

Appendix A. Search Strategy

SEARCHES RUN IN JULY/AUGUST 2015 [Surveillance]

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2006-7/10/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

“osteoarthritis, knee”[MH] OR (“osteoarthritis”[MH] AND (knee[tiab] OR knees[tiab])) OR (osteoarthritis*[tiab] AND (knee[tiab] OR knees[tiab])) OR (“osteoarthritis”[MH] AND (patellofemoral[tiab] OR patello-femoral[tiab])) AND
Glucosamine[MH] OR “Chondroitin”[MH] OR glucosamine OR acetylglucosamine OR “n-acetylglucosamine” OR “n-acetyl-d-glucosamine” OR chondroitin

NEW THERAPIES:

“osteoarthritis, knee”[MH] OR (“osteoarthritis”[MH] AND (knee[tiab] OR knees[tiab])) OR (osteoarthritis*[tiab] AND (knee[tiab] OR knees[tiab])) OR (“osteoarthritis”[MH] AND (patellofemoral[tiab] OR patello-femoral[tiab])) AND
monovisc OR duloxetine* OR cymbalta OR selective serotonin* OR ssri OR milnacipran OR savella OR venlafaxine OR effexor OR desvenlafaxine OR pristiq OR “il-1” OR interleukin* OR anakinra OR canakinumab OR “platelet rich plasma” OR “platelet-rich plasma” OR PRP OR “nerve growth factor” OR fibroblast growth OR shoe wedge* OR capsaicin

MANUALLY SEARCHED ENDNOTE TO FILTER ABOVE RESULTS FOR THE FOLLOWING TERMS REPRESENTING STUDY DESIGNS:

Comparative
Evaluation
Follow-up
Follow up
Prospective
Placebo
Clinical trial
Mask
Single-blind
Double-blind
Blind
Random
RCT
Research design
Control

Volunteer
Systematic review
Meta-analy*
Meta analy*
Metaanaly*
Database or Data base
Case series (for Arthroscopy only)

DATABASE SEARCHED & TIME PERIOD COVERED:

Embase – 1/1/2006-7/21/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

'knee osteoarthritis'/exp OR 'knee osteoarthritis' OR ('osteoarthritis'/exp OR osteoarthritis AND ('knee'/exp OR knee OR knees OR patellofemoral OR 'patello femoral'))

AND

'chondroitin' OR 'chondroitin'/exp OR chondroitin OR 'glucosamine' OR 'glucosamine'/exp OR glucosamine OR 'acetylglucosamine' OR 'acetylglucosamine'/exp OR acetylglucosamine OR 'n-acetylglucosamine'/exp OR 'n-acetylglucosamine' OR 'n-acetyl-d-glucosamine'/exp OR 'n-acetyl-d-glucosamine'

AND

Human/de

NEW THERAPIES:

'knee osteoarthritis'/exp OR 'knee osteoarthritis' OR ('osteoarthritis'/exp OR osteoarthritis AND ('knee'/exp OR knee OR knees OR patellofemoral OR 'patello femoral'))

AND

'monovisc' OR 'monovisc'/exp OR monovisc OR duloxetine* OR 'cymbalta' OR 'cymbalta'/exp OR cymbalta OR (selective AND serotonin*) OR 'ssnri' OR 'ssnri'/exp OR ssnri OR 'milnacipran' OR 'milnacipran'/exp OR milnacipran OR 'savella' OR 'savella'/exp OR savella OR 'venlafaxine' OR 'venlafaxine'/exp OR venlafaxine OR 'effexor' OR 'effexor'/exp OR effexor OR 'desvenlafaxine' OR 'desvenlafaxine'/exp OR desvenlafaxine OR 'pristiq' OR 'pristiq'/exp OR pristiq OR 'il-1'/exp OR 'il-1' OR interleukin* OR 'anakinra' OR 'anakinra'/exp OR anakinra OR 'canakinumab' OR 'canakinumab'/exp OR canakinumab OR 'platelet rich plasma'/exp OR 'platelet rich plasma' OR 'platelet-rich plasma'/exp OR 'platelet-rich plasma' OR 'prp' OR 'prp'/exp OR prp OR 'nerve growth factor'/exp OR 'nerve growth factor' OR (('fibroblast' OR 'fibroblast'/exp OR fibroblast) AND ('growth' OR 'growth'/exp OR growth)) OR (('shoe' OR 'shoe'/exp OR shoe) AND wedge*) OR capsaicin*

AND

Human/de

MANUALLY SEARCHED ENDNOTE TO FILTER ABOVE RESULTS FOR THE FOLLOWING TERMS REPRESENTING STUDY DESIGNS:

Comparative

Follow-up
Follow up
Prospective
Placebo
Trial
Mask
Single-blind
Double-blind
Blind
Random
RCT
Research design
Control
Volunteer
Systematic review
Meta-analy*
Meta analy*
Database or Data base
Case series (for Arthroscopy only)

DATABASE SEARCHED & TIME PERIOD COVERED:

Cochrane Databases of Systematic Reviews, Other Reviews, CENTRAL, Methods, Technology Assessment, Economic Evaluations – 1/1/2006-8/3/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

osteoarthritis and (knee or knees or patellofemoral or patello-femoral):ti,ab,kw

AND

glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin:ti,ab,kw

NEW THERAPIES:

osteoarthritis and (knee or knees or patellofemoral or patello-femoral):ti,ab,kw

AND

monovisc or duloxetine* or cymbalta or selective serotonin* or ssni or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin:ti,ab,kw

DATABASE SEARCHED & TIME PERIOD COVERED:

International Pharmaceutical Abstracts – 1/1/2006-8/4/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

ab(osteoarthritis and (knee or knees or patellofemoral or patello-femoral)) OR ti(osteoarthritis and (knee or knees or patellofemoral or patello-femoral)) OR su(osteoarthritis and (knee or knees or patellofemoral or patello-femoral))

AND

ab(glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin) OR ti(glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin) OR su(glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin)

NEW THERAPIES:

ab(osteoarthritis and (knee or knees or patellofemoral or patello-femoral)) OR ti(osteoarthritis and (knee or knees or patellofemoral or patello-femoral)) OR su(osteoarthritis and (knee or knees or patellofemoral or patello-femoral))

AND

ab(monovisc or duloxetine* or cymbalta or selective serotonin* or ssnri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin) OR ti(monovisc or duloxetine* or cymbalta or selective serotonin* or ssnri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin) OR su(monovisc or duloxetine* or cymbalta or selective serotonin* or ssnri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin)

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UPDATES RUN IN NOVEMBER/DECEMBER 2015 for the report

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 6/1/2015-11/4/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

“osteoarthritis, knee”[MH] OR (“osteoarthritis”[MH] AND (knee[tiab] OR knees[tiab])) OR (osteoarthritis*[tiab] AND (knee[tiab] OR knees[tiab])) OR (“osteoarthritis”[MH] AND (patellofemoral[tiab] OR patello-femoral[tiab]))

AND

Glucosamine[MH] OR "Chondroitin"[MH] OR glucosamine OR acetylglucosamine OR "n-acetylglucosamine" OR "n-acetyl-d-glucosamine" OR chondroitin

NEW THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 6/1/2015-12/2/2015

“osteoarthritis, knee”[MH] OR (“osteoarthritis”[MH] AND (knee[tiab] OR knees[tiab])) OR (osteoarthritis*[tiab] AND (knee[tiab] OR knees[tiab])) OR (“osteoarthritis”[MH] AND (patellofemoral[tiab] OR patello-femoral[tiab]))

AND

duloxetine* OR cymbalta OR selective serotonin* OR ssri OR milnacipran OR savella OR venlafaxine OR effexor OR desvenlafaxine OR pristiq OR "il-1" OR interleukin* OR anakinra OR canakinumab OR "platelet rich plasma" OR "platelet-rich plasma" OR PRP OR "nerve growth factor" OR fibroblast growth OR shoe wedge* OR capsaicin

ADDITIONAL THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed - 1/1/2006-12/11/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

“osteoarthritis, knee”[MH] OR (“osteoarthritis”[MH] AND (knee[tiab] OR knees[tiab])) OR (osteoarthritis*[tiab] AND (knee[tiab] OR knees[tiab])) OR (“osteoarthritis”[MH] AND (patellofemoral[tiab] OR patello-femoral[tiab])) OR (“osteoarthritis”[tiab] AND (patellofemoral[tiab] OR patello-femoral[tiab]))

AND

acupuncture[tiab] OR acupuncture[ot] OR braces OR orthotic* OR orthosis OR orthoses OR stem cell* OR physical therapy OR exercis* OR herbal supplement* OR transdermal OR topical analgesic* OR analgesic cream* OR prolotherap* OR weight loss OR losing weight OR diet OR dieting OR weight reduc* OR cell-based therap* OR "Acupuncture Therapy"[Mesh] OR "Orthotic Devices"[Mesh] OR "Stem Cells"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Exercise Movement Techniques"[Mesh] OR "Exercise Therapy"[Mesh] OR "Transdermal Patch"[Mesh] OR "Weight Loss"[Mesh] OR "Diet, Reducing"[Mesh] OR "Weight Reduction Programs"[Mesh] OR (dietary supplements[mh] AND (plants, medicinal[mh] OR plant extracts[mh])) OR (administration, topical[mh] AND analgesics[mh])

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DATABASE SEARCHED & TIME PERIOD COVERED:

Embase – 1/1/2015-11/5/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

'knee osteoarthritis'/exp OR 'knee osteoarthritis' OR ('osteoarthritis' OR 'osteoarthritis'/exp OR osteoarthritis AND ('knee' OR 'knee'/exp OR knee OR knees OR patellofemoral OR 'patello femoral')) AND [english]/lim AND [humans]/lim AND [2015-2015]/py AND 'chondroitin' OR 'chondroitin'/exp OR chondroitin OR 'glucosamine' OR 'glucosamine'/exp OR glucosamine OR 'acetylglucosamine' OR 'acetylglucosamine'/exp OR acetylglucosamine OR 'n-acetylglucosamine'/exp OR 'n-acetylglucosamine' OR 'n-acetyl-d-glucosamine'/exp OR 'n-acetyl-d-glucosamine'

NEW THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

Embase – 1/1/2015-11/5/2015

'knee osteoarthritis'/exp OR 'knee osteoarthritis' OR ('osteoarthritis' OR 'osteoarthritis'/exp OR osteoarthritis AND ('knee' OR 'knee'/exp OR knee OR knees OR patellofemoral OR 'patello femoral')) AND duloxetine* OR 'cymbalta' OR 'cymbalta'/exp OR cymbalta OR (selective AND serotonin*) OR 'ssnri' OR 'ssnri'/exp OR ssnri OR 'milnacipran' OR 'milnacipran'/exp OR milnacipran OR 'savella' OR 'savella'/exp OR savella OR 'venlafaxine' OR 'venlafaxine'/exp OR venlafaxine OR 'effexor' OR 'effexor'/exp OR effexor OR 'desvenlafaxine' OR 'desvenlafaxine'/exp OR desvenlafaxine OR 'pristiq' OR 'pristiq'/exp OR pristiq OR 'il-1'/exp OR 'il-1' OR interleukin* OR 'anakinra' OR 'anakinra'/exp OR anakinra OR 'canakinumab' OR 'canakinumab'/exp OR canakinumab OR 'platelet rich plasma'/exp OR 'platelet rich plasma' OR 'platelet-rich plasma'/exp OR 'platelet-rich plasma' OR 'prp' OR 'prp'/exp OR prp OR 'nerve growth factor'/exp OR 'nerve growth factor' OR ('fibroblast' OR 'fibroblast'/exp OR fibroblast AND ('growth' OR 'growth'/exp OR growth)) OR ('shoe' OR 'shoe'/exp OR shoe AND wedge*) OR capsaicin* AND Human

ADDITIONAL THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

Embase - 1/1/2006-12/11/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

'knee osteoarthritis'/exp OR 'knee osteoarthritis' OR 'osteoarthritis' OR 'osteoarthritis'/exp OR osteoarthritis AND ('knee' OR 'knee'/exp OR knee OR knees OR patellofemoral OR 'patello femoral')) AND 'acupuncture' OR 'acupuncture'/exp OR acupuncture OR 'braces' OR 'braces'/exp OR braces OR orthotic* OR 'orthosis' OR 'orthosis'/exp OR orthosis OR 'orthoses' OR 'orthoses'/exp OR orthoses OR (stem AND cell*) OR (physical AND ('therapy' OR 'therapy'/exp OR therapy)) OR exercis* OR herbal AND supplement* OR 'transdermal' OR 'transdermal'/exp OR transdermal OR ('topical' OR 'topical'/exp OR topical AND analgesic*) OR ('analgesic' OR 'analgesic'/exp OR analgesic AND cream*) OR prolotherap*

OR ('weight' OR 'weight'/exp OR weight AND (loss OR losing) OR 'diet' OR 'diet'/exp OR diet OR 'dieting' OR 'dieting'/exp OR dieting OR ('weight' OR 'weight'/exp OR weight AND reduc*) OR '(cell based' AND therap*)

AND

Humans

DATABASE SEARCHED & TIME PERIOD COVERED:

Cochrane – 1/1/2015-11/5/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

osteoarthritis and (knee or knees or patellofemoral or patello-femoral):ti,ab,kw (Word variations have been searched)

AND

glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin:ti,ab,kw (Word variations have been searched)

NEW THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

Cochrane – 1/1/2015-12/2/2015

SEARCH STRATEGY:

osteoarthritis and (knee or knees or patellofemoral or patello-femoral):ti,ab,kw Publication Year from 2015 to 2015 (Word variations have been searched)

AND

duloxetine* or cymbalta or selective serotonin* or ssnri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin:ti,ab,kw (Word variations have been searched)

ADDITIONAL THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

Cochrane - 1/1/2006-12/11/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

osteoarthritis and (knee or knees or patellofemoral or patello-femoral):ti,ab,kw (Word variations have been searched)

AND

acupuncture or braces or orthotic* or orthosis or orthoses or "stem cell" or "stem cells" or "physical therapy" or exercis* or "herbal supplement" or "herbal supplements" or transdermal or "topical analgesic" or "topical analgesics" or "analgesic cream" or "analgesic creams" or prolotherap* or weight or diet or dieting or "cell-based therapy" or "cell-based therapies" 143386

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DATABASE SEARCHED & TIME PERIOD COVERED:

CINAHL – 1/1/2006-11/12/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

TI (osteoarthritis AND (knee or knees or patellofemoral or patello-femoral)) OR AB (osteoarthritis AND (knee or knees or patellofemoral or patello-femoral)) OR SU (osteoarthritis AND (knee or knees or patellofemoral or patello-femoral))

AND

TI (glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin) OR AB (glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin) OR SU (glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin)

NEW THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

CINAHL – 1/1/2006-12/2/2015

SEARCH STRATEGY:

TI (osteoarthritis AND (knee or knees or patellofemoral or patello-femoral)) OR AB (osteoarthritis AND (knee or knees or patellofemoral or patello-femoral)) OR SU (osteoarthritis AND (knee or knees or patellofemoral or patello-femoral))

AND

TI (duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin) OR AB (duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin) OR SU (duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin)

ADDITIONAL THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

CINAHL - 1/1/2006-12/4/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

TI (osteoarthritis and (knee or knees or patellofemoral or patello-femoral)) OR AB (osteoarthritis and (knee or knees or patellofemoral or patello-femoral)) OR SU (osteoarthritis and (knee or knees or patellofemoral or patello-femoral)

AND

TI (acupuncture or braces or orthotic* or orthosis or orthoses or "stem cell" or "stem cells" or "physical therapy" or exercis* or "herbal supplement" or "herbal supplements" or transdermal or "topical analgesic" or "topical analgesics" or "analgesic cream" or "analgesic creams" or prolotherap* or weight or diet or dieting or "cell-based therapy" or "cell-based therapies") OR AB (acupuncture or braces or orthotic* or orthosis or orthoses or "stem cell" or "stem cells" or "physical therapy" or exercis* or "herbal supplement" or "herbal supplements" or transdermal or "topical analgesic" or "topical analgesics" or "analgesic cream" or "analgesic creams" or prolotherap* or weight or diet or dieting or "cell-based therapy" or "cell-based therapies") OR SU (acupuncture or braces or orthotic* or orthosis or orthoses or "stem cell" or "stem cells" or "physical therapy" or exercis* or "herbal supplement" or "herbal supplements" or transdermal or "topical analgesic" or "topical analgesics" or "analgesic cream" or "analgesic creams" or prolotherap* or weight or diet or dieting or "cell-based therapy" or "cell-based therapies")

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DATABASE SEARCHED & TIME PERIOD COVERED:

Web of Science – Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC 1/1/2006-12/2/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

TOPIC: (osteoarthritis and (knee or knees or patellofemoral or patello-femoral)

AND

TOPIC: (glucosamine or acetylglucosamine or "n-acetylglucosamine" or "n-acetyl-d-glucosamine" or chondroitin)

NEW THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

Web of Science – Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC 1/1/2006-12/2/2015

SEARCH STRATEGY:

TS=(osteoarthritis and (knee or knees or patellofemoral or patello-femoral)

AND

TS=(duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin)

ADDITIONAL THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

Web of Science Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC - 1/1/2006-12/14/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

ts=(osteoarthritis) AND ts=(knee or knees or patellofemoral or patello-femoral)

AND

ts=(acupuncture or braces or orthotic* or orthosis or orthoses or "stem cell" or "stem cells" or "physical therapy" or exercis* or "herbal supplement" or "herbal supplements" or transdermal or "topical analgesic" or "topical analgesics" or "analgesic cream" or "analgesic creams" or prolotherap* or weight or diet or dieting or "cell-based therapy" or "cell-based therapies")

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DATABASE SEARCHED & TIME PERIOD COVERED:

Scopus - 1/1/2006-11/6/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

TITLE-ABS-KEY (osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral))

AND

TITLE-ABS-KEY (glucosamine OR acetylglucosamine OR "n-acetylglucosamine" OR "n-acetyl-d-glucosamine" OR chondroitin))

AND

SUBJAREA (mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci)

NEW THERAPIES

DATABASE SEARCHED & TIME PERIOD COVERED:

Scopus - 1/1/2006-12/2/2015

SEARCH STRATEGY:

TITLE-ABS-KEY (osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral))
AND

SUBJAREA (mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs
OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci)
AND

TITLE-ABS-KEY (duloxetine* OR cymbalta OR selective serotonin* OR ssri OR milnacipran
OR savella OR venlafaxine OR effexor OR desvenlafaxine OR pristiq OR "il-1" OR interleukin*
OR anakinra OR canakinumab OR "platelet rich plasma" OR "platelet-rich plasma" OR prp OR ("nerve growth factor" OR fibroblast growth OR shoe wedge* OR capsaicin)
AND

SUBJAREA (mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs
OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci)

DATABASE SEARCHED & TIME PERIOD COVERED:

International Pharmaceutical Abstracts - 6/29/2015-11/18/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGY:

ab(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral)) OR ti(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral)) OR su(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral))

DATABASE SEARCHED & TIME PERIOD COVERED:

AMED (Allied & Complementary Medicine) - 6/29/2015-11/18/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

ab(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral)) OR ti(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral)) OR su(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral))
AND

ab(glucosamine OR acetylglucosamine OR "n-acetylglucosamine" OR "n-acetyl-d-glucosamine" OR chondroitin) OR ti(glucosamine OR acetylglucosamine OR "n-acetylglucosamine" OR "n-acetyl-d-glucosamine" OR chondroitin) OR su(glucosamine OR acetylglucosamine OR "n-acetylglucosamine" OR "n-acetyl-d-glucosamine" OR chondroitin)

NEW THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

AMED (Allied & Complementary Medicine) - 6/29/2015-11/18/2015

SEARCH STRATEGY:

ab(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral)) OR ti(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral)) OR su(osteoarthritis AND (knee OR knees OR patellofemoral OR patello-femoral))

AND

ab(duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin) OR ti(duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin) OR su(duloxetine* or cymbalta or selective serotonin* or ssri or milnacipran or savella or venlafaxine or effexor or desvenlafaxine or pristiq or "il-1" or interleukin* or anakinra or canakinumab or "platelet rich plasma" or "platelet-rich plasma" or PRP or "nerve growth factor" or fibroblast growth or shoe wedge* or capsaicin)

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DATABASE SEARCHED & TIME PERIOD COVERED:

ClinicalTrials.gov – 1/1/2006-11/10/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

GLUCOSAMINE:

KEYWORD :knee OR knees OR patellofemoral OR patello-femoral

AND

CONDITION:osteoarthritis

AND

INTERVENTION: glucosamine OR acetylglucosamine OR "n-acetylglucosamine" OR "n-acetyl-d-glucosamine" OR chondroitin

NEW THERAPIES:

KEYWORD:knee OR knees OR patellofemoral OR patello-femoral

AND

CONDITION:osteoarthritis

AND

INTERVENTION:duloxetine OR cymbalta OR selective serotonin OR ssri OR milnacipran OR savella OR venlafaxine OR effexor OR desvenlafaxine OR pristiq OR "il-1" OR interleukin OR anakinra OR canakinumab OR "platelet rich plasma" OR "platelet-rich plasma" OR PRP OR "nerve growth factor" OR fibroblast growth OR shoe wedge OR shoe wedges OR capsaicin

ADDITIONAL THERAPIES:

DATABASE SEARCHED & TIME PERIOD COVERED:

ClinicalTrials.gov - 1/1/2006-12/21/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

KEYWORD: knee OR knees OR patellofemoral OR patello-femoral

CONDITION: osteoarthritis

INTERVENTION: acupuncture OR stem cell OR stem cells OR physical therapy OR diet OR diets OR nutrition OR nutritional OR weight OR obese OR obesity OR dietary supplements OR transdermal OR patch OR plant OR plants OR exercise OR exercising OR topical analgesic OR topical analgesics OR analgesic cream OR analgesic creams OR brace OR braces OR orthotic OR orthotics OR orthosis OR orthoses OR herbal supplement OR herbal supplements OR prolotherapy or prolotherapies OR prolotherapeutic OR cell-based

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DATABASE SEARCHED & TIME PERIOD COVERED:

PEDRO - 1/1/2006-12/11/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGIES:

Abstract & Title: Osteoarthritis

AND

Abstract & Title: knee

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DATABASE SEARCHED & TIME PERIOD COVERED:

WHO International Clinical Trials Registry - 1/1/2006-12/15/2015

LANGUAGE:

English OR Non-English with English Abstract

SEARCH STRATEGY:

CONDITION: Osteoarthritis AND knee

Appendix B. List of Excluded Studies

This appendix lists all studies (publications) that were identified in our literature searches that were subsequently excluded during abstract or full-text screening.

