtassak J,Vojtassak J,Jacobs A,Rynn L,Waechter S,Richarz U. A Phase IIIb, Multicentre, Randomised, Parallel-Group, Placebo-Controlled, Double-Blind Study to Investigate the Efficacy and Safety of OROS Hydromorphone in Subjects with Moderate-to-Severe Chronic Pain Induced by Osteoarthritis of the Hip or the Knee. *Pain Res Treat* 2011;2011:239501.

Vorsanger G,Xiang J,Jordan D,Farrell J. Post hoc analysis of a randomized, double-blind, placebo-controlled efficacy and tolerability study of Tramadol extended release for the treatment of osteoarthritis pain in geriatric patients. *Clin Ther* 2007;29 Suppl:2520-2535.

Vrezas I,Elsner G,Bolm-Audorff U,Abolmaali N,Seidler A. Case-control study of knee osteoarthritis and lifestyle factors considering their interaction with physical workload. *Int Arch Occup Environ Health* 2010;83(3):291-300.

Waciakowski D,Urban K,Karpas K. Valgus High Tibial Osteotomy - Long-Term Results. *Acta Chir Orthop Traumatol Cech* 2011;78(3):225-231.

Wada J,Koshino T,Morii T,Sugimoto K. Natural course of osteoarthritis of the knee treated with or without intraarticular corticosteroid injections. *Bull Hosp Jt Dis* 1993;53(2):45-48.

Wada M,Imura S,Nagatani K,Baba H,Shimada S,Sasaki S. Relationship between gait and clinical results after high tibial osteotomy. *Clin Orthop Relat Res* 1998;(354):180-188.

Waddell DD,Bricker DC. Clinical experience with the effectiveness and tolerability of hylan G-F 20 in 1047 patients with osteoarthritis of the knee. *J Knee Surg* 2006;19(1):19-27.

Waddell DD,Cefalu CA,Bricker DC. A second course of hylan G-F 20 for the treatment of osteoarthritic knee pain: 12-month patient follow-up. *J Knee Surg* 2005;18(1):7-15.

Waddell DD,Cefalu CA,Bricker DC. An open-label study of a second course of hylan G-F 20 for the treatment of pain associated with knee osteoarthritis. *Curr Med Res Opin* 2003;19(6):499-507.

Waddell DD,Marino AA. Chronic knee effusions in patients with advanced osteoarthritis: implications for functional outcome of viscosupplementation. *J Knee Surg* 2007;20(3):181-184.

Wagenhauser FJ,Narozna H. The influence of Lonazolac-Ca (Irritren(Reg.trademark)) on active-stage osteoarthrosis. Results of a double-blind crossover study against Naproxen. <ORIGINAL> DER EINFLUSS VON LONAZOLAC-CA (IRRITREN(Reg.trademark)) AUF AKTIVIERTE ARTHROSEN. ERGEBNISSE EIN. *AKTUEL RHEUMATOL* 1982;7:194-198.

Wagenitz A,Mueller EA,Frentzel A,Cambon N. Comparative efficacy and tolerability of two sustained-release formulations of Diclofenac: results of a double-blind, randomised study in patients with osteoarthritis and a reappraisal of Diclofenac's use in this patient population. *Curr Med Res Opin* 2007;23(8):1957-1966.

Wai EK,Kreder HJ,Williams JI. Arthroscopic debridement of the knee for osteoarthritis in patients fifty years of age or older: utilization and outcomes in the Province of Ontario. *J Bone Joint Surg Am* 2002;84-A(1):17-22.

Waikakul S,Penkitti P,Soparat K,Boonsanong W. Topical analgesics for knee arthrosis: a parallel study of Ketoprofen gel and Diclofenac emulgel. *J Med Assoc Thai* 1997;80(9):593-597.

Walsh NE,Mitchell HL,Reeves BC,Hurley MV. Integrated exercise and self-management programmes in osteoarthritis of the hip and knee: a systematic review of effectiveness. *Physical Therapy Reviews* 2006;11(4):289-297.

Wandel S,Juni P,Tendal B,Nuesch E,Villiger PM,Welton NJ,Reichenbach S,Trelle S. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis (Structured abstract). *BMJ* 2010;341:c4675:.

Wandel S,Juni P,Tendal B,Nuesch E,Villiger PM,Welton NJ,Reichenbach S,Trelle S. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: Network meta-analysis. *BMJ* 2010 Oct 2;341(7775):711.

Wang C,Schmid CH,Hibberd PL,Kalish R,Roubenoff R,Rones R,McAlindon T. Tai Chi is effective in treating knee osteoarthritis: a randomized controlled trial. *Arthritis Rheum* 2009;61(11):1545-1553.

- Wang CX,Yu W,Wang G,Wei DG. Small needle-scalpel therapy combined with movement exercise for osteoarthritis of knee joint: A comprehensive analysis on the curative effect. [Chinese]. *Journal* 2004;8:8034-8035.
- Wang H,Ge J,Yin H,Feng X,Zhu L,Zhang J,Guo Z,Luo T. Analysis of fufang duzhong jianglu keli in improvement of knee joint function in 400 cases of knee osteoarthritis. *Chinese Journal of Clinical Rehabilitation* 2005;9(42):166-168.
- Wang J,Kuo KN,Galante JO. High tibial osteotomy for varus gonarthrosis. A six-year follow-up. *Journal of Surgical Association Republic of China* 1989;22(3):247-252.
- Wang JW,Hsu CC. Distal femoral varus osteotomy for osteoarthritis of the knee. *J Bone Joint Surg Am* 2005;87(1):127-133.
- Wang JW,Hsu CC. Distal femoral varus osteotomy for osteoarthritis of the knee. Surgical technique. *J Bone Joint Surg Am* 2006;88 Suppl 1 Pt 1:100-108.
- Wang KH,Hwang DH,Cho JH,Changale SD,Woo SJ,Nha KW. Arthroscopic direct repair for a complete radial tear of the posterior root of the medial meniscus. *Clin Orthop Surg* 2011 Dec;3(4):332-335.
- Wang SM,Kain ZN,White PF. Acupuncture analgesia: II. Clinical considerations. *Anesth Analg* 2008;106(2):611-21, table.
- Wang T,Liu Y,Xie A,Ding H,Teng S. Improvement of articular pain by arthroscopic douche in osteoarthritis of knee joint. *Chinese Journal of Clinical Rehabilitation* 2002;6(24):3769.
- Wang TJ,Belza B,Elaine TF,Whitney JD,Bennett K. Effects of aquatic exercise on flexibility, strength and aerobic fitness in adults with osteoarthritis of the hip or knee. *J Adv Nurs* 2007;57(2):141-152.
- Wang TJ,Lee SC,Liang SY,Tung HH,Wu SF,Lin YP. Comparing the efficacy of aquatic exercises and land-based exercises for patients with knee osteoarthritis. *J Clin Nurs* 2011 Sep;20(17-18):2609-2622.
- Wang X,Miller GD,Messier SP,Nicklas BJ. Knee strength maintained despite loss of lean body mass during weight loss in older obese adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci* 2007;62(8):866-871.
- Wang-Saegusa A,Cugat R,Ares O,Seijas R,Cusco X,Garcia-Balletbo M. Infiltration of plasma rich in growth factors for osteoarthritis of the knee short-term effects on function and quality of life. *Archives of Orthopaedic and Trauma Surgery* 2011;131(3):311-317.
- Ward DE,Veys EM,Bowdler JM,Roma J. Comparison of Aceclofenac with Diclofenac in the treatment of osteoarthritis. *Clin Rheumatol* 1995;14(6):656-662.
- Warholm O,Skaar S,Hedman E,Molmen HM,Eik L. The effects of a standardized herbal remedy made from a subtype of *Rosa canina* in patients with osteoarthritis: A double-blind, randomized, placebo-controlled clinical trial. *Current Therapeutic Research - Clinical and Experimental* 2003;64(1):21-31.
- Wassenaar MJ,Biermasz NR,Bijsterbosch J,Pereira AM,Meulenbelt I,Smit JW,Roelfsema F,Kroon HM,Romijn JA,Kloppenburger M. Arthropathy in long-term cured acromegaly is characterised by osteophytes without joint space narrowing: a comparison with generalised osteoarthritis. *Ann Rheum Dis* 2011 Feb;70(2):320-325.

