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Appendix 1 Search strategies

Phase one (identifying: (1) common comparators between exercise with oral non-steroidal anti-inflammatory drugs [NSAIDs] and paracetamol; (2) first part of direct evidence between exercise versus oral NSAIDs and paracetamol, i.e., randomised controlled trials [RCTs] comparing exercise with oral NSAIDs and paracetamol; and (3) first part of indirect evidence between exercise versus oral NSAIDs and paracetamol, i.e., RCTs comparing exercise with potential common comparators [e.g., usual care/no treatment/waiting list control, glucosamine sulphate/chondroitin sulphate, intra-articular hyaluronic acid, topical NSAIDs, acupuncture] that can connect exercise with oral NSAIDs and paracetamol):

MEDLINE (PubMed)

1. (exercise) OR (physical conditioning, human)
2. (Circuit-Based Exercise)
3. (exercise therapy) OR (motion therapy, continuous passive) OR (muscle stretching exercises) OR (plyometric exercise) OR (resistance training) OR (hydrotherapy) OR (rehabilitation) OR (activities of daily living) OR (dance therapy)
4. (muscle strength) OR (physical endurance) OR (anaerobic threshold) OR (exercise tolerance) OR (physical fitness) OR (postural balance) OR (posture) OR (psychomotor performance) OR (range of motion, articular)
5. (Pliability)
6. (movement) OR (motor activity) OR (exercise)
7. (Physical Exertion)
8. (Mind-Body Therapies)
9. (running) OR (jogging) OR (swimming) OR (walking)
10. (Isometric Contraction)
11. (exercise movement techniques) OR (breathing exercises) OR (qigong) OR (tai ji) OR (yoga) OR (pilates)
12. Propriocepti*[title/abstract]
13. Balanc*[title/abstract]
14. Aquat*[title/abstract]
15. Cycl*[title/abstract]
16. Aerobic[title/abstract]
17. Strength*[title/abstract]
18. (((((((tai-ji[Title/Abstract]) OR taiji[Title/Abstract]) OR taijiquan[Title/Abstract]) OR tai ji quan[Title/Abstract]) OR tai chi[Title/Abstract]) OR taichi[Title/Abstract]) OR t ai chi[Title/Abstract]) OR t'ai chi[Title/Abstract]) OR tai chi chuan[Title/Abstract]
19. (qigong)[title/abstract] OR (qi gong)[title/abstract] OR (chi kung)[title/abstract] OR (chikung)[title/abstract] OR (ch i kung)[title/abstract] OR (ch'i kung)[title/abstract]
20. Therap*[title/abstract]
21. Physiotherapy*[title/abstract]
22. Train*[title/abstract]
23. neuromuscular training[title/abstract]

24. treadmill[title/abstract]
25. OR/1-24
26. osteoarthriti*[tiab] OR osteoarthriti*[mh]
27. osteoarthro*[tiab] OR gonarthriti*[tiab] OR gonarthro*[tiab] OR coxarthriti*[tiab] OR coxarthro*[tiab] OR osteo?arthritis[tiab]
28. (knee*[tiab] OR hip[tiab] OR joint*[tiab]) AND (pain*[tiab] OR discomfort*[tiab])
29. (knee*[tiab] OR hip[tiab] OR joint*[tiab]) AND stiff*[tiab]
30. OR/26-29
31. random*[tiab] OR placebo[tiab] OR controlled[tiab] OR trial*[tiab]
32. (singl*[tiab] OR doubl*[tiab] OR tripl*[tiab]) and (mask*[tiab] OR blind*[tiab])
33. compar*[tiab]
34. OR/31-33
35. 25 AND 30 AND 34

Embase

1. 'exercise'/exp
2. (exercise) OR (physical conditioning, human)
3. (Circuit-Based Exercise)
4. (exercise therapy) OR (motion therapy, continuous passive) OR (muscle stretching exercises) OR (plyometric exercise) OR (resistance training) OR (hydrotherapy) OR (rehabilitation) OR (activities of daily living) OR (dance therapy)
5. (muscle strength) OR (physical endurance) OR (anaerobic threshold) OR (exercise tolerance) OR (physical fitness) OR (postural balance) OR (posture) OR (psychomotor performance) OR (range of motion, articular)
6. (Pliability)
7. (movement) OR (motor activity) OR (exercise)
8. (Physical Exertion)
9. (Mind-Body Therapies)
10. (running) OR (jogging) OR (swimming) OR (walking)
11. (Isometric Contraction)
12. (exercise movement techniques) OR (breathing exercises) OR (qigong) OR (tai ji) OR (yoga) OR (pilates)
13. Propriocepti*:ti,ab
14. Balanc*:ti,ab
15. Aquat*:ti,ab
16. Cycl*:ti,ab
17. Aerobic:ti,ab
18. Strength*:ti,ab
19. (tai-ji OR taiji OR taijiquan OR tai ji quan OR tai chi OR taichi OR tai chi chuan):ti,ab
20. (qigong OR qi gong OR chi kung OR chikung OR chi kung):ti,ab
21. Therap*:ti,ab
22. Physiotherapy*:ti,ab
23. Train*:ti,ab
24. neuromuscular training:ti,ab
25. treadmill:ti,ab
26. OR/1-25
27. 'osteoarthritis'/exp
28. (osteoarthriti* OR osteoarthro* OR gonarthriti* OR gonarthro* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*):ti,ab
29. ((knee* OR hip* OR joint*) near/3 (pain* OR ach* OR discomfort*)):ti,ab
30. ((knee* OR hip* OR joint*) near/3 stiff*):ti,ab
31. OR/27-30
32. (random* or controlled or trial* or placebo):ti,ab
33. ((singl* or doubl*or tripl*) and (mask* or blind*)):ti,ab
34. (compar*):ti,ab
35. OR/32-34
36. 26 AND 31 AND 35

Web of science

1. TITLE: ((exercise OR physical conditioning, human OR Circuit-Based Exercise OR exercise therapy OR motion therapy, continuous passive OR muscle stretching exercises OR plyometric exercise OR resistance training OR hydrotherapy OR rehabilitation OR activities of daily living OR dance therapy OR muscle strength OR physical endurance OR anaerobic threshold OR exercise tolerance OR physical fitness OR postural balance OR posture OR psychomotor performance OR range of motion, articular OR Pliability OR movement OR motor activity OR Physical Exertion OR Mind-Body Therapies OR running OR jogging OR swimming OR walking OR Isometric Contraction OR exercise movement techniques OR breathing exercises OR qigong OR tai ji OR yoga OR pilates OR Propriocepti* OR Balanc* OR Aquat* OR Cycl* OR Aerobic OR Strength* OR tai-ji OR taiji OR taijiquan OR tai ji quan OR tai chi OR taichi OR tai chi chuan OR qigong OR qi gong OR chikung OR chi kung OR Therap* OR Physiotherapy* OR Train* OR neuromuscular training OR treadmill))
2. TITLE: (osteoarthriti* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*)
3. TITLE: (random* OR control* OR placebo)
4. TITLE: ((singl* OR doubl* OR tripl*) and (mask* OR blind*))
5. TITLE: (compar*)
6. OR/3-5
7. 1 AND 2 AND 6

Cochrane Library

1. MeSH descriptor Osteoarthritis explode all trees
2. (osteoarthritis* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*):ti,ab,kw
3. 1 OR 2
4. MESH descriptor exercise explode all trees
5. (exercise) OR (physical conditioning, human)
6. (Circuit-Based Exercise)
7. (exercise therapy) OR (motion therapy, continuous passive) OR (muscle stretching exercises) OR (plyometric exercise) OR (resistance training) OR (hydrotherapy) OR (rehabilitation) OR (activities of daily living) OR (dance therapy)
8. (muscle strength) OR (physical endurance) OR (anaerobic threshold) OR (exercise tolerance) OR (physical fitness) OR (postural balance) OR (posture) OR (psychomotor performance) OR (range of motion, articular)
9. (Pliability)
10. (movement) OR (motor activity) OR (exercise)
11. (Physical Exertion)
12. (Mind-Body Therapies)
13. (running) OR (jogging) OR (swimming) OR (walking)
14. (Isometric Contraction)
15. (exercise movement techniques) OR (breathing exercises) OR (qigong) OR (tai ji) OR (yoga) OR (pilates)
16. Propriocepti*:ab,ti
17. Balanc*:ab,ti
18. Aquat*:ab,ti
19. Cycl*:ab,ti
20. Aerobic:ab,ti
21. Strength*:ab,ti
22. (tai-ji OR taiji OR taijiquan OR tai ji quan OR tai chi OR taichi OR tai chi chuan):ab,ti
23. (qigong OR qi gong OR chi kung OR chikung OR ch i kung):ab,ti
24. Therap*:ab,ti
25. Physiotherapy*:ab,ti
26. Train*:ab,ti
27. neuromuscular training:ab,ti
28. treadmill:ab,ti
29. OR/4-28
30. 3 AND 29

Scopus

1. TITLE-ABS(exercise)
2. TITLE-ABS((“exercise therapy”) OR (“motion therapy”) OR (“muscle stretching exercises”) OR (“plyometric exercise”) OR (“resistance training”) OR (“hydrotherapy”) OR (“rehabilitation”) OR (“activities of daily living”) OR (“dance therapy”) OR (“Mind-Body Therapies”) OR (“neuromuscular training”) OR ((running) OR (jogging) OR (swimming) OR (walking)))
3. TITLE-ABS(Propriocepti*)
4. TITLE-ABS(Balanc*)
5. TITLE-ABS(Aquat*)
6. TITLE-ABS(Cycl*)
7. TITLE-ABS(Aerobic)
8. TITLE-ABS(Strength*)
9. OR/1-8
10. TITLE-ABS(osteoarthriti*)
11. TITLE-ABS(osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR osteo?arthritis)
12. OR/10-11
13. TITLE-ABS(random* OR placebo OR controlled OR trial*)
14. TITLE-ABS(singl* OR doubl* OR tripl*) and TITLE-ABS(mask* OR blind*)
15. TITLE-ABS(compar*)
16. OR/13-15
17. 9 AND 12 AND 16

Phase two (identifying: (1) second part of direct evidence between exercise versus oral NSAIDs and paracetamol; and (2) second part of indirect evidence between exercise versus oral NSAIDs and paracetamol, i.e., RCTs comparing exercise or oral NSAIDs and paracetamol with potential common comparators [e.g., usual care/no treatment/waiting list control, glucosamine sulphate/chondroitin sulphate, intra-articular hyaluronic acid, topical NSAIDs, acupuncture] that can connect exercise with oral NSAIDs and paracetamol):

MEDLINE (PubMed)

1.1 Search strategies for oral NSAIDs and paracetamol vs. all interventions

1. "non-steroidal anti-inflammatory agents"[Text Word] OR "anti-inflammatory agents, non-steroidal"[Mesh] OR "antiinflammatory agents, non-steroidal"[Pharmacological Action] OR "Anti-Inflammatory Agents, Non-Steroidal"[Text Word] OR "NSAIDs"[tiab] OR "nonsteroidal antiinflammatory"[tiab] OR "Non-Steroidal Anti-Inflammator*"[tiab] OR "Selective Non-Steroidal Anti-Inflammator*"[tiab]
2. "Cyclooxygenase 2 Inhibitors"[Mesh] OR (cyclooxygenase-2[tiab] inhibitor*[tiab]) OR (cyclooxygenase-II[tiab] inhibitor*[tiab]) OR (cyclo-oxygenase-2[tiab] inhibitor*[tiab]) OR (cyclo-oxygenase-II[tiab] inhibitor*[tiab]) OR (COX2[tiab] inhibitor*[tiab]) OR (COX-2[tiab] inhibitor*[tiab]) OR (COX-II[tiab] inhibitor*[tiab]) OR (COXII[tiab] inhibitor*[tiab])
3. (cyclooxygenase-2[tiab] antagonist*[tiab]) OR (cyclooxygenase-II[tiab] antagonist*[tiab]) OR (cyclo-oxygenase-2[tiab] antagonist*[tiab]) OR (cyclo-oxygenase-II[tiab] antagonist*[tiab]) OR (COX2[tiab] antagonist*[tiab]) OR (COX-2[tiab] antagonist*[tiab]) OR (COX-II[tiab] antagonist*[tiab]) OR (COXII[tiab] antagonist*[tiab])
4. (prostaglandin[tiab] synthase[tiab] inhibitor[tiab]) OR (prostaglandin[tiab] synthase[tiab] inhibitor*[tiab]) OR (prostaglandin[tiab] synthase[tiab] antagonist[tiab]) OR (prostaglandin[tiab] synthase[tiab] antagonist*[tiab])
5. (Acetaminophen OR Paracetamol OR Tylenol OR ibuprofen OR ketoprofen OR fenoprofen OR oxaprozin OR sulindac OR flurbiprofen OR diclofenac OR naproxen OR tenoxicam OR piroxicam OR droxicam OR indometacin OR indomethacin OR feprazone OR phenylbutazone OR isoxicam OR meclofenamate OR ketorolac OR lornoxicam OR nabumetone OR meloxicam OR aceclofenac OR alclofenac OR dexibuprofen OR dexketoprofen OR metamizol OR phenazone OR propyphenazone OR Prenazone OR ximoprofen OR Apazone OR Bufexamac OR Clonixin OR Curcumin OR Dexibruprofen OR Dipyrone OR Epirizole OR Fenbufen OR Fenclofenac OR Lederfen OR "Niflumic Acid" OR Oxyphenbutazone OR pirazolac OR pirprofen OR Ponstan OR Suprofen OR "Tiaprofenic acid" OR "tolfenamic acid" OR Tolmetin OR "meclofenamic acid" OR "mefenamic acid")[tiab]
6. (coxib* OR apricoxib OR celecoxib OR cimicoxib OR darbufelone OR deracoxib OR etoricoxib OR firocoxib OR flosulide OR lumiracoxib OR mavacoxib OR methanesulfonamide OR nimesulide OR parecoxib OR robenacoxib OR tiracoxib OR valdecoxib OR vedaprofen OR etodolac OR rofecoxib OR vioxx OR Celebrex OR bextra OR prexige OR arcoxia OR floctafenine OR meclofenam* OR Mesalamine OR Ceoxx OR Ceeoxx OR Cimalgex OR Deramaxx OR Onsior OR "JTE-522" OR movalis OR mobec OR Mobic OR movicox OR mobicox OR parocin OR uticox OR Daypro OR Dayrun OR Duraprox OR meclomen OR Ponstan OR Xefo OR Seractil OR Antipyrine OR Metherazone OR Loxonin OR indoprofen OR Diflunisal

OR Carprofen OR “Flufenamic acid” OR Flunixin OR Ramifenazone)[tiab]

7. OR/1-6
8. osteoarthriti*[tiab] OR osteoarthriti*[mh]
9. osteoarthro*[tiab] OR gonarthriti*[tiab] OR gonarthro*[tiab] OR coxarthriti*[tiab] OR coxarthro*[tiab] OR osteo?arthritis[tiab]
10. 8 OR 9
11. random*[tiab] OR placebo[tiab] OR controlled[tiab] OR trial*[tiab]
12. (singl*[tiab] OR doubl*[tiab] OR tripl*[tiab]) and (mask*[tiab] OR blind*[tiab])
13. compar*[tiab]
14. OR/11-13
15. 7 AND 10 AND 14