Not Human – N = 6

1. Attur M, Al-Mussawir HE, Patel J, et al. Prostaglandin E(2) exerts catabolic effects in osteoarthritis cartilage: Evidence for signaling via the EP4 receptor. *Journal of Immunology*. 2008 Oct;181(7):5082-8. PMID: WOS:000259755700072.
2. Bougault C, Gosset M, Houard X, et al. Stress-Induced Cartilage Degradation Does Not Depend on the NLRP3 Inflammasome in Human Osteoarthritis and Mouse Models. *Arthritis and Rheumatism*. 2012 Dec;64(12):3972-81. PMID: WOS:000311706300018.
3. Calado GP, Lopes AJ, Costa Junior LM, et al. *Chenopodium ambrosioides* L. Reduces Synovial Inflammation and Pain in Experimental Osteoarthritis. *PLoS One*. 2015;10(11):e0141886. doi: 10.1371/journal.pone.0141886. PMID: 26524084.
4. Dunn SL, Wilkinson JM, Crawford A, et al. Cannabinoid WIN-55,212-2 mesylate inhibits interleukin-1 beta induced matrix metalloproteinase and tissue inhibitor of matrix metalloproteinase expression in human chondrocytes. *Osteoarthritis and Cartilage*. 2014 Jan;22(1):133-44. PMID: WOS:000330422000017.
5. Jayasuriya CT, Goldring MB, Terek R, et al. Matrilin-3 Induction of IL-1 receptor antagonist Is required for up-regulating collagen II and aggrecan and down-regulating ADAMTS-5 gene expression. *Arthritis Research & Therapy*. 2012;14(5) PMID: WOS:000315488700009.
6. van Buul GM, Koevoet WL, Kops N, et al. Platelet-rich plasma releasate inhibits inflammatory processes in osteoarthritic chondrocytes. *Am J Sports Med*. 2011 Nov;39(11):2362-70. doi: doi: 10.1177/0363546511419278.

Not a population of interest – N = 5

1. Edwards C, Rogers A, Lynch S, et al. The effects of bariatric surgery weight loss on knee pain in patients with osteoarthritis of the knee. *Arthritis*. 2012;2012:504189. doi: 10.1155/2012/504189. PMID: 23243506.
2. Edwards PK, Ackland TR, Ebert JR. Accelerated weightbearing rehabilitation after matrix-induced autologous chondrocyte implantation in the tibiofemoral joint: early clinical and radiological outcomes. *Am J Sports Med*. 2013 Oct;41(10):2314-24. doi: 10.1177/0363546513495637. PMID: 23880403.

3. Kim YS, Kwon OR, Choi YJ, et al. Comparative Matched-Pair Analysis of the Injection Versus Implantation of Mesenchymal Stem Cells for Knee Osteoarthritis. *Am J Sports Med.* 2015 Nov;43(11):2738-46. doi: 10.1177/0363546515599632. PMID: 26337418.
4. Soni A, Joshi A, Mudge N, et al. Supervised exercise plus acupuncture for moderate to severe knee osteoarthritis: a small randomised controlled trial. *Acupunct Med.* 2012 Sep;30(3):176-81. doi: 10.1136/acupmed-2012-010128. PMID: 22914302.
5. Yang PF, Li D, Zhang SM, et al. Efficacy of ultrasound in the treatment of osteoarthritis of the knee. *Orthop Surg.* 2011 Aug;3(3):181-7. doi: 10.1111/j.1757-7861.2011.00144.x. PMID: 22009649.

Not on OA of the knee – N = 27

1. Abbott JH, Chapple C, Pinto D, et al. Exercise therapy, manual therapy, or both, for management of osteoarthritis of the hip or knee: 2-year follow-up of a randomized clinical trial. *Osteoarthritis and cartilage*; 2014. p. S51.
2. Allen KD, Yancy WS, Jr., Bosworth HB, et al. A Combined Patient and Provider Intervention for Management of Osteoarthritis in Veterans: A Randomized Clinical Trial. *Ann Intern Med.* 2015 Dec 22doi: 10.7326/M15-0378. PMID: 26720751.
3. Barandun M, Iselin LD, Santini F, et al. Generation and Characterization of Osteochondral Grafts With Human Nasal Chondrocytes. *Journal of Orthopaedic Research.* 2015 Aug;33(8):1111-9. PMID: WOS:000357817400001.
4. Barry BK. Acute resistance exercise and pressure pain sensitivity in knee osteoarthritis: a randomised crossover trial. *Osteoarthritis and cartilage*; 2014. p. 407-14.
5. Bigoni M, Sacerdote P, Turati M, et al. Acute and Late Changes in Intraarticular Cytokine Levels Following Anterior Cruciate Ligament Injury. *Journal of Orthopaedic Research.* 2013 Feb;31(2):315-21. PMID: WOS:000313979700020.
6. Bossen D, Veenhof C, Van Beek KE, et al. Effectiveness of a web-based physical activity intervention in patients with knee and/or hip osteoarthritis: randomized controlled trial. *J Med Internet Res.* 2013;15(11):e257. doi: 10.2196/jmir.2662. PMID: 24269911.
7. Crossley KM, Marino GP, Macilquham MD, et al. Can patellar tape reduce the patellar malalignment and pain associated with patellofemoral osteoarthritis? *Arthritis Rheum.* 2009 Dec 15;61(12):1719-25. doi: 10.1002/art.24872. PMID: 19950307.
8. Ebert JR, Smith A, Fallon M, et al. Incidence, degree, and development of graft hypertrophy 24 months after matrix-induced autologous chondrocyte implantation: association with clinical outcomes. *Am J Sports Med.* 2015 Sep;43(9):2208-15. doi: 10.1177/0363546515591257. PMID: 26163536.

9. Gaynor PJ, Liu P, Weller MA, et al. Comparison of safety outcomes among Caucasian, Hispanic, Black, and Asian patients in duloxetine studies of chronic painful conditions. *Current Medical Research and Opinion*. 2013 May;29(5):549-60. PMID: WOS:000317593000013.
10. Hale LA, Waters D, Herbison P. A randomized controlled trial to investigate the effects of water-based exercise to improve falls risk and physical function in older adults with lower-extremity osteoarthritis. *Arch Phys Med Rehabil*. 2012 Jan;93(1):27-34. doi: 10.1016/j.apmr.2011.08.004. PMID: 21982325.
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12. Hughes SL, Seymour RB, Campbell RT, et al. Fit and Strong!: Bolstering Maintenance of Physical Activity Among Older Adults With Lower-extremity Osteoarthritis. *American Journal of Health Behavior*. 2010;34(6):750-63. PMID: WOS:000291935900010.
13. Jimenez SC, Fernandez GR, Zurita OF, et al. [Effects of education and strength training on functional tests among older people with osteoarthritis]. *Rev Med Chil*. 2014 Apr;142(4):436-42. doi: 10.4067/s0034-98872014000400004. PMID: 25117033.
14. Kanzaki N, Ono Y, Shibata H, et al. Glucosamine-containing supplement improves locomotor functions in subjects with knee pain: A randomized, double-blind, placebo-controlled study. *Clinical Interventions in Aging*. 2015 28;10:1743-53. PMID: 2015491213 FULL TEXT LINK <http://dx.doi.org/10.2147/CIA.S93077>.
15. Lansdown H, Howard K, Brealey S, et al. 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. doi: 10.1186/1471-2474-10-130. PMID: 19852841.
16. Martins F, Kaster T, Schutzler L, et al. Factors influencing further acupuncture usage and a more positive outcome in patients with osteoarthritis of the knee and the hip: a 3-year follow-up of a randomized pragmatic trial. *Clin J Pain*. 2014 Nov;30(11):953-9. doi: 10.1097/ajp.0000000000000062. PMID: 24346625.
17. Nawaz SZ, Dhinsa B, Gallagher KR, et al. Autologous chondrocyte implantation does not prevent the need for arthroplasty in patients with pre-existing osteoarthritis. *Arthroscopy - Journal of Arthroscopic and Related Surgery*. 2011 October;27(10 SUPPL. 1):e170-e1.
18. Parlar S, Fadiloglu C, Argon G, et al. The effects of self-pain management on the intensity of pain and pain management methods in arthritic patients. *Pain Manag Nurs*. 2013 Sep;14(3):133-42. doi: 10.1016/j.pmn.2010.08.002. PMID: 23972864.
19. Pisters M, Veenhof C, Schellevis F, et al. Long-term effect of exercise therapy in patients with osteoarthritis: A randomized controlled trial comparing two different physiotherapy interventions. *Physiotherapy (United Kingdom)*; 2011. p. eS1005.

20. Satpute A, Bhatt DL, Kashyap S, et al. Effects of Bariatric Surgery on Long-Term Quality of Life Outcomes for Obese Patients with Osteoarthritis [abstract]. . *Arthritis Rheumatol.* 2015;67(suppl 10).
21. Tollefsrud I, Askmann E. Effect of exercise and lifestyle interventions on an outpatient rehabilitation programme for patients with hip or knee OA. *Scandinavian Journal of Rheumatology.* 2014 2014;43 SUPPL. 127:78-9.
22. Tsuji T, Yoon J, Kitano N, et al. Effects of N-acetyl glucosamine and chondroitin sulfate supplementation on knee pain and self-reported knee function in middle-aged and older Japanese adults: a randomized, double-blind, placebo-controlled trial. *Aging Clin Exp Res.* 2015 Jul 16doi: 10.1007/s40520-015-0412-6. PMID: 26178634.
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26. White DK, Neogi T, Rejeski WJ, et al. Can an Intensive Diet and Exercise Program Prevent Knee Pain Among Overweight Adults at High Risk? *Arthritis Care & Research.* 2015 July;67(7):965-71.
27. 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 Jun;16(3):131-8. doi: 10.1016/j.ctim.2007.12.003. PMID: 18534325.

Not on treating/managing OA of the knee – N = 5

1. Catay E, Ruta S, Rosa J, et al. Ultrasound (US) Findings in Patients with Knee Pain: Sensitivity and Specificity for the Diagnosis of Knee Osteoarthritis and Development of an US Prediction Score [abstract]. 2012 ACR/ARHP Annual Meeting. *Arthritis rheumatol.* 2012;64 (suppl S10):S53.
2. Haxby Abbott J, Chapple C, Pinto D, et al. Exercise Therapy and/or Manual Therapy for Hip or Knee Osteoarthritis: 2-Year Follow-up of a Randomized Controlled Trial [abstract]. 2014 ACR/ARHP Annual Meeting. *Arthritis Rheumatol.* 2014;66 (suppl S10):S1266-7.
3. Lamas JR, Tornero-Esteban P, Garcia Fernández C, et al. A Double-Blind, Randomized, Placebo-Controlled Trial of Mesenchymal Stem Cells for the Treatment of Patients with Full-

Thickness Rotator Cuff Tears [abstract]. 2015 ACR/ARHP Annual Meeting. Arthritis Rheumatol. 2015;67 (suppl 10):1411.

4. Skou ST, Rasmussen S, Simonsen O, et al. Knee Confidence as It Relates to Self-reported and Objective Correlates of Knee Osteoarthritis: A Cross-sectional Study of 220 Patients. J Orthop Sports Phys Ther. 2015 Oct;45(10):765-71. doi: 10.2519/jospt.2015.5864. PMID: 26304646.

5. White D, Neogi T, Rejeski WJ, et al. Can Knee Pain be Prevented through Diet and Exercise Among Those at High Risk? the Look Ahead Study [abstract]. 2014 ACR/ARHP Annual Meeting. Arthritis Rheumatol. 2014;66 (suppl S10):S1314-5.

Not an intervention of interest – N = 93

1. Abou-Raya S, Abou-Raya A, Helmii M. Duloxetine for the management of pain in older adults with knee osteoarthritis: randomised placebo-controlled trial. Age Ageing. 2012 Sep;41(5):646-52. doi: 10.1093/ageing/afs072. PMID: 22743149.

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3. Anz AW, Hackel JG, Nilssen EC, et al. Application of Biologics in the Treatment of the Rotator Cuff, Meniscus, Cartilage, and Osteoarthritis. Journal of the American Academy of Orthopaedic Surgeons. 2014 Feb;22(2):68-79. PMID: WOS:000349452200002.

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6. Baraf HS, Gloth FM, Barthel HR, et al. Safety and efficacy of topical diclofenac sodium gel for knee osteoarthritis in elderly and younger patients: pooled data from three randomized, double-blind, parallel-group, placebo-controlled, multicentre trials. Drugs Aging. 2011 Jan 1;28(1):27-40. doi: 10.2165/11584880-000000000-00000. PMID: 21174485.

7. Barrett T, Franke R, Cheruvu N, et al. An assessment of the efficacy and tolerability of diclofenac sodium 2% topical solution for treating osteoarthritis of the knee. Journal of Pain. 2014 April;15(4 SUPPL. 1):S97.

8. Barthel HR, Haselwood D, Longley S, 3rd, et al. Randomized controlled trial of diclofenac sodium gel in knee osteoarthritis. Semin Arthritis Rheum. 2009 Dec;39(3):203-12. doi: 10.1016/j.semarthrit.2009.09.002. PMID: 19932833.

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10. Bennell KL, Kyriakides M, Metcalf B, et al. Neuromuscular versus quadriceps strengthening exercise in patients with medial knee osteoarthritis and varus malalignment: a randomized controlled trial. *Arthritis Rheumatol*. 2014 Apr;66(4):950-9. doi: 10.1002/art.38317. PMID: 24757146.
11. Bodick N, Lufkin J, Willwerth C, et al. An Intra-Articular, Extended-Release Formulation of Triamcinolone Acetonide Prolongs and Amplifies Analgesic Effect in Patients with Osteoarthritis of the Knee. *Journal of Bone and Joint Surgery-American Volume*. 2015 Jun;97A(11):877-88. PMID: WOS:000363418100003.
12. Chappell AS, Desai D, Liu-Seifert H, et al. A double-blind, randomized, placebo-controlled study of the efficacy and safety of duloxetine for the treatment of chronic pain due to osteoarthritis of the knee. *Pain Pract*. 2011 Jan-Feb;11(1):33-41. doi: 10.1111/j.1533-2500.2010.00401.x. PMID: 20602715.
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16. Chen XY, Spaeth RB, Freeman SG, et al. The modulation effect of longitudinal acupuncture on resting state functional connectivity in knee osteoarthritis patients. *Molecular Pain*. 2015 Oct;11 PMID: WOS:000363742900001.
17. Cheung RKH, Leung KK, Lee KC, et al. Sequential non-traumatic femoral shaft fractures in a patient on long-term alendronate. *Hong Kong Medical Journal*. 2007;13(6):485-9.
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19. Cho JJ, Kim TW, Park YM, et al. Tissuegene-C (Invossa™) in patients with osteoarthritis: A phase II trials. *Cytotherapy*. 2015 June;17(6 SUPPL. 1):S84.

20. Conaghan PG, Dickson J, Bolten W, et al. A multicentre, randomized, placebo- and active-controlled trial comparing the efficacy and safety of topical ketoprofen in Transfersome gel (IDEA-033) with ketoprofen-free vehicle (TDT 064) and oral celecoxib for knee pain associated with osteoarthritis. *Rheumatology (Oxford)*. 2013 Jul;52(7):1303-12. doi: 10.1093/rheumatology/ket133. PMID: 23542612.
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No usable data – N = 75

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Multi-component interventions – N = 27

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Duplicate or duplicate data – N = 32

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Appendix C. Evidence Table for All Included Studies

Table C1. Evidence table for all included studies

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Abbott, 2015 ⁵³ Study design: RCT Trial name: None Study Location: New Zealand Health care setting: Academic orthopedic surgery clinic/department, Physical therapy outpatient clinic Single Site	Total n = 75 Mean Age: 64 Arm 1, Mean Age: 64(10) BMI: 29.2(6.1) Arm 2, Mean Age: 65(10) BMI: 30.2(5.6) Arm 3, Mean Age: 61(12) BMI: 27.6(4.7) Arm 4, Mean Age: 64(10.2) BMI: 29.8(6.6) Female: 62% Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Subtype: NR Diagnosis: ACR Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Minimum Age: 40 ACR: NA	Surgery knee limb in prior previous hip or knee replacement of the affected joint or any other surgical procedure in the previous 6 months month(s) Pending surgery Analgesics use in the previous Injected opioid or analgesic use in the previous 30 days month(s) Injected corticosteroids in the prior 30 days, hip or knee month(s) RA Physical impairments that would prevent participation Inability to comprehend study instructions or to attend and complete the sessions and follow-up	Arm 1: Land-based exercise n = 19 Placebo/ Dose: 45 minutes per session Frequency: 12 sessions per 9 weeks Duration: 9 weeks Method of Blinding: NA Co-Intervention: none Arm 2: Land-based exercise n = 19 Dose: 45 minutes per session Frequency: 8 sessions in 9 weeks, 2 booster sessions at 5 months, 1 session at 8 months, 1 session at 11 months Duration: 11 months Method of Blinding: NA Co-Intervention: Booster sessions at 5, 8, and 11 months Arm 3: Land-based exercise + manipulation n = 18 Dose: 45 minutes per exercise session and 30-45 minutes per manual therapy session Frequency: 12 sessions exercise and manual therapy each in 9 weeks Duration: 9 weeks Method of Blinding: NA Co-Intervention: Manual therapy Arm 4: Land-based exercise plus manipulation n = 19 Dose: 45 minutes per exercise session and 30-45 minutes per manual therapy session Frequency: 12 sessions exercise and manual therapy each in 9 weeks plus 2 booster sessions at 5 months, 1 session at 8 months, 1 session at 11 months Duration: 11 months Method of Blinding: NA Co-Intervention: Booster sessions plus manual therapy	<u>TUG (s):</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-2.58, 0.58) Comparator: Arm 3 vs Arm 1 , MD : 0.00 95% CI: (-1.42, 1.42) Comparator: Arm 4 vs Arm 1 , MD : -0.10 95% CI: (-2.02, 1.82) <u>WOMAC total:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -56.10 95% CI: (-92.70, -19.50) Comparator: Arm 3 vs Arm 1 , MD : -39.20 95% CI: (-69.38, -9.02) Comparator: Arm 4 vs Arm 1 , MD : -8.30 95% CI: (-41.90, 25.30) <u>Pain intensity score:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.84, -0.16) Comparator: Arm 3 vs Arm 1 , MD : -2.30 95% CI: (-4.07, -0.53) Comparator: Arm 4 vs Arm 1 , MD : 0.20 95% CI: (-1.86, 2.26)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Acosta-Olivo, 2014 ²⁶	Total n = 42	Diagnosis of osteoarthritis of the knee	Surgery knee limb in prior 2 months month(s)	Arm 1: Control n = 21 Dose: 1g paracetamol Frequency: 3 times per day Duration: 1 month	<u>KOOS:</u> Follow-Up Time: 4 months : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-18.11, 0.11) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -6.90 95% CI: (-18.29, 4.49)
Study design: RCT	Age Range: NR	Duration of Symptoms: 3 months	Prior experience with the intervention of interest	Arm 2: Cell-based therapies n = 21 Dose: 5 ml plasma per injection Frequency: 2 doses per month Duration: 1 month	
Trial name: None	Arm 1, Mean Age: NR BMI: NR	Minimum Age: 40	Use of anticoagulants		
Study Location: Mexico	Arm 2, Mean Age: NR BMI: NR	Able to sign Consent	Varus-valgus deformities		
Health care setting: Academic orthopedic surgery clinic/department	Female: NR	Without previous treatment	Prior arthritis in the knee		
Single Site	Racial/Ethnic Distribution: NR	NR	Autoimmune disorders		
	Living Situation: Community Dwelling		Cerebrovascular diseases; hemoglobin <11; drug or alcohol abuse; active infections		
	Location of OA: NR				
	Subtype: NR				
	Diagnosis: K-L: Grade I				
	Analgesic Use: Yes				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Atamaz, 2012 ⁷²	Total n = 203 Study design: RCT Trial name: None Study Location: NR Health care setting: NR Multiple Sites: 4 Age Range: NR Arm 1, Mean Age: 60.7 (SD 6.5) BMI: 29.0 (SD 4.1) Arm 2, Mean Age: 61.9 (SD 6.9) BMI: 28.4 (SD 3.5) Female: 82.3% Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: NR Diagnosis: K-L: 2&3, ~Symptomatic with at least 40mm or 4cm severity of pain on the VAS for at least 6 months, ACR Analgesic Use: Yes, Patients were asked to discontinue any pretreatment with NSAIDs drugs 7 days before the start of the study. If the patient required analgesic medication for knee pain, paracetamol use was permitted and noted.	Diagnosis of osteoarthritis of the knee Duration of Symptoms: 6 months Minimum Age: 51 Maximum Age: 79 Otherwise Healthy K-L: 2&3 ACR: confirmed knee OA	Concomitant medical problems that prevent participation Surgery knee limb in prior 6 month(s) Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 1 month(s) Prior experience with the intervention of interest Diagnosis of joint infection, a specific condition (neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, etc), ascertained/suspected pregnancy or lactation, and poor general health status that would interfere with the functional assessments History of any contraindication for electrotherapy Received corticosteroid therapy or chondroprotective agents during the 30 days prior to the study or viscosupplementation treatment within 6 months prior to the study Undergone previous major surgery, such as joint replacement or arthroscopy, within 6 months prior to the study	Arm 1: Sham n = 37, Placebo/Sham TENS, Dose: 20 minutes, Frequency: 5 times per week, Duration: 3 weeks Method of Blinding: All patients, investigators, and analysts were blinded, with the exception of members of the data and safety monitoring board Co-Intervention: Exercise program in groups of 4-5 patients led by a physiotherapist 3x/week for 3 weeks, included 5- to 6-minutes of jogging, stretching exercises (approx. 10min), isometric quadriceps exercises (10–15 repetitions) in the seated position were performed for 10 seconds with 10-second breaks, and chair lift and minisquats exercises (10–15 reps). At the end of 3 weeks, the physiotherapist prescribed a home-based training program (3x/week) as well as group exercise. Before the treatments, all patients participated in a single education group session of approximately 1-hour duration. Arm 2: Neuromuscular electrical stimulation n = 37, Dose: 80Hz with 10- to 30-mA intensity for 20 minutes, Frequency: 5 times per week, Duration: 3 weeks Method of Blinding: All patients, investigators, and analysts were blinded, with the exception of members of the data and safety monitoring board Co-Intervention: Exercise program in groups of 4-5 patients led by a physiotherapist 3x/week for 3 weeks, included 5- to 6-minutes of jogging, stretching exercises (approx. 10min), isometric quadriceps exercises (10–15 repetitions) in the seated position were performed for 10 seconds with 10-second breaks, and chair lift and minisquats exercises (10–15 reps). At the end of 3 weeks, the physiotherapist prescribed a home-based training program (3x/week) as well as group exercise. Before the treatments, all patients participated in a single education group session of	<u>VAS pain:</u> Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 4.30 95% CI: (-5.99, 14.59) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-11.23, 11.63) <u>WOMAC function:</u> Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-8.66, 3.66) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-9.73, 4.73) <u>WOMAC pain:</u> Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -1.40 95% CI: (-3.69, 0.89) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.30 95% CI: (-3.89, 1.29)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Atkins, 2013 ¹⁰⁴	Total n = 40	Minimum Age: 50	Concomitant medical problems that prevent participation	Arm 1: Control n = 19	<u>WOMAC function:</u>
Study design: RCT	Total # of knees = NR	Ambulatory	Prior surgery on one or both knees	Placebo/Control, wait list	Follow-Up Time: 12 weeks :
Trial name: None	Age Range: NR	Willingness to attend 75% of scheduled self-massage sessions	Surgery knee limb in prior 6 month(s)	Dose: NA	Comparator: Arm 2 vs Arm 1 , MD : -0.80 95% CI: (NC, NC)
Study Location: US	Arm 1, Mean Age: NR BMI: NR	No limitations that prevented mobility of the knee	Injected corticosteroids in the prior 3 month(s)	Frequency: NA	<u>WOMAC pain:</u>
Health care setting: Wellness center	Arm 2, Mean Age: NR BMI: NR	Knee pain, pain on most days of the prior month, and morning stiffness lasting less than 30 minutes	Active rheumatoidarthritis or other serious medical conditions	Duration: 12 weeks	Follow-Up Time: 12 weeks :
Single Site	Female: NR	Crepitus on motion and bony enlargement at affected joints	Intra-articular knee injection of a steroid within the previous 3 months	Method of Blinding: None	Comparator: Arm 2 vs Arm 1 , MD : -0.65 95% CI: (NC, NC)
	Racial/Ethnic Distribution: NR	Agreement to practice no new exercise or stretching program and commitment to receiving no other mas sage therapy during the study	Surgical procedure on either lower extremity within the past 6 months	Co-Intervention: Usual care only and received optional future dates for the knee self-massage training	<u>WOMAC total:</u>
	Living Situation: NR			Arm 2: Massage n = 21	Follow-Up Time: 12 weeks :
	Location of OA: NR			Dose: Supervised sessions were 1 hour, including 20 minutes of the intervention. During the unsupervised weeks, participants were encouraged to continue their twice-weekly practice of self-massage.	Comparator: Arm 2 vs Arm 1 , MD : -0.70 95% CI: (NC, NC)
	Subtype: NR			Frequency: 2 times per week	
	Diagnosis: Written diagnosis of knee OA by participants' health care provider			Duration: 12 weeks	
	Analgesic Use: Yes			Method of Blinding: None	
				Co-Intervention: Usual care	