Watanabe K,Tsuchiya H,Matsubara H,Kitano S,Tomita K. Revision high tibial osteotomy with the Taylor spatial frame for failed opening-wedge high tibial osteotomy. *J Orthop Sci* 2008;13(2):145-149.

Waterworth RF,Petrie JP. Double-blind comparative study of etodolac and Piroxicam in patients with osteoarthritis of the knee. *Adv Ther* 1992;9:240-249.

Waterworth RF,Waterworth SM,Taylor KM. A comparison of tenoxicam and Piroxicam in a long-term clinical study in patients with osteoarthritis of hip or knee joints. *Eur J Rheumatol Inflamm* 1985;8(1):21-27.

We SR,Jeong E,Koog YH,Min B. Effects of nutraceuticals on knee osteoarthritis: Systematic review. *African Journal of Biotechnology* 2012;11(12):2814-2821.

Weale AE,Ackroyd CE,Mani GV,Winson IG. Day-case or short-stay admission for arthroscopic knee surgery: A randomised controlled trial. *Ann R Coll Surg Engl* 1998;80(2):146-149.

Weaver A,Rubin B,Caldwell J,McMahon FG,Lee D,Makarowski W,Offenberg H,Sack M,Sikes D,Trapp R,... Comparison of the efficacy and safety of oxaprozin and nabumetone in the treatment of patients with osteoarthritis of the knee. *Clin Ther* 1995;17(4):735-745.

Weaver AL,Messner RP,Storms WW,Polis AB,Najarian DK,Petruschke RA,Geba GP,Tershakovec AM. Treatment of patients with osteoarthritis with Rofecoxib compared with nabumetone. *J Clin Rheumatol* 2006;12(1):17-25.

Weber M. Interstitial and intraarticular laser therapy - A new option for difficult pain syndromes. *Pain Practice* 2012 Feb;12 SUPPL. 1:70-71.

Wegener T,Lupke NP. Treatment of patients with arthrosis of hip or knee with an aqueous extract of devil's claw (*Harpagophytum procumbens* DC.). *Phytother Res* 2003;17(10):1165-1172.

Wegman A,van der Windt D,van TM,Felson D. Review: Non-steroidal anti-inflammatory drugs are slightly better than Paracetamol for reducing pain in osteoarthritis. *Evidence-Based Medicine* 2004;9(6):180.

Wei N,Delauter SK,Erlichman MS. The holmium YAG laser in office based arthroscopy of the knee: comparison with standard interventional instruments in patients with arthritis. *J Rheumatol* 1997;24(9):1806-1808.

Weidenhielm L,Mattsson E,Brostrom LA,Wersall-Robertsson E. Effect of preoperative physiotherapy in unicompartmental prosthetic knee replacement. *Scand J Rehabil Med* 1993;25(1):33-39.

Weidenhielm L,Olsson E,Brostrom LA,Borjesson-Hederstrom M,Mattsson E. Improvement in gait one year after surgery for knee osteoarthrosis: a comparison between high tibial osteotomy and prosthetic replacement in a prospective randomized study. *Scand J Rehabil Med* 1993;25(1):25-31.

Weigl M,Angst F,Aeschlimann A,Lehmann S,Stucki G. Predictors for response to rehabilitation in patients with hip or knee osteoarthritis: a comparison of logistic regression models with three different definitions of responder. *Osteoarthritis and Cartilage* 2006;14(7):641-651.

Weigl M,Angst F,Stucki G,Lehmann S,Aeschlimann A. Inpatient rehabilitation for hip or knee osteoarthritis: 2 year follow up study. *Ann Rheum Dis* 2004;63(4):360-368.

Wein CR,Haupt JB,McMillan R,Russell AHK. Open trial of Glucosamine Hydrochloride (Arthroid) in the Treatment of Pain of Osteoarthritis of the Knee. *Unpublished* 1998;.

Weinberger A,Fadilah R,Lev A,Pinkhas J. Intra-articular temperature measurements after superficial heating. *Scand J Rehabil Med* 1989;21(1):55-57.

Weng MC,Lee CL,Chen CH,Hsu JJ,Lee WD,Huang MH,Chen TW. Effects of different stretching techniques on the outcomes of isokinetic exercise in patients with knee osteoarthritis. *Kaohsiung J Med Sci* 2009;25(6):306-315.

Wenham CY,Conaghan PG. Optimising pain control in osteoarthritis. *Practitioner* 2010 Dec;254(1735):23-23.

Wetzels R,van WC,Grol R,Wensing M. Family practice nurses supporting self-management in older patients with mild osteoarthritis: a randomized trial. *BMC Fam Pract* 2008;9:7.

Wheeler JW,Shull PB,Besier TF. Real-time knee adduction moment feedback for gait retraining through visual and tactile displays. *J Biomech Eng* 2011 Mar 15;133(4 Article Number):.

Whelton JC,Greenberg BP. Fenbufen and placebo treatment in osteoarthritis. Short-term double-blind parallel group study. *Pharmacology* 1982;25 Suppl 1:21-26.

White A,Foster N,Cummings M,Barlas P. The effectiveness of acupuncture for osteoarthritis of the knee - a systematic review [with consumer summary]. *Acupuncture in Medicine* 2006;24(Suppl):S40-S48.

White DK,Keysor JJ,LaValley MP,Lewis CE,Torner JC,Nevitt MC,Felson DT. Clinically Important Improvement in Function Is Common in People with or at High Risk of Knee OA: The MOST Study. *J Rheumatol* 2010;.

Wiesenhutter CW,Boice JA,Ko A,Sheldon EA,Murphy FT,Wittmer BA,Aversano ML,Reicin AS. Evaluation of the comparative efficacy of Etoricoxib and ibuprofen for treatment of patients with osteoarthritis: A randomized, double-blind, placebo-controlled trial. *Mayo Clin Proc* 2005;80(4):470-479.

Wild JE,Grond S,Kuperwasser B,Gilbert J,McCann B,Lange B,Steup A,Haufel T,Etropolski MS,Rauschkolb C,Lange R. Long-term safety and tolerability of tapentadol extended release for the management of chronic low back pain or osteoarthritis pain. *Pain Pract* 2010 Sep;10(5):416-427.

Wilder FV,Leaverton PE,Rogers MW,Lemrow NB. Vitamin supplements and radiographic knee osteoarthritis: The Clearwater Osteoarthritis Study. *Journal of Musculoskeletal Research* 2009;12(2):85-93.

Wildi LM,Raynauld JP,Martel PJ,Beaulieu A,Bessette L,Morin F,Abram F,Dorais M,Pelletier JP. Chondroitin sulphate reduces both cartilage volume loss and bone marrow lesions in knee osteoarthritis patients starting as early as 6 months after initiation of therapy: a randomised, double-blind, placebo-controlled pilot study using MRI. *Annals of the Rheumatic Diseases* 2011;70:982-989.

Wildi LM,Raynauld JP,Martel-Pelletier J,Abram F,Dorais M,Pelletier JP. Relationship between bone marrow lesions, cartilage loss and pain in knee osteoarthritis: results from a randomised controlled clinical trial using MRI. *Ann Rheum Dis* 2010 Dec;69(12):2118-2124.