1.2 Search strategies for exercise vs. all interventions

1. (exercise) OR (physical conditioning, human)
2. (Circuit-Based Exercise)
3. (exercise therapy) OR (motion therapy, continuous passive) OR (muscle stretching exercises) OR (plyometric exercise) OR (resistance training) OR (hydrotherapy) OR (rehabilitation) OR (activities of daily living) OR (dance therapy)
4. (muscle strength) OR (physical endurance) OR (anaerobic threshold) OR (exercise tolerance) OR (physical fitness) OR (postural balance) OR (posture) OR (psychomotor performance) OR (range of motion, articular)
5. (Pliability)
6. (movement) OR (motor activity) OR (exercise)
7. (Physical Exertion)
8. (Mind-Body Therapies)
9. (running) OR (jogging) OR (swimming) OR (walking)
10. (Isometric Contraction)
11. (exercise movement techniques) OR (breathing exercises) OR (qigong) OR (tai ji) OR (yoga) OR (pilates)
12. Propriocepti*[title/abstract]
13. Balanc*[title/abstract]
14. Aquat*[title/abstract]
15. Cycl*[title/abstract]
16. Aerobic[title/abstract]
17. Strength*[title/abstract]
18. (((((((tai-ji[Title/Abstract]) OR taiji[Title/Abstract]) OR taijiquan[Title/Abstract]) OR tai ji quan[Title/Abstract]) OR tai chi[Title/Abstract]) OR taichi[Title/Abstract]) OR t ai chi[Title/Abstract]) OR t'ai chi[Title/Abstract]) OR tai chi chuan[Title/Abstract]
19. (qigong)[title/abstract] OR (qi gong)[title/abstract] OR (chi kung)[title/abstract] OR (chikung)[title/abstract] OR (ch i kung)[title/abstract] OR (ch'i kung)[title/abstract]
20. Therap*[title/abstract]
21. Physiotherapy*[title/abstract]
22. Train*[title/abstract]
23. neuromuscular training[title/abstract]

24. treadmill[title/abstract]
25. OR/1-24
26. osteoarthriti*[tiab] OR osteoarthriti*[mh]
27. osteoarthro*[tiab] OR gonarthriti*[tiab] OR gonarthro*[tiab] OR coxarthriti*[tiab] OR coxarthro*[tiab] OR osteo?arthritis[tiab]
28. (knee*[tiab] OR hip[tiab] OR joint*[tiab]) AND (pain*[tiab] OR discomfort*[tiab])
29. (knee*[tiab] OR hip[tiab] OR joint*[tiab]) AND stiff*[tiab]
30. OR/26-29
31. random*[tiab] OR placebo[tiab] OR controlled[tiab] OR trial*[tiab]
32. (singl*[tiab] OR doubl*[tiab] OR tripl*[tiab]) and (mask*[tiab] OR blind*[tiab])
33. compar*[tiab]
34. OR/31-33
35. 25 AND 30 AND 34

Embase

2.1 Search strategies for oral NSAIDs and paracetamol vs. all interventions

1. ((nonsteroid antiinflammatory agent*) OR (non-steroidal anti-inflammatory agent*) OR NSAIDs):ti,ab
2. ((Cyclooxygenase 2 Inhibitor*) OR (cyclooxygenase-2 inhibitor*) OR (cyclooxygenase-II inhibitor*) OR (cyclo-oxygenase-2 inhibitor*) OR (cyclo-oxygenase-II inhibitor*) OR (COX2 inhibitor*) OR (COX-2 inhibitor*) OR (COX-II inhibitor*) OR (COXII inhibitor*)):ti,ab
3. (Acetaminophen OR Paracetamol OR Tylenol OR ibuprofen OR ketoprofen OR fenoprofen OR oxaprozin OR sulindac OR flurbiprofen OR diclofenac OR naproxen OR tenoxicam OR piroxicam OR droxicam OR indometacin OR indomethacin OR feprazone OR phenylbutazone OR isoxicam OR meclofenamate OR ketorolac OR lornoxicam OR nabumetone OR meloxicam OR aceclofenac OR alclofenac OR dexibuprofen OR dexketoprofen OR metamizol OR phenazone OR propyphenazone OR Prenazone OR ximoprofen OR Apazone OR Bufexamac OR Clonixin OR Curcumin OR Dexibruprofen OR Dipyrone OR Epirizole OR Fenbufen OR Fenclofenac OR Lederfen OR “Niflumic Acid” OR Oxyphenbutazone OR pirazolac OR pirprofen OR Ponstan OR Suprofen OR “Tiaprofenic acid” OR “tolfenamic acid” OR Tolmetin OR “meclofenamic acid” OR “mefenamic acid”):ti,ab
4. (coxib* OR apricoxib OR celecoxib OR cimicoxib OR darbufelone OR deracoxib OR etoricoxib OR firocoxib OR flosulide OR lumiracoxib OR mavacoxib OR methanesulfonamide OR nimesulide OR parecoxib OR robenacoxib OR tiracoxib OR valdecoxib OR vedaprofen OR etodolac OR rofecoxib OR vioxx OR Celebrex OR bextra OR prexige OR arcoxia OR floctafenine OR meclofenam* OR Mesalamine OR Ceoxx OR Ceeoxx OR Cimalgex OR Deramaxx OR Onsior OR “JTE-522” OR movalis OR mobec OR Mobic OR movicox OR mobicox OR parocin OR uticox OR Daypro OR Dayrun OR Duraprox OR meclomen OR Ponstan OR Xefo OR Seractil OR Antipyrine OR Metherazone OR Loxonin OR indoprofen OR Diflunisal OR Carprofen OR “Flufenamic acid” OR Flunixin OR Ramifenazone):ti,ab
5. OR/1-4
6. (osteoarthriti* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*):ti,ab
7. (random* OR controlled OR trial* OR placebo):ti,ab
8. ((singl* OR doubl*OR tripl*) and (mask* OR blind*)):ti,ab
9. (compar*):ti,ab
10. OR/7-9
11. 5 AND 6 AND 10

2.2 Search strategies for exercise vs. all interventions

1 ‘exercise’/exp
2 (exercise) OR (physical conditioning, human)
3 (Circuit-Based Exercise)
4 (exercise therapy) OR (motion therapy, continuous passive) OR (muscle stretching exercises) OR (plyometric exercise) OR (resistance training) OR (hydrotherapy) OR (rehabilitation) OR (activities of daily living) OR (dance therapy)
5 (muscle strength) OR (physical endurance) OR (anaerobic threshold) OR (exercise tolerance) OR (physical fitness) OR (postural balance) OR (posture) OR (psychomotor performance) OR (range

of motion, articular)
6 (Pliability)
7 (movement) OR (motor activity) OR (exercise)
8 (Physical Exertion)
9 (Mind-Body Therapies)
10 (running) OR (jogging) OR (swimming) OR (walking)
11 (Isometric Contraction)
12 (exercise movement techniques) OR (breathing exercises) OR (qigong) OR (tai ji) OR (yoga) OR (pilates)
13 Propriocepti*:ti,ab
14 Balanc*:ti,ab
15 Aquat*:ti,ab
16 Cycl*:ti,ab
17 Aerobic:ti,ab
18 Strength*:ti,ab
19 (tai-ji OR taiji OR taijiquan OR tai ji quan OR tai chi OR taichi OR tai chi chuan):ti,ab
20 (qigong OR qi gong OR chi kung OR chikung OR chi kung):ti,ab
21 Therap*:ti,ab
22 Physiotherapy*:ti,ab
23 Train*:ti,ab
24 neuromuscular training:ti,ab
25 treadmill:ti,ab
26 OR/1-25
27 'osteoarthritis'/exp
28 (osteoarthriti* OR osteoarthro* OR gonarthriti* OR gonarthro* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*):ti,ab
29 ((knee* OR hip* OR joint*) near/3 (pain* OR ach* OR discomfort*)):ti,ab
30 ((knee* OR hip* OR joint*) near/3 stiff*):ti,ab
31 OR/27-30
32 (random* or controlled or trial* or placebo):ti,ab
33 ((singl* or doubl*or tripl*) and (mask* or blind*)):ti,ab
34 (compar*):ti,ab
35 OR/32-34
36 26 AND 31 AND 35

Web of science

3.1 Search strategies for oral NSAIDs and paracetamol vs. all interventions

1. TITLE: (("non-steroidal anti-inflammatory agents" OR "anti-inflammatory agents, non-steroidal" OR "antiinflammatory agents, non-steroidal" OR "Anti-Inflammatory Agents, Non-Steroidal" OR "NSAID*" OR "nonsteroidal antiinflammatory" OR "non-steroidal anti-inflammatory"))
2. TITLE: ((Cyclooxygenase 2 Inhibitor*) OR (cyclooxygenase-2 inhibitor*) OR (cyclooxygenase-II inhibitor*) OR (cyclo-oxygenase-2 inhibitor*) OR (cyclo-oxygenase-II inhibitor*) OR (COX2 inhibitor*) OR (COX-2 inhibitor*) OR (COX-II inhibitor*) OR (COXII inhibitor*))
3. TITLE: (Acetaminophen OR Paracetamol OR Tylenol OR ibuprofen OR ketoprofen OR fenoprofen OR oxaprozin OR sulindac OR flurbiprofen OR diclofenac OR naproxen OR tenoxicam OR piroxicam OR droxicam OR indometacin OR indomethacin OR feprazone OR phenylbutazone OR isoxicam OR meclofenamate OR ketorolac OR lornoxicam OR nabumetone OR meloxicam OR aceclofenac OR alclofenac OR dexibuprofen OR dexketoprofen OR metamizol OR phenazone OR propyphenazone OR Prenazone OR ximoprofen OR Apazone OR Bufexamac OR Clonixin OR Curcumin OR Dexibruprofen OR Dipyrone OR Epirizole OR Fenbufen OR Fenclofenac OR Lederfen OR "Niflumic Acid" OR Oxyphenbutazone OR pirazolac OR pirprofen OR Ponstan OR Suprofen OR "Tiaprofenic acid" OR "tolfenamic acid" OR Tolmetin OR "meclofenamic acid" OR "mefenamic acid" OR coxib* OR apricoxib OR celecoxib OR cimicoxib OR darbufelone OR deracoxib OR etoricoxib OR firocoxib OR flosulide OR lumiracoxib OR mavacoxib OR methanesulfonamide OR nimesulide OR parecoxib OR robenacoxib OR tiracoxib OR valdecoxib OR vedaprofen OR etodolac OR rofecoxib OR vioxx OR Celebrex OR bextra OR prexige OR arcoxia OR floctafenine OR meclofenam* OR Mesalamine OR Ceoxx OR Ceeoxx OR Cimalgex OR Deramaxx OR Onsior OR "JTE-522" OR movalis OR mobec OR Mobic OR movicox OR mobicox OR parocin OR uticox OR Daypro OR Dayrun OR Duraprox OR meclomen OR Ponstan OR Xefo OR Seractil OR Antipyrine OR Metherazone OR Loxonin OR indoprofen OR Diflunisal OR Carprofen OR "Flufenamic acid" OR Flunixin OR Ramifenazone)
4. OR/1-3
5. TITLE: (osteoarthriti* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*)
6. TITLE: (random* OR control* OR placebo)
7. TITLE: ((singl* OR doubl* OR tripl*) and (mask* OR blind*))
8. TITLE: (compar*)
9. OR/6-8
10. 4 AND 5 AND 9

3.2 Search strategies for exercise vs. all interventions

1. TITLE: ((exercise OR physical conditioning, human OR Circuit-Based Exercise OR exercise therapy OR motion therapy, continuous passive OR muscle stretching exercises OR plyometric exercise OR resistance training OR hydrotherapy OR rehabilitation OR activities of daily living OR dance therapy OR muscle strength OR physical endurance OR anaerobic threshold OR exercise tolerance OR physical fitness OR postural balance OR posture OR psychomotor performance OR range of motion, articular OR Pliability OR movement OR motor activity OR Physical Exertion OR Mind-Body Therapies OR running OR jogging OR swimming OR walking

OR Isometric Contraction OR exercise movement techniques OR breathing exercises OR qigong OR tai ji OR yoga OR pilates OR Propriocepti* OR Balanc* OR Aquat* OR Cycl* OR Aerobic OR Strength* OR tai-ji OR taiji OR taijiquan OR tai ji quan OR tai chi OR taichi OR tai chi chuan OR qigong OR qi gong OR chikung OR chi kung OR Therap* OR Physiotherapy* OR Train* OR neuromuscular training OR treadmill))

2. TITLE: (osteoarthriti* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*)
3. TITLE: (random* OR control* OR placebo)
4. TITLE: ((singl* OR doubl* OR tripl*) and (mask* OR blind*))
5. TITLE: (compar*)
6. OR/3-5
7. 1 AND 2 AND 6

Cochrane Library

4.1 Search strategies for oral NSAIDs and paracetamol vs. all interventions

1. MeSH descriptor Osteoarthritis explode all trees
2. (osteoarthritis* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*):ti,ab,kw
3. 1 OR 2
4. MESH descriptor “anti-inflammatory agents, non-steroidal” explode all trees
5. MESH descriptor “cyclooxygenase 2 inhibitor” explode all trees
6. (Acetaminophen OR Paracetamol OR Tylenol OR ibuprofen OR ketoprofen OR fenoprofen OR oxaprozin OR sulindac OR flurbiprofen OR diclofenac OR naproxen OR tenoxicam OR piroxicam OR droxicam OR indometacin OR indomethacin OR feprazone OR phenylbutazone OR isoxicam OR meclofenamate OR ketorolac OR lornoxicam OR nabumetone OR meloxicam OR aceclofenac OR alclofenac OR dexibuprofen OR dexketoprofen OR metamizol OR phenazone OR propyphenazone OR Prenazone OR ximoprofen OR Apazone OR Bufexamac OR Clonixin OR Curcumin OR Dexibruprofen OR Dipyrone OR Epirizole OR Fenbufen OR Fenclofenac OR Lederfen OR “Niflumic Acid” OR Oxyphenbutazone OR pirazolac OR pirprofen OR Ponstan OR Suprofen OR “Tiaprofenic acid” OR “tolfenamic acid” OR Tolmetin OR “meclofenamic acid” OR “mefenamic acid”):ti,ab,kw
7. (coxib* OR apricoxib OR celecoxib OR cimicoxib OR darbufelone OR deracoxib OR etoricoxib OR firocoxib OR flosulide OR lumiracoxib OR mavacoxib OR methanesulfonamide OR nimesulide OR parecoxib OR robenacoxib OR tiracoxib OR valdecoxib OR vedaprofen OR etodolac OR rofecoxib OR vioxx OR Celebrex OR bextra OR prexige OR arcoxia OR floctafenine OR meclofenam* OR Mesalamine OR Ceoxx OR Ceeoxx OR Cimalgex OR Deramaxx OR Onsior OR “JTE-522” OR movalis OR mobec OR Mobic OR movicox OR mobicox OR parocin OR uticox OR Daypro OR Dayrun OR Duraprox OR meclomen OR Ponstan OR Xefo OR Seractil OR Antipyrine OR Metherazone OR Loxonin OR indoprofen OR Diflunisal OR Carprofen OR “Flufenamic acid” OR Flunixin OR Ramifenazone):ti,ab,kw
8. OR/4-7
9. 3 AND 8

4.2 Search strategies for exercise vs. all interventions

1. MeSH descriptor Osteoarthritis explode all trees
2. (osteoarthritis* OR osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR arthros* OR arthrot*):ti,ab,kw
3. 1 OR 2
4. MESH descriptor exercise explode all trees
5. (exercise) OR (physical conditioning, human)
6. (Circuit-Based Exercise)
7. (exercise therapy) OR (motion therapy, continuous passive) OR (muscle stretching exercises) OR (plyometric exercise) OR (resistance training) OR (hydrotherapy) OR (rehabilitation) OR (activities of daily living) OR (dance therapy)
8. (muscle strength) OR (physical endurance) OR (anaerobic threshold) OR (exercise tolerance) OR (physical fitness) OR (postural balance) OR (posture) OR (psychomotor performance) OR (range of motion, articular)