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Atukorala, 2016 ¹¹⁰ Study design: Single arm trial Trial name: Healthy weight for life Study Location: Australia Health care setting: internet and phone-based program Multiple Sites: NR (internet-based)	Total n = 1383 Mean Age(SD): Mean age 64.0(8.7) Arm 1, Mean Age: 64(8.7) BMI: 34.4(5.2) Female: 70.9% Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: NR Subtype: NR Diagnosis: K-L: not specified, Mean KOOS pain 56.3(6.8) Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee BMI>28 Referral to orthopedist for KR Enrollment in OAHWFL program Radiographic or arthroscopy: NR	Exclusion : NR	Arm 1: Weight loss and exercise n = 1383 Dose: NA Frequency: NA Duration: 18 weeks	<u>KOOS function:</u> Follow-Up Time: 18 weeks : Comparator: >10% weight change (post-pre) , MD : 17.40 95% CI: (15.9, 18.9) Comparator: 7.6-10% weight change (post-pre) , MD : 13.60 95% CI: (11.9, 15.3) Comparator: 5.1-7.5% weight change (post-pre) , MD : 12.00 95% CI: (10.2, 13.8) Comparator: 2.5-5% weight change (post-pre) , MD : 8.90 95% CI: (7.0, 10.8) Comparator: <2.5% weight change (post-pre) , MD : 7.80 95% CI: (4.8, 10.8) <u>KOOS pain:</u> Follow-Up Time: 18 weeks : Comparator: >10% weight change (post-pre) , MD : 16.70 95% CI: (15.2, 18.2) Comparator: 7.6-10% weight change (post-pre) , MD : 13.30 95% CI: (11.6, 15.0) Comparator: 5.1-7.5% weight change (post-pre) , MD : 12.00 95% CI: (10.2, 13.8) Comparator: 2.5-5% weight change (post-pre) , MD : 9.90 95% CI: (7.7, 12.1) Comparator: <2.5% weight change (post-pre) , MD : 6.10 95% CI: (3.2, 9.0)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Avelar, 2011²²</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: NR</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 23</p> <p>Total # of knees = NR</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 71 (SD 4) BMI: NR</p> <p>Arm 2, Mean Age: 75 (SD 5) BMI: NR</p> <p>Female: 86.96%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: bilateral 34.8% (of 21), unilateral 56.5% (of 21)</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 1-4, Knee OA in at least 1 knee clinical and radiographic criteria according to ACR</p> <p>Analgesic Use: Yes</p>	<p>Minimum Age: 60</p> <p>Ambulatory</p> <p>Able to sign Consent</p> <p>Not requiring a walking aid</p> <p>Any cognitive deficit as determined by the Mini-Mental Status Examination</p>	<p>Concomitant medical problems that prevent participation</p> <p>Concomitant or prior use of other meds</p> <p>Prior acute injury to the knee</p> <p>Not having suffered any recent knee injury</p> <p>Any orthopedic, neurological, respiratory, or acute cardiac diseases that would preclude the study</p> <p>Not having been submitted to any rehabilitation procedure in the previous 3 months</p> <p>Not having used glucocorticoids for at least 2 months prior the study</p>	<p>Arm 1: Control n = 11</p> <p>Placebo/Control</p> <p>Dose: NA</p> <p>Frequency: NA</p> <p>Duration: 12 weeks</p> <p>Method of Blinding: Blinded, not otherwise described</p> <p>Co-Intervention: Squatting exercises, for each repetition, individuals were instructed to perform 3 seconds of isometric flexion of the quadriceps to 60 degrees and 3 seconds of isometric flexion of the quadriceps to 10 degrees. Prior to the squatting exercises, both groups warmed-up on an ergometric bicycle at 70% of the predicted maximum heart rate for age for 10 minutes</p> <p>Arm 2: Vibrating platform (whole body vibration) n = 12</p> <p>Dose: Frequency of 35Hz–40Hz, amplitude of 4mm, and acceleration that ranged from 2.78G to 3.26G</p> <p>Frequency: 3 times per week</p> <p>Duration: 12 weeks</p> <p>Method of Blinding: Blinded, not otherwise described</p> <p>Co-Intervention: Squatting exercises, for each repetition, individuals were instructed to perform 3 seconds of isometric flexion of the quadriceps to 60 degrees and 3 seconds of isometric flexion of the quadriceps to 10 degrees. Prior to the squatting exercises, both groups warmed-up on an ergometric bicycle at 70% of the predicted maximum heart rate for age for 10 minutes</p>	<p><u>6 min walk (meter):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -27.62 95% CI: (-42.80, -12.44)</p> <p><u>TGUG (s):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.02 95% CI: (-0.27, 0.31)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -59.00 95% CI: (-373.43, 255.43)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 24.00 95% CI: (-60.64, 108.64)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Azlin, 2011⁹⁸</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Malaysia</p> <p>Health care setting: Physiotherapy unit in academic medical center</p> <p>Single Site</p>	<p>Total n = 13</p> <p>Age Range: 40</p> <p>Arm 1, Mean Age: 59.7(4.9) BMI: 26.2</p> <p>Arm 2, Mean Age: 63.1 (10.8) BMI: 28.5</p> <p>Female: 85%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: bilateral 85%, unilateral 15%</p> <p>Subtype: NR</p> <p>Diagnosis: By orthopedic specialist</p> <p>Analgesic Use: Yes, Continued normal medications</p>	<p>Diagnosis of osteoarthritis of the knee: By orthopedic specialist</p> <p>Ambulatory</p> <p>Ascend and descend at least a flight of stair</p> <p>Willingness to be randomized</p> <p>Sub-acute or chronic OA</p> <p>Number of knees >=1</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Prior acute injury to the knee</p> <p>Acute inflammation or contracture</p> <p>Cognitive problem (MMSE<20)</p> <p>Pain during exercise</p>	<p>Arm 1: Control n = 6 Placebo/Conventional physical therapy Frequency: Twice a week Duration: 4 weeks</p> <p>Arm 2: Passive joint mobilization n = 7 Frequency: Twice a week Duration: 4 weeks Co-Intervention: Conventional physiotherapy (exercises followed by thermal therapy with hot pack)</p>	<p><u>VAS pain stairs:</u></p> <p>Follow-Up Time: 4 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -2.99 95% CI: (-21.54, 15.56)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Barduzzi, 2013⁵¹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 15</p> <p>Arm 1, Mean Age: 70.8(6.3) BMI: NR</p> <p>Arm 2, Mean Age: 71.6(7.0) BMI: NR</p> <p>Arm 3, Mean Age: 66.4(5.1) BMI: NR</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: bilateral 60%</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 60</p> <p>Maximum Age:79</p> <p>Able to sign Consent</p> <p>ACR: NA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Pending surgery</p> <p>Physical Therapy or Rehab or exercise in the previous 3 months month(s)</p> <p>Use of assistive walking devices</p> <p>Neurological dysfunction that promoted cognitive changes</p>	<p>Arm 1: Control n = 5 Dose: NA Frequency: NA Duration: NA</p> <p>Arm 2: Water based physical therapy n = 5 Dose: 60 minutes per session (2-4 sets, 20-25 repetitions) Frequency: 3 sessions per week Duration: 4 months (45 day break between 12th and 13th session) 24 sessions total</p> <p>Arm 3: Land-based physical therapy n = 5 Dose: 60 minutes per session (2-4 sets, 20-25 repetitions) Frequency: 3 sessions per week Duration: 4 months (45 day break between 12th and 13th session) 24 sessions total</p>	<p><u>Walking speed:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -1.18 95% CI: (-5.39, 3.03)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -0.29 95% CI: (-4.77, 4.19)</p> <p>Follow-Up Time: 4.5 months : Comparator: Arm 3 vs Arm 2 , MD : 4.03 95% CI: (-0.51, 8.57)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Bartels, 2014⁵⁵</p> <p>Study design: Single arm trial</p> <p>Trial name: CAROT</p> <p>Study Location: Denmark</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 192</p> <p>Total # of knees = NR</p> <p>Mean Age(SD): 62.6 (SD 6.3) (for 175 who</p> <p>Arm 1, Mean Age: 62.6 (SD 6.3) BMI: 37.1 (SD 4.4)</p> <p>Female: NR</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: ACR primary knee OA</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 51</p> <p>BMI >= 30 kg/m²</p> <p>ACR: Primary knee OA</p> <p>NR: Clinical symptoms and radiographic verification of the diagnosis</p>	<p>Exclusion : NR</p>	<p>Arm 1: Weight loss, self-management n = 192</p> <p>Dose: 8-week formula weight loss diet 415-810 kcal/day, followed by 8 weeks on a hypo-energetic 1200 kcal/day diet of normal food and formula products</p> <p>Frequency: Diet was daily. Weekly sessions (1.5 h/week) by a dietician giving nutritional instructions and behavioral therapy</p> <p>Duration: 16 weeks</p> <p>Method of Blinding: NA</p> <p>Co-Intervention: NR</p>	<p><u>KOOS function:</u></p> <p>Follow-Up Time: 16 weeks : Comparator: post-pre , MD : 12.10 95% CI: (10.0, 14.2)</p> <p><u>KOOS pain:</u></p> <p>Follow-Up Time: 16 weeks : Comparator: post-pre , MD : 10.70 95% CI: (8.5, 12.9)</p> <p><u>Weight (kg):</u></p> <p>Follow-Up Time: 16 weeks : Comparator: pre-post , MD : 14.00 95% CI: (13.3, 14.7)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Bellare, 2014²⁹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: India</p> <p>Health care setting: Orthopedic clinics</p> <p>Multiple Sites: 3</p>	<p>Total n = 117</p> <p>Age Range: >=50</p> <p>Arm 1, Mean Age: 60.70 (8.31) BMI: 27.68 (3.03)</p> <p>Arm 2, Mean Age: 59.98 (8.81) BMI: 27.36 (3.71)</p> <p>Female: 23%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee: ACR</p>	<p>Exclusion : NR</p>	<p>Arm 1: Diet therapy n = 56 Dose: 1200-1400 kcal/d Duration: 1 year</p> <p>Arm 2: Diet therapy + Glucosamine-chondroitin n = 61 Dose: Glucosamine 1500mg/day; Chondroitin 1200mg/day Frequency: Twice daily (G 750mg+C 600mg) Duration: 1 year</p>	<p><u>Lequesne Index Score:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -3.20 95% CI: (-3.86, -2.54)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.56 95% CI: (-3.35, -1.77)</p> <p><u>VAS score:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-1.99, -1.41)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.08 95% CI: (-2.40, -1.76)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -7.90 95% CI: (-10.06, -5.74)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.86 95% CI: (-6.16, -1.56)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -3.10 95% CI: (-3.69, -2.51)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.59 95% CI: (-2.31, -0.87)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Bennell, 2011 ⁹¹	Total n = 200 Study design: RCT Trial name: None Study Location: Australia Health care setting: NR Site size: NR	Diagnosis of osteoarthritis of the knee Minimum Age: 50 Able to sign Consent Pain on walking >=3 Radiological knee alignment <=185 degrees X-ray: Osteophytes or joint space narrowing in medial compartment	Concomitant medical problems that prevent participation Prior surgery on one or both knees Surgery knee limb in prior 6 month(s) Concomitant or prior use of other meds Injected corticosteroids in the prior 6 month(s) Prior experience with the intervention of interest K-L: 1 or 4 Predominant patellofemoral joint symptoms Systemic arthritic conditions	Arm 1: Control Insoles n = 97 Placebo/No-wedging insoles Frequency: All day every day Duration: 12 months Arm 2: Wedge Insoles n = 103 Frequency: All day every day Duration: 12 months	<u>Quality of life:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-0.06, 0.06) <u>WOMAC function:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.70 95% CI: (-2.79, 4.19) <u>WOMAC pain:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-0.75, 1.15)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Bennell, 2015⁴⁵</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Australia</p> <p>Health care setting: Academic sports medicine clinic/department</p> <p>Single Site</p>	<p>Total n = 222</p> <p>Mean Age: 63</p> <p>Arm 1, Mean Age: 62.7 (7.9) BMI: 31.5 (5.9)</p> <p>Arm 2, Mean Age: 63.0 (7.9) BMI: 30.8 (6.4)</p> <p>Arm 3, Mean Age: 64.6 (8.3) BMI: 31.0 (6.0)</p> <p>Female: 60%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 73%, unilateral 27%</p> <p>Diagnosis: K-L: 30% Grade II; 21% grade III; 23% grade IV</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: knee pain \geq3 months</p> <p>Minimum Age: 50</p> <p>Average pain \geq40/100mm on VAS in preceding week</p> <p>At least moderate difficulty with daily functioning (WOMAC physical function \geq 25/68 units)</p> <p>ACR Criteria: NA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 months month(s)</p> <p>Pending surgery</p> <p>Injected corticosteroids in the prior 3 months month(s)</p> <p>Physical Therapy or Rehab or exercise in the previous 6 months month(s)</p> <p>Prior experience with the intervention of interest</p> <p>Systemic arthritis</p> <p>Self-reported history of serious mental illness, such as schizophrenia, or self reported diagnosis of current clinical depression; neurological condition such as Parkinson's disease, multiple sclerosis or stroke</p> <p>Walking exercise for $>$30 minutes continuously daily; participating in a regular (more than twice a week) structured and/or supervised exercise program such as attending exercise classes in a gym or use of a personal trainer</p> <p>Inability to walk unaided</p> <p>Inadequate written and spoken English; inability to comply with the study protocol such as inability to attend physical therapy sessions or attend assessment appointments at the University</p>	<p>Arm 1: Land-based Exercise strength/resistance training n = 75 Dose: 25 minutes exercise Frequency: 10 sessions per 12 weeks plus home practice Duration: 12 weeks</p> <p>Arm 2: Self-management n = 74 Dose: NR Frequency: 10 sessions per 12 weeks plus home practice Duration: 12 weeks</p> <p>Arm 3: Self-management plus Land-based exercise: strength training n = 73 Dose: 25 minute exercise sessions plus educational session Frequency: 10 sessions per 12 weeks plus home practice Duration: 12 weeks</p>	<p><u>AQoL-6D:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-0.05, 0.05)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -0.02 95% CI: (-0.07, 0.03)</p> <p>Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.03 95% CI: (-0.08, 0.02)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -0.06 95% CI: (-0.11, -0.01)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.20 95% CI: (0.31, 2.09)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.10 95% CI: (-0.69, 0.89)</p> <p>Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (0.34, 1.86)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.00 95% CI: (-0.58, 0.58)</p> <p><u>VAS overall pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.40 95% CI: (-6.18, 8.98)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -5.40 95% CI: (-12.30, 1.50)</p> <p>Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-7.70, 8.30)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -2.80 95% CI: (-10.94, 5.34)</p> <p><u>VAS walking:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-8.11, 8.11)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -8.20 95% CI: (-15.32, -1.08)</p> <p>Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-9.00, 8.60)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Bennell, 2015 ⁴⁵ -Continued					<p>Comparator: Arm 3 vs Arm 1 , MD : -5.10 95% CI: (-13.94, 3.74)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 4.30 95% CI: (0.78, 7.82)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -3.80 95% CI: (-7.06, -0.54)</p> <p>Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : 3.20 95% CI: (-0.53, 6.93)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -2.10 95% CI: (-5.88, 1.68)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.80 95% CI: (-0.14, 1.74)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -0.70 95% CI: (-1.61, 0.21)</p> <p>Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-0.74, 1.54)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -0.20 95% CI: (-1.38, 0.98)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Bliddal, 2011 ¹⁰⁸	Total n = 96 Age Range: 36-90 Arm 1, Mean Age: 64.1 (10.5) BMI: 35.2 (4.5) Arm 2, Mean Age: 61.1 (11.1) BMI: 35 (5.5) Female: 89% Racial/Ethnic Distribution: NR Living Situation: NR Subtype: NR Diagnosis: K-L: 2&3, ACR Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Minimum Age: 18 Overweight was defined as a body mass index (BMI) ≥ 28 kg/m ² . Only patients who explicitly expressed a clear, unequivocal desire for weight loss Fluent in Danish ACR	Concomitant medical problems that prevent participation History of other rheumatic diseases possibly responsible for secondary OA, diabetes mellitus or other endocrine disorders, and substantial abnormalities in haematological, hepatic, renal or cardiac function	Arm 1: Conventional diet program n = 45 Placebo/Control Dose: 1200 calories/day Frequency: Daily Duration: 52 weeks Method of Blinding: Single-blinded Arm 2: Low-energy diet n = 44 Dose: 810-1200 cal/day Frequency: Daily Duration: 52 weeks Method of Blinding: Single-blinded	<u>WOMAC disability:</u> Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.60 95% CI: (-9.14, 1.94) <u>WOMAC pain:</u> Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.20 95% CI: (-13.30, -1.10) <u>WOMAC total:</u> Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.30 95% CI: (-9.57, 0.97) <u>Weightloss, kg:</u> Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.30 95% CI: (-9.52, -5.08)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Brosseau, 2012²⁷</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Health care setting: Physical therapy outpatient clinic</p> <p>Single Site</p>	<p>Total n = 222</p> <p>Mean Age(SD): Mean age 63.4(8.6)</p> <p>Arm 1, Mean Age: 62.3(6.8) BMI: 29.9(5.3)</p> <p>Arm 2, Mean Age: 63.9(10.3) BMI: 29.4(5.4)</p> <p>Female: 69%</p> <p>Racial/Ethnic Distribution: African American 2.3%, Asian 4.5%, Caucasian 88.7%, Hispanic 3.6%, 0.5% American Indian, 0.5% Other</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 23%, unilateral 77%</p> <p>Subtype: NR</p> <p>Diagnosis: Mild to moderate according to ACR clinical and radiographic criteria</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: pain for at least 3 months</p> <p>Ambulatory</p> <p>Expected medications to change during study period</p> <p>Demonstrated ability to walk for a minimum of 20 minutes with minimal pain (<=3/10 on VAS)</p> <p>Able to be treated as outpatients</p> <p>Available 3 times a week for 12 months</p> <p>mild to moderate according to ACR clinical and radiographic criteria: NR</p>	<p>Injected hyaluronic acid in the past or during the past 12 months month(s)</p> <p>Injected corticosteroids in the prior 12 months month(s)</p> <p>Physical Therapy or Rehab or exercise in the previous regular activity program 2 or more times per week for more than 20 minutes per session/durion previous 6 months or rehab treatment within prior 12 months month(s)</p> <p>Severe OA of the knee or other weight bearing joints of the lower extremity</p> <p>Pain at rest or at night</p> <p>Any other treatment for knee OA besides analgesic for prior 12 months</p> <p>Uncontrolled HTN or other condition, such as rheumatoid arthritis that would make participation difficult</p> <p>Significant cognitive difcits, inability to communicate in English, intention to move within the year, unwillingness to sign consent</p>	<p>Arm 1: Control n = 74 Placebo/Educational materials (pamphlet) Dose: NA Frequency: NA Duration: 12 months Method of Blinding: NA</p> <p>Arm 2: Walking n = 79 Dose: 45 minutes walking and 20 minutes warm-up/cool down per session Frequency: 3 sessions per week Duration: 12 months Method of Blinding: NA Co-Intervention:</p> <p>Arm 3: Walking + Co-Intervention: behavioral intevention adapted from Program for Arthritis Control through Education and Exercise program: education and behavioral counseling</p>	<p><u>6 min walk (meter):</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 47.44 95% CI: (4.45, 90.43)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 40.20 95% CI: (-1.29, 81.69)</p> <p><u>SF-36 pain:</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 2.40 95% CI: (-5.89, 10.69)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 6.28 95% CI: (-1.94, 14.49)</p> <p><u>SF-36 physical function:</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 7.54 95% CI: (-1.57, 16.64)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 12.44 95% CI: (2.30, 22.58)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.53 95% CI: (-0.35, 1.41)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.52 95% CI: (-0.23, 1.27)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : -1.20 95% CI: (-8.35, 5.95)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 4.75 95% CI: (-2.94, 12.44)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-7.32, 7.52)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 2.66 95% CI: (-5.35, 10.67)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-7.54, 6.34)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 4.68 95% CI: (-2.80, 12.16)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Bruce-Brand, 2012⁴⁰</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Ireland</p> <p>Health care setting: Academic orthopedic surgery clinic/department</p> <p>Single Site</p>	<p>Total n = 26</p> <p>Mean Age: 64</p> <p>Arm 1, Mean Age: 65.2 ± 3.1 BMI: 31.7 ± 4.1</p> <p>Arm 2, Mean Age: 63.4 ± 5.9 BMI: 33.9 ± 8.3</p> <p>Arm 3, Mean Age: 63.9 ± 5.8 BMI: 33.7 ± 5.6</p> <p>Female: 42%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 3&4, Noderate-to-severe, Outerbridge Scale 3-4</p> <p>Analgesic Use: Yes, Subjects in all 3 groups were advised to maintain any pre-existing treatment of their OA such as pharmacologic therapy.