- Wildner M,Peters A,Hellich J,Reichelt A. Complications of high tibial osteotomy and internal fixation with staples. *Arch Orthop Trauma Surg* 1992;111(4):210-212.
- Wiley AM. Reconstruction of the osteoarthritic knee by high tibial osteotomy and joint clearance. *Can J Surg* 1967;10(1):28-35.
- Will R,Laing B,Edelman J,Lovegrove F,Surveyor I. Comparison of two yttrium-90 regimens in inflammatory and osteoarthropathies. *Ann Rheum Dis* 1992;51(2):262-265.
- Williams FM,Skinner J,Spector TD,Cassidy A,Clark IM,Davidson RM,MacGregor AJ. Dietary garlic and hip osteoarthritis: evidence of a protective effect and putative mechanism of action. *BMC Musculoskelet Disord* 2010;11:280.
- Williams HJ,Ward JR,Egger MJ,Neuner R,Brooks RH,Clegg DO,Field EH,Skosey JL,Alarcon GS,Willkens RF,.. Comparison of Naproxen and Acetaminophen in a two-year study of treatment of osteoarthritis of the knee. *Arthritis Rheum* 1993;36(9):1196-1206.
- Williams PI,Hosie J,Scott DL. Etodolac therapy for osteoarthritis: a double-blind, placebo-controlled trial. *Curr Med Res Opin* 1989;11(7):463-470.
- Williamson L,Wyatt MR,Yein K,Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology (Oxford)* 2007;46(9):1445-1449.
- Wills AK,Black S,Cooper R,Coppack RJ,Hardy R,Martin KR,Cooper C,Kuh D. Life course body mass index and risk of knee osteoarthritis at the age of 53 years: evidence from the 1946 British birth cohort study. *Ann Rheum Dis* 2011 Oct 6;.
- Winter CC,Brandes M,Muller C,Schubert T,Ringling M,Hillmann A,Rosenbaum D,Schulte TL. Walking ability during daily life in patients with osteoarthritis of the knee or the hip and lumbar spinal stenosis: A cross sectional study. *BMC Musculoskeletal Disorders* 2010;11 Article Number(233. Date of Publication):.
- Winther K,Apel K,Thamsborg G. A powder made from seeds and shells of a rose-hip subspecies (*Rosa canina*) reduces symptoms of knee and hip osteoarthritis: a randomized, double-blind, placebo-controlled clinical trial. *Scand J Rheumatol* 2005;34(4):302-308.
- Wislowska M,Jablonska B. Serum cartilage oligomeric matrix protein (COMP) in rheumatoid arthritis and knee osteoarthritis. *Clin Rheumatol* 2005;24(3):278-284.
- Witt CM,Jena S,Brinkhaus B,Liecker B,Wegscheider K,Willich SN. Acupuncture in patients with osteoarthritis of the knee or hip: a randomized, controlled trial with an additional nonrandomized arm. *Arthritis Rheum* 2006;54(11):3485-3493.
- Witt CM,Pach D,Brinkhaus B,Wruck K,Tag B,Mank S,Willich SN. Safety of acupuncture: results of a prospective observational study with 229,230 patients and introduction of a medical information and consent form. *Forsch Komplementmed* 2009;16(2):91-97.

- Wittenberg RH,Schell E,Krehan G,Maeumbaed R,Runge H,Schluter P,Fashola TO,Thurston HJ,Burger KJ,Trechsel U. First-dose analgesic effect of the cyclo-oxygenase-2 selective inhibitor Lumiracoxib in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled comparison with Celecoxib [NCT00267215]. *Arthritis Res Ther* 2006;8(2):R35.
- Wluka AE,Stuckey S,Brand C,Cicuttini FM. Supplementary vitamin E does not affect the loss of cartilage volume in knee osteoarthritis: a 2 year double blind randomized placebo controlled study. *J Rheumatol* 2002;29(12):2585-2591.
- Wobig M,Beks P,Dickhut A,Maier R,Vetter G. Open-label multicenter trial of the safety and efficacy of viscosupplementation with Hylan G-F 20 (Synvisc) in primary osteoarthritis of the knee. *Journal of Clinical Rheumatology* 1999;5(6 SUPPL.):S24-S31.
- Wobig M. Hylan G-F 20 (Synvisc) for the treatment of osteoarthritis of the knee: Clinical studies and practical considerations. *Journal of Clinical Rheumatology* 1999;5(6 SUPPL.):S12-S17.
- Wojtulewski JA,Hart FD,Huskisson EC. Fenoprofen in treatment of osteoarthrosis of hip and knee. *Br Med J* 1974;2(5917):475-476.
- Wolf S,Foley S,Budiman-Mak E,Moritz T,O'Connell S,Jelinek C,Collins EG. Predictors of weight loss in overweight veterans with knee osteoarthritis who participated in a clinical trial. *J Rehabil Res Dev* 2010;47(3):171-181.
- Wolfe F,Hawley DJ,Peloso PM,Wilson K,Anderson J. Back pain in osteoarthritis of the knee. *Arthritis Care Res* 1996;9(5):376-383.
- Wolfe F,Lane NE. The longterm outcome of osteoarthritis: rates and predictors of joint space narrowing in symptomatic patients with knee osteoarthritis. *J Rheumatol* 2002;29(1):139-146.
- Wolsko PM,Eisenberg DM,Simon LS,Davis RB,Walleczek J,Mayo SM,Kaptchuk TJ,Phillips RS. Double-blind placebo-controlled trial of static magnets for the treatment of osteoarthritis of the knee: results of a pilot study. *Altern Ther Health Med* 2004;10:36-43.
- Wong H,Yuan WQ,Zhao Y,Li YJ. [External application of reparil-gel accompanied with intra-articular injection of sodium hyaluronate for treatment of knee osteoarthritis]. *Chinese Journal of Clinical Rehabilitation* 2006;10:39-41.
- Wong SHS,Wong CSM,Li TTL. Steroids in regional analgesia. *Expert Opinion on Pharmacotherapy* 2010;11(17):2839-2848.
- Wood L,Peat G,Thomas E,Hay EM,Sim J. Associations between physical examination and self-reported physical function in older community-dwelling adults with knee pain. *Phys Ther* 2008;88(1):33-42.
- Woolley SM,Topp RV,Commager JA. The performance of functional activities in patient with knee osteoarthritis. *Gait Posture* 1998;7(2):145.
- Wright V,Haslock DI,Dowson D,Seller PC,Reeves B. Evaluation of silicone as an artificial lubricant in osteoarthrotic joints. *Br Med J* 1971;2(5758):370-373.

Wu CW,Morrell MR,Heinze E,Concoff AL,Wollaston SJ,Arnold EL,Singh R,Charles C,Skovrun ML,FitzGerald JD,Moreland LW,Kalunian KC. Validation of American College of Rheumatology classification criteria for knee osteoarthritis using arthroscopically defined cartilage damage scores. *Semin Arthritis Rheum* 2005;35(3):197-201.

Wu HB,Du JY,Yang SH,Shao ZW,Xiong XQ. [Evaluation on the effects of hyaluronan combined with different dosages of Celecoxib for relieving pain and ankylosis induced by knee osteoarthritis]. *Zhongguo Linchuang Kangfu* 2004;8:5491-5493.

Wu JJ,Shih LY,Hsu HC,Chen TH. The double-blind test of sodium hyaluronate (ARTZ) on osteoarthritis knee. *Zhonghua Yi Xue Za Zhi (Taipei)* 1997;59(2):99-106.

Wu LD,Hahne HJ,Hassenpflug T. A long-term follow-up study of high tibial osteotomy for medial compartment osteoarthrosis. *Chin J Traumatol* 2004;7(6):348-353.

Wu MX,Li XH,Lin MN,Jia XR,Mu R,Wan WR,Chen RH,Chen LH,Lin WQ,Huang CY,Zhang XR,Hong KD,Li L,Liu XX. Clinical study on the treatment of knee osteoarthritis of Shen-Sui insufficiency syndrome type by electroacupuncture. *Chin J Integr Med* 2010 Aug;16(4):291-297.

Wu SS,Tuan K. Current concepts in nonoperative management of knee osteoarthritis. *Orthopedics* 2005;28(2):134-139.