9. (Pliability)
10. (movement) OR (motor activity) OR (exercise)
11. (Physical Exertion)
12. (Mind-Body Therapies)
13. (running) OR (jogging) OR (swimming) OR (walking)
14. (Isometric Contraction)
15. (exercise movement techniques) OR (breathing exercises) OR (qigong) OR (tai ji) OR (yoga) OR (pilates)
16. Propriocepti*:ab,ti
17. Balanc*:ab,ti
18. Aquat*:ab,ti
19. Cycl*:ab,ti
20. Aerobic:ab,ti
21. Strength*:ab,ti
22. (tai-ji OR taiji OR taijiquan OR tai ji quan OR tai chi OR taichi OR tai chi chuan):ab,ti
23. (qigong OR qi gong OR chi kung OR chikung OR ch i kung):ab,ti
24. Therap*:ab,ti
25. Physiotherapy*:ab,ti
26. Train*:ab,ti
27. neuromuscular training:ab,ti
28. treadmill:ab,ti
29. OR/4-28
30. 3 AND 29

Scopus:

5.1 Search strategies for oral NSAIDs and paracetamol vs. all interventions

1. TITLE-ABS(“non-steroidal anti-inflammatory agents”) OR ALL(“anti-inflammatory agents, on-steroidal”) OR (“antiinflammatory agents, non-steroidal”) OR (“Anti-Inflammatory Agents, Non-Steroidal”) OR TITLE-ABS(“NSAIDs”) OR TITLE-ABS (“nonsteroidal antinflammatory”) OR TITLE-ABS (“Non-Steroidal Anti-Inflammator*”) OR TITLE-ABS (“Selective Non-Steroidal Anti-Inflammator*”)
2. ("Cyclooxygenase 2 Inhibitors") OR TITLE-ABS(cyclooxygenase-2 and inhibitor*) OR TITLE-ABS(cyclooxygenase-II and inhibitor*) OR TITLE-ABS(cyclo-oxygenase-2 and inhibitor*) OR TITLE-ABS(cyclo-oxygenase-II and inhibitor*) OR TITLE-ABS(COX2 and inhibitor*) OR TITLE-ABS(COX-2 and inhibitor*) OR TITLE-ABS(COX-II and inhibitor*) OR TITLE-ABS(COXII and inhibitor*)
3. TITLE-ABS(cyclooxygenase-2 and antagonist*) OR TITLE-ABS(cyclooxygenase-II and antagonist*) OR TITLE-ABS(cyclo-oxygenase-2 and antagonist*) OR TITLE-ABS(cyclo-oxygenase-II and antagonist*) OR TITLE-ABS(COX2 and antagonist*) OR TITLE-ABS(COX -2 and antagonist*) OR TITLE-ABS(COX-II and antagonist*) OR TITLE-ABS(COXII and antagonist*)
4. TITLE-ABS(prostaglandin and synthase and inhibitor) OR TITLE-ABS(prostaglandin and synthase and inhibitor*) OR TITLE-ABS(prostaglandin and synthase and antagonist) OR TITLE-ABS(prostaglandin and synthase and antagonist*)
5. TITLE-ABS((Acetaminophen) OR (Paracetamol) OR (Tylenol) OR (ibuprofen) OR (ketoprofen) OR (fenoprofen) OR (oxaprozin) OR (sulindac) OR (flurbiprofen) OR (diclofenac) OR (naproxen) OR (tenoxicam) OR (piroxicam) OR (droxicam) OR (indomethacin) OR (indomethacin) OR (feprazone) OR (phenylbutazone) OR (isoxicam) OR (meclofenamate) OR (ketorolac) OR (lornoxicam) OR (nabumetone) OR (meloxicam) OR (aceclofenac) OR (alclofenac) OR (dexibuprofen) OR (dexketoprofen) OR (metamizole) OR (phenazone) OR (propyphenazone) OR (Prenazone) OR (ximoprofen) OR (Apazone) OR (Bufexamac) OR (Clonixin) OR (Curcumin) OR (Dexibruprofen) OR (Dipyrone) OR (Epirizole) OR (Fenbufen) OR (Fenclofenac) OR (Lederfen) OR (“Niflumic Acid") OR (Oxyphenbutazone) OR (pirazolac) OR (pirprofen) OR (Ponstan) OR (Suprofen) OR (“Tiaprofenic acid") OR (“tolfenamic acid") OR (Tolmetin) OR (“meclofenamic acid") OR (“mefenamic acid"))
6. TITLE-ABS((coxib*) OR (apricoxib) OR (celecoxib) OR (cimicoxib) OR (darbufelone) OR (deracoxib) OR (etoricoxib) OR (firocoxib) OR (flosulide) OR (lumiracoxib) OR (mavacoxib) OR (methanesulfonamide) OR (nimesulide) OR (parecoxib) OR (robenacoxib) OR (tiracoxib) OR (valdecoxib) OR (vedaprofen) OR (etodolac) OR (rofecoxib) OR (vioxx) OR (Celebrex) OR (bextra) OR prexige OR arcoxia OR floctafenine OR meclofenam* OR Mesalamine OR Ceoxx OR Ceeoxx OR Cimalgex OR Deramaxx OR Onsior OR “JTE-522” OR movalis OR mobec OR Mobic OR movicox OR mobicox OR parocin OR uticox OR Daypro OR Dayrun OR Duraprox OR meclomen OR Ponstan OR Xefo OR Seractil OR Antipyrine OR Metherazone OR Loxonin OR indoprofen OR Diflunisal OR Carprofen OR “Flufenamic acid" OR Flunixin OR Ramifenazone)
7. OR/1-6
8. TITLE-ABS(osteoarthriti*)
9. TITLE-ABS((osteoarthro*) OR (gonarthriti*) OR (gonarthro*) OR (coxarthriti*) OR (coxarthro*)

OR (osteo?arthritis))
10. 8 OR 9
11. TITLE-ABS(random* OR placebo OR controlled OR trial*)
12. TITLE-ABS((singl* OR doubl* OR tripl*) and (mask* OR blind*))
13. TITLE-ABS(compar*)
14. OR/11-13
15. 7 AND 10 AND 14

5.2 Search strategies for exercise vs. all interventions
1. TITLE-ABS(exercise)
2. TITLE-ABS((“exercise therapy”) OR (“motion therapy”) OR (“muscle stretching exercises”) OR (“plyometric exercise”) OR (“resistance training”) OR (“hydrotherapy”) OR (“rehabilitation”) OR (“activities of daily living”) OR (“dance therapy”) OR (“Mind-Body Therapies”) OR (“neuromuscular training”) OR ((running) OR (jogging) OR (swimming) OR (walking)))
3. TITLE-ABS(Propriocepti*)
4. TITLE-ABS(Balanc*)
5. TITLE-ABS(Aquat*)
6. TITLE-ABS(Cycl*)
7. TITLE-ABS(Aerobic)
8. TITLE-ABS(Strength*)
9. OR/1-8
10. TITLE-ABS(osteoarthriti*)
11. TITLE-ABS(osteoarthro* OR gonarthriti* OR gonarthro* OR coxarthriti* OR coxarthro* OR osteo?arthritis)
12. OR/10-11
13. TITLE-ABS(random* OR placebo OR controlled OR trial*)
14. TITLE-ABS(singl* OR doubl* OR tripl*) and TITLE-ABS(mask* OR blind*)
15. TITLE-ABS(compar*)
16. OR/13-15
17. 9 AND 12 AND 16

Appendix 2 NMA-SoF table for comparison between exercise and oral NSAIDs and paracetamol

Bayesian NMA-SoF table

BENEFITS

Comparative efficacy of exercise therapy and oral non-steroidal anti-inflammatory drugs and paracetamol for knee or hip osteoarthritis: a network meta-analysis of randomised controlled trials

Patient or population: Patients with knee or hip osteoarthritis
Interventions: Exercise
Comparator (reference): Oral NSAIDs and paracetamol
Outcome: Pain and function at or nearest to four weeks, at eight weeks and at 24 weeks
Setting: Outpatient or community

Outcomes* **		**Total studies: Total participants:**	**Comparative efficacy* and ranks****		**Certainty of evidence**	**Interpretation of Findings**
			Exercise	***Oral NSAIDs and paracetamol***		
At or nearest to four weeks	Pain	47 RCTs 4,377 participants	SMD: -0.12 (-1.74, 1.50) Ranks: 3.2	SMD: reference Ranks: 3.0	⊕⊕◯◯ **Low** Due to Risk of bias and Inconsistency	-
	Function	40 RCTs 2,968 participants	SMD: 0.09 (-1.69, 1.85) Ranks: 2.8	SMD: reference Ranks: 3.1	⊕⊕◯◯ **Low** Due to Risk of bias and Inconsistency	-
At eight weeks	Pain	2 RCTs 210 participants	SMD: 0.22 (-0.05, 0.49) Ranks: 1.3	SMD: reference Ranks: 1.7	⊕⊕⊕⊕ **High**	-
	Function	2 RCTs 214 participants	SMD: 0.06 (-0.20, 0.33) Ranks: 1.4	SMD: reference Ranks: 1.6	⊕⊕⊕⊕ **High**	-
At 24 weeks	Pain	9 RCTs 2,141 participants	SMD: 0.17 (-0.77, 1.12) Ranks: 2.3	SMD: reference Ranks: 2.9	⊕⊕⊕◯ **Moderate** Due to Risk of bias	-
	Function	9 RCTs 2,141 participants	SMD: 0.05 (-1.15, 1.24) Ranks: 2.6	SMD: reference Ranks: 2.7	⊕⊕⊕◯ **Moderate** Due to Risk of bias	-

NMA-SoF table definitions

* Estimates are reported as mean difference and credible interval (CrI). Results are expressed in credible intervals as opposed to the confidence intervals since a Bayesian analysis has been conducted.

** Ranking and confidence intervals for efficacy outcome are presented. Rank statistics is defined as the probabilities that a treatment out of *n* treatments in a network meta-analysis is the best, the second, the third and so on until the least effective treatment.

*** Studies without a common comparator (such as usual care or acupuncture arm) that provides connections through a network of different regimens were excluded from analysis.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Appendix 3 Funnel plots

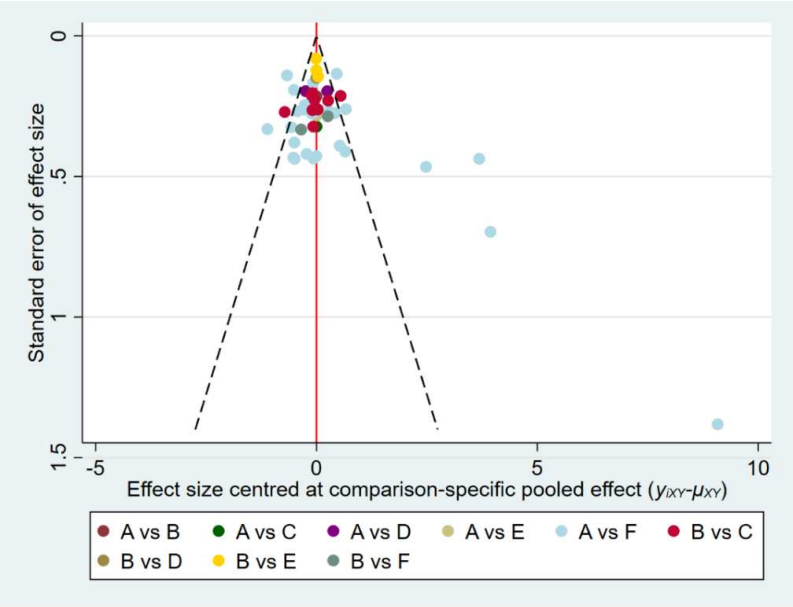


Figure 3.1. Funnel plot for assessment of publication bias on pain reduction in the overall network and individual comparisons at or nearest to four weeks.

A= exercise; B= oral NSAIDs and paracetamol; C= acupuncture; D= intra-articular hyaluronic acid; E= topical NSAIDs; F= usual care.

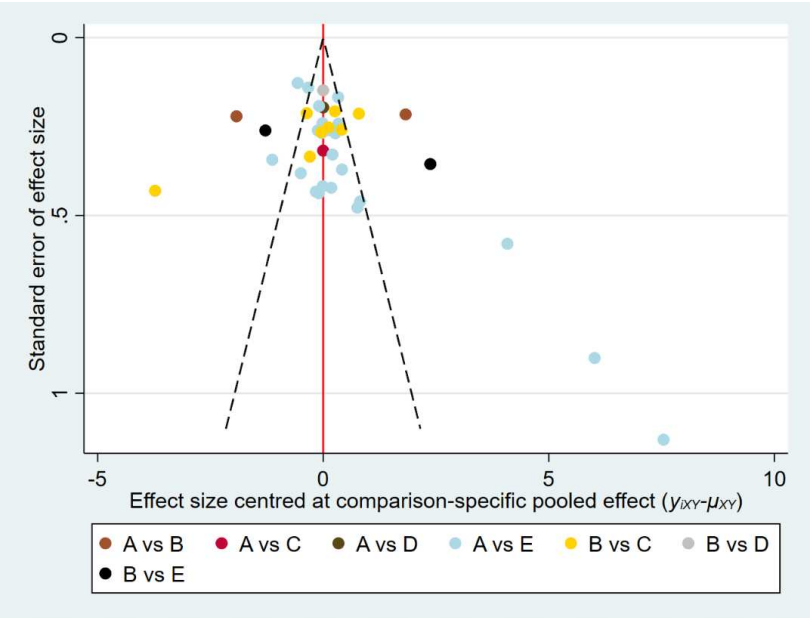


Figure 3.2. Funnel plot for assessment of publication bias on functional improvement in the overall network and individual comparisons at or nearest to four weeks.

A= exercise; B= oral NSAIDs and paracetamol; C= acupuncture; D= intra-articular hyaluronic acid; E= usual care.

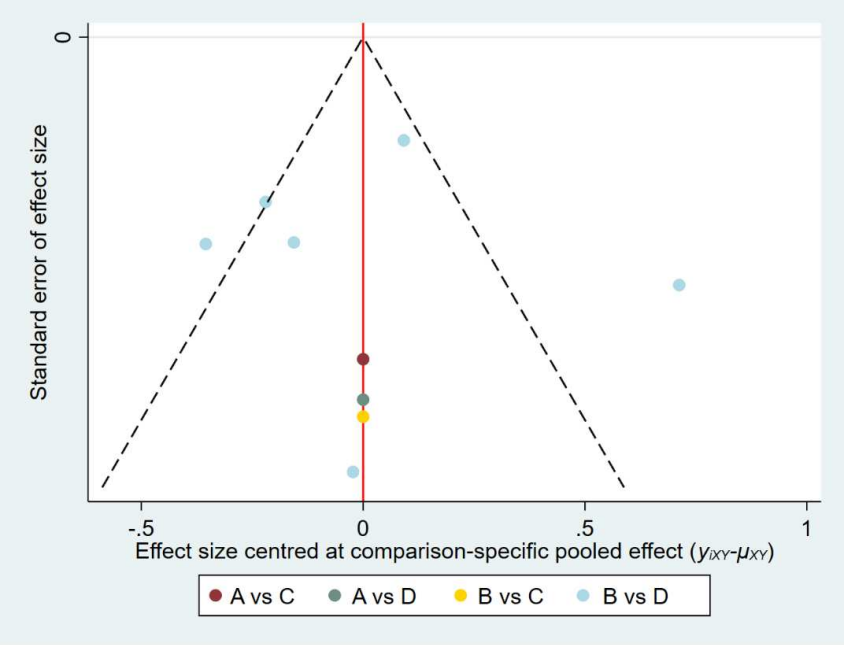


Figure 3.3. Funnel plot for assessment of publication bias on pain reduction in the overall network and individual comparisons at 24 weeks.