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 55</p> <p>Maximum Age:74</p> <p>Ambulatory</p> <p>Wait list for arthroplasty</p> <p>K-L: 3&4</p> <p>Outerbridge scale: 3-4</p>	<p>Surgery knee limb in prior 3 month(s)</p> <p>Pending surgery</p> <p>Physical Therapy or Rehab or exercise in the previous 6 months month(s)</p> <p>Prior experience with the intervention of interest</p> <p>Medical co-morbidities precluding participation in an exercise program</p> <p>Implanted electrical devices</p> <p>Neurological disorders, inflammatory arthritis</p> <p>Significant cognitive impairment</p> <p>Anticoagulant therapy</p>	<p>Arm 1: Standard care n = 6 Placebo/OA education, weight loss, pharmacologic therapy, and physical therapy Dose: not applicable Frequency: not applicable Duration: 6 weeks</p> <p>Arm 2: Strength/resistance training n = 10 Dose: 30 minutes Frequency: 3 sessions per week Duration: 6 weeks</p> <p>Arm 3: NMES n = 10 Dose: 20 minutes per session Frequency: 5 sessions per week Duration: 6 weeks</p>	<p><u>SF-36 mental:</u></p> <p>Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 5.20 95% CI: (-18.46, 28.86)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 5.10 95% CI: (-14.55, 24.75)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.64 95% CI: (-23.41, 20.13)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -5.67 95% CI: (-27.62, 16.28)</p> <p><u>SF-36 physical:</u></p> <p>Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 14.63 95% CI: (-8.68, 37.94)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 20.23 95% CI: (1.63, 38.83)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 6.00 95% CI: (-15.16, 27.16)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 5.50 95% CI: (-13.19, 24.19)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 9.83 95% CI: (-7.73, 27.39)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 9.83 95% CI: (-7.20, 26.86)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 7.80 95% CI: (-4.79, 20.39)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 7.77 95% CI: (-4.54, 20.08)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.27 95% CI: (-2.88, 5.42)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.17 95% CI: (-3.50, 3.84)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 2.45 95% CI: (-1.37, 6.27)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.55 95% CI: (-2.85, 3.95)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Bruyere, 2008³¹</p> <p>Study design: Post-hoc analysis of two RCTs</p> <p>Trial name: None</p> <p>Study Location: Belgium, Czech Republic</p> <p>Health care setting: Academic orthopedic surgery clinic/department, Institute of Rheumatology</p> <p>Multiple Sites: 2</p>	<p>Total n = 275</p> <p>Age Range: 63.2</p> <p>Arm 1, Mean Age: 63.6 BMI: 26.6</p> <p>Arm 2, Mean Age: 62.9 BMI: 26.6</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Inclusion : NR</p> <p>ACR</p>	<p>Exclusion : NR</p>	<p>Arm 1: Placebo n = 131 Placebo/Tablets;packets Dose: Frequency: Once daily Duration: 12 months</p> <p>Arm 2: Glucosamine sulfate use n = 144 Dose: 1500mg Frequency: Once daily Duration: 12 months</p>	<p><u>Total knee replacement:</u></p> <p>Follow-Up Time: 5 years :</p> <p>Comparator: Arm 2 vs Arm 1 , RR : 0.43 95% CI: (0.20, 0.92)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Cakir, 2014 ⁶⁵	Total n = 60 Age Range: 40-80 Arm 1, Mean Age: 57.1 (7.8) BMI: 29.5 (5.9) Arm 2, Mean Age: 56.9 (8.8) BMI: 27.9 (4.4) Arm 3, Mean Age: 58.2 (9.9) BMI: 30.9 (4.0) Female: 15.5% Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: NR Diagnosis: K-L: 2&3, ACR Analgesic Use: Yes, Paracetamol up to 2000 mg/day	Diagnosis of osteoarthritis of the knee Duration of Symptoms: 6 months Minimum Age: 40 Maximum Age: 79 K-L: 2&3	Concomitant medical problems that prevent participation Concomitant or prior use of other meds Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 1 month(s) Physical Therapy or Rehab or exercise in the previous month(s) Prior experience with the intervention of interest Joint infection, neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, ascertained/suspected pregnancy or lactating and poor general health status	Arm 1: Control n = 20 Placebo/Sham procedure Frequency: 5 times a week Duration: 12 months Co-Intervention: Isometric exercise, strengthening, stretching Arm 2: Continuous Ultrasound n = 20 Dose: Frequency of 1 MHz with intensity of 1 W/cm ² Frequency: 5 times a week Duration: 12 months Co-Intervention: Isometric exercise, strengthening, stretching Arm 3: Pulse Ultrasound n = 20 Dose: Frequency of 1 MHz with intensity of 1 W/cm ² Frequency: 5 times a week Duration: 12 months Co-Intervention: Isometric exercise, strengthening, stretching	<u>VAS pain at rest:</u> Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : -0.90 95% CI: (-11.14, 9.34) Comparator: Arm 3 vs Arm 1 , MD : -2.10 95% CI: (-10.99, 6.79) <u>VAS pain on movement:</u> Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : 0.60 95% CI: (-13.56, 14.76) Comparator: Arm 3 vs Arm 1 , MD : -0.60 95% CI: (-16.69, 15.49) <u>WOMAC function:</u> Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : -2.90 95% CI: (-9.15, 3.35) Comparator: Arm 3 vs Arm 1 , MD : 1.60 95% CI: (-2.94, 6.14) <u>WOMAC pain:</u> Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : -1.60 95% CI: (-3.25, 0.05) Comparator: Arm 3 vs Arm 1 , MD : 0.20 95% CI: (-1.32, 1.72)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Callaghan, 2015 ⁸² Study design: RCT Trial name: None Study Location: UK Health care setting: NR Single Site	Total n = 126 Age Range: 40-70 Arm 1, Mean Age: 56.4 (8.1) BMI: 30.5 (5.1) Arm 2, Mean Age: 54.5 (6.7) BMI: 31.4 Female: 57.1 Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: NR Subtype: Patellofemora 100% Diagnosis: K-L: 2&3 Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Duration of Symptoms: 3 months; >=4 on VAS scale Taking same medication for past 3 months K-L: 2&3 Patellofemoral OA: PL OA is present and greater than tibiofemoral OA	Concomitant medical problems that prevent participation Prior surgery on one or both knees Injected corticosteroids in the prior 1 month(s) Initiating new treatment	Arm 1: No brace n = 63 Placebo/Control Duration: 6 weeks Method of Blinding: Single-blind Arm 2: Brace n = 63 Duration: 6 weeks Method of Blinding: Single-blind	<u>Koos pain subscale:</u> Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.70 95% CI: (-10.76, -0.64) <u>VAS:</u> Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.30 95% CI: (-2.01, -0.59)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Campos, 2015 ⁸⁸	Total n = 58 Mean Age: 64.3 Arm 1, Mean Age: 63.3 (7.5) BMI: 30.3 (5.1) Arm 2, Mean Age: 65.2 (9.6) BMI: 30.8 (6.1) Female: 63.8 Racial/Ethnic Distribution: African American 10.3%, Asian 3.4%, Caucasian 74.1%, 12.1% Mixed Living Situation: NR Location of OA: NR Subtype: Medial 100% Diagnosis: K-L: 1-4, ACR Analgesic Use: Yes, Unlimited	Diagnosis of osteoarthritis of the knee Duration of Symptoms: 6 months of usual care treatment Able to sign Consent ACR	Concomitant medical problems that prevent participation Pending surgery Concomitant or prior use of other meds	Arm 1: Neutral insole n = 29 Placebo/Sham Dose: 5-10 hrs/day Frequency: Daily Duration: 6 months Method of Blinding: Unblinded Arm 2: Wedged insole n = 29 Dose: 5-10 hrs/day Frequency: Daily Duration: 6 months Method of Blinding: Unblinded	<u>Lequesne index:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-1.19, 3.39) Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.00 95% CI: (-1.02, 3.02) <u>VAS:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.20 95% CI: (-14.34, 9.94) Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-11.99, 11.39) <u>WOMAC pain:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (-2.30, 2.10) Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.70 95% CI: (-2.64, 1.24) <u>WOMAC total:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.70 95% CI: (-13.38, 7.98) Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-11.04, 9.04)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Carlos, 2012⁶⁶</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Physical therapy outpatient clinic</p> <p>Single Site</p>	<p>Total n = 30</p> <p>Arm 1, Mean Age: 62.7(8.7) BMI: 31.1(3.2)</p> <p>Arm 2, Mean Age: 63.4(4.6) BMI: 27.8(3.8)</p> <p>Arm 3, Mean Age: 63.9(6.3) BMI: 31.8(4.1)</p> <p>Female: 70%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: bilateral 86.7%, unilateral 13.3%</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: Grade II-4 on at least one knee</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: 3 months</p> <p>Minimum Age: 50</p> <p>Maximum Age: 75</p> <p>K-L:-grade II-4</p>	<p>Concomitant medical problems that prevent participation</p> <p>Continued Use of Analgesics</p> <p>Diabetes, uncontrolled hypertension, morbid obesity</p> <p>Dementia</p> <p>OA of the hip</p> <p>Use of antiinflammatory or anxiolytic drugs during the past 6 months</p>	<p>Arm 1: Exercise n = 10 Dose: 45 minutes (2 sets of 30 reps) Frequency: 3 sessions per week Duration: 8 weeks</p> <p>Arm 2: Ultrasound n = 10 Dose: 2.5W/cm², 20%, 100Hz Frequency: 3 sessions per week for 4 weeks Duration: 8 weeks (4 weeks US, 4 weeks exercise) Co-Intervention: strength/resistance training 3 sessions per week for 4 weeks</p> <p>Arm 3: Ultrasound n = 10 Dose: Frequency: 3 sessions per week for 4 weeks Duration: 8 weeks (4 weeks US, 4 weeks exercise) Co-Intervention: strength/resistance training 3 sessions per week for 4 weeks</p>	<p><u>VAS movement:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.05 95% CI: (-0.23, 0.14)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.03 95% CI: (-0.08, 0.14)</p> <p><u>VAS rest:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.42 95% CI: (0.13, 0.71)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.17 95% CI: (-0.17, 0.50)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.38 95% CI: (0.16, 0.60)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.31 95% CI: (0.08, 0.54)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.42 95% CI: (0.25, 0.59)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.32 95% CI: (0.09, 0.55)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.43 95% CI: (0.15, 0.71)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.28 95% CI: (-0.01, 0.57)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Cheawthamai, 2014⁹⁹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Thailand</p> <p>Health care setting: Academic physical therapy department</p> <p>Single Site</p>	<p>Total n = 43</p> <p>Age Range: 65.3</p> <p>Arm 1, Mean Age: 64.1(7.9) BMI: 27.1(3.6)</p> <p>Arm 2, Mean Age: 66.6(8.8) BMI: 27.0(4.6)</p> <p>Female: 100%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 51%, unilateral 48%</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes, Participants were instructed to continue any current medication and not to start any new medication</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Female</p> <p>ACR: NR</p>	<p>Surgery knee limb in prior 1.5 months month(s)</p> <p>Injected corticosteroids in the prior 1month month(s)</p> <p>Systemic joint disease, cerebrovascular disease, Parkinson's</p> <p>Back and limb surgery in the prior 1.5 months</p>	<p>Arm 1: Home-exercise program n = 22 Placebo/Home-exercise Dose: Customized Frequency: Daily Duration: 12 weeks</p> <p>Arm 2: Manipulation/manual therapy n = 21 Dose: Customized Frequency: Daily Duration: 12 weeks Co-Intervention: home-based exercise</p>	<p><u>6 min walk (meter):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.00 95% CI: (NC, NC)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (NC, NC)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (NC, NC)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.90 95% CI: (NC, NC)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Cherian, 2015⁸³</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: US</p> <p>Health care setting: NR</p> <p>Single Site</p>	<p>Total n = 52</p> <p>Age Range: 41-80</p> <p>Arm 1, Mean Age: 54 Arm 2, Mean Age: 59</p> <p>Female: 48.1%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 3&4</p> <p>Analgesic Use: Yes, Both treatment and the matched cohorts were not prohibited from receiving previously prescribed NSAIDs. However, we instructed patients to remain taking the same dosage of NSAIDs medication throughout the study, and that if increase or change of dosage was needed, this would only occur after their three month follow-up appointment. In addition, no patients in the study were started on new pain medications at the time of enrollment and throughout the trial period by our institution. The rationale behind our choices for a corticosteroid injection/ physical therapy and to allow the use of NSAID as the matching cohort was to compare the use of the brace to the current initial standard of care at our institution.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 41</p> <p>Maximum Age: 79</p> <p>Able to sign Consent</p> <p>Medial or lateral OA</p> <p>Persistent pain beyond treatment</p> <p>Ability to comply with treatment</p> <p>K-L: 3&4</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 month(s)</p> <p>Injected corticosteroids in the prior 3 month(s)</p> <p>Equal medial/lateral OA</p> <p>History of traumatic onset of knee pain</p>	<p>Arm 1: Usual care n = 26</p> <p>Placebo/Usual care Dose: 1 mL Kenalog 40 mg and 4 mL of 1% lidocaine (corticosteroids); unspecified length of time (physical therapy)</p> <p>Frequency: Unspecified (corticosteroids); gait training three times a week for six weeks, self-directed physical therapy every other day (physical therapy)</p> <p>Duration: 3 months</p> <p>Method of Blinding: Single-blinded</p> <p>Arm 2: Brace n = 26</p> <p>Dose: 3+ hrs per day</p> <p>Frequency: Daily</p> <p>Duration: 3 months</p> <p>Method of Blinding: Single-blinded</p>	<p><u>SF-36 mental:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 2.30 95% CI: (NC, NC)</p> <p><u>SF-36 physical:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -5.90 95% CI: (NC, NC)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.10 95% CI: (NC, NC)</p> <p><u>VAS:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (NC, NC)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Cheung, 2014 ⁵⁷ Study design: RCT Trial name: None Study Location: US Health care setting: Home home, NR Site size: NR	Total n = 36 Mean Age: 72 Arm 1, Mean Age: 71.9 (69.3, 74.6) 95% CI Arm 2, Mean Age: 71.9 (69.0, 75.0) 95% CI BMI: 29.1 (26.7, 31.7) 95% CI BMI: 28.8 (26.0, 31.7) 95% CI Female: 100% Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: NR Subtype: NR Diagnosis: ACR Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Duration of Symptoms: 6 months Minimum Age: 65 Maximum Age: 89 ACR	Concomitant medical problems that prevent participation Surgery knee limb in prior 24 month(s) Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 3 month(s) Prior experience with the intervention of interest Not currently participating in a supervised exercise program Cognitive/mental impairment Symptoms of joint locking; in stability indicated by chronic use of a knee brace, cane, walker, or wheelchair Prior joint replacement : a) uncontrolled high blood pressure or existing heart condition; and b) other comorbid condition with overlapping symptoms (i.e. fibromyalgia, rheumatoid arthritis) were also be excluded.	