Xie F,Lo NN,Pullenayegum EM,Tarride JE,O'Reilly DJ,Goeree R,Lee HP. Evaluation of health outcomes in osteoarthritis patients after total knee replacement: a two-year follow-up. *Health Qual Life Outcomes* 2010;8:87.

Xu H,Wu HG. [Clinical observation of electroacupuncture combined with low-dose Diclofenac in treating osteoarthritis of the knee]. *Zhong xi yi jie he xue bao = Journal of Chinese integrative medicine* 2007;5:457-459.

Xu P,Guo X,Jin WZ,Yao J,Zhang Y,Cai Q. [Clinical observation on effect of intra-articular injection of sodium hyaluronate accompanied with external application of sanhua ointment for knee osteoarthritis]. *Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi = Chinese journal of integrated traditional and Western medicine / Zhongguo Zhong xi yi jie he xue hui , Zhongguo Zhong yi yan jiu yuan zhu ban* 2005;25:620-622.

Yamashita H,Masuyama S,Otsuki K,Tsukayama H. Safety of acupuncture for osteoarthritis of the knee - A review of randomised controlled trials, focusing on specific reactions to acupuncture. *Acupuncture in Medicine* 2006;24(SUPPL.):S49-S52.

Yang D,Xu F,Ma L,Gan J. Ultrasonic wave in combination with quadriceps exercise for the treatment of senile knee osteoarthritis. *Chinese Journal of Clinical Rehabilitation* 2005;9(26):252-254.

Yang DJ. (Ultrasonic wave in combination with quadriceps exercise for the treatment of senile knee osteoarthritis). 2005.

Yang KG,Raijmakers NJ,van Arkel ER,Caron JJ,Rijk PC,Willems WJ,Zijl JA,Verbout AJ,Dhert WJ,Saris DB. Autologous interleukin-1 receptor antagonist improves function and symptoms in osteoarthritis when compared to placebo in a prospective randomized controlled trial. *Osteoarthritis Cartilage* 2008;16(4):498-505.

- Yang W. Forty-seven cases of gonitis treated by a combined therapy of Chinese drugs and acupuncture. *J Tradit Chin Med* 2001;21(2):127-129.
- Yasuda K,Majima T,Tanabe Y,Kaneda K. Long-term evaluation of high tibial osteotomy for medial osteoarthritis of the knee. *Bull Hosp Jt Dis Orthop Inst* 1991;51(2):236-248.
- Yasuda K,Majima T,Tsuchida T,Kaneda K. A ten- to 15-year follow-up observation of high tibial osteotomy in medial compartment osteoarthritis. *Clin Orthop Relat Res* 1992;(282):186-195.
- Yasuda K,Sasaki T. The mechanics of treatment of the osteoarthritic knee with a wedged insole. *Clin Orthop Relat Res* 1987;(215):162-172.
- Yates DA. The treatment of osteoarthritis. *Practitioner* 1972;208(243):43-47.
- Yavuz U,Sokucu S,Albayrak A,Ozturk K. Efficacy comparisons of the intraarticular steroidal agents in the patients with knee osteoarthritis. *Rheumatol Int* 2011 Nov 5;.
- Yavuz U,Sokucu S,Albayrak A,Ozturk K. Efficacy comparisons of the intraarticular steroidal agents in the patients with knee osteoarthritis. *Rheumatol Int* 2011:1-6.
- Yavuzer G,Sonel B,Suldur N,Ergin S. Effects of intra-articular hylan G-F 20 injections on clinical and biomechanical characteristics of the knee in osteoarthritis. *Int J Rehabil Res* 2005;28(4):371-374.
- Yelland MJ,Nikles CJ,McNairn N,Del Mar CB,Schluter PJ,Brown RM. Celecoxib compared with sustained-release Paracetamol for osteoarthritis: a series of n-of-1 trials. *Rheumatology (Oxford)* 2007;46(1):135-140.
- Yen ZS,Lai MS,Wang CT,Chen LS,Chen SC,Chen WJ,Hou SM. Cost-effectiveness of treatment strategies for osteoarthritis of the knee in Taiwan. *J Rheumatol* 2004;31(9):1797-1803.
- Yeung E,Jackson M,Sexton S,Walter W,Zicat B,Walter W. The effect of obesity on the outcome of hip and knee arthroplasty. *Int Orthop* 2010 May 29;.
- Yilmaz B,Goktepe AS,Alaca R,Mohur H,Kayar AH. Comparison of a generic and a disease specific quality of life scale to assess a comprehensive spa therapy program for knee osteoarthritis. *Joint Bone Spine* 2004;71(6):563-566.
- Yilmaz OO,Wu M. Efficacy of Emg-biofeedback in knee osteoarthritisClinical study on the treatment of knee osteoarthritis of Shen-Sui insufficiency syndrome type by electroacupuncture. 2010.
- Yip Y,Yip YB. A 1-year follow-up of an experimental study of a self-management arthritis programme with an added exercise component of clients with osteoarthritis of the kneeEffects of a self-management arthritis programme with an added exercise component for osteoart. 2008.
- Yip YB,Sit JW,Fung KK,Wong DY,Chong SY,Chung LH,Ng TP. Effects of a self-management arthritis programme with an added exercise component for osteoarthritic knee: randomized controlled trial. *J Adv Nurs* 2007;59(1):20-28.

Yip YB,Sit JW,Fung KK,Wong DY,Chong SY,Chung LH,Ng TP. Impact of an Arthritis Self-Management Programme with an added exercise component for osteoarthritic knee sufferers on improving pain, functional outcomes, and use of health care services: An experimental study. *Patient Educ Couns* 2007;65(1):113-121.

Yip YB,Sit JW,Wong DY,Chong SY,Chung LH. A 1-year follow-up of an experimental study of a self-management arthritis programme with an added exercise component of clients with osteoarthritis of the knee. *Psychol Health Med* 2008;13(4):402-414.

Yip YB,Tam AC. An experimental study on the effectiveness of massage with aromatic ginger and orange essential oil for moderate-to-severe knee pain among the elderly in Hong Kong. *Complement Ther Med* 2008;16(3):131-138.

Yocum D,Fleischmann R,Dalgin P,Caldwell J,Hall D,Roszko P. Safety and efficacy of meloxicam in the treatment of osteoarthritis: a 12-week, double-blind, multiple-dose, placebo-controlled trial. The Meloxicam Osteoarthritis Investigators. *Arch Intern Med* 2000;160(19):2947-2954.

Yoon Y,Rah J,Park H. A prospective study of the accuracy of clinical examination evaluated by arthroscopy of the knee. *Int Orthop* 1997;21(4):223-227.

Yoshimura N,Muraki S,Oka H,Kawaguchi H,Nakamura K,Akune T. Association of knee osteoarthritis with the accumulation of metabolic risk factors such as overweight, hypertension, dyslipidemia, and impaired glucose tolerance in Japanese men and women: The ROAD study. *J Rheumatol* 2011 May;38(5):921-930.

Young S,Woodbury mg,Fryday FK,Donovan Ta. Efficacy of interferential current stimulation alone for pain reduction in patients with osteoarthritis of the knee: A randomized placebo control clinical trial. *Phys Ther* 1991;71:852.

Yurtkuran M,Alp A,Konur S,Ozcakir S,Bingol U. Laser acupuncture in knee osteoarthritis: a double-blind, randomized controlled study. *Photomed Laser Surg* 2007;25(1):14-20.

Yurtkuran M,Kocagil T. TENS, electroacupuncture and ice massage: comparison of treatment for osteoarthritis of the knee. *Am J Acupunct* 1999;27(3-4):133-140.

Yurtkuran M,Yurtkuran M,Alp A,Nasircilar A,Bingol U,Altan L,Sarpdere G. Balneotherapy and tap water therapy in the treatment of knee osteoarthritis. *Rheumatol Int* 2006;27(1):19-27.