A= exercise; B= oral NSAIDs and paracetamol; C= intra-articular hyaluronic acid; D= glucosamine sulphate/chondroitin sulphate.

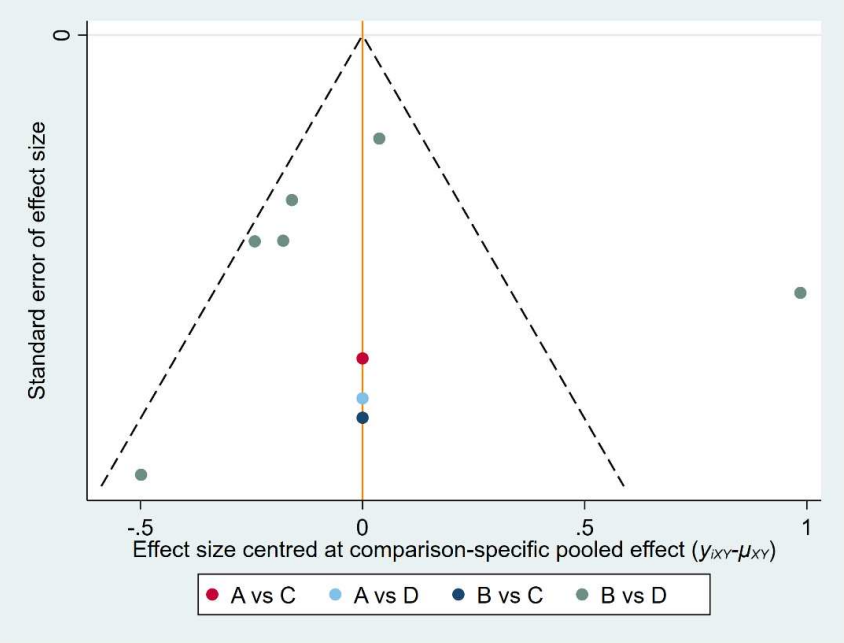


Figure 3.4. Funnel plot for assessment of publication bias on functional improvement in the overall network and individual comparisons at 24 weeks.

A= exercise; B= oral NSAIDs and paracetamol; C= intra-articular hyaluronic acid; D= glucosamine sulphate/chondroitin sulphate.

Appendix 4 Results of SUCRA

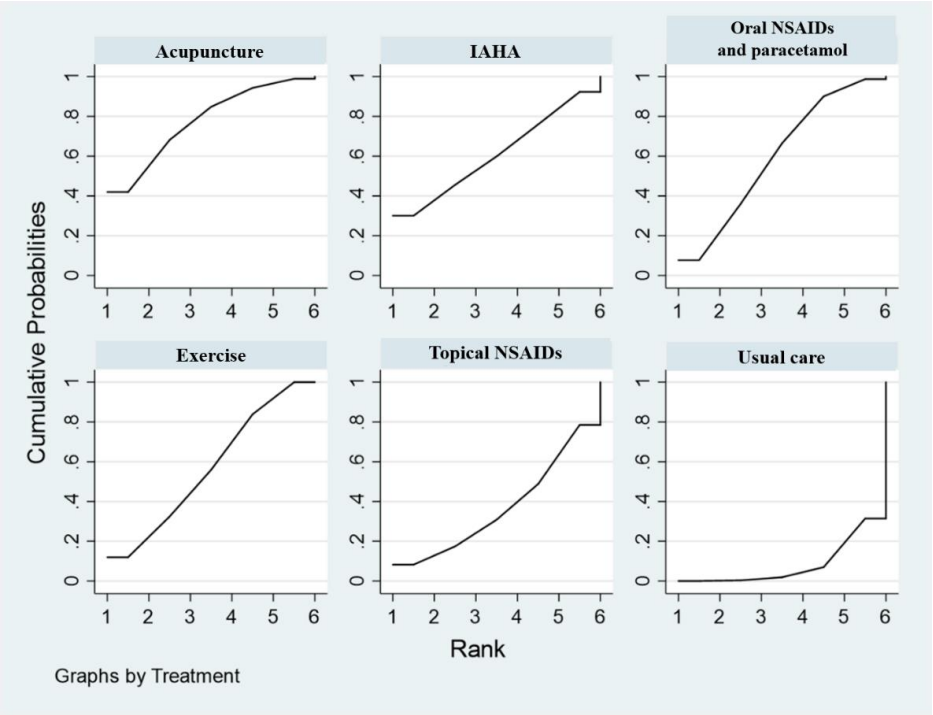


Figure 4.1. Rankings for effects on pain relief at or nearest to four weeks. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
Acupuncture	77.7
IAHA	60.8
Oral NSAIDs and paracetamol	59.8
Exercise	56.8
Topical NSAIDs	36.8
Usual care	8.1

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid.

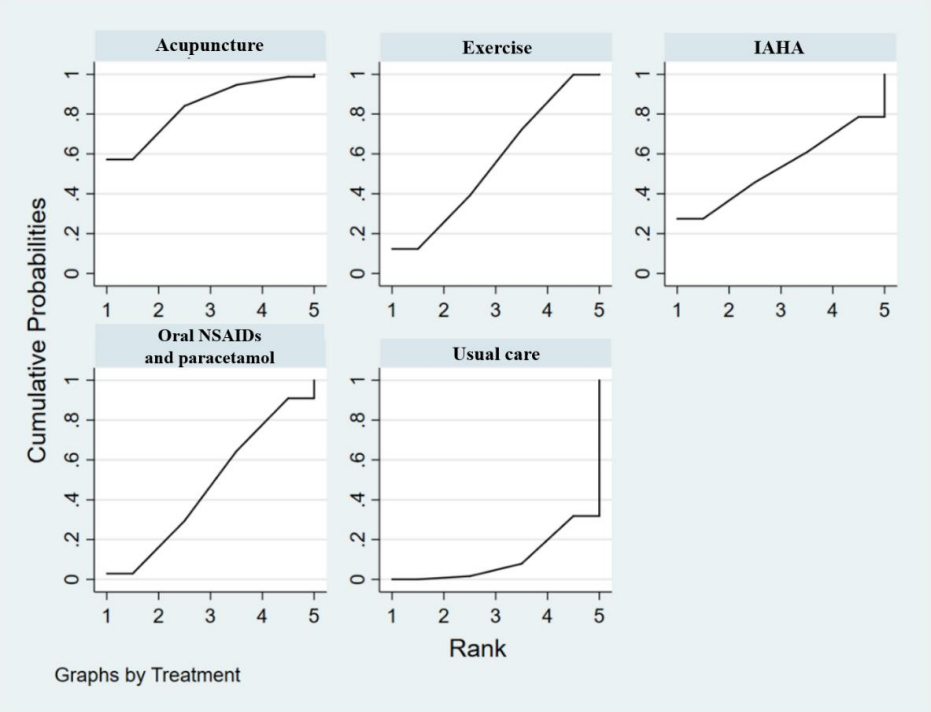


Figure 4.2. Rankings for effects on functional improvement at or nearest to four weeks.
Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
Acupuncture	83.7
Exercise	55.8
IAHA	53.2
Oral NSAIDs and paracetamol	46.9
Usual care	10.3

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid.

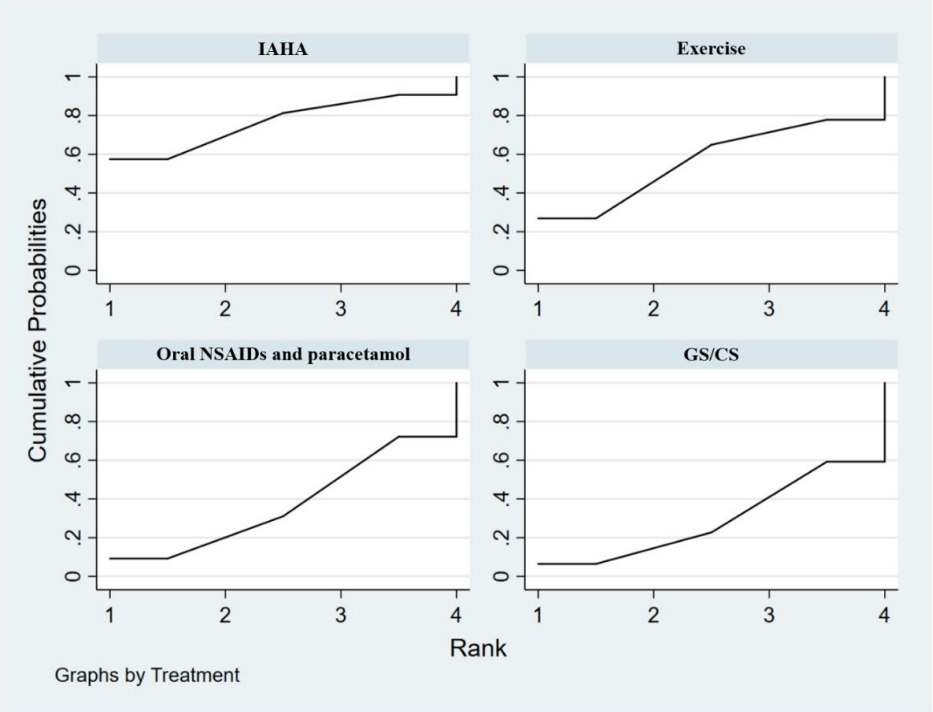


Figure 4.3. Rankings for effects on pain relief at 24 weeks. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
IAHA	76.5
Exercise	56.5
Oral NSAIDs and paracetamol	37.5
GS/CS	29.5

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; GS/CS, glucosamine sulphate/chondroitin sulphate.

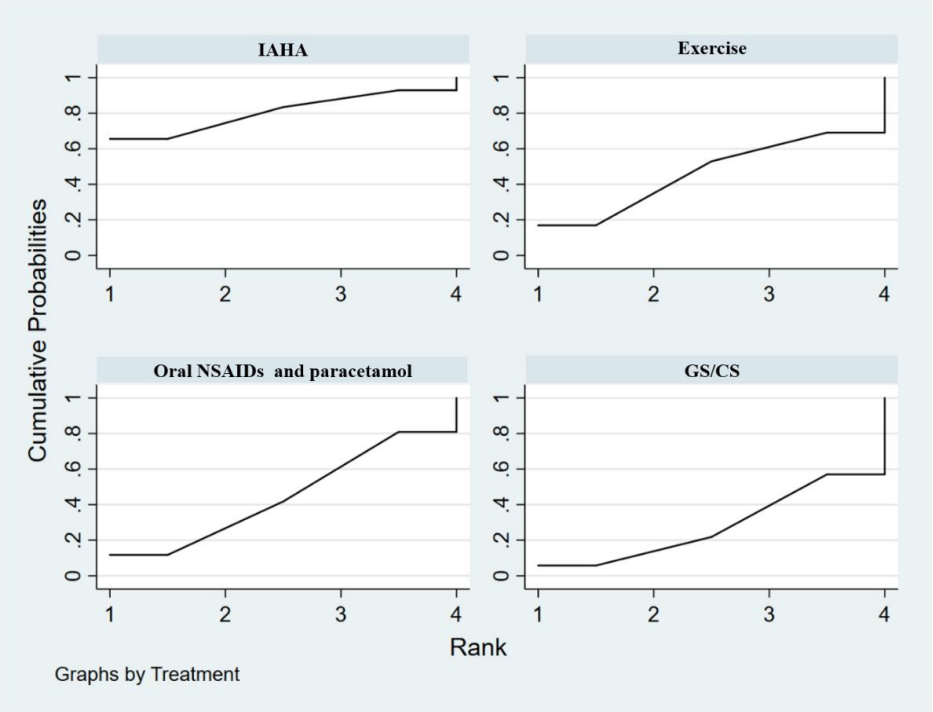


Figure 4.4. Rankings for effects on functional improvement at 24 weeks. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
IAHA	80.6
Exercise	46.3
Oral NSAIDs and paracetamol	44.8
GS/CS	28.2

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; GS/CS, glucosamine sulphate/chondroitin sulphate.

Appendix 5 Networks plots for each outcome

The size of the circle in each network is proportional to the number of participants randomly assigned to the treatment comparison. The width of each line is proportional to the number of trials comparing the two connected treatments. When a line is absent, this indicates that there were no head-to-head trials of the corresponding treatments reporting the outcome of interest. Numbers (n/n) near the line indicate 'number of studies/number of participants' of the related comparisons.

Figure 5.1. Structure of network formed by interventions for pain relief at eight weeks.

NSAIDs, non-steroidal anti-inflammatory drugs.

Figure 5.2. Structure of network formed by interventions for functional improvement at eight weeks.

NSAIDs, non-steroidal anti-inflammatory drugs.

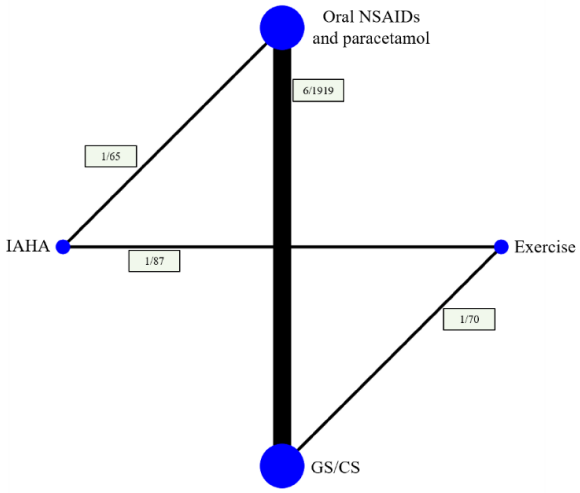


Figure 5.3. Structure of network formed by interventions for pain relief at 24 weeks.

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; GS/CS, glucosamine sulphate/chondroitin sulphate.

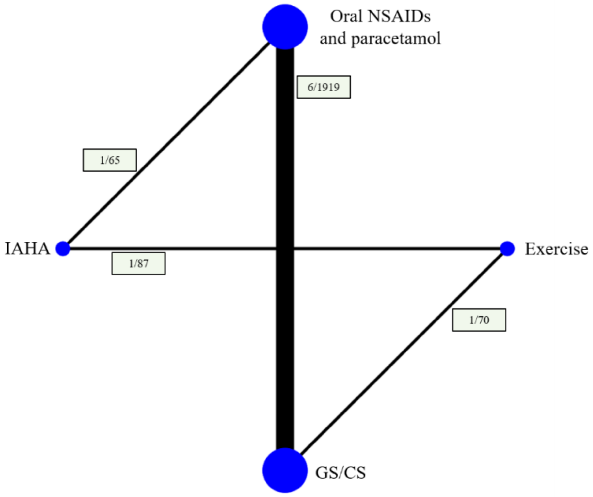


Figure 5.4. Structure of network formed by interventions for functional improvement at 24 weeks. NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; GS/CS, glucosamine sulphate/chondroitin sulphate.