Arm 1: Wait list control n = 18 Placebo/Wait list Duration: 8 weeks Method of Blinding: Single-blind Arm 2: Hatha yoga n = 18 Dose: 60 minutes Frequency: Weekly Duration: 8 weeks Method of Blinding: Single-blind	<u>SF-12 mental component:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 2.00 95% CI: (-1.33, 5.33) <u>SF-12 physical component:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.70 95% CI: (-2.04, 3.44) <u>WOMAC function:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.20 95% CI: (-10.58, 2.18) <u>WOMAC pain:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-4.36, -0.64) <u>WOMAC total:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.30 95% CI: (-16.62, 0.02)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Christensen, 2015 ³⁴ Study design: RCT Trial name: CAROT Study Location: Denmark Health care setting: Home home, Hospital-outpatient, Dietary unit Site size: NR	Total n = 192 Total # of knees = NR Age Range: NR Arm 1, Mean Age: 61.7 (SD 6.8) BMI: NR Arm 2, Mean Age: 63.0 (SD 6.5) BMI: NR Arm 3, Mean Age: 62.9 (SD 5.8) BMI: NR Female: 80.7% Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: bilateral 89%, unilateral 11% Subtype: NR Diagnosis: Confirmed knee OA based on clinical symptoms, including pain, and on standing radiographs in at least 1 joint compartment Analgesic Use: Yes, Participants were asked not to change any medication or nutritional supplements during the study	Diagnosis of osteoarthritis of the knee Minimum Age: 50 BMI >= 30 kg/m2 NR: Confirmed knee OA based on clinical symptoms, including pain, and on standing radiographs in at least 1 joint compartment	Pending surgery Lack of motivation to lose weight Inability to speak Danish Planned antiobesity surgery, total knee alloplasty (TKA), or receiving pharmacologic therapy for obesity	Arm 1: Control n = 64 Placebo/Control Dose: NA Frequency: NA Duration: 68 weeks (16 on co-intervention, 52 on control) Method of Blinding: NR Co-Intervention: Initial 16-week intensive dietary therapy Arm 2: Weight loss n = 64 Dose: 1 hour sessions Frequency: Weekly sessions for 52 weeks Duration: 68 weeks (16 on co-intervention, 52 on additional weight loss intervention) Method of Blinding: NR Co-Intervention: Initial 16-week intensive dietary therapy Arm 3: Home exercise program; strength/resistance training n = 64 Dose: 60 minutes per session Frequency: 3 days per week Duration: 68 weeks (16 on co-intervention, 52 on additional exercise intervention) Method of Blinding: NR Co-Intervention: Initial 16-week intensive dietary therapy	<u>6 min walk (meter):</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.63 95% CI: (-35.67, 6.41) Comparator: Arm 3 vs Arm 1 , MD : -15.59 95% CI: (-36.63, 5.45) <u>KOOS pain:</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-4.13, 6.33) Comparator: Arm 3 vs Arm 1 , MD : 1.90 95% CI: (-3.33, 7.13) <u>SF-36 mental health:</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.60 95% CI: (-1.09, 4.29) Comparator: Arm 3 vs Arm 1 , MD : 1.20 95% CI: (-1.49, 3.89) <u>SF-36 physical component:</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-3.86, 1.66) Comparator: Arm 3 vs Arm 1 , MD : 0.60 95% CI: (-2.16, 3.36) <u>VAS pain:</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-7.67, 6.47) Comparator: Arm 3 vs Arm 1 , MD : -0.10 95% CI: (-7.17, 6.97) <u>Change in BMI:</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-2.09, -0.11) Comparator: Arm 3 vs Arm 1 , MD : 0.60 95% CI: (-0.39, 1.59) <u>Weightloss, kg:</u> Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.73 95% CI: (-5.37, -0.09) Comparator: Arm 3 vs Arm 1 , MD : 1.99 95% CI: (-0.65, 4.63)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Claes, 2015¹¹²</p> <p>Study design: Single arm trial</p> <p>Trial name: Osteoarthritis Chronic CAre Program (OACCP)</p> <p>Study Location: Australia</p> <p>Health care setting: Hospital-outpatient</p> <p>Multiple Sites: 11</p>	<p>Total n = 203</p> <p>Arm 1, Mean Age: 67.3(9.7) BMI: 31.3(6.6)</p> <p>Female: 64.5</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: VAS >=4/10 at initial assessment; waiting list for TKR or orthopaedic referral</p>	<p>VAS >=4/10 at recruitment visit</p> <p>Pain associated with affected joint on most days of prior month</p>	<p>Exclusion : NR</p>	<p>Arm 1: Weight loss n = 203</p> <p>Placebo/NA</p> <p>Dose: NA</p> <p>Frequency: NA</p> <p>Duration: 1 year</p> <p>Method of Blinding: NA</p> <p>Co-Intervention: NA</p>	<p><u>6-minute walk test (m):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: post-pre , MD : 36.70 95% CI: (27.2, 46.2)</p> <p>Follow-Up Time: 26 weeks : Comparator: post-pre , MD : 44.00 95% CI: (31.5, 56.5)</p> <p><u>BMI:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 0.50 95% CI: (0.3, 0.7)</p> <p>Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 0.80 95% CI: (0.5, 1.1)</p> <p><u>KOOS pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: post-pre , MD : 5.00 95% CI: (2.0, 7.9)</p> <p>Follow-Up Time: 26 weeks : Comparator: post-pre , MD : 5.60 95% CI: (1.6, 9.6)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 1.40 95% CI: (1.1, 1.7)</p> <p>Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 2.00 95% CI: (1.4, 2.6)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 1.00 95% CI: (0.7, 1.3)</p> <p>Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 0.90 95% CI: (0.4, 1.4)</p> <p><u>Weight (kg):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 1.40 95% CI: (0.8, 2.0)</p> <p>Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 2.10 95% CI: (1.2, 3.0)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Coleman, 2012¹¹⁵</p> <p>Study design: RCT</p> <p>Trial name: Osteoarthritis of the Knee Self Management Program</p> <p>Study Location: Australia</p> <p>Health care setting: Community venue</p> <p>Site size: NR</p>	<p>Total n = 146</p> <p>Total # of knees = NR</p> <p>Mean Age(SD): 65 (SD 8)</p> <p>Arm 1, Mean Age: 65 (SD 8.7) BMI: NR</p> <p>Arm 2, Mean Age: 65 (SD 7.9) BMI: NR</p> <p>Female: 74.7%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: X-ray or clinical diagnosis of OA</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 18</p> <p>English-speaking</p> <p>Referral from general practitioner or specialist</p> <p>Able to meet program requirements</p> <p>NR: X-ray or clinical diagnosis of OA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 month(s)</p> <p>Coexisting inflammatory arthritis</p> <p>Serious comorbidity</p> <p>Knee replacement scheduled in < 6 months</p> <p>Cannot meet program time points</p>	<p>Arm 1: Control group n = 75 Placebo/Control Dose: NA Frequency: NA Duration: 6 weeks Method of Blinding: Patients were not blind, physiotherapists performing the assessments were blind to group allocation Co-Intervention: NR</p> <p>Arm 2: Self-management program n = 71 Dose: 2.5 hours Frequency: Once per week Duration: 6 weeks Method of Blinding: Patients were not blind, physiotherapists performing the assessments were blind to group allocation Co-Intervention: NR</p>	<p><u>SF-36 body pain:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -6.00 95% CI: (-11.96, -0.04)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.20 95% CI: (-12.47, -1.93)</p> <p><u>SF-36 physical function:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -5.70 95% CI: (-10.97, -0.43)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.60 95% CI: (-9.48, -1.72)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-1.55, -0.45)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-1.55, -0.45)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-6.14, -0.86)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.30 95% CI: (-7.24, -3.36)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.43, 0.23)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-2.33, -0.67)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -4.10 95% CI: (-7.43, -0.77)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.20 95% CI: (-9.97, -4.43)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Coleman, 2012 ¹¹⁵ -Continued					<p><u>Number with MCII SF36 pain:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.81 95% CI: (0.54, 1.21)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.73 95% CI: (0.43, 1.24)</p> <p><u>Number with MCII SF36 physical function:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.73 95% CI: (0.52, 1.02)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.57 95% CI: (0.38, 0.84)</p> <p><u>Number with MCII TUG:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.68 95% CI: (0.47, 0.99)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.32 95% CI: (0.20, 0.52)</p> <p><u>Number with MCII VAS Pain:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.20 95% CI: (0.08, 0.49)</p> <p><u>Number with MCII WOMAC physical function:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.56 95% CI: (0.33, 0.95)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.24 95% CI: (0.11, 0.51)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Cortes, 2014 ¹⁰⁰	Total n = 18	Able to sign Consent	Concomitant medical problems that prevent participation	Arm 1: Control n = 9	<u>TUG (s):</u>
Study design: RCT	Total # of knees = NR	Knee pain most days within the last month	Surgery knee limb in prior 12 month(s)	Placebo/Control	Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 3.94 95% CI: (-4.01, 11.89)
Trial name: None	Age Range: 67-91	Disabling knee pain during at least one of the following activities: going down stairs or up stairs; walking at a pace of 0.4 km; and standing up or sitting down on the toilet or bed	Injected hyaluronic acid in the past or during the past 6 month(s)	Dose: NA Frequency: NA Duration: 6 weeks Method of Blinding:	Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 2.84 95% CI: (-4.61, 10.29)
Study Location: Spain	Arm 1, Mean Age: NR BMI: NR	No changes in drug administration, including NSAIDs, during the study	Injected corticosteroids in the prior 6 month(s)	Arm 2: Massage	<u>VAS pain:</u>
Health care setting: NR	Female: NR Racial/Ethnic Distribution: NR		Rheumatoid arthritis or other inflammatory joint disease		Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 3.10 95% CI: (0.76, 5.44)
Site size: NR	Living Situation: Community Dwelling Location of OA: NR Subtype: NR		Intra-articular injection within the last 6 months		Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 2.28 95% CI: (0.44, 4.12)
	Diagnosis: Radiologic evidence and/or clinical signs of knee OA		Cognitive impairment that may bias the research		<u>WOMAC total:</u>
	Analgesic Use: Yes, No changes in drug administration, including NSAIDs, during the study				Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 21.42 95% CI: (9.79, 33.05)
					Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 14.04 95% CI: (4.71, 23.37)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
da Silva, 2015 ⁴⁸	Total n = 30 Study design: RCT Trial name: None Study Location: Brazil Health care setting: Physical therapy outpatient clinic Single Site	Diagnosis of osteoarthritis of the knee Minimum Age: 18 Pain iwthin the past year; on most days for at least 3 months Stable doses of NSAIDs ACR: NA Lequesne Index: 5-13	Concomitant medical problems that prevent participation Prior experience with the intervention of interest Other cause of pain in the lower limb Refusal to continue Two consecutive or 3 non-consecutive absences	Arm 1: Control n = 15 Duration: 8 weeks Co-Intervention: Pre-randomization self-management program Arm 2: Land-based exercise program n = 15 Dose: 45 minutes per session Frequency: 2 sessions per week Duration: 8 weeks Co-Intervention: Pre-randomization self-management program plus weekly educational sessions	<u>6 min walk:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -50.40 95% CI: (-94.26, -6.54) <u>Lequesne Index Function:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.83 95% CI: (-1.84, 0.18) <u>SF-36 bodily pain:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.80 95% CI: (-27.39, -2.21) <u>SF-36 physical function:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.00 95% CI: (-26.24, -1.76) <u>SF-36 role physical:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -53.33 95% CI: (-76.10, -30.56) <u>TUG (s):</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.05 95% CI: (-3.12, -0.98)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Dundar, 2015²⁵</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Turkey</p> <p>Health care setting: Academic Physical Medicine and Rehabilitation Department</p> <p>Single Site</p>	<p>Total n = 40</p> <p>Total # of knees = NR</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 57.6 BMI: 31.2</p> <p>Arm 2, Mean Age: 56.8 BMI: 31.7</p> <p>Female: 72.5%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: bilateral 100%</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 2&3, Bilateral knee OA diagnosis according to ACR criteria</p> <p>Analgesic Use: Yes, Patients were not allowed to change the dosage of their routine pain medication or begin a new pain medication during the study.</p>	<p>Inclusion : NR</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 month(s)</p> <p>Injected hyaluronic acid in the past or during the past 6 month(s)</p> <p>Injected corticosteroids in the prior 6 month(s)</p> <p>Pregnant</p> <p>Not allowed to change dosage of their routine pain medication</p> <p>Not allowed to begin new pain medication</p>	<p>Arm 1: Sham Procedure n = 20 Placebo/Sham Procedure Dose: NR Frequency: 5 times per week Duration: 4 weeks Method of Blinding: The WOMAC questionnaire and VAS for pain were performed by a physiatrist who was blind to the patient's treatment protocol. Another clinician blinded to the patient's clinical and treatment data, performed the ultrasound. Co-Intervention: Both groups received 20 sessions (5 sessions in a week, each lasting 60 min) of physical therapy, including hot pack, ultrasound, TENS and isometric knee exercise</p> <p>Arm 2: Neuromuscular electrical stimulation n = 20 Dose: frequency of 50Hz, intensity 100 microT for 20 minutes Frequency: 5 times per week Duration: 4 weeks Method of Blinding: The WOMAC questionnaire and VAS for pain were performed by a physiatrist who was blind to the patient's treatment protocol. Another clinician blinded to the patient's clinical and treatment data, performed the ultrasound. Co-Intervention: Both groups received 20 sessions (5 sessions in a week, each lasting 60 min) of physical therapy, including hot pack, ultrasound, TENS and isometric knee exercise</p>	<p><u>Total WOMAC:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 7.00 95% CI: (NC, NC)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (NC, NC)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 7.00 95% CI: (NC, NC)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Dwyer, 2015 ¹⁰²	Total n = 78	Diagnosis of osteoarthritis of the knee	Surgery knee limb in prior 6 month(s)	Arm 1: Rehabilitation n = 26 Placebo/Usual care Dose: 20 min Frequency: 6 times Duration: 4 weeks Method of Blinding: Unblinded	<u>WOMAC function:</u> Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -22.00 95% CI: (-162.58, 118.58) Comparator: Arm 3 vs Arm 1 , MD : -32.80 95% CI: (-191.40, 125.80)
Study design: RCT	Total # of knees = 85	Duration of Symptoms: >=1 year	Prior experience with the intervention of interest	Arm 2: Manual and manipulative therapy (MMT) n = 26 Dose: 20 minutes Frequency: 12 times Duration: 4 weeks Method of Blinding: Unblinded	<u>WOMAC pain:</u> Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -26.90 95% CI: (-68.88, 15.08) Comparator: Arm 3 vs Arm 1 , MD : -31.50 95% CI: (-72.40, 9.40)
Trial name: None	Age Range: 38-80	Minimum Age: 38	>=720/2400 on WOMAC	Arm 3: Rehabilitation + Manual and manipulative therapy (MMT) n = 26 Dose: 20-40 minutes Frequency: 6 session β- 3 with extra training Duration: 4 weeks Method of Blinding: Unblinded Co-Intervention: Rehab or MMT	<u>WOMAC total:</u> Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -80.50 95% CI: (-281.64, 120.64) Comparator: Arm 3 vs Arm 1 , MD : -63.20 95% CI: (-273.72, 147.32)
Study Location: US, South Africa	Arm 1, Mean Age: 60.9 (10.3) BMI: 28.6 (5.2)	Maximum Age:79			
Health care setting: Chiropractic university-based outpatient teaching clinics	Arm 2, Mean Age: 63.5 (10.9) BMI: 28.6 (5.2)	Ambulatory			
Multiple Sites: 2	Arm 3, Mean Age: 62.2 (11.8) BMI: 30.6 (7.6)	K-L: 0-3			
	Female: 63	1 of three clinical criteria involving knee pain, crepitus, morning stiffness, and bony enlargement: 1 of 3 criteria			
	Racial/Ethnic Distribution: NR				
	Living Situation: Community Dwelling				
	Location of OA: bilateral 91%, unilateral 9%				
	Subtype: NR				
	Diagnosis: K-L: 0-3, of three clinical criteria involving knee pain, crepitus, morning stiffness, and bony enlargement				
	Analgesic Use: Yes				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Elboim-Gabyzon, 2013⁷⁰</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Israel</p> <p>Health care setting: Physical therapy outpatient clinic</p> <p>Single Site</p>	<p>Total n = 63</p> <p>Mean Age(SD): 68.9 (SD 7.7)</p> <p>Arm 1, Mean Age: NR BMI: NR</p> <p>Arm 2, Mean Age: NR BMI: NR</p> <p>Female: 82.5%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: >=2, Diagnosis of idiopathic knee OA</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: Knee pain atleast 3 months, with pain presenting at least three days a week during the last month</p> <p>Minimum Age: 51</p> <p>Ambulatory</p> <p>Ability to follow instructions</p> <p>K-L: >=2</p> <p>ACR: Compliance with the classification of ACR</p> <p>NR: Diagnosis of idiopathic knee OA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Injected hyaluronic acid in the past or during the past 6 month(s)</p> <p>Injected corticosteroids in the prior 6 month(s)</p> <p>Existence of a pacemaker</p> <p>History of cardiovascular, neurological or orthopedic problems that could affect functional performance or previous knee surgery other than arthroscopy</p> <p>Inability to tolerate electrical stimulation at a level of current sufficient to elicit full knee extension</p> <p>Change in pain medication in the previous month</p> <p>Injections to the knee joint during the previous six months</p>	<p>Arm 1: Control n = 30, Placebo/Control, Dose: NA, Frequency: NA, Duration: NA Method of Blinding: Assessor was blind to treatment allocation only at the initial assessment. Physical therapists leading group exercise program were familiar with the study protocol were not aware of treatment allocation. Co-Intervention: Group exercise program consisting of 12 45-minute sessions, biweekly for six weeks, with 6–8 subjects in each group led by one of 3 physical therapists. To be included in final analysis, subjects had to complete the 12 sessions within 8 weeks. The program included: range of motion exercises; knee and lower extremity muscle-strengthening exercises; functional activities; and balance training. Sessions also included patient education on self-management; activity and exercise planning, and discussion of pain-coping strategies.</p> <p>Arm 2: Neuromuscular electrical stimulation n = 33, Dose: 75 Hz frequency; 2s ramp-up time; 10s on time; 2s off time; amplitude to tolerance (max 100mA); 10 contractions, Frequency: Biweekly, Duration: 6 weeks Method of Blinding: Assessor was blind to treatment allocation only at the initial assessment. Physical therapists leading group exercise program were familiar with the study protocol were not aware of treatment allocation. Co-Intervention: Group exercise program consisting of 12 45-minute sessions, biweekly for six weeks, with 6–8 subjects in each group led by one of 3 physical therapists. To be included in final analysis, subjects had to complete the 12 sessions within 8 weeks. The program included: range of motion exercises; knee and lower extremity muscle-strengthening exercises; functional activities; and balance training. Sessions also included patient education on self-management; activity</p>	<p><u>TUG (s):</u></p> <p>Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-1.60, 2.00)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-2.98, -0.42)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -23.20 95% CI: (-49.20, 2.80)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Erhart, 2010 ⁹⁵	Total n = 79	Minimum Age: 40	Concomitant medical problems that prevent participation	Arm 1: Control n = 26	<u>WOMAC pain:</u>
Study design: RCT	Total # of knees = NR	Maximum Age:79	Prior surgery on one or both knees	Placebo/Control shoes	Follow-Up Time: 6 months :
Trial name: None	Age Range: >=60.2	Ambulatory	Concomitant or prior use of other meds	Dose: NA	Comparator: Arm 2 vs Arm 1 , MD : -3.70 95% CI: (NC, NC)
Study Location: US	Arm 1, Mean Age: 62.1 BMI: 27.4	Able to sign Consent	Prior acute injury to the knee	Frequency: Suggested minimum wear time 4hr/day, average monthly reports 7.9-9.5h/day	<u>Clinically significant on WOMAC pain:</u>
Health care setting: NR	Arm 2, Mean Age: 61.4 BMI: 27.6		BMI >35 kg/m2	Duration: 6 months	Follow-Up Time: 6 months :
Site size: NR	Female: 51.39%		Use of shoe insert or hinged knee brace	Method of Blinding: Subjects were blinded to the shoe type, researcher was not blinded	Comparator: Arm 2 vs Arm 1 , RR : 0.49 95% CI: (0.31, 0.79)
	Racial/Ethnic Distribution: NR		Narcotic pain medication use	Co-Intervention: NR	
	Living Situation: NR		Intraarticular joint injection in previous 2 months	Arm 2: Variable-stiffness shoes n = 34	
	Location of OA: NR		Nerve or muscle disease associated with walking difficulty, Gout or recurrent pseudogout, and Diagnosed or symptomatic osteoarthritis in other lower extremity joints, and Serious injury to foot, ankle, back, or hips	Dose: NA	
	Subtype: Medial 100%			Frequency: Suggested minimum wear time 4hr/day, average monthly reports 6.9-8.0h/day	
	Diagnosis: Osteoarthritic changes based on MRI (cartilage thinning and/or osteophytes)			Duration: 6 months	
	Analgesic Use: Yes			Method of Blinding: Subjects were blinded to the shoe type, researcher was not blinded	
				Co-Intervention: NR	