Yusong L,Liang G,Shanzhi M. Treatment of 256 cases of osteoarthritis of knee joint with Guo Jianhua's four-step therapy. *J Tradit Chin Med* 2008;28(2):114-117.

Yusuf E,Bijsterbosch J,Slagboom PE,Kroon HM,Rosendaal FR,Huizinga TW,Kloppenburg M. Association between Several Clinical and Radiological Determinants with Long-Term Clinical Progression and Good Prognosis of Lower Limb Osteoarthritis. *PLoS One* 2011;6(10):e25426.

Za ZG,Song YC,Zao MJ,Liu CF. Comparison of therapeutic results of Danshen and sodium hyaluronate injection for knee osteoarthritis. *Chinese Journal of Clinical Rehabilitation* 2002;6:3746-3747.

Zachariae E,Sylvest J. Osteoarthritis of the knee treated with tolafenamic acid. *Scand J Rheumatol* 1972;1(3):97-99.

- Zacher J, Feldman D, Gerli R, Scott D, Hou SM, Uebelhart D, Rodger IW, Ozturk ZE. A comparison of the therapeutic efficacy and tolerability of Etoricoxib and Diclofenac in patients with osteoarthritis. *Curr Med Res Opin* 2003;19(8):725-736.
- Zaki SH, Rae PJ. High tibial valgus osteotomy using the Tomofix plate--medium-term results in young patients. *Acta Orthop Belg* 2009;75(3):360-367.
- Zeng HW, Nie B, Shi LL. [Observation on therapeutic effect of blood-letting puncture combined with red-hot needle therapy on knee osteoarthritis]. *Zhongguo zhen jiu = Chinese acupuncture & moxibustion* 2008;28:493-495.
- Zgradie I. Comparison of therapeutic efficacy of nimesulide and Diclofenac in patients with degenerative joint diseases. *J Indian Med Assoc* 1999;97(4):119-123.
- Zhang BM, Wu YC. Clinical study on the treatment of knee osteoarthritis with point penetration method of long needle. *J Acu Tuina Sci* 2003;1:49.
- Zhang HN, Zhang J, Lv CY, Leng P, Wang YZ, Wang XD, Wang CY. Modified biplanar open-wedge high tibial osteotomy with rigid locking plate to treat varus knee. *J Zhejiang Univ Sci B* 2009;10(9):689-695.
- Zhang W, McWilliams DF, Ingham SL, Doherty SA, Muthuri S, Muir KR, Doherty M. Nottingham knee osteoarthritis risk prediction models. *Ann Rheum Dis* 2011 Sep;70(9):1599-1604.
- Zhang Y, Jordan JM. Epidemiology of osteoarthritis. *Clin Geriatr Med* 2010 Aug;26(3):355-369.
- Zhao L, Shen X, Cheng K, Deng H, Ding G, Tan M, Lao L. Validating a Nonacupoint Sham Control for Laser Treatment of Knee Osteoarthritis. *Photomed Laser Surg* 2009;..
- Zhao SZ, Dedhiya SD, Bocanegra TS, Fort JG, Kuss ME, Rush SM. Health-related quality-of-life effects of oxaprozin and nabumetone in patients with osteoarthritis of the knee. *Clin Ther* 1999;21(1):205-217.
- Zhao SZ, McMillen JJ, Markenson JA, Dedhiya SD, Zhao WW, Osterhaus JT, Yu SS. Evaluation of the functional status aspects of health-related quality of life of patients with osteoarthritis treated with Celecoxib. *Pharmacotherapy* 1999;19(11):1269-1278.
- Zheng P, Tong Z, Jin R, Wang Q, Shi G, Dong Z. One-year follow-up of knee joint function in patients with osteoarthritis after synovectomy under arthroscopy. *Chinese Journal of Clinical Rehabilitation* 2006;10(36):160-162.
- Zheng WJ, Tang FL, Li J, Zhang FC, Li ZG, Su Y, Wu DH, Ma L, Zhou HQ, Huang F, Zhang JL, Liang DF, Zhou YX, Xu H. Evaluation of efficacy and safety of Diacerein in knee osteoarthritis in Chinese patients. *Chin Med Sci J* 2006;21(2):75-80.
- Zhong Q, Ye G, Wang H, Lin S. Treatment of knee osteoarthritis by invigorating the kidney, dispelling the cold and activating the collaterals: A randomized controlled study. *Chinese Journal of Clinical Rehabilitation* 2006;10(47):177-179.
- Zhou SF. Acupuncture as an adjunct to exercise-based physiotherapy does not improve the pain of knee osteoarthritis. *Aust J Acupunct Chin Med* 2008;3:53-55.

Zhu Y,Chen RL,Miao FR,Ji L. [Clinical observation on the therapeutic effect of drugs-paste separated moxibustion combined with electroacupuncture for knee osteoarthritis patients of cold-damp type]. *Zhen ci yan jiu = Acupuncture research / [Zhongguo yi xue ke xue yuan Yi xue qing bao yan jiu suo bian ji]* 2010;35:293-297.

Zietz PM,Selesnick H. The use of hylan G-F 20 after knee arthroscopy in an active patient population with knee osteoarthritis. *Arthroscopy* 2008;24(4):416-422.

Zlnay D,Masaryk P,Rovensky J. Aulin (Nimesulid) - Selective inhibitor of cyclooxygenase-2 in the treatment of osteoarthritis. [Slovak]. *Rheumatologia* 1998;12:19-24.

Zochling J,March L,Lapsley H,Cross M,Tribe K,Brooks P. Use of complementary medicines for osteoarthritis--a prospective study. *Ann Rheum Dis* 2004;63(5):549-554.

Zuegel NP,Braun WG,Kundel KP,Rueter AE. Stabilization of high tibial osteotomy with staples. *Arch Orthop Trauma Surg* 1996;115(5):290-294.

Reference List

- (21) Coleman S, Briffa NK, Carroll G, Inderjeeth C, Cook N, McQuade J. A randomised controlled trial of a self-management education program for osteoarthritis of the knee delivered by health care professionals. *Arthritis Res Ther* 2012;14(1):R21. **PM:22284848**
- (22) Fransen M, Crosbie J, Edmonds J. Physical therapy is effective for patients with osteoarthritis of the knee: a randomized controlled clinical trial. *J Rheumatol* 2001;28(1):156-164. **PM:11196518**
- (23) Bennell KL, Hinman RS, Metcalf BR et al. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis* 2005;64(6):906-912. **PM:15897310**
- (24) Borjesson M, Robertson E, Weidenhielm L, Mattsson E, Olsson E. Physiotherapy in knee osteoarthritis: effect on pain and walking. *Physiother Res Int* 1996;1(2):89-97. **PM:9238726**
- (25) Deyle GD, Henderson NE, Matekel RL, Ryder MG, Garber MB, Allison SC. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med* 2000;132(3):173-181. **PM:10651597**
- (26) Huang MH, Lin YS, Yang RC, Lee CL. A comparison of various therapeutic exercises on the functional status of patients with knee osteoarthritis. *Semin Arthritis Rheum* 2003;32(6):398-406. **PM:12833248**
- (27) Jan MH, Lin CH, Lin YF, Lin JJ, Lin DH. Effects of weight-bearing versus nonweight-bearing exercise on function, walking speed, and position sense in participants with knee osteoarthritis: a randomized controlled trial. *Arch Phys Med Rehabil* 2009;90(6):897-904. **PM:19480863**
- (28) Jan MH, Lin JJ, Liao JJ, Lin YF, Lin DH. Investigation of clinical effects of high- and low-resistance training for patients with knee osteoarthritis: a randomized controlled trial. *Phys Ther* 2008;88(4):427-436. **PM:18218827**
- (29) Ebnezar J, Nagarathna R, Bali Y, Nagendra HR. Effect of an integrated approach of yoga therapy on quality of life in osteoarthritis of the knee joint: A randomized control study. *Int J Yoga* 2011;4(2):55-63. **PM:22022123**
- (30) Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effects of an integrated approach of hatha yoga therapy on functional disability, pain, and flexibility in osteoarthritis of the knee joint: a randomized controlled study. *J Altern Complement Med* 2012;18(5):463-472. **PM:22537508**