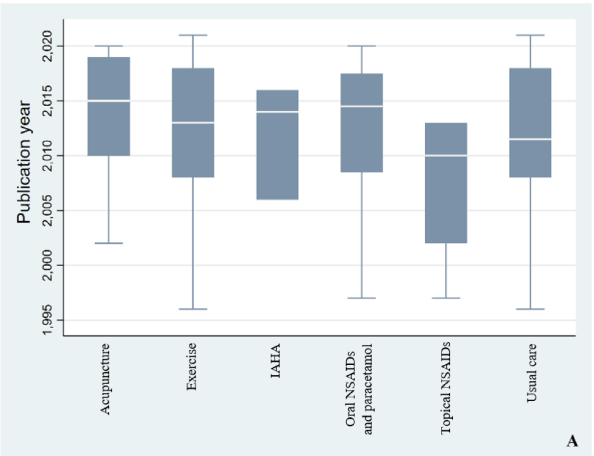
Appendix 6 Assessment of transitivity

Before conducting the statistical analysis, we estimated whether the studies included in the NMA were on average similar in terms of characteristics that might modify the treatment effect (so that the transitivity assumption is plausible). Indirect comparisons, in contrast to direct comparisons, are not protected by randomisation and may be confounded by differences between the trials. In our analysis we deemed the following parameters as possible confounders: publication year, percentage female, mean age, baseline pain and function score.

The plausibility of the transitivity assumption was assessed by comparing the distribution of these potential effect modifiers across trials grouped by comparison.

6.1 Publication year

We examined the distribution of publication year over each intervention. The overall range was between 1996 and 2021 with a median of 2013 at or nearest to four weeks; the overall range was between 2006 and 2018 with a median of 2015 at 24 weeks. Obviously, treatment recommendations for OA may differ considerably with regards to publication year. We examined publication year as a potential effect modifier, because it can be a proxy parameter for a number of factors that may have changed over the years (e.g., changes in trial design, monitoring, etc), that could have possibly influenced the effect size. We found no significant difference in publication year between the all interwentions at or nearest to four weeks or 24 weeks ($P > 0.05$).



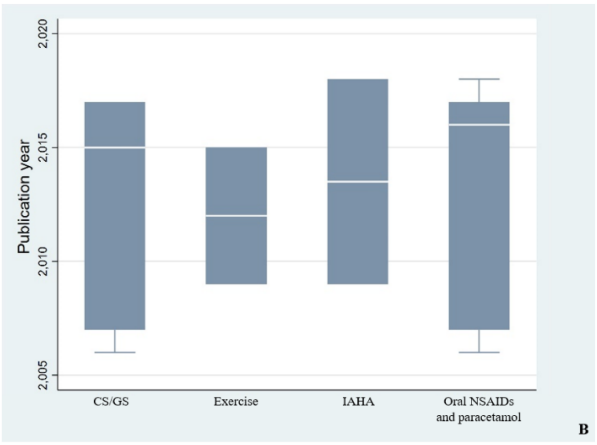


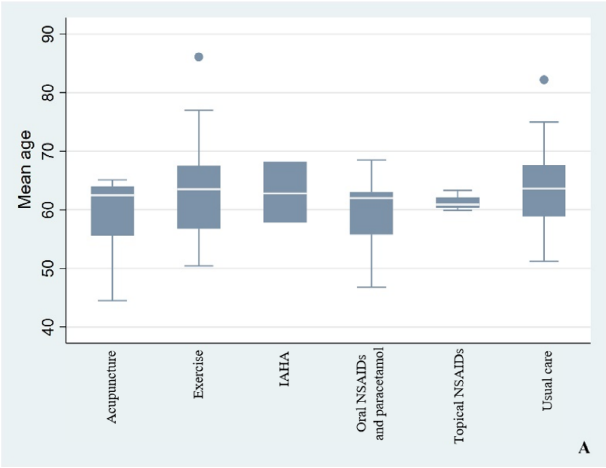
Figure 1.A. Boxplot for distribution of publication year across comparisons at or nearest to four weeks

Figure 1.B. Boxplot for distribution of publication year across comparisons at 24 weeks

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; CS/GS, glucosamine sulphate/chondroitin sulphate.

6.2 Mean age

We examined the distribution of mean age over each intervention. The overall range was between 44.5 and 86.1 with a median of 61.2 at or nearest to four weeks; the overall range was between 55.5 and 71.2 with a median of 61.4 at 24 weeks. Age is a major risk factor for OA; thus, we inspected the effects of mean age as a potential effect modifier. We found no significant difference in mean age between the all interwentions at or nearest to four weeks or 24 weeks ($P > 0.05$).



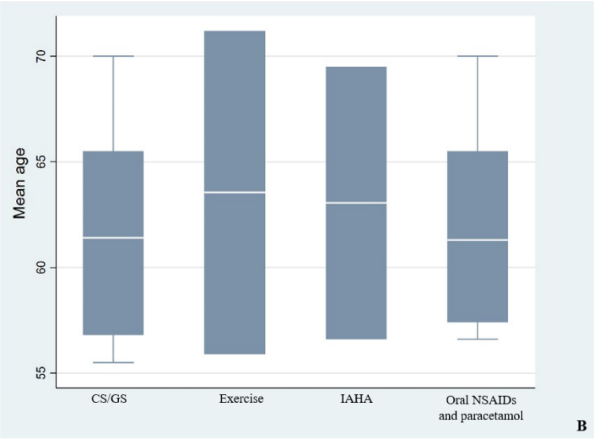


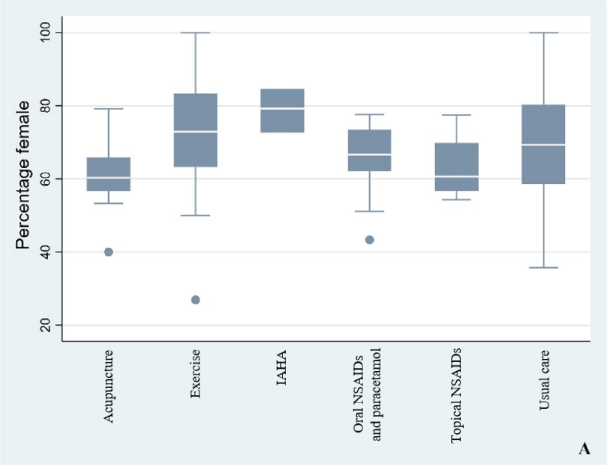
Figure 2.A. Boxplot for distribution of mean age across comparisons at or nearest to four weeks

Figure 2.B. Boxplot for distribution of mean age across comparisons at 24 weeks

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; CS/GS, glucosamine sulphate/chondroitin sulphate.

6.3 Percentage female

We examined the distribution of percentage female over each intervention. The overall range was between 26.9 and 100 with a median of 69.5 at or nearest to four weeks; the overall range was between 51.5 and 100 with a median of 74.7 at 24 weeks. Some studies had only male or only female participants. Female genderis a risk factor for OA; thus, we inspected the effects of percentage female a potential effect modifier. We found no significant difference in percentage female between the all interwentions at or nearest to four weeks or 24 weeks ($P > 0.05$).



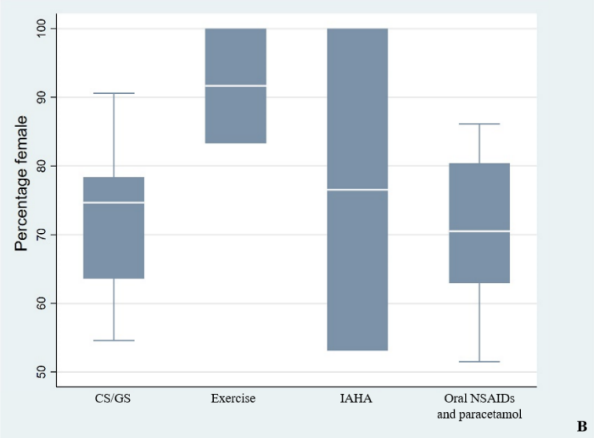


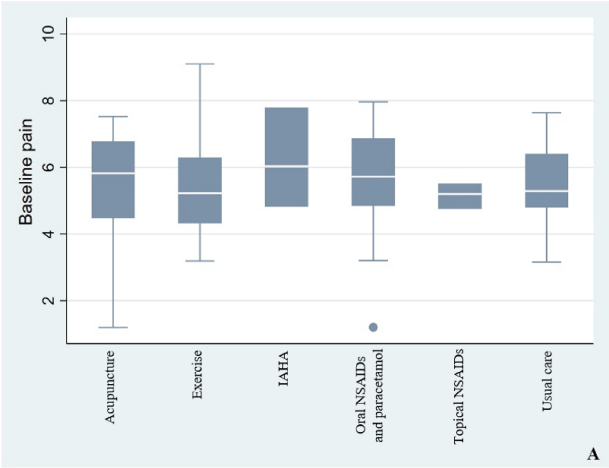
Figure 3.A. Boxplot for distribution of percentage female across comparisons at or nearest to four weeks

Figure 3.B. Boxplot for distribution of percentage female across comparisons at 24 weeks

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; CS/GS, glucosamine sulphate/chondroitin sulphate.

6.4 Baseline pain score

We examined the distribution of baseline pain score over each intervention. The overall range was between 1.2 and 9.1 with a median of 5.41 at or nearest to four weeks; the overall range was between 3.9 and 7.7 with a median of 5.84 at 24 weeks. Our results may be susceptible to selection bias due to severity of disease at presentation; thus, we inspected the effects of baseline pain score as a potential effect modifier. We found no significant difference in baseline pain score between the all interwentions at or nearest to four weeks or 24 weeks ($P > 0.05$).



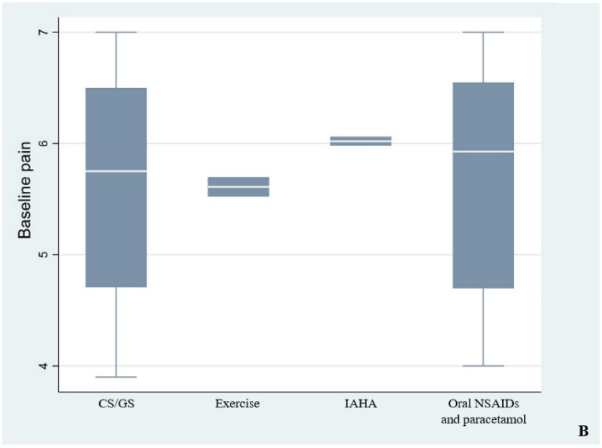


Figure 4.A. Boxplot for distribution of baseline pain score across comparisons at or nearest to four weeks

Figure 4.B. Boxplot for distribution of baseline pain score across comparisons at 24 weeks

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; CS/GS, glucosamine sulphate/chondroitin sulphate.

6.5 Baseline function score

We examined the distribution of baseline function score over each intervention. The overall range was between 28 and 78.7 with a median of 50.0 at or nearest to four weeks; the overall range was between 38.8 and 60.0 with a median of 48.0 at 24 weeks. Our results may be susceptible to selection bias due to severity of disease at presentation; thus, we inspected the effects of baseline function score as a potential effect modifier. We found no significant difference in baseline function score between the all interwentions at or nearest to four weeks or 24 weeks ($P > 0.05$).

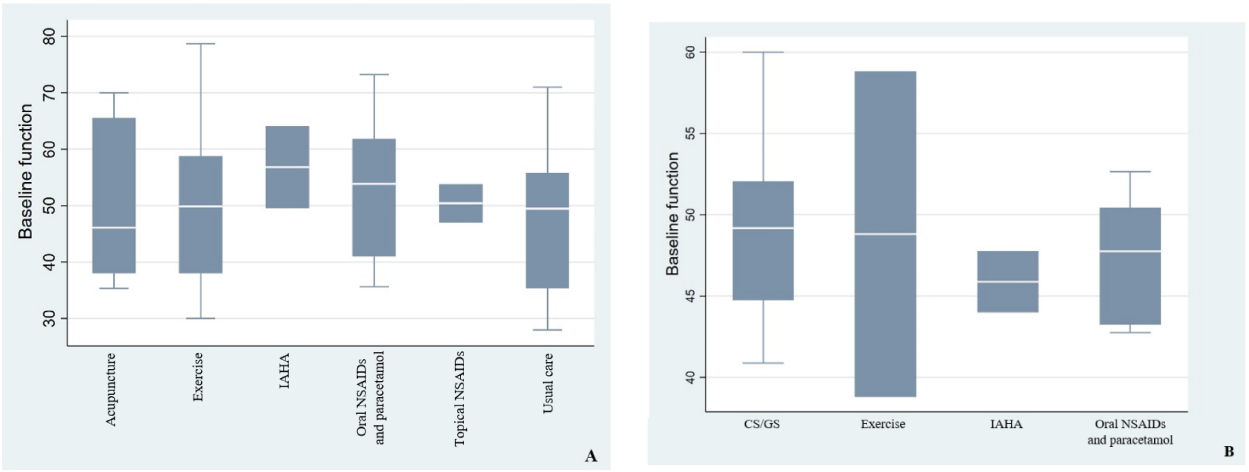


Figure 5.A. Boxplot for distribution of baseline function score across comparisons at or nearest to four weeks

Figure 5.B. Boxplot for distribution of baseline function score across comparisons at 24 week

NSAIDs, non-steroidal anti-inflammatory drugs; IAHA, intra-articular hyaluronic acid; CS/GS, glucosamine sulphate/chondroitin sulphate.