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Erhart-Hledik, 2012 ⁹⁶	Total n = 79	Diagnosis of osteoarthritis of the knee	Concomitant medical problems that prevent participation	Arm 1: Control n = 39	<u>WOMAC pain:</u>
Study design: RCT	Total # of knees = NR	Duration of Symptoms: Persistent medial compartment knee joint pain	Prior surgery on one or both knees	Placebo/Control, constant-stiffness shoe	Follow-Up Time: 12 months :
Trial name: None	Mean Age(SD): 60.2 (SD 9.8)	Minimum Age: 40	Concomitant or prior use of other meds	Dose: Instructed to use their assigned shoes as their main walking shoes, a minimum 4 h of wear per day	Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (NC, NC)
Study Location: NR	Arm 1, Mean Age: 61.0 (SD 12.0) BMI: NR	Maximum Age:80	Injected hyaluronic acid in the past or during the past 2 month(s)	Frequency: Daily Duration: 12 months	
Health care setting: NR	Arm 2, Mean Age: 57.3 (SD 8.5) BMI: NR	Ambulatory	Injected corticosteroids in the prior 2 month(s)	Method of Blinding: Patients were blinded to their shoe type. The researcher performing the gait analysis was not blinded to shoe type.	
Site size: NR	Female: 46.8%	Able to sign Consent	Prior acute injury to the knee	Co-Intervention: NR	
	Racial/Ethnic Distribution: NR	NR: Symptomatic medial compartment knee OA	BMI > 35 kg/m2	Arm 2: Orthotics/shoes n = 40	
	Living Situation: NR	NR: Osteoarthritic changes based on MRI/radiograph	Total knee replacement	Dose: Instructed to use their assigned shoes as their main walking shoes, a minimum 4 h of wear per day	
	Location of OA: NR		Intraarticular joint injection in previous 2 months	Frequency: Daily Duration: 12 months	
	Subtype: Medial 100%		Use of shoe insert or hinged knee brace or narcotic pain medication	Method of Blinding: Patients were blinded to their shoe type. The researcher performing the gait analysis was not blinded to shoe type.	
	Diagnosis: Symptomatic medial compartment knee OA, osteoarthritic changes based on MRI/radiograph		Nerve or muscle disease associated with walking difficulty; serious injury to foot, ankle, back, or hips; gout or recurrent pseudogout; or OA in other lower extremity joint	Co-Intervention: NR	
	Analgesic Use: Yes				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Fioravanti, 2012⁵⁸</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Italy</p> <p>Health care setting: Academic rheumatology clinic/department, health spa</p> <p>Single Site</p>	<p>Total n = 60</p> <p>Mean Age: 70.5</p> <p>Arm 1, Mean Age: 72.45±7.14 BMI: 26.53±4</p> <p>Arm 2, Mean Age: 69.33±7.63 BMI: 27.52±3</p> <p>Female: 50%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 100%</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes, Patients in both groups were advised to continue their established pharmacological and non-pharmacological treatments, with the exception of analgesic drugs (500 mg acetaminophen tablets) and NSAIDs (150 mg Diclofenac tablets, 20 mg Piroxicam tablets, 750 mg Naproxen tablets, 200 mg Aceclofenac), which were to be consumed as required and noted daily in a diary.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: >+3 months</p> <p>Minimum Age: 50</p> <p>Maximum Age: 75</p> <p>ACR: NA</p> <p>VAS: >30mm</p> <p>K-L: 1-3</p>	<p>Concomitant medical problems that prevent participation</p> <p>Injected hyaluronic acid in the past or during the past 6 months month(s)</p> <p>Injected corticosteroids in the prior 3 months month(s)</p> <p>Physical Therapy or Rehab or exercise in the previous thermal treatments in the previous 6 months month(s)</p> <p>Severe comorbidity of the heart, lungs, liver, cerebrum or kidney, varices, systemic blood disease, neoplasm</p> <p>Acute illness</p> <p>Type 1 diabetes</p> <p>Pregnancy or nursing</p> <p>Arthroscopy with or without joint lavage in the previous 6 months, chondroprotective agents in the previous 6 months</p>	<p>Arm 1: Control n = 30 Duration: NA</p> <p>Arm 2: Balneotherapy n = 30 Dose: 20 minutes per treatment Frequency: 12 treatments per 2 weeks Duration: 2 weeks</p>	<p><u>Lequesne index:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -7.50 95% CI: (-9.57, -5.43)</p> <p><u>SF-36 mental component:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -17.00 95% CI: (-25.14, -8.86)</p> <p><u>SF-36 physical component:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -32.60 95% CI: (-49.62, -15.58)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -42.50 95% CI: (-53.67, -31.33)</p> <p><u>WOMAC total function score:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -37.47 95% CI: (-46.61, -28.33)</p> <p><u>WOMAC total pain score:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -25.70 95% CI: (-34.06, -17.34)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Fioravanti, 2015⁶¹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Italy</p> <p>Health care setting: Spa resort</p> <p>Single Site</p>	<p>Total n = 103</p> <p>Age Range: 40-80</p> <p>Arm 1, Mean Age: 69.66 (11.1) BMI: 28.01 (4.18)</p> <p>Arm 2, Mean Age: 68.49 (9.01) BMI: 28.58 (4.01)</p> <p>Female: 72</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 100%</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 1-3, ACR</p> <p>Analgesic Use: Yes, Allowed but washout of concomitant acetaminophen or NSAIDs was required for an entire week before randomization and 24 h before every assessment.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: 6</p> <p>Minimum Age: 40</p> <p>Maximum Age: 79</p> <p>VAS: \geq30mm in last 3 months</p> <p>K-L: 1-3</p>	<p>Concomitant medical problems that prevent participation</p> <p>Injected hyaluronic acid in the past or during the past 3 month(s)</p> <p>Injected corticosteroids in the prior 3 month(s)</p> <p>Prior experience with the intervention of interest</p> <p>Symptomatic Slow Acting Drugs for OA (SYSADOA) in last 3 months</p>	<p>Arm 1: Usual care n = 50 Duration: 2 weeks Method of Blinding: Unblinded</p> <p>Arm 2: Mud-bath therapy n = 53 Dose: 35 minutes Frequency: 12 sessions Duration: 2 weeks Method of Blinding: Unblinded</p>	<p><u>EQ-5D:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (NC, NC)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.24 95% CI: (NC, NC)</p> <p><u>EQ-5D-VAS:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 22.09 95% CI: (NC, NC)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 14.35 95% CI: (NC, NC)</p> <p><u>SF-12 mental component:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -2.71 95% CI: (NC, NC)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.92 95% CI: (NC, NC)</p> <p><u>SF-12 physical component:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 11.85 95% CI: (NC, NC)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 12.46 95% CI: (NC, NC)</p> <p><u>VAS:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-21.31, 1.31)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -15.00 95% CI: (-25.63, -4.37)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -5.50 95% CI: (-10.81, -0.19)</p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-15.00, -5.00)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Fitzgerald, 2011 ⁵⁰	Total n = 183 Study design: RCT Trial name: None Study Location: US Health care setting: NR Single Site	Diagnosis of osteoarthritis of the knee Minimum Age: 40 ACR: meet criteria for OAK K-L: ≥ 2	Concomitant medical problems that prevent participation Prior surgery on one or both knees	Arm 1: Strength training; agility training; aerobic exercise n = 84 Placebo/Control Dose: N/A Frequency: Twice a week Duration: 6 weeks Method of Blinding: Unblinded Arm 2: Standard exercise + agility and perturbation training n = 75 Dose: N/A Frequency: Twice a week Duration: 6 weeks Method of Blinding: Unblinded	<u>WOMAC physical function score:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-3.59, 4.19) Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-5.87, 1.07) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-7.32, 0.32) <u>Get up and go test score (s):</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 1.40 95% CI: (-0.13, 2.93) Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-0.94, 0.34) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-0.75, 0.15) <u>Knee pain:</u> Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-0.89, 1.09) Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.38, 0.18) Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.45, 0.25)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Foroughi, 2011 ⁴²	Total n = 54 Study design: RCT Trial name: None Study Location: Australia Health care setting: NR Single Site	Diagnosis of osteoarthritis of the knee Minimum Age: >40 ACR	Concomitant medical problems that prevent participation Surgery knee limb in prior 6 month(s) Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 6 month(s) Prior acute injury to the knee Secondary OA Men	Arm 1: Sham exercise n = 28 Placebo/Sham Dose: approx.40 minutes () Frequency: Daily Duration: 6 months Method of Blinding: Single-blinded Arm 2: Progressive resistance training (PRT) n = 26 Dose: approx.60 minutes Frequency: Daily Duration: 6 months Method of Blinding: Single-blinded	<u>WOMAC function:</u> Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.49 95% CI: (-15.08, 0.10) <u>WOMAC pain:</u> Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.67 95% CI: (-3.71, 0.37) <u>WOMAC total:</u> Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -10.40 95% CI: (-19.94, -0.86)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Fransen, 2014 ³⁰	Total n = 605	Diagnosis of osteoarthritis of the knee	Concomitant medical problems that prevent participation	Arm 1: Placebo n = 151 Placebo/Capsules Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy	<u>SF-12 mental:</u> Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-3.90, 0.90) Comparator: Arm 3 vs Arm 1 , MD : -3.00 95% CI: (-5.11, -0.89) Comparator: Arm 4 vs Arm 1 , MD : -2.00 95% CI: (-4.37, 0.37)
Study design: RCT	Age Range: 45-75	Duration of Symptoms: 6 months	Surgery knee limb in prior 6 month(s)	Arm 2: Glucosamine n = 152 Dose: 1500 mg Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy	<u>SF-12 physical:</u> Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-1.96, 2.56) Comparator: Arm 3 vs Arm 1 , MD : 1.60 95% CI: (-0.74, 3.94) Comparator: Arm 4 vs Arm 1 , MD : 0.10 95% CI: (-2.18, 2.38)
Trial name: LEGS	Arm 1, Mean Age: 60.6 (8.1) BMI: 29.1 (5.8)	Pain >=4/10	Pending surgery	Arm 3: Glucosamine–chondroitin n = 151 Dose: 1500mg Glucosamine+ 800 mg Chondroitin Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy	<u>WOMAC function:</u> Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-3.23, 3.23) Comparator: Arm 3 vs Arm 1 , MD : 0.00 95% CI: (-3.29, 3.29) Comparator: Arm 4 vs Arm 1 , MD : -0.40 95% CI: (-3.62, 2.82)
Study Location: Australia	Arm 2, Mean Age: 61.2 (7.7) BMI: 28.4 (4.7)	Radiographs: Reduced joint space in medial tibial-femoral compartment but > 2mm	Injected hyaluronic acid in the past or during the past 3 month(s)	Arm 4: Chondroitin n = 151 Dose: 800 mg Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy	<u>WOMAC pain:</u> Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (-0.98, 0.78) Comparator: Arm 3 vs Arm 1 , MD : 0.10 95% CI: (-0.79, 0.99) Comparator: Arm 4 vs Arm 1 , MD : -0.20 95% CI: (-1.08, 0.68)
Health care setting: NR	Arm 3, Mean Age: 60.7 (8.4) BMI: 28.8 (6.0)		Injected corticosteroids in the prior 3 month(s)		
Site size: NR	Arm 4, Mean Age: 59.5 (8.0) BMI: 29.6 (5.4)		Rheumatoid arthritis		
	Female: 56%		Unstable diabetes		
	Racial/Ethnic Distribution: NR		Allergy to shellfish		
	Living Situation: Community Dwelling		Bilateral knee replacement		
	Location of OA: NR				
	Subtype: Medial 100%				
	Diagnosis: K-L: <2				
	Analgesic Use: Yes, Not restricted				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Ghroubi, 2008 ¹⁰⁵	Total n = 56 Study design: RCT Trial name: None Study Location: Tunisia Health care setting: Physical therapy outpatient clinic Single Site Female: NR Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: NR Subtype: NR Diagnosis: K-L: mean 2.25, Mild to moderate Analgesic Use: Yes, Patients who changed their medication use during the study were excluded.	Diagnosis of osteoarthritis of the knee Minimum Age: 18 BMI>=35 or 30-35 with at least one chronic health risk factor Pain in the knee several days per week and having functional difficulties due to the OA, such as walking>1km, climbing stairs, housework, doing errands, lifting heavy load K-L: I=III	Prior surgery on one or both knees Prior acute injury to the knee An orthopedic problem that would prevent walking on a treadmill Treatment for another form of arthritis Contraindication to exercising Precursors to CVD or prior recent MI Serious psychiatric disorders	Arm 1: Control n = 14 Placebo/No diet or exercise Dose: NA Frequency: NA Duration: 2 months Arm 2: Land-based exercise n = 13 Dose: 60 minutes aerobic and strength training per session Frequency: 3 sessions per week Duration: 2 months Arm 3: Diet and exercise n = 15 Dose: 60 minutes per session Frequency: 3 sessions per week Duration: 2 months Arm 4: Diet only n = 14 Dose: NA Frequency: NA Duration: 2 months	<u>6 min walk:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -39.00 95% CI: (-46.47, -31.53) Comparator: Arm 3 vs Arm 1 , MD : -53.00 95% CI: (-59.33, -46.67) Comparator: Arm 4 vs Arm 1 , MD : 2.00 95% CI: (-6.51, 10.51) <u>Lequesne Index:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.41 95% CI: (-3.52, -1.30) Comparator: Arm 3 vs Arm 1 , MD : -3.73 95% CI: (-4.65, -2.81) Comparator: Arm 4 vs Arm 1 , MD : -2.23 95% CI: (-3.30, -1.16) <u>VAS:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.90 95% CI: (-4.52, -1.28) Comparator: Arm 3 vs Arm 1 , MD : -4.56 95% CI: (-5.82, -3.30) Comparator: Arm 4 vs Arm 1 , MD : -2.10 95% CI: (-3.32, -0.88) <u>WOMAC function:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.09 95% CI: (-4.46, -1.72) Comparator: Arm 3 vs Arm 1 , MD : -4.01 95% CI: (-5.56, -2.46) Comparator: Arm 4 vs Arm 1 , MD : -2.34 95% CI: (-3.71, -0.97) <u>Number with significant improvement in WOMAC:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.23 95% CI: (0.02, 2.23) Comparator: Arm 3 vs Arm 1 , RR : 0.16 95% CI: (0.02, 1.39) Comparator: Arm 4 vs Arm 1 , RR : 0.33 95% CI: (0.03, 3.43)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Gormeli, 2015 ²⁴	Total n = 182 Study design: RCT Trial name: None Study Location: Turkey Health care setting: NR Site size: NR Age Range: 53.5 Arm 1, Mean Age: 52.8 (12.8) BMI: 29.5 (3.2) Arm 2, Mean Age: 53.8 (13.4) BMI: 28.4 (4.4) Arm 3, Mean Age: 53.7 (13.1) BMI: 28.7 (4.8) Arm 4, Mean Age: 53.5 (14) BMI: 29.7 (3.7) Female: 55.6% Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: Tibiofemoral 100% Diagnosis: K-L: 1-4 Analgesic Use: Yes, Paracetamol was prescribed for discomfort.	Diagnosis of osteoarthritis of the knee Duration of Symptoms: > 4 months K-L: 1-4	Surgery knee limb in prior month(s) Systemic disorders (diabetes, rheumatic diseases, severe cardiovascular diseases, haematological diseases, infections) Generalized OA, Undergoing anticoagulant or antiaggregant therapy Use of NSAIDs in the 5 days before injection Hemoglobin values < 11 g/dL and platelet values < 150,000/mm ³	Arm 1: Control n = 40 Frequency: One time treatment Arm 2: PRP1 n = 44 Frequency: One time treatment Arm 3: PRP3 n = 39 Frequency: One time treatment Arm 4: HA n = 39 Frequency: One time treatment	<u>EQ-VAS:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 14.00 95% CI: (11.56, 16.44) Comparator: Arm 3 vs Arm 1 , MD : 23.40 95% CI: (19.66, 27.14) Comparator: Arm 4 vs Arm 1 , MD : 12.80 95% CI: (10.04, 15.56) <u>EuroQol-VAS:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -14.00 95% CI: (-16.44, -11.56) Comparator: Arm 3 vs Arm 1 , MD : -23.40 95% CI: (-27.14, -19.66) Comparator: Arm 4 vs Arm 1 , MD : -12.80 95% CI: (-15.56, -10.04)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Gschiel, 2010⁷¹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Germany</p> <p>Health care setting: Academic pain clinic</p> <p>Single Site</p>	<p>Total n = 45</p> <p>Mean Age: 58</p> <p>Arm 1, Mean Age: 57.7(3.5) BMI: 29.6</p> <p>Arm 2, Mean Age: 58.4(2.4) BMI: 27</p> <p>Female: 75%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: NR</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 18</p> <p>Maximum Age: 79</p> <p>Body weight 50-100kg</p> <p>Chronic pain (at least 4/11 NRS)</p> <p>radiologically verified diagnosis: NR</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior experience with the intervention of interest</p> <p>CVD</p> <p>Permanent pacemaker</p> <p>Neurologic disease</p> <p>Inflammatory joint disease</p> <p>Cancer</p>	<p>Arm 1: Placebo n = 20 Dose: 30 minutes per treatment session Frequency: two sessions per day Duration: 3 weeks</p> <p>Arm 2: TENS n = 25 Dose: 30 minutes per treatment session Frequency: two sessions per day Duration: 3 weeks</p>	<p><u>WOMAC Pain:</u></p> <p>Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-2.85, 0.85)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.20 95% CI: (-18.43, 10.03)</p>
<p>Hatef, 2014⁸⁷</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Iran</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 150</p> <p>Arm 1, Mean Age: 48.6 (10) at endline</p> <p>Arm 2, Mean Age: 48.21 (12) at endline</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: Medial 100%, Tibiofemoral 100%</p> <p>Diagnosis: Mild-to-moderate, ACR</p> <p>Analgesic Use: Yes, Unrestricted? Not detailed</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: Pain on a daily basis for at least 1 month during the previous 3 months</p> <p>K-L: >2</p> <p>Clinical diagnosis: Medial femoro-tibial OA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Injected corticosteroids in the prior 1 month(s)</p> <p>Knee joint lavage within the previous 3 months</p> <p>Tibial osteotomy within the previous 5 years</p> <p>Drug treatment for OA within the previous week</p> <p>Greater or similar reduction in lateral than medial femoro-tibial joint space width</p> <p>Secondary knee or hip OA</p>	<p>Arm 1: Neutral insoles n = 75 Placebo/Sham Duration: 2 months Method of Blinding: Double-blinded</p> <p>Arm 2: Lateral wedged insoles n = 75 Duration: 2 months Method of Blinding: Double-blinded</p>	<p><u>VAS:</u></p> <p>Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -23.05 95% CI: (-28.34, -17.76)</p> <p><u>VAS - number pain mild (21-40):</u></p> <p>Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , RR : 0.13 95% CI: (0.05, 0.36)</p> <p><u>VAS - number pain none to scant (0-20):</u></p> <p>Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , RR : 0.23 95% CI: (0.03, 2.03)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Henriksen, 2013 ⁴⁹ Study design: RCT Trial name: None Study Location: Denmark Health care setting: NR Site size: NR	Total n = 60 Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: NR Analgesic Use: Yes	Inclusion : NR	Exclusion : NR	Arm 1: Control n = 23 Duration: 12 weeks Arm 2: Exercise n = 25 Frequency: 3 sessions per week Duration: 12 weeks	<u>KOOS pain:</u> Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 6.8 95% CI: (1.2, 12.4)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Hochberg, 2008¹¹⁶</p> <p>Study design: RCT</p> <p>Trial name: GAIT</p> <p>Study Location: US</p> <p>Health care setting: Academic rheumatology clinic/department</p> <p>Multiple Sites: 16</p>	<p>Total n = 1583</p> <p>Total # of knees = NR</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 58(10) BMI: 31.9(7.3)</p> <p>Arm 2, Mean Age: 59(10) BMI: 31.8(6.8)</p> <p>Arm 3, Mean Age: 58(10) BMI: 32.0(7.6)</p> <p>Arm 4, Mean Age: 59(11) BMI: 31.5(6.6)</p> <p>Arm 5, Mean Age: 59(11) BMI: 31.5(7.1)</p> <p>Female: 64%</p> <p>Racial/Ethnic Distribution: African American 14%, Asian NR, Caucasian 78%, NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 2&3, WOMAC pain scores 125-400 out of 500, Functional class I, II, or III</p> <p>Analgesic Use: Yes, Patients were allowed to take up to 4000 mg of acetaminophen (Tylenol, McNeil) daily, except during the 24 hours before a clinical evaluation for joint pain. Other analgesics, including narcotics and NSAIDs, were not permitted.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 40</p> <p>Ambulatory</p> <p>Knee pain for at least six months and on the majority of days during the preceding month</p> <p>K-L: 2&3</p> <p>ACR: 1, II, or III</p> <p>WOMAC: 125-400mm</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Prior acute injury to the knee</p> <p>Concurrent medical or arthritic conditions that could confound evaluation of the index joint</p> <p>Concurrent use of analgesics other than acetaminophen, including NSAIDs or narcotics</p> <p>Predominant patellofemoral disease</p> <p>A history of clinically significant trauma or surgery to the index knee</p>	<p>Arm 1: Placebo n = 313 Dose: NA (not applicable) Frequency: 3 times a day Duration: 24 weeks Method of Blinding: NR</p> <p>Arm 2: Glucosamine n = 317 Dose: 500mg Frequency: three times a day Duration: 24 weeks Method of Blinding: NA</p> <p>Arm 3: Chondroitin sulfate n = 318 Dose: 400 mg Frequency: three times a day Duration: 24 weeks Method of Blinding: NA</p> <p>Arm 4: Glucosamine+chondroitin sulfate n = 317 Dose: 500 mg G + 400 mg CS Frequency: three times a day Duration: 24 weeks Method of Blinding: NA</p> <p>Arm 5: Celecoxib n = 318 Dose: 200 mg Frequency: once a day Duration: 24 weeks Method of Blinding: NA</p>	<p><u>WOMAC pain (% with 20% or better improvement in pain):</u></p> <p>Follow-Up Time: 24 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , RR : 0.94 95% CI: (0.83, 1.06)</p> <p>Comparator: Arm 3 vs Arm 1 , RR : 0.92 95% CI: (0.81, 1.04)</p> <p>Comparator: Arm 4 vs Arm 1 , RR : 0.90 95% CI: (0.80, 1.02)</p> <p>Comparator: Arm 5 vs Arm 1 , RR : 0.86 95% CI: (0.76, 0.96)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Hochberg, 2015 ²⁸ Study design: RCT Trial name: MOVES Study Location: France, Germany, Poland and Spain Health care setting: NR Multiple Sites: 42	Total n = 606 Age Range: >=40 Arm 1, Mean Age: 63.2 (9.0) BMI: 30.9 (18.0) Arm 2, Mean Age: 62.2 (8.8) BMI: 31.1 (5.8) Female: 83.9% Racial/Ethnic Distribution: Caucasian 98.7%, 1.3% Living Situation: NR Location of OA: NR Subtype: NR Diagnosis: K-L: 2&3, ACR Analgesic Use: Yes, Up to 3 g/day of acetaminophen except during the 48 h before clinical evaluation	Diagnosis of osteoarthritis of the knee: ACR Duration of Symptoms: 1 month Minimum Age: 40 Otherwise Healthy Able to sign Consent No clinical or significant laboratory abnormalities Negative pregnancy test and use of birth control Not participating in another clinical trial Agree to attend all study-related visits K-L: 2&3 WOMAC: >301	Concomitant medical problems that prevent participation Prior surgery on one or both knees Surgery knee limb in prior 6 month(s) Pending surgery Concomitant or prior use of other meds Known allergy to chondroitin, glucosamine, celecoxib, sulphonamides, aspirin, lactose, NSAIDs, Allergy to shellfish, Intolerance to acetaminophen History of systemic diseases (heart attack or stroke, DM, hypertension, chronic liver/kidney diseases, infections); history of psychiatric disorders, alcohol/drug abuse Active malignancy or history of a malignancy within the past 5 years Concurrent arthritic disease, pain in other parts of the body, fibromyalgia	Arm 1: Celecoxib n = 282 Dose: 200mg Frequency: Once daily Duration: 6 months Method of Blinding: Matching capsules Arm 2: Glucosamine-chondroitin n = 286 Dose: 500 mg Glucosamine+400 mg Chondroitin Frequency: Three time daily Duration: 6 months	<u>% clinically significant on WOMAC pain:</u> Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , RR : 1.00 95% CI: (0.85, 1.17) <u>EuroQoL-5D mobility:</u> Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-0.00, 0.00) <u>EuroQoL-5D pain/discomfort:</u> Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (0.10, 0.10) <u>WOMAC function:</u> Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 21.20 95% CI: (-44.99, 87.39) Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : 71.50 95% CI: (NC, NC) <u>WOMAC pain:</u> Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-19.76, 21.96) Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : 25.00 95% CI: (NC, NC) <u>Clinically significant on WOMAC function:</u> Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , RR : 1.02 95% CI: (0.86, 1.21)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Hsieh, 2012⁶⁴</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Taiwan</p> <p>Health care setting: NR</p> <p>Single Site</p>	<p>Total n = 72</p> <p>Mean Age(SD): Mean: 60.3 (10.4)</p> <p>Arm 1, Mean Age: 61.3 (12) BMI: 26 (4.5)</p> <p>Arm 2, Mean Age: 61.1 (9.4) BMI: 26.4 (5.0)</p> <p>Female: 86%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: II+ in both knees, ACT</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>K-L: II+ in both knees</p> <p>ACR</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior Ever month(s)</p> <p>Pregnant or plan ning to become pregnant, and those who had a self-reported history of malignancy, vertigo, or stroke.