- (31) Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effect of integrated yoga therapy on pain, morning stiffness and anxiety in osteoarthritis of the knee joint: A randomized control study. *Int J Yoga* 2012;5(1):28-36. **PM:22346063**
- (32) Silva LE, Valim V, Pessanha AP et al. Hydrotherapy versus conventional land-based exercise for the management of patients with osteoarthritis of the knee: a randomized clinical trial. *Phys Ther* 2008;88(1):12-21. **PM:17986497**
- (33) O'Reilly SC, Muir KR, Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. *Ann Rheum Dis* 1999;58(1):15-19. **PM:10343535**
- (34) Kovar PA, Allegrante JP, MacKenzie CR, Peterson MG, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med* 1992;116(7):529-534. **PM:1543305**
- (35) Fitzgerald GK, Piva SR, Gil AB, Wisniewski SR, Oddis CV, Irrgang JJ. Agility and perturbation training techniques in exercise therapy for reducing pain and improving function in people with knee osteoarthritis: a randomized clinical trial. *Phys Ther* 2011;91:452-469.
- (36) Lin DH, Lin CH, Lin YF, Jan MH. Efficacy of 2 non-weight-bearing interventions, proprioception training versus strength training, for patients with knee osteoarthritis: a randomized clinical trial. *J Orthop Sports Phys Ther* 2009;39(6):450-457. **PM:19531879**
- (37) Topp R, Woolley S, Hornyak J, III, Khuder S, Kahaleh B. The effect of dynamic versus isometric resistance training on pain and functioning among adults with osteoarthritis of the knee. *Arch Phys Med Rehabil* 2002;83(9):1187-1195. **PM:12235596**
- (38) Bennell KL, Hunt MA, Wrigley TV et al. Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomised controlled trial. *Osteoarthritis Cartilage* 2010;18(5):621-628. **PM:20175973**
- (39) Shakoor MA, Rahman MS, Azad AK, Islam MS. Effects of isometric quadriceps muscle strengthening exercise on chronic osteoarthritis of the knee. *Bangladesh Med Res Counc Bull* 2010;36(1):20-22. **PM:21280554**
- (40) Maurer BT, Stern AG, Kinossian B, Cook KD, Schumacher HR, Jr. Osteoarthritis of the knee: isokinetic quadriceps exercise versus an educational intervention. *Arch Phys Med Rehabil* 1999;80(10):1293-1299. **PM:10527090**
- (41) Azad AK, Nabi G, Shakoor MA, Moyeenuzzaman M. Role of muscle strengthening exercise on osteoarthritis of the knee joint. *J Med* 2011;12(2):120-124.
- (42) Ettinger WH, Jr., Burns R, Messier SP et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;277(1):25-31. **PM:8980206**

- (43) Diracoglu D, Aydin R, Baskent A, Celik A. Effects of kinesthesia and balance exercises in knee osteoarthritis. *J Clin Rheumatol* 2005;11(6):303-310. **PM:16371799**
- (44) Teixeira PE, Piva SR, Fitzgerald GK. Effects of Impairment-Based Exercise on Performance of Specific Self-Reported Functional Tasks in Individuals With Knee Osteoarthritis. *Phys Ther* 2011. **PM:22003157**
- (45) Yip YB, Sit JW, Fung KK et al. Effects of a self-management arthritis programme with an added exercise component for osteoarthritic knee: randomized controlled trial. *J Adv Nurs* 2007;59(1):20-28. **PM:17559610**
- (46) Focht BC, Rejeski WJ, Ambrosius WT, Katula JA, Messier SP. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum* 2005;53(5):659-665. **PM:16208674**
- (47) Rejeski WJ, Focht BC, Messier SP, Morgan T, Pahor M, Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol* 2002;21(5):419-426. **PM:12211508**
- (48) McCarthy CJ, Mills PM, Pullen R, Roberts C, Silman A, Oldham JA. Supplementing a home exercise programme with a class-based exercise programme is more effective than home exercise alone in the treatment of knee osteoarthritis. *Rheumatology (Oxford)* 2004;43(7):880-886. **PM:15113993**
- (49) Tunay VB, Baltaci G, Atay AO. Hospital-based versus home-based proprioceptive and strengthening exercise programs in knee osteoarthritis. *Acta Orthop Traumatol Turc* 2010;44(4):270-277. **PM:21252603**
- (50) Allen KD, Oddone EZ, Coffman CJ et al. Telephone-based self-management of osteoarthritis: A randomized trial. *Ann Intern Med* 2010;153(9):570-579. **PM:21041576**
- (51) Hurley MV, Walsh NE, Mitchell HL et al. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster randomized trial. *Arthritis Rheum* 2007;57(7):1211-1219. **PM:17907147**
- (52) Ravaud P, Flipo RM, Boutron I et al. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *BMJ* 2009;338):b421. **PM:19237406**
- (53) Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord* 2008;9):132. **PM:18831740**
- (54) Lee R, Kean WF. Obesity and knee osteoarthritis. *Inflammopharmacology* 2012;20(2):53-58. **PM:22237485**

- (55) Muthuri SG, Hui M, Doherty M, Zhang W. What if we prevent obesity? Risk reduction in knee osteoarthritis estimated through a meta-analysis of observational studies. *Arthritis Care and Research* 2011;63(7):982-990.
- (56) Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring)* 2006;14(7):1219-1230. **PM:16899803**
- (57) Bliddal H, Leeds AR, Stigsgaard L, Astrup A, Christensen R. Weight loss as treatment for knee osteoarthritis symptoms in obese patients: 1-year results from a randomised controlled trial. *Ann Rheum Dis* 2011;70(10):1798-1803. **PM:21821622**
- (58) Riecke BF, Christensen R, Christensen P et al. Comparing two low-energy diets for the treatment of knee osteoarthritis symptoms in obese patients: a pragmatic randomized clinical trial. *Osteoarthritis Cartilage* 2010;18(6):746-754. **PM:20206314**
- (59) Christensen R, Astrup A, Bliddal H. Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. *Osteoarthritis Cartilage* 2005;13(1):20-27. **PM:15639633**
- (60) Jenkinson CM, Doherty M, Avery AJ et al. Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. *BMJ* 2009;339:b3170. **PM:19690345**
- (61) Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 2004;141(12):901-910. **PM:15611487**
- (62) Suarez-Almazor ME, Looney C, Liu Y et al. A randomized controlled trial of acupuncture for osteoarthritis of the knee: effects of patient-provider communication. *Arthritis Care Res (Hoboken)* 2010;62(9):1229-1236. **PM:20506122**
- (63) Weiner DK, Rudy TE, Morone N, Glick R, Kwok CK. Efficacy of periosteal stimulation therapy for the treatment of osteoarthritis-associated chronic knee pain: an initial controlled clinical trial. *J Am Geriatr Soc* 2007;55(10):1541-1547. **PM:17908057**
- (64) Williamson L, Wyatt MR, Yein K, Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology (Oxford)* 2007;46(9):1445-1449. **PM:17604311**
- (65) Taechaarpornkul W, Suvapan D, Theppanom C, Chanthipwaree C, Chirawatkul A. Comparison of the effectiveness of six and two acupuncture point regimens in osteoarthritis of the knee: a randomised trial. *Acupunct Med* 2009;27(1):3-8. **PM:19369186**