Appendix 7 Basic characteristics of included randomised controlled trials (n=152 studies)

Studies	Location of OA	Groups	Sample Size (female, %)	Mean Age (years)	Treatment Duration	Follow-up Time Point	Outcomes
Oral NSAIDs and paracetamol vs. Exercise							
Doi 2008[1]	Knee	G1: Oral NSAIDs (one of loxoprofen tablet, diclofenac tablet or zaltoprofen) G2: Exercise (strength exercise)	G1: 70 (75.7) G2: 72 (76.4)	G1: 68.9 G2: 66.8	8 weeks	4, 8 weeks	Pain, function, QoL
Zhang 2015[2]	Knee	G1: Oral NSAIDs (celecoxib) G2: Exercise (strength exercise)	G1: 48 (77.1) G2: 46 (73.9)	G1: 64.5 G2: 63.5	4 weeks	4 weeks	Pain, function
Holsgaard-Larsen 2018[3]	Knee	G1: Paracetamol G2: Exercise (neuromotor exercise)	G1: 46 (54.3) G2: 47 (61.7)	G1: 58.3 G2: 57.9	8 weeks	8 weeks	Pain, function, QoL
Jing 2020[4]	Knee	G1: Oral NSAIDs (one of naproxen, diclofenac or celecoxib) G2: Exercise (mixed exercise)	G1: 74 (73.5) G2: 92 (71.6)	G1: 55.8 G2: 56.7	5 weeks	1, 3, 5 weeks	Function, QoL
Acupuncture vs. Oral NSAIDs and paracetamol							
Gang 2016[5]	Knee	G1: Acupuncture (electroacupuncture) G2: Oral NSAIDs (meloxicam)	G1: 45 (53.3) G2: 45 (51.1)	G1: 54.0 G2: 54.0	6 weeks	6 weeks	Pain, function
Li 2015[6]	Knee	G1: Acupuncture (electroacupuncture) G2: Oral NSAIDs (celecoxib)	G1: 38 (NA) G2: 38 (NA)	NA	3 weeks	3 weeks	Pain, function
Liu 2013[7]	Knee	G1: Acupuncture (long-needle) G2: Oral NSAIDs (ibuprofen)	G1: 97 (NA) G2: 95 (NA)	NA	3 months	3 weeks, 3 months	Data not available
Nie 2015[8]	Knee	G1: Acupuncture G2: Oral NSAIDs (ibuprofen)	G1: 60 (61.7) G2: 30 (66.7)	G1: 61.7 G2: 62.0	2 weeks	2 weeks	Pain
Hou 2019[9]	Knee	G1: Acupuncture (fan-needle) G2: Oral NSAIDs (celecoxib)	G1: 50 (70.0) G2: 50 (66.0)	G1: 64.0 G2: 63.0	4 weeks	4 weeks	Pain, function
Sangdee 2002[10]	Knee	G1: Acupuncture (electroacupuncture) G2: Oral NSAIDs (diclofenac)	G1: 48 (79.2) G2: 49 (77.6)	G1: 65.1 G2: 62.1	4 weeks	4 weeks	Pain, function
Sheng 2010[11]	Hip	G1: Acupuncture (electroacupuncture) G2: Oral NSAIDs (diclofenac)	G1: 30 (60.0) G2: 30 (63.3)	G1: 63.2 G2: 61.1	4 weeks	4 weeks	Pain, function
Wu 2008[12]	Knee	G1: Acupuncture (electroacupuncture) G2: Oral NSAIDs (diclofenac)	G1: 20 (60.0) G2: 20 (65.0)	G1: 62.5 G2: 61.2	4 weeks	4 weeks	Pain, function

Zheng 2004[13]	Hip	G1: Acupuncture (electroacupuncture) G2: Oral NSAIDs (diclofenac)	G1: 60 (NA) G2: 60 (NA)	NA	2 years	2 years	Pain, function
Wang 2020[14]	Knee	G1: Acupuncture G2: Oral NSAIDs (celecoxib)	G1: 33 (60.6) G2: 32 (53.1)	G1: 44.5 G2: 46.8	4 weeks	4 weeks	Pain, function
Wang 2020[15]	Knee	G1: Acupuncture G2: Oral NSAIDs (celecoxib)	G1: 30 (40.0) G2: 30 (43.3)	G1: 64.8 G2: 65.4	4 weeks	4 weeks	Pain, function
Acupuncture vs. Exercise							
Saleki 2013[16]	Knee	G1: Acupuncture G2: Exercise (strength exercise)	G1: 20 (NA) G2: 20 (NA)	G1: 55.6 G2: 50.4	4 weeks	4 weeks	Pain, function, QoL
CS/GS vs. Oral NSAIDs and paracetamol							
Antonio 1982[17]	Knee	G1: Glucosamine sulphate G2: Oral NSAIDs (ibuprofen)	G1: 18 (83.3) G2: 20 (65.0)	G1: 58.4 G2: 57.2	8 weeks	1, 2, 4, 8 weeks	Pain
Chopra 2013[18]	Knee	G1: Glucosamine sulphate G2: Oral NSAIDs (celecoxib)	G1: 108 (NA) G2: 105 (NA)	G1: 55.5 G2: 56.6	24 weeks	2, 4, 8, 12, 16, 20, 24 weeks	Pain, function
Clegg 2006[19]	Knee	G1: Chondroitin Sulphate G2: Oral NSAIDs (celecoxib)	G1: 635 (63.6) G2: 318 (66.7)	G1: 58.4 G2: 59.4	24 weeks	4, 8, 16, 24 weeks	Pain, function
HANS 1994[20]	Knee	G1: Glucosamine sulphate G2: Oral NSAIDs (ibuprofen)	G1: 100 (42.0) G2: 99 (53.5)	G1: 54.0 G2: 54.0	4 weeks	1, 2, 3, 4 weeks	Pain, function
Herrero-Beaumont 2007[21]	Knee	G1: Glucosamine sulphate G2: Paracetamol	G1: 106 (90.6) G2: 108 (86.1)	G1: 63.4 G2: 63.8	6 months	1, 3, 6 months	Pain, function
Korkmaz 2013[22]	Knee	G1: Glucosamine sulphate G2: Oral NSAIDs (diclofenac sodium)	G1: 25 (75.0) G2: 27 (70.4)	G1: 57.2 G2: 56.6	12 weeks	12 weeks	Pain, function
Morreale 1996[23] (Double dummy)	Knee	G1: Chondroitin Sulphate (chondroitin sulphate + placebo diclofenac sodium) G2: Oral NSAIDs (diclofenac sodium + placebo chondroitin sulphate)	G1: 74 (58.1) G2: 72 (59.7)	G1: 55.4 G2: 56.4	30 days	10, 20, 30 days	Pain, function
Pelletier 2016[24]	Knee	G1: Chondroitin Sulphate G2: Oral NSAIDs (celecoxib + placebo)	G1: 97 (54.6) G2: 97 (62.9)	G1: 61.4 G2: 61.3	24 months	3, 6, 12, 18, 24 months	Pain, function
Qiu 1998[25] (Double dummy)	Knee	G1: Glucosamine sulphate (glucosamine sulphate + placebo ibuprofen) G2: Oral NSAIDs (ibuprofen + placebo glucosamine sulphate)	G1: 88 (72.7) G2: 90 (84.4)	G1: 56.5 G2: 56.3	4 weeks	2, 4 weeks	Pain

Reginster 2017[26] (Double dummy)	Knee	G1: Chondroitin Sulphate (chondroitin sulphate + placebo celecoxib) G2: Oral NSAIDs (celecoxib + placebo chondroitin sulphate)	G1: 199 (78.4) G2: 199 (80.4)	G1: 65.5 G2: 65.5	6 months	30, 91, 182 days	Pain, function
Sawitzke 2010[27]	Knee	G1: Chondroitin Sulphate G2: Oral NSAIDs (celecoxib)	G1: 126 (73.0) G2: 142 (65.5)	G1: 56.3 G2: 57.6	24 months	24 months	Data not available
Tío 2017[28]	Knee	G1: Chondroitin Sulphate G2: Paracetamol	G1: 35 (74.3) G2: 35 (74.3)	G1: 70.0 G2: 70.0	6 months	6 weeks, 3, 6 months	Pain, function
Lee 2001[29]	Knee	G1: Glucosamine G2: Oral NSAIDs (etodolac)	G1: 43 (83.7) G2: 26 (88.5)	G1: 62.0 G2: 60.0	6 weeks	3, 6 weeks	Pain, function
CS/GS vs. Exercise							
Armagan 2015[30]	Knee	G1: Glucosamine sulphate G2: Exercise (strength exercise)	G1: 40 (75.0) G2: 30 (83.3)	G1: 56.8 G2: 55.9	6 months	6 months	Pain, function
IAHA vs. Oral NSAIDs and paracetamol							
Wu 2004[31]	Knee	G1: Intra-articular hyaluronic acid G2: Oral NSAIDs (celecoxib)	G1: 30 (60.0) G2: 30 (56.7)	G1: 65.8 G2: 64.7	16 weeks	1, 2, 4, 6, 8, 10, 12, 14, 16 weeks	Data not available
Ishijima 2014[32]	Knee	G1: Intra-articular hyaluronic acid G2: Oral NSAIDs	G1: 99 (72.7) G2: 93 (76.3)	G1: 68.2 G2: 68.5	5 weeks	5 weeks	Pain, function
Buendía-López 2018[33]	Knee	G1: Intra-articular hyaluronic acid G2: Oral NSAIDs	G1: 32 (53.1) G2: 33 (51.5)	G1: 56.6 G2: 57.4	52 weeks	26, 52 weeks	Pain, function
IAHA vs. Exercise							
Karatosun 2006[34]	Knee	G1: Intra-articular hyaluronic acid G2: Exercise (mixed exercise)	G1: 52 (84.6) G2: 53 (86.8)	G1: 57.8 G2: 55.3	6 weeks	1, 2, 3, 6 weeks	Pain
Kawasaki 2009[35]	Knee	G1: Intra-articular hyaluronic acid G2: Exercise (mixed exercise)	G1: 42 (100.0) G2: 45 (100.0)	G1: 69.5 G2: 71.2	24 weeks	24 weeks	Pain, function
Saccomanno 2016[36]	Knee	G1: Intra-articular hyaluronic acid G2: Exercise (mixed exercise)	G1: 53 (79.2) G2: 51 (64.7)	G1: 62.8 G2: 61.2	1 month	1 month	Pain, function
Topical NSAIDs vs. Oral NSAIDs and paracetamol							
Mu 2014[37] (Double dummy)	Knee	G1: Topical NSAIDs (loxoprofen hydrogel patch + tablet placebo) G2: Oral NSAIDs (loxoprofen sodium + patch placebo)	G1: 81 (76.5) G2: 83 (80.7)	G1: 57.3 G2: 56.9	4 weeks	2, 4 weeks	Data not available

Rother 2007[38] (Double dummy)	Knee	G1: Topical NSAIDs (ketoprofen gel + placebo tablet) G2: Oral NSAIDs (celecoxib + placebo gel)	G1: 138 (54.3) G2: 132 (62.1)	G1: 63.3 G2: 62.4	6 weeks	2, 4, 6 weeks	Pain, function
Sandelin 1997[39] (Double dummy)	Knee	G1: Topical NSAIDs (eltenac gel + placebo tablet) G2: Oral NSAIDs (diclofenac + placebo gel)	G1: 124 (62.1) G2: 78 (73.1)	G1: 61.0 G2: 61.0	4 weeks	2, 3, 4 weeks	Pain, function
Simon 2009[40] (Double dummy)	Knee	G1: Topical NSAIDs (diclofenac solution + placebo tablets) G2: Oral NSAIDs (diclofenac + placebo solution)	G1: 154 (67.5) G2: 151 (62.9)	G1: 61.7 G2: 62.0	12 weeks	4, 8, 12 weeks	Pain, function
Conaghan 2013[41]	Knee	G1: Topical NSAIDs (ketoprofen gel) G2: Oral NSAIDs (celecoxib)	G1: 463 (59.2) G2: 233 (66.9)	G1: 60.8 G2: 62.0	12 weeks	2, 6, 9, 12 weeks	Pain, function
Tugwell 2004[42] (Double dummy)	Knee	G1: Topical NSAIDs (diclofenac solution + placebo tablets) G2: Oral NSAIDs (diclofenac + placebo solution + placebo tablets)	G1: 311 (57.0) G2: 311 (57.0)	G1: 64.0 G2: 63.0	12 weeks	12 weeks	Pain, function
Dickson 1991[43]	Knee	G1: Topical NSAIDs (piroxicam gel) G2: Oral NSAIDs (ibuprofen + placebo gel)	G1: 118 (64) G2: 117 (68)	G1: 63.0 G2: 62.0	4 weeks	4 weeks	Data not available
Topical NSAIDs vs. Exercise							
Yavuz 2013[44]	Knee	G1: Topical NSAIDs (diclofenac gel) G2: Exercise (strength exercise)	G1: 40 (77.5) G2: 40 (72.5)	G1: 59.9 G2: 58.9	6 weeks	6 weeks	Pain
Usual care/wait list/no treatment vs. Oral NSAIDs and paracetamol							
Ding 2009[45]	Knee	G1: No treatment G2: Oral NSAIDs (ibuprofen)	G1: 30 (73.3) G2: 30 (70.0)	G1: 58.9 G2: 52.0	2 weeks	2 weeks	Pain, function, QoL
Nannoni 2020[46]	Knee	G1: Wait list G2: Oral NSAIDs (celecoxib)	G1: 50 (78.0) G2: 50 (76.0)	G1: 57.1 G2: 57.4	2 weeks	1, 2 weeks	Pain, function
Usual care/wait list/no treatment vs. Exercise							
Abbott 2013[47]	Knee or hip	G1: Usual care G2: Exercise (mixed exercise + usual care)	G1: 51 (49.0) G2: 51 (62.7)	G1: 66.1 G2: 66.9	9 weeks	9 weeks	Pain, function

An 2008[48]	Knee	G1: No treatment G2: Exercise (mind-body exercise)	G1: 14 (100.0) G2: 14 (100.0)	G1: 64.6 G2: 65.4	8 weeks	8 weeks	Pain, function, QoL
Songül 2019[49]	Knee	G1: No treatment G2: Exercise (strength exercise)	G1: 17 (88.2) G2: 15 (73.3)	G1: 58.5 G2: 58.7	4 weeks	4 weeks	Pain, function
Aoki 2009[50]	Knee	G1: Usual care G2: Exercise (flexibility exercise)	G1: 19 (100.0) G2: 17 (100.0)	G1: 74.4 G2: 72.3	80 days	80 days	Pain, function
Arnold 2010[51]	Hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 25 (64.0) G2: 26 (76.9)	G1: 75.8 G2: 74.4	11 weeks	11 weeks	Function
Bennell 2010[52]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 44 (45.5) G2: 45 (51.1)	G1: 64.6 G2: 64.5	13 weeks	13 weeks	Pain, function
Borjesson 1996[53]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 34 (50.0) G2: 34 (50.0)	G1: 64.0 G2: 64.0	12 weeks	12 weeks	Pain, function
Braghin 2017[54]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 16 (87.5) G2: 26 (65.4)	G1: 60.2 G2: 61.8	8 weeks	8 weeks	Pain, function
Gur 2002[55]	Knee	G1: No treatment G2: Exercise (strength exercise)	G1: 17 (NA) G2: 6 (NA)	G1: 55.5 G2: 57.0	8 weeks	8 weeks	Pain, function
Henriksen 2014[56]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 29 (72.4) G2: 31 (87.1)	G1: 61.3 G2: 65.9	12 weeks	12 weeks	Pain, function, QoL
Huang 2005[57]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 35 (NA) G2: 35 (NA)	NA	8 weeks	8 weeks	Pain, function
Jan 2008[58]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 30 (83.3) G2: 68 (79.4)	G1: 62.8 G2: 62.6	8 weeks	8 weeks	Pain, function
Juhakoski 2011[59]	Hip	G1: Usual care G2: Exercise (mixed exercise + usual care)	G1: 58 (72.4) G2: 60 (68.3)	G1: 66.3 G2: 66.9	12 months	3, 6, 12 months	Pain, function,
Krauss 2014[60]	Hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 68 (39.1) G2: 71 (40.8)	G1: 60.0 G2: 58.0	12 weeks	12 weeks	Pain, function, QoL
Lee 2008[61]	Knee	G1: Usual care G2: Exercise (mind-body exercise)	G1: 24 (62.5) G2: 22 (95.5)	G1: 75.0 G2: 76.0	12 weeks	12 weeks	Pain, function
Lim 2008[62]	Knee	G1: No treatment G2: Exercise (strength exercise)	G1: 54 (53.7) G2: 53 (56.6)	G1: 63.6 G2: 65.6	12 weeks	12 weeks	Pain, function
Lin 2009[63]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 36 (72.2) G2: 72 (68.1)	G1: 62.2 G2: 62.7	8 weeks	8 weeks	Pain, function
Monica 2015[64]	Knee or hip	G1: Usual care G2: Exercise (flexibility exercise)	G1: 12 (75.0) G2: 12 (83.3)	G1: 54.9 G2: 52.8	12 weeks	12 weeks	Pain, function