</p>	<p>Arm 1: Sham monochromatic infrared energy (MIRE) n = 35 Placebo/Sham Dose: 40 minutes Frequency: 3 times a week Duration: 2 weeks Method of Blinding: Double-blind</p> <p>Arm 2: Monochromatic infrared energy (MIRE) n = 37 Dose: 40 minutes Frequency: 3 times a week Duration: 2 weeks Method of Blinding: Double-blind</p>	<p><u>KOOS pain:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-7.74, 4.34)</p> <p><u>KOOS quality of life:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-6.39, 6.59)</p> <p><u>OAQOL:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-2.70, 2.10)</p> <p><u>WHOQOL-BREF physical:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.80 95% CI: (-8.48, 4.88)</p> <p><u>WHOQOL-BREF psychological:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.40 95% CI: (-11.19, 2.39)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Imoto, 2012³⁹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Academic rheumatology clinic/department</p> <p>Single Site</p>	<p>Arm 1, Mean Age: 58.78 (9.60) BMI: 30.00 (5.05)</p> <p>Arm 2, Mean Age: 61.50 (6.94) BMI: 29.72 (4.11)</p> <p>Female: 92%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 26%, unilateral 74%</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 92% Grade II, 5% Grade III, 3% Grade IV, NRS pain 7.2</p> <p>Analgesic Use: Yes, Patients were allowed to continue their medications, but paracetamol, diacerein, and chloroquin were used</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 50</p> <p>Maximum Age: 75</p> <p>Knee pain</p> <p>Less than 30 minutes morning stiffness and crepitation in active movement and osteophytes</p> <p>ACR</p> <p>K-L: 2 or above in past 12 months</p>	<p>Physical therapy more than twice a week</p> <p>Inability to pedal a bike</p> <p>Unstable heart condition</p> <p>Fibromyalgia</p> <p>Prior knee arthroplasty</p>	<p>Arm 1: Control n = 50</p> <p>Placebo/Educational manual and 2 phone calls</p> <p>Dose: NA</p> <p>Frequency: NA</p> <p>Duration: 8 weeks</p> <p>Method of Blinding: NR</p> <p>Arm 2: Land-based strength training n = 50</p> <p>Dose: 30-40 minutes per session</p> <p>Frequency: two sessions per week</p> <p>Duration: 8 weeks</p> <p>Method of Blinding: NR</p> <p>Co-Intervention: Orientation manual</p>	<p><u>Numerical Rating Scale for pain:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.47 95% CI: (-2.71, -0.23)</p> <p><u>SF-36 functional capacity:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.83 95% CI: (-18.92, 3.26)</p> <p><u>SF-36 pain:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.98 95% CI: (-13.94, 7.98)</p> <p><u>SF-36 physical aspects:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -13.47 95% CI: (-33.97, 7.03)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.80 95% CI: (-2.97, -0.63)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Imoto, 2013 ⁶⁹	Total n = 100 Mean Age: 59.7 Arm 1, Mean Age: 58.8 (9.6) BMI: 30 (5) Arm 2, Mean Age: 60.6 (6.7) BMI: 30 (4) Female: 93% Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: bilateral 72% (96% for NMES group) Subtype: NR Diagnosis: K-L: 93% grade II, 4% grade III, 3% grade IV Analgesic Use: Yes, Patients' continued medications during intervention but paracetamol, diacerein, and chloroquine were prescribed	Diagnosis of osteoarthritis of the knee Minimum Age: 50 Maximum Age:75 ACR: NA K-L: Grade 2 or more in the prior 12 months	Use of pacemaker, unstable cardiac status, Attendance in a physical activity program more than twice a week Inability to ride a stationary bike, or to walk Previous arthroplasty	Arm 1: Control group n = 50 Placebo/Educational materials Dose: NA Frequency: NA Duration: 8 weeks Method of Blinding: NR Arm 2: NMES n = 50 Dose: 40 minutes per session Frequency: NR Duration: 8 weeks Method of Blinding: NR Co-Intervention: Educational guide	<u>Lequesne Index:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.81 95% CI: (-4.53, -1.09) <u>NRS:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.44 95% CI: (-2.65, -0.23) <u>TUG (s):</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.45 95% CI: (-3.42, -1.48)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Jones, 2012⁹⁷</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Academic rheumatology clinic/department</p> <p>Single Site</p>	<p>Total n = 64</p> <p>Arm 1, Mean Age: 62.56 (5.88) BMI: 29.54 (3.42)</p> <p>Arm 2, Mean Age: 61.75 (5.92) BMI: 29.01 (2.83)</p> <p>Living Situation: Community Dwelling</p> <p>Diagnosis: VAS 5.56/10, WOMAC 51.0/96</p> <p>Analgesic Use: Yes, Stable use of analgesics</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Stable doses of antiinflammatory drugs</p> <p>No regular physical exercise in the month before the study</p> <p>ACR: NA</p> <p>VAS: 3-7/10</p>	<p>Injected hyaluronic acid in the past or during the past 3 months month(s)</p> <p>Injected corticosteroids in the prior 3 months month(s)</p> <p>Physical Therapy or Rehab or exercise in the previous physical therapy in the previous 6 months or rehab in the previous 3 months month(s)</p> <p>Prior experience with the intervention of interest</p> <p>Symptomatic heart disease</p> <p>Symptomatic disease of the lower limbs (other than knee osteoarthritis) or upper limb that would secure the cane</p> <p>Symptomatic lung disease; severe systemic disease; severe psychiatric illness</p> <p>Regular physical exercise; (three or more times per week for at least 3 months)</p> <p>Inability to walk; geographic inaccessibility</p>	<p>Arm 1: Control n = 32 Duration: 2 months</p> <p>Arm 2: Braces or Canes n = 32 Dose: NA Frequency: NA Duration: 2 months Co-Intervention: usual therapy</p>	<p><u>6 min walk with cane (m):</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : 83.28 95% CI: (62.38, 104.18)</p> <p><u>6 min walk without cane (m):</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -6.50 95% CI: (-24.86, 11.86)</p> <p><u>Lequesne:</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -2.53 95% CI: (-4.34, -0.72)</p> <p><u>SF-36 bodily pain:</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -14.16 95% CI: (-24.30, -4.02)</p> <p><u>SF-36 physical function:</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -9.06 95% CI: (-17.81, -0.31)</p> <p><u>SF-36 role physical:</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -16.75 95% CI: (-31.69, -1.81)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -2.11 95% CI: (-2.83, -1.39)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -1.06 95% CI: (-8.87, 6.75)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Ju, 2015⁴⁷</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Korea</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 14</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 65.1 ± 2.9 BMI: Average weight: 60.6 ± 7.69 kg, average height 153.1 ± 4.5 cm and</p> <p>Arm 2, Mean Age: 65.7 ± 3.5 BMI: average weight of 64.7 ± 2.3 kg, height 152.4 ± 5.1 cm and an</p> <p>Female: 100%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes</p>	<p>Minimum Age: 60</p>	<p>Exclusion : NR</p>	<p>Arm 1: Control n = 7 Duration: NR</p> <p>Arm 2: Agility-type exercise n = 7 Dose: 20 minutes (3 sets of 10 repetitions per exercise) per session Frequency: 3 sessions per week Duration: 8 weeks</p>	<p><u>VAS pain:</u></p> <p>Follow-Up Time: 8 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -4.00 95% CI: (-5.32, -2.68)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Kahan, 2009³⁶</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: US, France, Belgium, Switzerland, Austria</p> <p>Health care setting: Hospital-outpatient</p> <p>Multiple Sites: 35</p>	<p>Total n = 622</p> <p>Age Range: 45-80</p> <p>Arm 1, Mean Age: 61.8(0.5) BMI: 28.8</p> <p>Arm 2, Mean Age: 62.9(0.5) BMI: 28.5</p> <p>Female: 68.5%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: Medial 100%</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes, Acetaminophen in 500-mg tablets (maximum dosage 4 gm/day); NSAIDs were allowed in cases of acute pain.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: 3 months</p> <p>Minimum Age: 45</p> <p>Maximum Age: 79</p> <p>ACR</p> <p>VAS: ≥ 30 mm</p> <p>JSW: ≥ 1 mm</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Concomitant or prior use of other meds</p> <p>Injected hyaluronic acid in the past or during the past 3 month(s)</p> <p>Injected corticosteroids in the prior 3 month(s)</p> <p>Prior acute injury to the knee</p> <p>K-L: 4</p> <p>Isolated lateral tibiofemoral OA; isolated patellofemoral OA</p> <p>A history or the active presence of other rheumatic diseases that could be responsible for secondary OA</p> <p>A history of hip OA or hip surgery</p>	<p>Arm 1: Placebo n = 313 Placebo/Sachet Frequency: Once daily</p> <p>Arm 2: Chondroitins sulfate n = 309 Dose: 800 mg Frequency: Once daily</p>	<p><u>VAS pain last 48 hours:</u></p> <p>Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : 0.50 95% CI: (-2.27, 3.27)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -4.00 95% CI: (-8.16, 0.16)</p> <p><u>WOMAC pain score last 48 hours:</u></p> <p>Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-6.16, 2.16)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-7.66, 0.66)</p> <p><u>Responder: reduction in pain score of at least 40% WOMAC:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.83 95% CI: (0.68, 1.02)</p> <p><u>Responder: reduction in pain score of at least 40mm:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.68 95% CI: (0.51, 0.91)</p> <p><u>Responder: reduction in pain score of at least 60mm:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.44 95% CI: (0.23, 0.85)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Knoop, 2013⁴⁶</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Netherlands</p> <p>Health care setting: Physical therapy outpatient clinic</p> <p>Single Site</p>	<p>Total n = 159</p> <p>Mean Age: 62</p> <p>Arm 1, Mean Age: 61.8 (6.6) BMI: 28.3(4.5)</p> <p>Arm 2, Mean Age: 62.1(7.6) BMI: 28.8(4.8)</p> <p>Female: 66% intervention; 56% control</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 75%, unilateral 25%</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 35% K-L: I; 28% K-L: II; 26% K-L: III; 12% K-L: IV</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 40</p> <p>Maximum Age: 75</p> <p>Ambulatory</p> <p>Self-reported or bio-assessed knee instability</p> <p>ACR: NA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Pending surgery</p> <p>Other diagnosed forms of arthritis</p> <p>Severe knee pain (NRS>8)</p> <p>Inability to comprehend Dutch, be scheduled for therapy or provide consent</p>	<p>Arm 1: Land-based exercise n = 79 Dose: 60 minutes per session Frequency: 2 sessions per week plus home exercises 5 days per week Duration: 12 weeks Method of Blinding: NR</p> <p>Arm 2: Agility type training n = 80 Dose: 60 minutes per session Frequency: 2 sessions per week plus home exercises 5 days per week Duration: 12 weeks Method of Blinding: NR</p>	<p><u>NRS:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.50 95% CI: (-1.16, 0.16)</p> <p>Follow-Up Time: 38 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.37, 0.17)</p> <p>Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-0.83, 0.43)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-0.16, 0.96)</p> <p>Follow-Up Time: 38 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-0.47, 0.67)</p> <p>Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-0.63, 0.83)</p> <p><u>WOMAC physical function:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-5.53, 1.73)</p> <p>Follow-Up Time: 38 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-4.49, 3.89)</p> <p>Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 4.10 95% CI: (0.62, 7.58)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Koca, 2009⁸⁶</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Turkey</p> <p>Health care setting: Physical therapy outpatient clinic</p> <p>Single Site</p>	<p>Total n = 37</p> <p>Total # of knees = 37</p> <p>Arm 1, Mean Age: 54.83 (9.27) BMI: 29.64</p> <p>Arm 2, Mean Age: 55.36 (11.50) BMI: 31.33</p> <p>Female: 100%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 2&3, ACR</p> <p>Analgesic Use: Yes, Paracetamol 1500 mg/day</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>K-L: 2&3</p> <p>ACR</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Injected hyaluronic acid in the past or during the past 6 month(s)</p> <p>Injected corticosteroids in the prior 6 month(s)</p> <p>Prior acute injury to the knee</p> <p>Physical Therapy or Rehab or exercise in the previous 12 month(s)</p> <p>Involvement of the lateral compartment of the knee</p> <p>Meniscopathy</p> <p>Infective or inflammatory pathologies of knee</p>	<p>Arm 1: Control n = 18 Dose: Paracetamol 1500 mg; quadriceps strengthening exercises Frequency: Paracetamol once daily; Duration: 3 months Co-Intervention: Paracetamol and exercise</p> <p>Arm 2: Insole n = 19 Dose: 6 mm wedge Frequency: All day long Duration: 3 months Co-Intervention: Paracetamol and exercise</p>	<p><u>VAS at rest:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -1.22 95% CI: (-2.89, 0.45)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -1.22 95% CI: (-2.89, 0.45)</p> <p><u>VAS at standing:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -0.93 95% CI: (-2.25, 0.39)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -0.93 95% CI: (-2.25, 0.39)</p> <p><u>VAS at walking:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -0.62 95% CI: (-2.01, 0.77)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -0.62 95% CI: (-2.01, 0.77)</p> <p><u>WOMAC function score:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -10.06 95% CI: (-19.68, -0.44)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -10.06 95% CI: (-19.68, -0.44)</p> <p><u>WOMAC pain score:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -3.14 95% CI: (-5.96, -0.32)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.14 95% CI: (-5.96, -0.32)</p> <p><u>WOMAC total:</u></p> <p>Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -15.16 95% CI: (-28.42, -1.90)</p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -17.68 95% CI: (-30.37, -4.99)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Kulich, 2014⁵⁹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Hungary</p> <p>Health care setting: Academic rheumatology clinic/department, mineral spa</p> <p>Single Site</p>	<p>Total n = 77</p> <p>Mean Age: 65.6</p> <p>Arm 1, Mean Age: 65.5(7.7) BMI: NR</p> <p>Arm 2, Mean Age: 65.6(6.4) BMI: NR</p> <p>Female: 78%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 100%</p> <p>Subtype: NR</p> <p>Diagnosis: Mild to moderate</p> <p>Analgesic Use: Yes, Any change in NSAID or chondroprotective therapy during the study was not allowed.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: at least 3 months</p> <p>Minimum Age: 45</p> <p>Maximum Age:75</p> <p>ACR: NA</p> <p>Radiographic imaging: NR</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 months month(s)</p> <p>Injected hyaluronic acid in the past or during the past 6 months month(s)</p> <p>Injected corticosteroids in the prior 1 month month(s)</p> <p>Prior acute injury to the knee</p> <p>Physical Therapy or Rehab or exercise in the previous month(s)</p> <p>Severe internal, rheumatic, urogenital, or skin diseases, radiculopathy</p> <p>Conditions for which warm baths were contraindicated</p> <p>Inflammatory rheumatic diseases</p> <p>Effusion</p> <p>Knee fracture or injury in prior 6 months or plate in knee, hip or spine surgery within previous year</p>	<p>Arm 1: Control n = 39 Dose: 30 minutes per session Frequency: 5 days per week Duration: 3 weeks</p> <p>Arm 2: Balneotherapy n = 38 Dose: 30 minutes per session Frequency: 5 days per week Duration: 3 weeks</p>	<p><u>VAS pain at rest:</u></p> <p>Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -16.00 95% CI: (-26.68, -5.32)</p> <p><u>VAS pain on exertion:</u></p> <p>Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -16.60 95% CI: (-25.79, -7.41)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.10 95% CI: (-15.82, -0.38)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-9.45, 4.65)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Laufer, 2014 ⁶⁷	Total n = 63 Study design: RCT Trial name: None Study Location: Israel Health care setting: Physical therapy outpatient clinic Single Site Female: 82.5% Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: NR Diagnosis: K-L: >=2 Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Duration of Symptoms: knee pain for atleast 3 months Minimum Age: 51 Ambulatory K-L: >=2	Concomitant medical problems that prevent participation Prior surgery on one or both knees Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 6 month(s) Physical Therapy or Rehab or exercise in the previous 3 month(s) Pacemaker or medical condition that could affect functional performance Injections to the knee joint during the previous six months Cardiovascular, neurological problems or other orthopedic problems Inability to follow instructions, difficulties with communication and cooperation or schedule inconvenient for them Medical conditions with contraindications for electrical stimulation	Arm 1: Control n = 25 Placebo/Control Dose: NA Frequency: NA Duration: NA Method of Blinding: The person conducting the exercise program was blinded to treatment allocation, blindness of the assessor was not maintained in the posttreatment and follow-up assessments Co-Intervention: Group exercise program delivered biweekly Arm 2: Neuromuscular electrical stimulation n = 25 Dose: Ten contractions were delivered at each session, at maximal tolerated intensity Frequency: Biweekly Duration: 6 weeks Method of Blinding: The person conducting the exercise program was blinded to treatment allocation, blindness of the assessor was not maintained in the posttreatment and follow-up assessments Co-Intervention: Group exercise program delivered biweekly	<u>TUG (s):</u> Follow-Up Time: 18 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-2.32, 1.92) Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-1.21, 1.61) <u>VAS pain:</u> Follow-Up Time: 18 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-3.25, -0.55) Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-2.70, -0.70) <u>WOMAC total:</u> Follow-Up Time: 18 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.70 95% CI: (-44.05, 14.65) Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -23.20 95% CI: (-43.20, -3.20)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Mahboob, 2009⁶⁰</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Iran</p> <p>Health care setting: Hospital-outpatient</p> <p>Single Site</p>	<p>Total n = 50</p> <p>Age Range: 44-79</p> <p>Arm 1, Mean Age: NR BMI: NR</p> <p>Arm 2, Mean Age: NR BMI: NR</p> <p>Female: 100%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Subtype: NR</p> <p>Diagnosis: ACR, severity not reported</p> <p>Analgesic Use: Yes, During the therapy program, if needed, patients were allowed to take paracetamol in a dose of less than 1500 mg per day (and drug use was assessed at followup).</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>ACR: not applicable</p>	<p>Prior surgery on one or both knees</p> <p>Injected hyaluronic acid in the past or during the past 6 months month(s)</p> <p>Injected corticosteroids in the prior 6 months month(s)</p> <p>Physical Therapy or Rehab or exercise in the previous 6 months month(s)</p> <p>Effusion</p> <p>Severe CVD and PVD</p>	<p>Arm 1: Placebo n = 25 Placebo/Placebo gel (lacking only mud) Dose: 20 minutes per treatment, each knee Frequency: once per day Duration: 30 days</p> <p>Arm 2: Mudpacks n = 25 Dose: 20 minutes per treatment, each knee Frequency: one treatment per day Duration: 30 days</p>	<p><u>WOMAC function:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -13.76 95% CI: (-31.63, 4.11)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.44 95% CI: (-11.34, 0.46)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Makovey, 2015¹¹¹</p> <p>Study design: Conference abstract</p> <p>Trial name: Healthy weight for life</p> <p>Study Location: NR</p> <p>Health care setting: Remotely delivered</p> <p>Site size: NR</p>	<p>Total n = 2175</p> <p>Total # of knees = NR</p> <p>Mean Age(SD): 64 (SD 8.6)</p> <p>Arm 1, Mean Age: 64 (SD 8.6) BMI: 34.4 (SD 5.2)</p> <p>Female: 71%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Analgesic Use: Yes</p>	Inclusion : NR	Exclusion : NR	<p>Arm 1: Weight loss n = 2175</p> <p>Dose: Phase 1 - motivational weight loss utilizing low calorie diet meal replacement, with controlled portions, and free foods for 6 weeks; phase 2 - consolidation weight loss for 6 weeks and phase 3 - short term weight maintenance</p> <p>Frequency: NR</p> <p>Duration: 18 weeks</p> <p>Method of Blinding: NA</p> <p>Co-Intervention: NR</p>	<p><u>SF-12 Mental Health Composite Score (PCS):</u></p> <p>Follow-Up Time: 18 weeks :</p> <p>Comparator: <2.5% weight change (post-pre) , MD : 3.58 95% CI: (1.8, 5.4)</p> <p>Comparator: 2.5-5% weight change (post-pre) , MD : 2.38 95% CI: (1.3, 3.5)</p> <p>Comparator: 5.1-7.5% weight change (post-pre) , MD : 5.11 95% CI: (4.2, 6.0)</p> <p>Comparator: 7.6-10% weight change (post-pre) , MD : 5.89 95% CI: (5.0, 6.8)</p> <p>Comparator: >10% weight change (post-pre) , MD : 6.66 95% CI: (5.8, 7.5)</p> <p><u>SF-12 Physical Health Composite Score (PCS):</u></p> <p>Follow-Up Time: 18 weeks :</p> <p>Comparator: <2.5% weight change (post-pre) , MD : 3.16 95% CI: (1.7, 4.6)</p> <p>Comparator: 2.5-5% weight change (post-pre) , MD : 4.07 95% CI: (3.2, 5.0)</p> <p>Comparator: 5.1-7.5% weight change (post-pre) , MD : 6.73 95% CI: (6.0, 7.4)</p> <p>Comparator: 7.6-10% weight change (post-pre) , MD : 6.65 95% CI: (5.8, 7.5)</p> <p>Comparator: >10% weight change (post-pre) , MD : 8.60 95% CI: (7.9, 9.3)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Messier, 2013 ¹⁰⁷	Total n = 454 Study design: RCT Trial name: IDEA Study Location: US Health care setting: Single Site Mean Age(SD): 66(6) Arm 1, Mean Age: 66(6) BMI: 33.6(3.7) Arm 2, Mean Age: 66(6) BMI: 33.7(3.8) Arm 3, Mean Age: 65(6) BMI: 33.6(3.7) Female: 72% Racial/Ethnic Distribution: Caucasian 81%, Nonwhite 19% Living Situation: Community Dwelling Location of OA: bilateral, unilateral Subtype: Patellofemora, Tibiofemoral Diagnosis: K-L: 2&3, Mild or moderate Analgesic Use: Yes, Patients were allowed to continue using any medications they were taking prior to the study,	Diagnosis of osteoarthritis of the knee: K-L: Minimum Age: 55 Ambulatory Able to sign Consent BMI 27-41 Pain on most days Sedentary lifestyle K-L: 2&3	Concomitant medical problems that prevent participation Prior surgery on one or both knees Knee or hip replacement Heart problems or cancer Injected knee medications Difficulty with ADLs, other knee-related activities >=21 drinks per week	Arm 1: Land-based Exercise n = 150 Placebo/Exercise Dose: 1 hour Frequency: 3 times per week Duration: 18 months Method of Blinding: NR Arm 2: Weight loss n = 152 Dose: 800-1000 calorie deficit per day Frequency: Not applicable Duration: 18 months Method of Blinding: NR Arm 3: Weight loss + land-based exercise n = 152 Dose: 1 hour exercise, 800-1000 calorie deficit Frequency: Exercise 3 times per week Duration: 18 months Method of Blinding: NR	<u>6 min walk (meter):</u> Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 23.00 95% CI: (3.15, 42.85) Comparator: Arm 3 vs Arm 1 , MD : -12.00 95% CI: (-33.93, 9.93) <u>SF-36 mental:</u> Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.50 95% CI: (-1.34, 2.34) Comparator: Arm 3 vs Arm 1 , MD : -0.70 95% CI: (-2.48, 1.08) <u>SF-36 physical:</u> Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-2.33, 2.33) Comparator: Arm 3 vs Arm 1 , MD : -2.70 95% CI: (-4.89, -0.51) <u>WOMAC function:</u> Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-2.67, 2.87) Comparator: Arm 3 vs Arm 1 , MD : -3.40 95% CI: (-6.02, -0.78) <u>WOMAC pain:</u> Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-0.31, 1.11) Comparator: Arm 3 vs Arm 1 , MD : -0.70 95% CI: (-1.41, 0.01) <u>Weight (kg):</u> Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : -6.00 95% CI: (-9.75, -2.25) Comparator: Arm 3 vs Arm 1 , MD : -8.10 95% CI: (-11.92, -4.28)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Miller, 2006 ¹⁰⁶	Total n = 87 Study design: RCT Trial name: None Study Location: US Health care setting: Academic exercise science department Single Site Living Situation: Community Dwelling Location of OA: NR Subtype: NR Diagnosis: Symptomatic knee OA Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Minimum Age: 60 BMI>=30 Self-reported difficulty in performing ADLs attributed to knee pain symptomatic knee OA	Unstable medical condition or condition whererapid weight loss or exercise contraindicated Unwillingness to modify diet or physical activity or inability to comply because of food allergy Excessive alcohol consumption	Arm 1: Control n = 43 Placebo/Educational sessions Dose: NA Frequency: two sessions per month Duration: 6 months Method of Blinding: NR Arm 2: Weight loss n = 44 Dose: 60 minutes per session Frequency: 1 session per week Duration: 6 months Method of Blinding: NR Co-Intervention: educational and behavioral sessions	<u>6 min walk (meter):</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -51.00 95% CI: (-96.03, -5.97) <u>BMI:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-4.48, -0.32) <u>WOMAC function:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -8.60 95% CI: (-13.50, -3.70) <u>WOMAC pain:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.25, -0.75) <u>WOMAC total:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -10.70 95% CI: (-17.01, -4.39) <u>Weight (kg):</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -9.10 95% CI: (-16.87, -1.33)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Mizusaki, 2013⁶⁸</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Academic rheumatology clinic/department</p> <p>Single Site</p>	<p>Total n = 100</p> <p>Mean Age: 61</p> <p>Arm 1, Mean Age: 61.50 ± 6.94 BMI: 29.72 ± 4.11</p> <p>Arm 2, Mean Age: 60.60 ± 6.72 BMI: 30.08 ± 3.80</p> <p>Female: 86%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 52%, unilateral 48%, NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L, ACR</p> <p>Analgesic Use: Yes, Patient medication was standardized and not modified during the study period. Paracetamol was prescribed for pain, and diacerein and chloroquine for OA control.