- (66) Sangdee C, Teekachunhatean S, Sananpanich K et al. Electroacupuncture versus diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *BMC Complement Altern Med* 2002;2):3. **PM:11914160**
- (67) Vas J, Mendez C, Perea-Milla E et al. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. *BMJ* 2004;329(7476):1216. **PM:15494348**
- (68) Witt C, Brinkhaus B, Jena S et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet* 2005;366(9480):136-143. **PM:16005336**
- (69) Berman BM, Singh BB, Lao L et al. A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. *Rheumatology (Oxford)* 1999;38(4):346-354. **PM:10378713**
- (70) Fary RE, Carroll GJ, Briffa TG, Briffa NK. The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: results of a double-blind, randomized, placebo-controlled, repeated-measures trial. 2011.
[http://dx.doi.org/10.1002/art.30258;](http://dx.doi.org/10.1002/art.30258)
[http://www.ncbi.nlm.nih.gov/pubmed/21312188;](http://www.ncbi.nlm.nih.gov/pubmed/21312188)
<http://onlinelibrary.wiley.com/journal/10.1002/%28ISSN%291529-0131/issues>
- (71) Zizic TM, Hoffman KC, Holt PA et al. The treatment of osteoarthritis of the knee with pulsed electrical stimulation. 1995.
[https://www.cebp.nl/vault_public/filesystem/?ID=2503;](https://www.cebp.nl/vault_public/filesystem/?ID=2503)
[http://www.ncbi.nlm.nih.gov/pubmed/8523357;](http://www.ncbi.nlm.nih.gov/pubmed/8523357) <http://www.jrheum.com/>
- (72) Trock DH, Bollet AJ, Markoll R. The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee and cervical spine. Report of randomized, double blind, placebo controlled trials. *J Rheumatol* 1994;21(10):1903-1911. **PM:7837158**
- (73) Atamaz FC, Durmaz B, Baydar M et al. Comparison of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled, multicenter study. *Arch Phys Med Rehabil* 2012;93(5):748-756. **PM:22459699**
- (74) Battisti E, Piazza E, Rigato M et al. Efficacy and safety of a musically modulated electromagnetic field (TAMMEF) in patients affected by knee osteoarthritis. *Clin Exp Rheumatol* 2004;22(5):568-572. **PM:15485009**
- (75) Huang MH, Yang RC, Lee CL, Chen TW, Wang MC. Preliminary results of integrated therapy for patients with knee osteoarthritis. *Arthritis Rheum* 2005;53(6):812-820. **PM:16342083**
- (76) Yang PF, Li D, Zhang SM et al. Efficacy of ultrasound in the treatment of osteoarthritis of the knee. *Orthop Surg* 2011;3(3):181-187. **PM:22009649**

- (77) Perlman AI, Sabina A, Williams AL, Njike VY, Katz DL. Massage therapy for osteoarthritis of the knee: a randomized controlled trial. *Arch Intern Med* 2006;166(22):2533-2538. **PM:17159021**
- (78) Kirkley A, Webster-Bogaert S, Litchfield R et al. The effect of bracing on varus gonarthrosis. *J Bone Joint Surg Am* 1999;81(4):539-548. **PM:10225800**
- (79) van-Raaij TM, Reijman M, Brouwer RW, Bierma-Zeinstra SM, Verhaar JA. Medial knee osteoarthritis treated by insoles or braces: a randomized trial. *Clin Orthop* 2010;468):1926-1932.
- (80) Brouwer RW, van Raaij TM, Verhaar JA, Coene LN, Bierma-Zeinstra SM. Brace treatment for osteoarthritis of the knee: a prospective randomized multi-centre trial. *Osteoarthritis Cartilage* 2006;14(8):777-783. **PM:16563810**
- (81) Bennell KL, Bowles KA, Payne C et al. Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial. *BMJ* 2011;342):d2912. **PM:21593096**
- (82) Baker K, Goggins J, Xie H et al. A randomized crossover trial of a wedged insole for treatment of knee osteoarthritis. *Arthritis Rheum* 2007;56(4):1198-1203. **PM:17393448**
- (83) Maillefert JF, Hudry C, Baron G et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis: a prospective randomized controlled study. *Osteoarthritis Cartilage* 2001;9(8):738-745. **PM:11795993**
- (84) Pham T, Maillefert JF, Hudry C et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis. A two-year prospective randomized controlled study. *Osteoarthritis Cartilage* 2004;12(1):46-55. **PM:14697682**
- (85) Toda Y, Tsukimura N. A comparative study on the effect of the insole materials with subtalar strapping in patients with medial compartment osteoarthritis of the knee. *Modern Rheumatology* 2004;14(6):459-465.
- (86) Clegg DO, Reda DJ, Harris CL et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006;354(8):795-808. **PM:16495392**
- (87) Mehta K, Gala J, Bhasale S et al. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial [ISRCTN25438351]. *BMC Complement Altern Med* 2007;7):34. **PM:17974032**
- (88) Trc T, Bohmova J. Efficacy and tolerance of enzymatic hydrolysed collagen (EHC) vs. glucosamine sulphate (GS) in the treatment of knee osteoarthritis (KOA). *Int Orthop* 2010. **PM:20401752**
- (89) Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum* 2001;44(11):2531-2538. **PM:11710709**

- (90) Zakeri Z, Izadi S, Bari Z, Soltani F, Narouie B, Ghasemi-Rad M. Evaluating the effects of ginger extract on knee pain, stiffness and difficulty in patients with knee osteoarthritis. *Journal of Medicinal Plant Research* 2011;5(15):3375-3379.
- (91) Pavelka K, Jr., Sedlackova M, Gatterova J, Becvar R, Pavelka K, Sr. Glycosaminoglycan polysulfuric acid (GAGPS) in osteoarthritis of the knee. *Osteoarthritis Cartilage* 1995;3(1):15-23. **PM:7536623**
- (92) Cibere J, Kopec JA, Thorne A et al. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *Arthritis Rheum* 2004;51(5):738-745. **PM:15478160**
- (93) Mazieres B, Combe B, Phan VA, Tondut J, Grynfeldt M. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study. *J Rheumatol* 2001;28(1):173-181. **PM:11196521**
- (94) Pavelka K, Coste P, Geher P, Krejci G. Efficacy and safety of piascledine 300 versus chondroitin sulfate in a 6 months treatment plus 2 months observation in patients with osteoarthritis of the knee. *Clin Rheumatol* 2010;29(6):659-670. **PM:20179981**
- (95) Fishman RL, Kistler CJ, Ellerbusch MT et al. Efficacy and safety of 12 weeks of osteoarthritic pain therapy with once-daily tramadol (Tramadol Contramid OAD). *J Opioid Manag* 2007;3(5):273-280. **PM:18181382**
- (96) Beaulieu AD, Peloso PM, Haraoui B et al. Once-daily, controlled-release tramadol and sustained-release diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial. *Pain Res Manag* 2008;13(2):103-110. **PM:18443672**
- (97) Miceli-Richard C, Le BM, Schmidely N, Dougados M. Paracetamol in osteoarthritis of the knee. *Ann Rheum Dis* 2004;63(8):923-930. **PM:15249319**
- (98) Schnitzer TJ, Weaver AL, Polis AB, Petruschke RA, Geba GP. Efficacy of rofecoxib, celecoxib, and acetaminophen in patients with osteoarthritis of the knee. A combined analysis of the VACT studies. *J Rheumatol* 2005;32(6):1093-1105. **PM:15940774**
- (99) Evcik D, Maralcan G, Kuru I. The efficacy of intra-articular tenoxicam in the treatment of knee osteoarthritis. *Pain Clinic* 2003;15(4):405-408.
- (100) Ottillinger B, Gomor B, Michel BA, Pavelka K, Beck W, Elsasser U. Efficacy and safety of eltenac gel in the treatment of knee osteoarthritis. *Osteoarthritis Cartilage* 2001;9(3):273-280. **PM:11300751**
- (101) Rother M, Lavins BJ, Kneer W, Lehnhardt K, Seidel EJ, Mazgareanu S. Efficacy and safety of epicutaneous ketoprofen in Transfersome (IDEA-033) versus oral celecoxib and placebo in osteoarthritis of the knee: multicentre randomised controlled trial. *Ann Rheum Dis* 2007;66(9):1178-1183. **PM:17363401**