Koli 2015[65]	Knee	G1: Usual care G2: Exercise (aerobic exercise)	G1: 40 (100.0) G2: 38 (100.0)	G1: 59.0 G2: 58.0	12 months	12 months	Pain, function, QoL
O'Reilly 1999[66]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 72 (68.1) G2: 108 (64.8)	G1: 62.2 G2: 61.9	6 months	6 months	Pain, function, QoL
Salacinski 2012[67]	Knee	G1: Usual care G2: Exercise (aerobic exercise)	G1: 18 (66.7) G2: 19 (78.9)	G1: 60.6 G2: 55.1	12 weeks	12 weeks	Pain, function, QoL
Schilke 1996[68]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 10 (NA) G2: 10 (NA)	G1: 68.4 G2: 64.5	8 weeks	8 weeks	Pain, function
Sekir 2005[69]	Knee	G1: No treatment G2: Exercise (neuromotor exercise)	G1: 10 (70.0) G2: 12 (75.0)	G1: 62.0 G2: 59.0	6 weeks	6 weeks	Pain, function
Simão 2012[70]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 11 (91.0) G2: 10 (90.0)	G1: 71.0 G2: 69.0	12 weeks	12 weeks	Pain, function
Swank 2011[71]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 35 (62.9) G2: 36 (66.7)	G1: 62.6 G2: 63.1	6 weeks	6 weeks	Pain
Takacs 2017[72]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 20 (65.0) G2: 20 (95.0)	G1: 67.1 G2: 66.1	10 weeks	10 weeks	Pain, function
Thorstensson 2005[73]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 31 (51.6) G2: 30 (50.0)	G1: 57.3 G2: 54.8	6 weeks	6 weeks	Pain, function, QoL
Topp 2002[74]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 35 (80.0) G2: 67 (68.7)	G1: 60.9 G2: 64.6	16 weeks	16 weeks	Pain, function
Trans 2009[75]	Knee	G1: No treatment G2: Exercise (strength exercise)	G1: 17 (100.0) G2: 35 (100.0)	G1: 61.1 G2: 60.1	8 weeks	8 weeks	Data not available
Waller 2017[76]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 44 (100.0) G2: 43 (100.0)	G1: 63.9 G2: 63.8	4 months	4 months	Pain, function, QoL
Wang 2007[77]	Knee or hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 18 (88.9) G2: 20 (80.0)	G1: 62.7 G2: 69.3	12 weeks	6, 12 weeks	Pain, function
Wortley 2013[78]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 6 (66.7) G2: 25 (72.0)	G1: 70.5 G2: 68.8	10 weeks	10 weeks	Pain, function
Hermann 2016[79]	Hip	G1: Usual care G2: Exercise (strength exercise)	G1: 40 (62.5) G2: 40 (67.5)	G1: 70.8 G2: 70.0	10 weeks	10 weeks	Pain, function, QoL
Hoogeboom 2010[80]	Hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 11 (63.6) G2: 10 (70.0)	G1: 75.0 G2: 77.0	4 weeks	4 weeks	Pain, function, QoL
Krasilshchikov 2011[81]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 8 (100.0) G2: 8 (100.0)	G1: 58.3 G2: 58.4	8 weeks	8 weeks	Pain, function

Wang 2011[82]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 26 (84.6) G2: 52 (86.5)	G1: 67.9 G2: 67.5	12 weeks	6, 12 weeks	Pain, function, QoL
Aglamis 2009[83]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 9 (100.0) G2: 16 (100.0)	G1: 54.4 G2: 56.8	12 weeks	6, 12 weeks	Pain, function, QoL
Beaupre 2004[84]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 66 (50.0) G2: 65 (60.0)	G1: 67.0 G2: 67.0	6 weeks	6 weeks	Pain, function, QoL
Bruce-Brand 2012[85]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 6 (50.0) G2: 10 (40.0)	G1: 65.2 G2: 63.4	7 weeks	7 weeks	Pain, function, QoL
Calatayud 2017[86]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 25 (NA) G2: 25 (NA)	G1: 66.7 G2: 66.8	8 weeks	8 weeks	Pain, function, QoL
Christensen 2015[87]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 64 (79.7) G2: 64 (81.3)	G1: 61.7 G2: 62.9	68 weeks	68 weeks	Pain, function, QoL
Cochrane 2005[88]	Knee or hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 158 (62.7) G2: 153 (63.4)	G1: 69.6 G2: 69.9	12 months	6, 12 months	Pain, function, QoL
Deepeshwar 2018[89]	Knee	G1: Usual care G2: Exercise (mind-body exercise)	G1: 35 (71.4) G2: 31 (80.6)	G1: 59.6 G2: 60.2	7 days	7 days	Function
Espejo 2012[90]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 14 (NA) G2: 17 (NA)	G1: 82.2 G2: 86.1	4 weeks	4 weeks	Pain, function, QoL
Evgeniadis 2008[91]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 20 (70.0) G2: 18 (83.3)	G1: 69.4 G2: 67.1	4 weeks	4 weeks	Pain, function, QoL
Ghroubi 2008[92]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 14 (NA) G2: 13 (NA)	G1: 42.4 G2: 39.8	8 weeks	8 weeks	Pain, function
Gstoettner 2011[93]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 20 (70.0) G2: 18 (88.9)	G1: 66.9 G2: 72.8	6 weeks	6 weeks	Data not available
Huang 2017[94]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 122 (80.3) G2: 128 (78.9)	G1: 67.4 G2: 68.1	12 weeks	4, 12 weeks	Pain, function
Kuptniratsaikul 2002[95]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 193 (76.7) G2: 199 (79.4)	G1: 67.6 G2: 67.9	2 months	2 months	Pain, function
Lund 2008[96]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 27 (66.7) G2: 52 (84.6)	G1: 70.0 G2: 66.4	8 weeks	8 weeks	Pain, function
Messier 2004[97]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 78 (68.0) G2: 80 (74.0)	G1: 69.0 G2: 69.0	18 months	6, 18 months	Pain, function
Song 2003[98]	Knee	G1: Usual care G2: Exercise (mind-body exercise)	G1: 21 (100.0) G2: 22 (100.0)	G1: 62.5 G2: 64.8	12 weeks	12 weeks	Pain, function

D'Lima 1996[99]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 8 (NA) G2: 16 (NA)	NA	5 weeks	5 weeks	Pain, function
Moghadam 2017[100]	Knee	G1: Usual care G2: Exercise (aerobic exercise)	G1: 9 (0) G2: 9 (0)	G1: 68.8 G2: 64.7	8 weeks	8 weeks	Function
Oida 2008[101]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 44 (88.6) G2: 44 (84.1)	G1: 72.5 G2: 74.8	3 months	3 months	Function
Oosting 2012[102]	Hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 15 (66.7) G2: 15 (93.3)	G1: 75.0 G2: 76.9	4 weeks	4 weeks	Pain, function, QoL
Peloquin 1999[103]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 65 (69.2) G2: 59 (71.2)	G1: 66.4 G2: 65.6	3 months	3 months	Pain, function, QoL
Rapp 2009[104]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 9 (66.7) G2: 15 (66.7)	G1: 60.0 G2: 57.0	8 weeks	8 weeks	Pain
Pisters 2010[105]	Knee or hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 103 (78.6) G2: 97 (75.3)	G1: 64.5 G2: 65.1	15 months	3, 9, 15 months	Pain, function
Ravaud 2004[106]	Knee or hip	G1: Usual care G2: Exercise (strength exercise)	G1: 760 (72.5) G2: 735 (70.7)	G1: 67.3 G2: 66.9	24 weeks	4, 12, 24 weeks	Pain, function
Salli 2006[107]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 20 (NA) G2: 58 (NA)	G1: 58.3 G2: 55.3	8 weeks	4, 8 weeks	Pain, function, QoL
Skoffer 2016[108]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 29 (58.6) G2: 30 (63.3)	G1: 70.1 G2: 70.7	5 weeks	5 weeks	Pain, function, QoL
Teirlinck 2016[109]	Hip	G1: Usual care G2: Exercise (mixed exercise + usual care)	G1: 102 (54.9) G2: 101 (62.4)	G1: 67.0 G2: 64.0	9 months	6 weeks, 3, 6, 9 months	Pain, function, QoL
Topp 2009[110]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 28 (35.7) G2: 26 (26.9)	G1: 63.5 G2: 64.1	3 weeks	3 weeks	Pain
Villadsen 2014[111]	Knee or hip	G1: Usual care G2: Exercise (neuromotor exercise)	G1: 81 (55.6) G2: 84 (56.0)	G1: 66.9 G2: 67.9	8 weeks	8 weeks	Pain, function, QoL
Wallis 2017[112]	Knee	G1: Usual care G2: Exercise (aerobic exercise)	G1: 23 (47.8) G2: 23 (39.1)	G1: 67.0 G2: 68.0	12 weeks	12 weeks	Pain, function, QoL
Weidenhielm 1993[113]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 20 (45.0) G2: 19 (57.9)	G1: 63.0 G2: 64.0	3 months	3 months	Pain
Young Moo 2000[114]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 40 (85.0) G2: 40 (90.0)	NA	6 weeks	6 weeks	Data not available

Van Baar 2001[115]	Knee or hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 102 (79.4) G2: 98 (77.6)	G1: 67.7 G2: 68.3	12 weeks	12 weeks	Data not available
Mazloum 2018[116]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 13 (NA) G2: 28 (NA)	G1: 50.8 G2: 52.7	8 weeks	8 weeks	Function
DeVita 2018[117]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 15 (53.3) G2: 15 (66.7)	G1: 56.2 G2: 58.1	12 weeks	12 weeks	Pain, function
Isaramalai 2018[118]	Knee	G1: Usual care G2: Exercise (strength exercise)	G1: 25 (80.0) G2: 50 (76.0)	G1: 63.7 G2: 67.5	2 months	1, 2 months	Pain, function
Jahic 2018[119]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 10 (70.0) G2: 10 (70.0)	G1: NA G2: NA	6 weeks	6 weeks	Function
Pazit 2018[120]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 9 (56.0) G2: 19 (52.6)	G1: 70.4 G2: 66.4	8 weeks	8 weeks	Pain, function, QoL
De Matos 2019[121]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 15 (80.0) G2: 15 (66.7)	G1: 60.8 G2: 58.6	8 weeks	8 weeks	Pain, function
Doiron-Cadrin 2020[122]	Knee or Hip	G1: Usual care G2: Exercise (strength exercise)	G1: 11 (72.7) G2: 11 (83.3)	G1: 66.7 G2: 61.3	12 weeks	12 weeks	Pain, function, QoL
Rewald 2020[123]	Knee	G1: Usual care G2: Exercise (aerobic exercise)	G1: 47 (51.1) G2: 55 (70.9)	G1: 61.0 G2: 59.0	12 weeks	12 weeks	Pain, function, QoL
Rezasoltani 2020[124]	Knee	G1: Usual care G2: Exercise (aerobic exercise)	G1: 15 (NA) G2: 15 (NA)	G1: 51.2 G2: 50.8	4 weeks	4 weeks	Pain, function
Kim 2020[125]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 35 (91.4) G2: 40 (77.5)	G1: 73.4 G2: 76.2	12 weeks	12 weeks	Function, QoL
Duarte 2020[126]	Knee or Hip	G1: Usual care G2: Exercise (mixed exercise)	G1: 8 (87.5) G2: 23 (65.2)	G1: 59.5 G2: 68.5	8 weeks	8 weeks	Data not available
Ye 2020[127]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 28 (71.4) G2: 28 (60.7)	G1: 63.6 G2: 65.1	12 weeks	8, 12 weeks	Pain, function
Guo 2021[128]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 52 (53.8) G2: 50 (54.0)	G1: 61.5 G2: 63.2	16 weeks	8, 16 weeks	Pain, function
Karimi 2021[129]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 10 (100.0) G2: 20 (100.0)	G1: 65.6 G2: 50.3	8 weeks	8 weeks	Data not available
Moharrami, M R 2021[130]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 21 (100.0) G2: 21 (100.0)	G1: 57.1 G2: 55.5	4 weeks	4 weeks	Pain, function
Xiao 2021[131]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 134 (NA) G2: 132 (NA)	G1: 69.0 G2: 71.0	24 weeks	12, 24 weeks	Pain, function, QoL

Azizi 2020[132]	Knee	G1: Usual care G2: Exercise (mixed exercise)	G1: 16 (NA) G2: 15 (NA)	G1: 65.5 G2: 63.5	8 weeks	8 weeks	Pain
Cheung 2014[133]	Knee	G1: Wait list G2: Exercise (mind-body exercise)	G1: 18 (100.0) G2: 18 (100.0)	G1: 71.9 G2: 71.9	8 weeks	4, 8 weeks	Pain, function, QoL
Chopp Hurley 2017[134]	Knee or hip	G1: Wait list G2: Exercise (strength exercise)	G1: 12 (75.0) G2: 12 (83.3)	G1: 54.9 G2: 52.8	12 weeks	12 weeks	Pain, function
Ferrara 2008[135]	Hip	G1: Wait list G2: Exercise (mixed exercise)	G1: 12 (58.3) G2: 11 (63.6)	G1: 63.1 G2: 63.8	4 weeks	4 weeks	Pain, function, QoL
Fransen 2001[136]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 43 (67.0) G2: 40 (78.0)	G1: 66.1 G2: 65.3	8 weeks	8 weeks	Pain, function, QoL
Fransen 2007[137]	Knee or hip	G1: Wait list G2: Exercise (mixed exercise)	G1: 41 (82.9) G2: 111 (70.3)	G1: 69.6 G2: 70.4	12 weeks	12 weeks	Pain, function, QoL
French 2013[138]	Hip	G1: Wait list G2: Exercise (mixed exercise)	G1: 43 (53.5) G2: 45 (75.6)	G1: 60.8 G2: 61.8	8 weeks	8 weeks	Pain, function, QoL
Hinman 2007[139]	Knee or hip	G1: Wait list G2: Exercise (mixed exercise)	G1: 35 (68.6) G2: 36 (66.7)	G1: 61.5 G2: 63.3	6 weeks	6 weeks	Pain, function, QoL
Jan 2009[140]	Knee	G1: Wait list G2: Exercise (strength exercise)	G1: 35 (68.6) G2: 71 (69.0)	G1: 62.2 G2: 62.6	8 weeks	8 weeks	Function
Jorge 2014[141]	Knee	G1: Wait list G2: Exercise (strength exercise)	G1: 31 (100.0) G2: 29 (100.0)	G1: 59.9 G1: 61.7	12 weeks	6, 12 weeks	Pain, function, QoL
Lee 2009[142]	Knee	G1: Wait list G2: Exercise (mind-body exercise)	G1: 15 (93.3) G2: 29 (93.1)	G1: 66.9 G2: 70.2	8 weeks	8 weeks	Pain, function, QoL
Rogind 1998[143]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 12 (91.7) G2: 11 (90.9)	G1: 73.0 G2: 69.3	3 months	3 months	Pain, function,
Rooij 2017[144]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 63 (73.0) G2: 63 (77.8)	G1: 63.9 G2: 63.2	20 weeks	10, 20 weeks	Pain, function, QoL
Rosedale 2014[145]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 59 (57.6) G2: 99 (55.6)	G1: 64.0 G2: 66.0	2 weeks	2 weeks	Pain, function, QoL
Thompson 2019[146]	Hip	G1: Wait list G2: Exercise (mixed exercise)	G1: 10 (70.0) G2: 21 (42.9)	G1: 60.8 G2: 59.7	12 weeks	12 weeks	Data not available
Vincent 2019[147]	Knee	G1: Wait list G2: Exercise (strength exercise)	G1: 32 (66.0) G2: 58 (68.6)	G1: 68.6 G2: 68.1	4 months	4 months	Pain, function
Shellington 2019[148]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 12 (75.0) G2: 10 (60.6)	G1: 69.3 G2: 69.7	24 weeks	12, 24 weeks	Pain, function

Domínguez-Navarro 2020[149]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 21 (66.7) G2: 44 (60.6)	G1: 70.2 G2: 70.6	1 month	1 month	Pain, function, QoL
Song 2020[150]	Knee	G1: Wait list G2: Exercise (neuromotor exercise)	G1: 16 (62.5) G2: 13 (61.5)	G1: 67.4 G2: 68.5	12 weeks	6, 12 weeks	Pain
Allen 2018[151]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 68 (77.9) G2: 140 (71.4)	G1: 64.3 G2: 65.7	4 months	4 months	Pain, function
Li 2018[152]	Knee	G1: Wait list G2: Exercise (mixed exercise)	G1: 31 (90.3) G2: 30 (73.3)	G1: 62.1 G2: 61.3	2 months	2 months	Pain, function, QoL

G, group; NA, not available; NSAIDs, non-steroidal anti-inflammatory drugs; QoL, quality of life.