- (102) Chao J, Wu C, Sun B et al. Inflammatory characteristics on ultrasound predict poorer longterm response to intraarticular corticosteroid injections in knee osteoarthritis. *J Rheumatol* 2010;37(3):650-655. **PM:20080918**
- (103) Gaffney K, Ledingham J, Perry JD. Intra-articular triamcinolone hexacetonide in knee osteoarthritis: factors influencing the clinical response. *Ann Rheum Dis* 1995;54(5):379-381. **PM:7794044**
- (104) Raynauld JP, Buckland-Wright C, Ward R et al. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2003;48(2):370-377. **PM:12571845**
- (105) Jones A, Doherty M. Intra-articular corticosteroids are effective in osteoarthritis but there are no clinical predictors of response. *Ann Rheum Dis* 1996;55(11):829-832. **PM:8976640**
- (106) Caborn D, Rush J, Lanzer W, Parenti D, Murray C. A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. *J Rheumatol* 2004;31(2):333-343. **PM:14760806**
- (107) Arden NK, Reading IC, Jordan KM et al. A randomised controlled trial of tidal irrigation vs corticosteroid injection in knee osteoarthritis: the KIVIS Study. *Osteoarthritis Cartilage* 2008;16(6):733-739. **PM:18077189**
- (108) Lundsgaard C, Dufour N, Fallentin E, Winkel P, Gluud C. Intra-articular sodium hyaluronate 2 mL versus physiological saline 20 mL versus physiological saline 2 mL for painful knee osteoarthritis: a randomized clinical trial. *Scand J Rheumatol* 2008;37(2):142-150. **PM:18415773**
- (109) Huang TL, Chang CC, Lee CH, Chen SC, Lai CH, Tsai CL. Intra-articular injections of sodium hyaluronate (Hyalgan(R)) in osteoarthritis of the knee. a randomized, controlled, double-blind, multicenter trial in the asian population. *BMC Musculoskelet Disord* 2011;12):221. **PM:21978211**
- (110) Puhl W, Bernau A, Greiling H et al. Intra-articular sodium hyaluronate in osteoarthritis of the knee: a multicenter, double-blind study. *Osteoarthritis Cartilage* 1993;1(4):233-241. **PM:15449510**
- (111) Day R, Brooks P, Conaghan PG, Petersen M. A double blind, randomized, multicenter, parallel group study of the effectiveness and tolerance of intraarticular hyaluronan in osteoarthritis of the knee. *J Rheumatol* 2004;31(4):775-782. **PM:15088306**
- (112) Juni P, Reichenbach S, Trelle S et al. Efficacy and safety of intraarticular hylan or hyaluronic acids for osteoarthritis of the knee: a randomized controlled trial. *Arthritis Rheum* 2007;56(11):3610-3619. **PM:17968921**

- (113) Maheu E, Zaim M, Appelboom T et al. Comparative efficacy and safety of two different molecular weight (MW) hyaluronans F60027 and Hylan G-F20 in symptomatic osteoarthritis of the knee (KOA). Results of a non inferiority, prospective, randomized, controlled trial. Clin Exp Rheumatol 2011;29(3):527-535. **PM:21722501**
- (114) Lee PB, Kim YC, Lim YJ et al. Comparison between high and low molecular weight hyaluronates in knee osteoarthritis patients: open-label, randomized, multicentre clinical trial. J Int Med Res 2006;34(1):77-87. **PM:16604827**
- (115) Raman R, Dutta A, Day N, Sharma HK, Shaw CJ, Johnson GV. Efficacy of Hylan G-F 20 and Sodium Hyaluronate in the treatment of osteoarthritis of the knee -- a prospective randomized clinical trial. Knee 2008;15(4):318-324. **PM:18430574**
- (116) Karlsson J, Sjogren LS, Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. Rheumatology (Oxford) 2002;41(11):1240-1248. **PM:12421996**
- (117) Kahan A, Lleo PL, Salin L. Prospective randomized study comparing the medicoeconomic benefits of Hylan GF-20 vs. conventional treatment in knee osteoarthritis. Joint Bone Spine 2003;70(4):276-281. **PM:12951310**
- (118) Altman RD, Akemark C, Beaulieu AD, Schnitzer T. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. Osteoarthritis Cartilage 2004;12(8):642-649. **PM:15262244**
- (119) Sanchez M, Fiz N, Azofra J et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. Arthroscopy 2012;28(8):1070-1078. **PM:22840987**
- (120) Sanchez M, Anitua E, Azofra J, Aguirre JJ, Andia I. Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. Clin Exp Rheumatol 2008;26(5):910-913. **PM:19032827**
- (121) Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil 2012;91(5):411-417. **PM:22513879**
- (122) Bradley JD, Heilman DK, Katz BP, Gsell P, Wallick JE, Brandt KD. Tidal irrigation as treatment for knee osteoarthritis: a sham-controlled, randomized, double-blinded evaluation. Arthritis Rheum 2002;46(1):100-108. **PM:11817581**
- (123) Vad VB, Bhat AL, Sculco TP, Wickiewicz TL. Management of knee osteoarthritis: knee lavage combined with hylan versus hylan alone. Arch Phys Med Rehabil 2003;84(5):634-637. **PM:12736873**

- (124) Kirkley A, Birmingham TB, Litchfield RB et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2008;359(11):1097-1107. **PM:18784099**
- (125) Kalunian KC, Moreland LW, Klashman DJ et al. Visually-guided irrigation in patients with early knee osteoarthritis: a multicenter randomized, controlled trial. *Osteoarthritis Cartilage* 2000;8(6):412-418. **PM:11069725**
- (126) Moseley JB, O'Malley K, Petersen NJ et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002;347(2):81-88. **PM:12110735**
- (127) Herrlin S, Hallander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. *Knee Surg Sports Traumatol Arthrosc* 2007;15(4):393-401. **PM:17216272**
- (128) Brouwer RW, Bierma-Zeinstra SM, van Raaij TM, Verhaar JA. Osteotomy for medial compartment arthritis of the knee using a closing wedge or an opening wedge controlled by a Puddu plate. A one-year randomised, controlled study. *J Bone Joint Surg Br* 2006;88(11):1454-1459. **PM:17075089**
- (129) Song IH, Song EK, Seo HY, Lee KB, Yim JH, Seon JK. Patellofemoral Alignment and Anterior Knee Pain After Closing- and Opening-Wedge Valgus High Tibial Osteotomy. *Arthroscopy* 2012. **PM:22520445**
- (130) Pongsoipetch B, Tantikul C. Open-wedge high tibial osteotomy in varus knee osteoarthritis: a 5-year prospective cohort study. *J Med Assoc Thai* 2009;92 Suppl 6):S109-S114. **PM:20128075**
- (131) El-Azab HM, Morgenstern M, Ahrens P, Schuster T, Imhoff AB, Lorenz SGF. Limb alignment after open-wedge high tibial osteotomy and its effect on the clinical outcome. *Orthopedics* 2011;34(10):e622-e628.
- (132) Rudan JF, Simurda MA. High tibial osteotomy. A prospective clinical and roentgenographic review. *Clin Orthop Relat Res* 1990;(255):251-256. **PM:2347159**
- (133) Sisto DJ, Mitchell IL. UniSpacer arthroplasty of the knee. *J Bone Joint Surg Am* 2005;87(8):1706-1711. **PM:16085608**
- (134) Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Lawrence Erlbaum Associates, 1998.
- (135) Thorpe KE, Zwarenstein M, Oxman AD et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clin Epidemiol* 2009;62(5):464-475. **PM:19348971**
- (136) Petitti DB, Teutsch SM, Barton MB, Sawaya GF, Ockene JK, DeWitt T. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. *Ann Intern Med* 2009;150(3):199-205. **PM:19189910**

- (137) Murphy MK, Black LA, Lamping DL, McKee CM, Sanderson C.F., Askam J. Consensus development methods, and their use in clinical guideline development. *Health Technol Assess* 1998.