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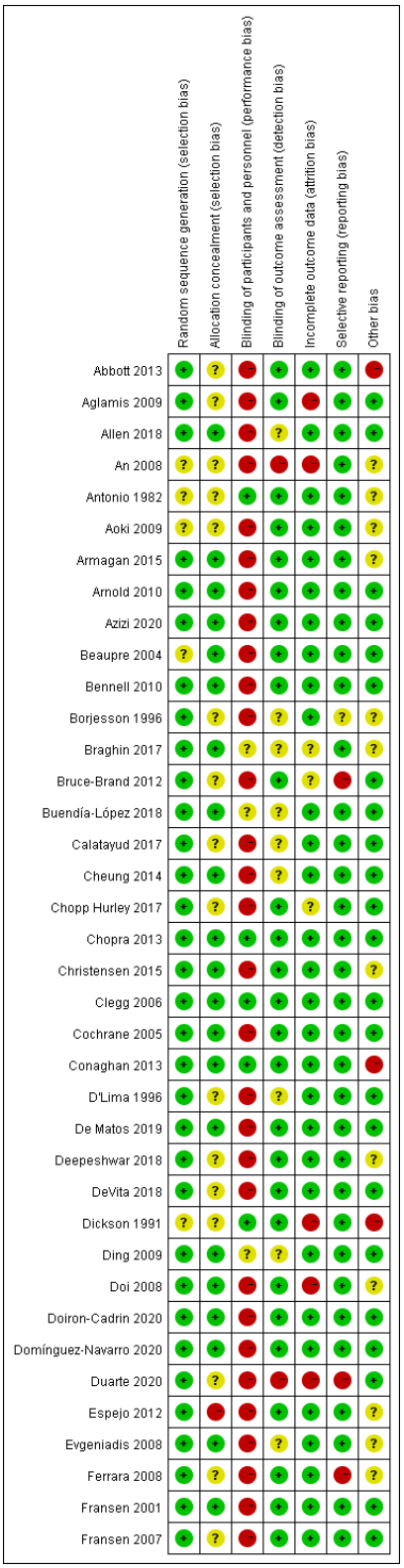
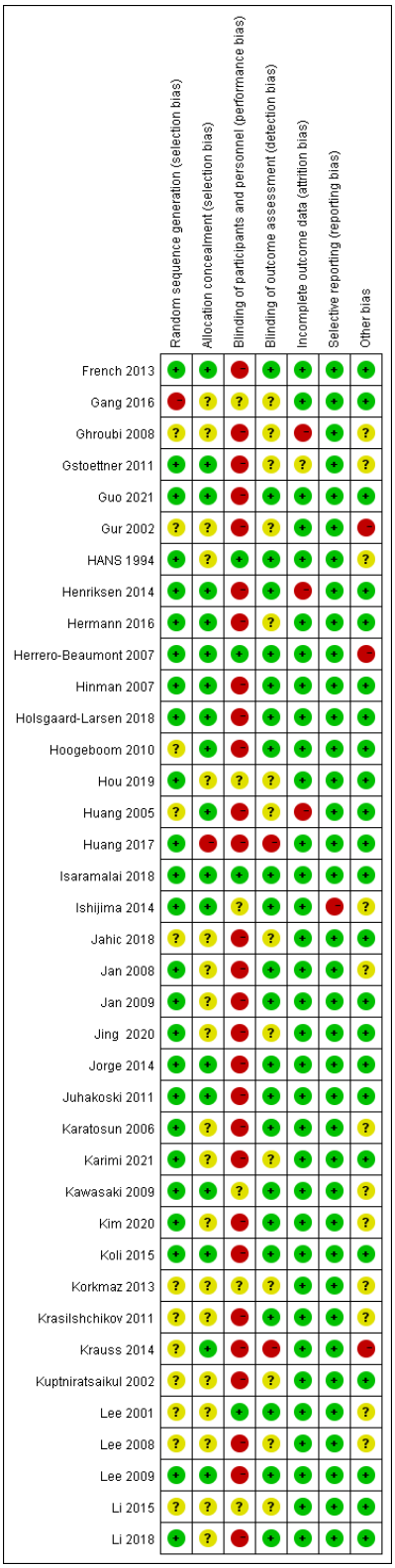
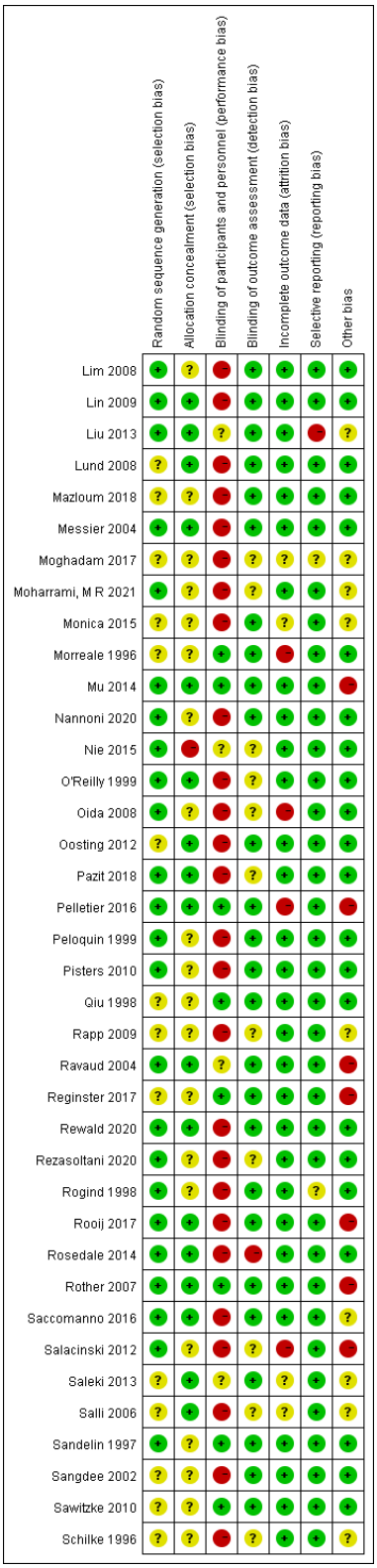
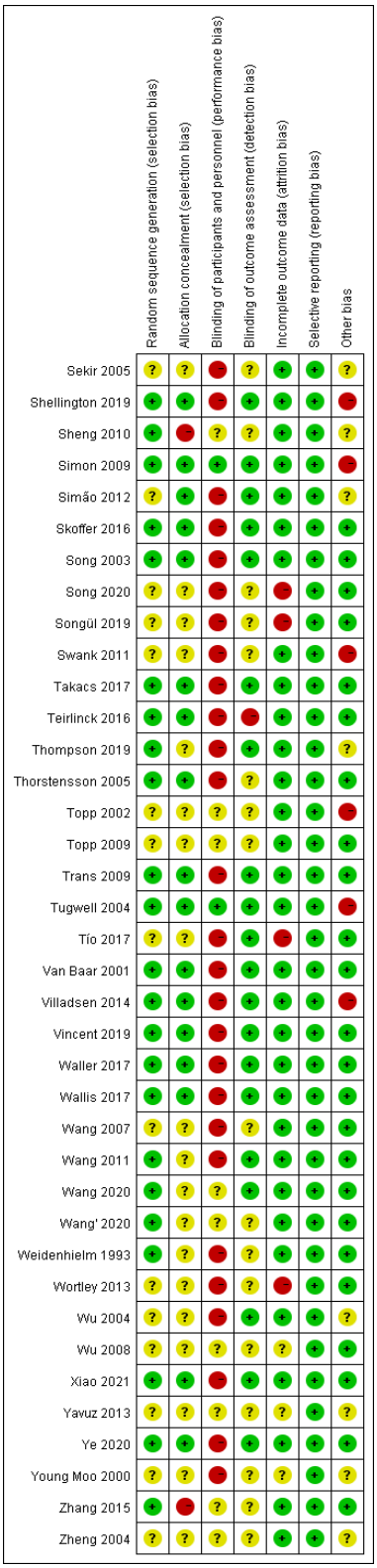
Appendix 8 Methodological quality of the included studies






Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Lim 2008
Lin 2009
Liu 2013
Lund 2008
Mazloum 2018
Messier 2004
Moghadam 2017
Moharrami, M R 2021
Monica 2015
Morreale 1996
Mu 2014
Nannoni 2020
Nie 2015
O'Reilly 1999
Oida 2008
Oosting 2012
Pazit 2018
Pelletier 2016
Peloquin 1999
Pisters 2010
Qiu 1998
Rapp 2009
Ravaud 2004
Reginster 2017
Rewald 2020
Rezasoltani 2020
Rogind 1998
Rooij 2017
Rosedale 2014
Rother 2007
Saccomanno 2016
Salacinski 2012
Saleki 2013
Salli 2006
Sandelin 1997
Sangdee 2002
Sawitzke 2010
Schilke 1996


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Sekir 2005
Shellington 2019
Sheng 2010
Simon 2009
Simão 2012
Skoffer 2016
Song 2003
Song 2020
Songül 2019
Swank 2011
Takacs 2017
Teirlinck 2016
Thompson 2019
Thorstensson 2005
Topp 2002
Topp 2009
Trans 2009
Tugwell 2004
Tío 2017
Van Baar 2001
Villadsen 2014
Vincent 2019
Waller 2017
Wallis 2017
Wang 2007
Wang 2011
Wang 2020
Wang' 2020
Weidenhielm 1993
Wortley 2013
Wu 2004
Wu 2008
Xiao 2021
Yavuz 2013
Ye 2020
Young Moo 2000
Zhang 2015
Zheng 2004

Appendix 9 League table

Network league tables for all the interventions in regard to the pain reduction and fuctional improvement at or nearest to four week and at 24 weeks. Results of the fuctional improvement are presented in the left lower half and results of pain reduction in the upper right half. Comparisons between treatments should be read from left to right and the estimate is in the cell in common between the column-defining treatment and the row-defining treatment. Estimates are presented as mean standard mean difference (SMD) with 95% confidence interval in parentheses. SMD above 0 favour the column intervention and SMD below 0 favour the row intervention. Interventions in bold are significantly different since the 95% credible interval does not include 0.

Pain reduction and fuctional improvement at or nearest to four weeks

Exercise	-0.12 (-1.74, 1.50)	-0.53 (-2.39, 1.34)	-0.16 (-2.36, 2.03)	0.50 (-1.7, 2.73)	**1.31 (0.61, 2.01)**
0.09 (-1.69, 1.85)	**Oral NSAIDs and paracetamol**	-0.41 (-1.59, 0.77)	-0.04 (-2.42, 2.35)	0.62 (-1.25, 2.50)	1.43 (-0.22, 3.09)
-0.83 (-2.91, 1.26)	-0.92 (-2.29, 0.45)	**Acupuncture**	0.37 (-2.22, 2.96)	1.03 (-1.14, 3.22)	1.84 (-0.06, 3.75)
-0.05 (-3.03, 2.95)	-0.13 (-3.12, 2.88)	0.79 (-2.47, 4.04)	**IAHA**	0.66 (-2.21, 3.56)	1.48 (-0.81, 3.76)
-	-	-	-	**Topical NSAIDs**	0.81 (-1.46, 3.05)
1.08 (0.29, 1.88)	0.99 (-0.82, 2.82)	1.91 (-0.24, 4.04)	1.13 (-1.94, 4.19)	-	**Usual care**

Pain reduction and fuctional improvement at 24 weeks

Exercise	0.17 (-0.77, 1.12)	-0.17 (-1.07, 0.72)	0.21 (-0.70, 1.12)
0.05 (-1.15, 1.24)	**Oral NSAIDs and paracetamol**	-0.34 (-1.26, 0.56)	0.04 (-0.38, 0.45)
-0.37 (-1.52, 0.77)	-0.42 (-1.58, 0.73)	**IAHA**	0.38 (-0.55, 1.33)
0.16 (-1.01, 1.30)	0.11 (-0.44, 0.64)	0.53 (-0.68, 1.72)	**CS/GS**

NSAIDs, non-steroidal anti-inflammatory drugs; CS/GS, glucosamine sulphate/chondroitin sulphate;IAHA, intra-articular hyaluronic acid.

Appendix 10 Results of global inconsistency test for the primary analyses

Time-point	Pain relief	Functional improvement
At or nearest to four weeks	Chi^2=8.12, *P*=0.087	Chi^2=1.91, *P*=0.592

The results was assessed by the design-by-treatment inconsistenc moldel and estimates in bold denote significance at $P < 0.05$.

Appendix 11 Sensitivity analysis

	SMD (95% CrI) [a]				
	Primary analysis	Sensitivity analysis			
		Non-outlier ES < 5	Allocation concealment-low risk	Sample size ≥ 30/arm	Intervention without prescribing paracetamol
Pain					
At or nearest to four weeks	**47 trials (n=4,377)**	**46 trials (n=4,347)**	**16 trials (n=1,367)**	**16 trials (n=2,755)**	**47 trials (n=4,377)**
	-0.12 (-1.74, 1.50)	-0.25 (-1.25, 0.75)	-1.04 (-2.18, 0.06)	-0.31 (-1.77, 1.16)	-0.12 (-1.74, 1.50)
At 24 weeks	**9 trials (n=2,141)**	**9 trials (n=2,141)**	**7 trials (n=1,760)**	**8 trials (n=2,093)**	**7 trials (n=1,879)**
	0.17 (-0.77, 1.12)	0.17 (-0.77, 1.12)	0.15 (-1.28, 1.58)	0.18 (-0.93, 1.28)	0.15 (-1.30, 1.58)
Function					
At or nearest to four weeks	**40 trials (n=2,968)**	**38 trials (n=2,906)**	**16 trials (n=1,367)**	**11 trials (n=1,499)**	**40 trials (n=2,968)**
	0.09 (-1.69, 1.85)	-0.10 (-1.31, 1.10)	-0.02 (-0.52, 0.49)	-0.21 (-2.48, 2.03)	0.09 (-1.69, 1.85)
At 24 weeks	**9 trials (n=2,141)**	**9 trials (n=2,141)**	**7 trials (n=1,760)**	**8 trials (n=2,093)**	**7 trials (n=1,879)**
	0.05 (-1.15, 1.24)	0.05 (-1.15, 1.24)	-0.02 (-1.76, 1.68)	0.00 (-1.31, 1.32)	-0.04 (-1.76, 1.67)

CrI, credible interval; ES, effect size; SMD, standard mean difference.

[a]For SMD, negative value favours oral NSAIDs and paracetamol; whereas the positive value favours of exercise.

Sensitivity analyses performed to show if some underlying assumptions (i.e., sample size < 30/arm, high or unclear risk of allocation concealment, intervention prescribing paracetamol and also studies that included outliers or had an effect size > 5) which would significantly alter the conclusion of primary analysis.