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 50</p> <p>Maximum Age: 74</p> <p>K-L: >=2</p> <p>ACR</p>	<p>Physical Therapy or Rehab or exercise in the previous current month(s)</p> <p>Use of a pacemaker, unstable heart conditions</p> <p>Inability to exercise on a stationary bicycle ergometer, inability to walk</p> <p>Diagnosis of fibromyalgia, epilepsy, and skin tumor or lesion at the NMES application site</p> <p>Previous hip or knee arthroplasty</p>	<p>Arm 1: Exercise n = 50 Dose: 40 minutes per session Frequency: two sessions per week Duration: 8 weeks Co-Intervention: a manual including guidelines on how not to overload the knee during daily activities and instructions on the use of ice packs in case of pain and inflammation and warm compresses in case of pain without inflammation</p> <p>Arm 2: NMES n = 50 Dose: 40 minutes per session Frequency: two sessions per week Duration: 8 weeks Co-Intervention: Exercise and a manual including guidelines on how not to overload the knee during daily activities and instructions on the use of ice packs in case of pain and inflammation and warm compresses in case of pain without inflammation</p>	<p><u>NRS pain score:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.03 95% CI: (-1.12, 1.18)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.65 95% CI: (-1.25, -0.05)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.92 95% CI: (-9.14, 3.30)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.65 95% CI: (-2.39, 1.09)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Nam, 2014⁴⁴</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: NR</p> <p>Health care setting: Academic orthopedic surgery clinic/department</p> <p>Single Site</p>	<p>Total n = 30</p> <p>Total # of knees = NR</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 63.7 (SD 5.6)</p> <p>BMI: NR</p> <p>Arm 2, Mean Age: 64.9 (SD 6.8)</p> <p>BMI: NR</p> <p>Female: 60%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: > 2</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 61</p> <p>Able to sign Consent</p> <p>Not currently exercising</p> <p>Ability to understand the exercise</p> <p>K-L: >2</p>	<p>Prior surgery on one or both knees</p>	<p>Arm 1: Control n = 15</p> <p>Placebo/Control</p> <p>Dose: 3 1-min sets, with 1-min breaks between sets for each exercise</p> <p>Frequency: 3 times per week</p> <p>Duration: 6 weeks</p> <p>Method of Blinding: NR</p> <p>Co-Intervention: NR</p> <p>Arm 2: Land-based exercise: Strength/Other n = 15</p> <p>Dose: 3 times per week</p> <p>Frequency: 3 1-min sets, with 1-min breaks between sets for each exercise</p> <p>Duration: 6 weeks</p> <p>Method of Blinding: NR</p> <p>Co-Intervention: NR</p>	<p><u>WOMAC total:</u></p> <p>Follow-Up Time: 6 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -2.99 95% CI: (-5.48, -0.50)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Nelson, 2013 ²⁴	Total n = 34 Mean Age(SD): 55.5 (2.5) Active; 58.4 (2) Arm 1, Mean Age: 58.4 BMI: 34.7 Arm 2, Mean Age: 55.5 BMI: 33.5 Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: NR Analgesic Use: Yes, Unrestricted use of NSAIDs	Diagnosis of osteoarthritis of the knee Duration of Symptoms: 3 months >= 2 h of daily standing activity in a physical occupation Imaging study: Confirmed articular cartilage loss VAS: >=4	Concomitant medical problems that prevent participation Surgery knee limb in prior 6 month(s) Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 6 month(s) Implanted electronic devices On disability or with third party claims	Arm 1: Heat/ultrasound/diathermy n = 19 Placebo/Sham Dose: 15 minutes Frequency: Twice a day Duration: 6 weeks Method of Blinding: Double-blind Arm 2: Heat/ultrasound/diathermy n = 15 Dose: 15 minutes Frequency: Twice a day Duration: 6 weeks Method of Blinding: Double-blind	<u>VAS:</u> Follow-Up Time: 42 days : Comparator: Arm 2 vs Arm 1 , MD : -1.92 95% CI: (-2.35, -1.49)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Oliveira, 2012³⁸</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Academic rheumatology clinic/department</p> <p>Single Site</p>	<p>Total n = 100</p> <p>Mean Age: 60</p> <p>Arm 1, Mean Age: 58.78 (9.60) BMI: 30.00 ± 5.05</p> <p>Arm 2, Mean Age: 61.50 (6.94) BMI: 29.72 ± 4.11</p> <p>Female: 92%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: bilateral 25%, unilateral 75%</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: mean: 2</p> <p>Analgesic Use: Yes, The patients' medication was standardized and not modified during the study.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 50</p> <p>Maximum Age: 75</p> <p>K-L: >=2</p> <p>ACR: NA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Pacemaker use; unstable heart conditions</p> <p>Participation in another exercise program</p> <p>Inability to pedal a stationary bike; inability to walk</p> <p>Previous knee or hip arthroplasty</p> <p>Diagnosis of fibromyalgia; epilepsy; and presence of a tumor or cutaneous lesion that could interfere with the procedure</p>	<p>Arm 1: Control n = 50 Duration: 8 weeks</p> <p>Arm 2: Land-based exercise n = 50 Dose: NR Frequency: two sessions per week Duration: 8 weeks</p>	<p><u>Lequesne Index:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.98 95% CI: (-3.75, -0.21)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.61 95% CI: (-11.67, 0.45)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.77 95% CI: (-2.38, 0.84)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Palmer, 2014 ⁷³	Total n = 224 Age Range: >=18 Arm 1, Mean Age: 62 (9.4) BMI: 29.8 (7.4) Arm 2, Mean Age: 61.2 (11.4) BMI: 29.7 (11.1) Arm 3, Mean Age: 60.9 (10.8) BMI: 29.1 (9.0) Female: 37% Racial/Ethnic Distribution: NR Living Situation: NR Location of OA: NR Subtype: NR Diagnosis: ACR Analgesic Use: Yes	Diagnosis of osteoarthritis of the knee Minimum Age: >=18 ACR: 3 of 6 signs and symptoms	Concomitant medical problems that prevent participation Prior experience with the intervention of interest Contraindications to TENS	Arm 1: Exercise program n = 77 Placebo/Control Dose: 1 hour Frequency: Weekly Duration: 6 weeks Method of Blinding: Single-blinded Arm 2: TENS n = 73 Dose: As needed; 30 minutes instructional program Frequency: As needed Duration: 6 weeks Method of Blinding: Single-blinded Co-Intervention: Exercise program Arm 3: Sham TENS n = 74 Dose: As needed; 30 minutes instructional program Frequency: As needed Duration: 6 weeks Method of Blinding: Single-blinded Co-Intervention: Exercise program	<u>WOMAC function:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 3 , MD : 0.50 95% CI: (-4.16, 5.16) Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.30 95% CI: (-3.38, 5.98) <u>WOMAC pain:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.00 95% CI: (-0.92, 2.92) Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , MD : -2.00 95% CI: (-3.46, -0.54) <u>WOMAC total:</u> Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.00 95% CI: (-5.48, 7.48) Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.60 95% CI: (-4.76, 7.96) <u>Clinically significant on WOMAC function:</u> Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , RR : 1.25 95% CI: (0.82, 1.91) Comparator: Arm 3 vs Arm 1 , RR : 1.16 95% CI: (0.77, 1.73)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Park, 2013 ⁷⁶ Study design: RCT Trial name: None Study Location: Korea Health care setting: NR NR Single Site	Total n = 44 Arm 1, Mean Age: 60 (6.22) BMI: 24.8 (1.76) Arm 2, Mean Age: 62.5 (5.66) BMI: 25.3 (2.92) Female: 100 Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Subtype: NR Diagnosis: K-L: 2&3, ACR Analgesic Use: Yes, One control group patient took NSAIDs for a heart condition.	Diagnosis of osteoarthritis of the knee Duration of Symptoms: >= 6 months Minimum Age: >=40 ACR K-L: 2&3	Concomitant medical problems that prevent participation Surgery knee limb in prior 6 month(s) Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 6 month(s) No serious knee trauma in last six months No acute symptomatic OA, comorbidities such as any peripheral or central neuro logic disorders in last 6 months K-L IV	Arm 1: Home-based exercise (HBE) n = 19 Placebo/Control Dose: 10 repetitions of each exercise Frequency: Daily; 3 instructional sessions/week for 8 weeks Duration: 8 weeks Arm 2: Whole body vibration (WBV) n = 17 Dose: 20 minutes Frequency: 3 times a week Duration: 8 weeks	<u>NRS:</u> Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.77, -0.23) <u>WOMAC total:</u> Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -3.36 95% CI: (-10.01, 3.29)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Patel, 2013 ²³	Total n = 78	Diagnosis of osteoarthritis of the knee: ACR	Surgery knee limb in prior 12 month(s)	Arm 1: Control n = 23 Placebo/Normal saline injection Dose: 8 mL Frequency: Single injection	<u>VAS:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.45 95% CI: (-3.12, -1.78) Comparator: Arm 3 vs Arm 1 , MD : -2.07 95% CI: (-2.81, -1.33)
Study design: RCT	Total # of knees = 156		Injected hyaluronic acid in the past or during the past 3 month(s)		
Trial name: None	Age Range: 33-80	Ahlback grade: 1-2			
Study Location: India	Arm 1, Mean Age: 53.65 (8.17) BMI: 26.21 (2.93) Arm 2, Mean Age: 53.11 (11.55)		Injected corticosteroids in the prior 3 month(s)	Arm 2: Single PRP Injection n = 27 Dose: 8 mL Frequency: Single injection	<u>WOMAC function:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -19.38 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -17.06 95% CI: (NC, NC)
Health care setting: Academic orthopedic surgery clinic/department	BMI: 26.28 (3.23) Arm 3, Mean Age: 51.64 (9.22) BMI: 25.81 (3.31)		Secondary OA due to joint inflammatory diseases, Generalized OA, Advanced stages of OA	Co-Intervention: 1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP	Comparator: Arm 2 vs Arm 1 , MD : -19.38 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -17.06 95% CI: (NC, NC)
Single Site	Female: 70.7%		Metabolic diseases of the bone	Arm 3: 2 PRP Injections n = 25 Dose: 8 mL Frequency: 2 injections 3 weeks apart	Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -15.56 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -16.24 95% CI: (NC, NC)
	Racial/Ethnic Distribution: NR		Coexisting backache	Co-Intervention: 1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP	<u>WOMAC pain:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -5.87 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -4.69 95% CI: (NC, NC)
	Living Situation: NR		Receiving anticoagulant therapy		Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.22 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -5.10 95% CI: (NC, NC)
	Location of OA: bilateral 100%		Hemoglobin level less than 10 gm% or associated comorbidities, infection, tumor, crystal arthropathies, or tense joint effusion		<u>WOMAC total:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -25.91 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -22.61 95% CI: (NC, NC)
	Subtype: NR				Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -21.42 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : -21.82 95% CI: (NC, NC)
	Diagnosis: Ahlback grade 1-2, ACR				
	Analgesic Use: Yes, Paracetamol 500mg if discomfort				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Perlman, 2012¹⁰³</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: US</p> <p>Health care setting: Hospital-outpatient</p> <p>Multiple Sites: 2</p>	<p>Total n = 125</p> <p>Total # of knees = NR</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 63.6 (SD 10.2) BMI: 31.7 (SD 6.5)</p> <p>Arm 2, Mean Age: 69.9 (SD 8.6) BMI: 31.0 (SD 7.5)</p> <p>Arm 3, Mean Age: 61.9 (SD 9.5) BMI: 32.1 (SD 6.8)</p> <p>Arm 4, Mean Age: 62.6 (SD 10.6) BMI: 31.8 (SD 6.7)</p> <p>Arm 5, Mean Age: 63.6 (SD 13.0) BMI: 31.3 (SD 7.1)</p> <p>Female: 70.4%</p> <p>Racial/Ethnic Distribution: African American 11.2%, Asian 0.8%, Caucasian 84.8%, Hispanic 0.8%, 0.8% White/Asian, 1.6% Unknown</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: Met the ACR criteria for knee OA</p> <p>Analgesic Use: Yes, Subjects using NSAIDs or other medications to control pain were included if their doses remained stable 3 months prior to starting the intervention</p>	<p>Minimum Age: 35</p> <p>Pre-randomization score of 40-90 on the visual analog pain scale</p> <p>Subjects using NSAIDs or other medications to control pain were included if their doses remained stable 3 months prior to starting the intervention</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Concomitant or prior use of other meds</p> <p>Injected hyaluronic acid in the past or during the past 1-12 months prior to enrollment month(s)</p> <p>Injected corticosteroids in the prior 1-12 months prior to enrollment month(s)</p> <p>Rheumatoid arthritis, fibromyalgia, recurrent or active pseudogout, cancer, or other serious medical conditions</p> <p>A rash or open wound over the knee and regular use of massage therapy (greater than once a month)</p> <p>Signs or history of kidney or liver failure; unstable asthma; knee replacement of both knees; reported recent use (4 weeks–1 year prior to enrollment) of oral or intra-articular corticosteroids or intra-articular hyaluronate; or knee arthroscopy or significant knee injury one year prior to enrollment</p>	<p>Arm 1: Control (usual care) n = 25, Dose: NR, Frequency: NR, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR</p> <p>Arm 2: Massage n = 25, Dose: 30 minutes, Frequency: Once per week, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR</p> <p>Arm 3: Massage n = 25, Dose: 30 minutes, Frequency: 2 times per week for 4 weeks, followed by once per week for 4 weeks, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR</p> <p>Arm 4: Massage n = 25, Dose: 60 minutes, Frequency: Once per week, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR</p> <p>Arm 5: Massage n = 25, Dose: 60 minutes, Frequency: 2 times per week for 4 weeks, followed by once per week for 4 weeks, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR</p>	<p><u>VAS pain:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.90 95% CI: (-17.89, 12.09)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -2.50 95% CI: (-16.81, 11.81)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -7.00 95% CI: (-21.09, 7.09)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -11.30 95% CI: (-27.16, 4.56)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.40 95% CI: (-18.27, 9.47)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -16.30 95% CI: (-30.17, -2.43)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -30.00 95% CI: (-42.09, -17.91)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -21.40 95% CI: (-33.42, -9.38)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -11.10 95% CI: (-22.60, 0.40)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -3.20 95% CI: (-13.32, 6.92)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -7.90 95% CI: (-20.05, 4.25)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -10.20 95% CI: (-21.54, 1.14)</p> <p>Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -11.40 95% CI: (-20.90, -1.90)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -10.60 95% CI: (-21.76, 0.56)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -14.60 95% CI: (-24.50, -4.70)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -15.40 95% CI: (-26.48, -4.32)</p> <p><u>WOMAC global:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.30 95% CI: (-19.08, 2.48)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Perlman, 2012 ¹⁰³ -Continued					<p>Comparator: Arm 3 vs Arm 1 , MD : -1.00 95% CI: (-11.78, 9.78)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -8.20 95% CI: (-19.46, 3.06)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -9.10 95% CI: (-21.03, 2.83)</p> <p>Follow-Up Time: 8 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -11.10 95% CI: (-21.34, -0.86)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -12.10 95% CI: (-23.31, -0.89)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -17.70 95% CI: (-28.02, -7.38)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -17.70 95% CI: (-28.50, -6.90)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 24 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -4.70 95% CI: (-18.04, 8.64)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 3.60 95% CI: (-8.70, 15.90)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -6.20 95% CI: (-19.16, 6.76)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -6.70 95% CI: (-20.19, 6.79)</p> <p>Follow-Up Time: 8 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -9.50 95% CI: (-20.69, 1.69)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -8.80 95% CI: (-20.75, 3.15)</p> <p>Comparator: Arm 4 vs Arm 1 , MD : -21.60 95% CI: (-33.47, -9.73)</p> <p>Comparator: Arm 5 vs Arm 1 , MD : -22.10 95% CI: (-33.89, -10.31)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Rabini, 2015⁸⁰</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Italy</p> <p>Health care setting: Hospital-outpatient</p> <p>Single Site</p>	<p>Total n = 50</p> <p>Total # of knees = NR</p> <p>Mean Age(SD): 73.72 (SD 5.24) 75.08 (SD 5.74)</p> <p>Arm 1, Mean Age: 75.08 (SD 5.74)</p> <p>BMI: NR</p> <p>Arm 2, Mean Age: 73.72 (SD 5.24)</p> <p>BMI: NR</p> <p>Female: 78%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 2&3</p> <p>Analgesic Use: Yes, Allowed rescue dose the use of 3 g of paracetamol for a maximum of 2 consecutive days.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: chronic knee pain, for at least 3 months</p> <p>Minimum Age: 60</p> <p>Able to sign Consent</p> <p>K-L: 2&3</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior surgery on one or both knees</p> <p>Surgery knee limb in prior 24 month(s)</p> <p>BMI > 30 kg/m2</p> <p>Neurological diseases involving the lower limbs or causing balance problems, systemic inflammatory diseases; severe heart disease; acute infections or bone tuberculosis</p> <p>Arthroprosthesis of lower limbs</p> <p>History of surgery on the affected knee in the last two years</p> <p>Active cancer or anticancer treatment</p>	<p>Arm 1: Sham procedure n = 25</p> <p>Placebo/Sham procedure</p> <p>Dose: NR</p> <p>Frequency: 10 minutes</p> <p>Duration: NR</p> <p>Method of Blinding: Patients and the researcher responsible of the outcome assessments were unaware of patients' allocation</p> <p>Co-Intervention: Allowed rescue dose of 3g of paracetamol for a maximum of 2 consecutive days and the application of ice package</p> <p>Arm 2: Vibrating platform (whole body vibration) n = 25</p> <p>Dose: Frequency of 100 Hz and an amplitude of approximately 0.2-0.5 mm for 10 minutes</p> <p>Frequency: 3 doses per day, for 3 consecutive days</p> <p>Duration: NR</p> <p>Method of Blinding: patients and the researcher responsible of the outcome assessments were unaware of patients' allocation</p> <p>Co-Intervention: Allowed rescue dose of 3g of paracetamol for a maximum of 2 consecutive days and the application of ice package</p>	<p><u>WOMAC total:</u></p> <p>Follow-Up Time: 24 weeks :</p> <p>Comparator: Arm 2 vs Arm 1 , MD : -19.04 95% CI: (-27.43, -10.65)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Rayegani, 2014 ²⁵	Total n = 62 Study design: RCT Trial name: None Study Location: Iran Health care setting: Hospital-outpatient Single Site	Diagnosis of osteoarthritis of the knee: ACR Duration of Symptoms: 3 months K-L: 1-4	Concomitant or prior use of other meds Analgesics use in the previous 3 days month(s) Injected corticosteroids in the prior 3 weeks (systemic in prior 2 weeks) month(s) Prior acute injury to the knee Age > 75 Diabetes mellitus, immunosuppressive and collagen vascular disorders, history of vasovagal shock, history or presence of cancer or malignant disorders, infection or active wound of the knee, Autoimmune and platelet disorders, treatment with anticoagulant and anti-platelet medications 10 days before injection, Hb < 12 g/dL platelet counts < 150,000/mL Pregnancy or breastfeeding Genu valgum/varum greater than 20 degrees	Arm 1: Control n = 31 Method of Blinding: No blinding Co-Intervention: Exercise and acetaminophen 500 mg without codeine Arm 2: Platelet Rich Plasma n = 31 Dose: 4-6 mL Frequency: 2 doses 4 weeks apart Duration: 4 weeks Method of Blinding: No blinding Co-Intervention: Exercise and acetaminophen 500 mg without codeine Arm 3: n = Dose: Frequency: Duration: Method of Blinding: Co-Intervention:	<u>SF-36 mental health:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (NC, NC) <u>SF-36 physical health:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (NC, NC) <u>WOMAC function:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.17 95% CI: (-5.54, 5.88) <u>WOMAC pain:</u> Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.96 95% CI: (-2.88, 0.96)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Richette, 2011¹¹³</p> <p>Study design: Single arm trial</p> <p>Trial name: None</p> <p>Study Location: France</p> <p>Health care setting: Department of Nutrition, Center of Reference for Medical and Surgical Care of Obesity</p> <p>Single Site</p>	<p>Total n = 44</p> <p>Mean Age(SD): 44 (10.3)</p> <p>Arm 1, Mean Age: 44 (10.3) BMI: 50.7 (7.2)</p> <p>Female: 82%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 2-4</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: 1 month</p> <p>K-L: 2-4</p> <p>VAS: >= 30 mm</p>	<p>Concomitant medical problems that prevent participation</p> <p>Concomitant or prior use of other meds</p> <p>Injected hyaluronic acid in the past or during the past 6 month(s)</p> <p>Injected corticosteroids in the prior 1 month(s)</p> <p>K-L: stage 1</p> <p>Inflammatory joint disease, chondrocalcinosis of the knee</p> <p>Current use of symptomatic slow-acting drugs, viscosupplementation within the past 6 month</p>	<p>Arm 1: Bariatric surgery n = 44 Duration: 6 months</p>	<p>BMI:</p> <p>Follow-Up Time: 6 months : Comparator: pre-post , MD : 10.30 95% CI: (7.4, 13.2)</p> <p>VAS pain:</p> <p>Follow-Up Time: 6 months : Comparator: pre-post , MD : 25.50 95% CI: (15.5, 35.5)</p> <p>WOMAC function:</p> <p>Follow-Up Time: 6 months : Comparator: pre-post , MD : 371.30 95% CI: (219.6, 523.0)</p> <p>WOMAC pain:</p> <p>Follow-Up Time: 6 months : Comparator: pre-post , MD : 93.20 95% CI: (47.1, 139.3)</p> <p>WOMAC stiffness:</p> <p>Follow-Up Time: 6 months : Comparator: pre-post , MD : 31.80 95% CI: (11.7, 51.9)</p> <p>Weight (kg):</p> <p>Follow-Up Time: 6 months : Comparator: pre-post , MD : 28.60 95% CI: (19.4, 37.8)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Rodrigues, 2008 ⁸⁵	Total n = 30 Age Range: 45-86 Arm 1, Mean Age: 61.9 (11.3) BMI: 30.6 (3.1) Arm 2, Mean Age: 61.6 (11.4) BMI: 28.9 (3.5) Female: 100% Racial/Ethnic Distribution: Caucasian 50% Living Situation: NR Location of OA: bilateral 100% Subtype: Lateral 100% Diagnosis: K-L: 2-4 Analgesic Use: Yes, If prescribed at least 4 weeks and 8 weeks, respectively, before entry and remained unchanged throughout the study.	Diagnosis of osteoarthritis of the knee K-L: >=2 at lateral compartment K-L: 0&1 at medial compartment VAS on movement: >=2	Prior surgery on one or both knees Injected hyaluronic acid in the past or during the past 6 month(s) Injected corticosteroids in the prior 3 month(s) BMI>=40 Difference in lower limb length > _x0001_1 cm Hallux rigidus History of rheumatologic disease (rheumatoid arthritis, connective tissue disease, microcrystalline arthropathy, and seronegative arthropathy) Soft tissue involvement (anserine, patellar, and calcaneal tendinopathy); foot/lower leg symptoms	Arm 1: Control n = 14 Dose: 3– 6 hours daily Duration: 8 weeks Method of Blinding: Received new shoes with insoles Arm 2: Medial insole n = 16 Dose: 3– 6 hours daily Duration: 8 weeks Method of Blinding: Received new shoes with insoles	<u>Lequesne index:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-5.28, 0.48) <u>VAS movement:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.20 95% CI: (-4.04, -0.36) <u>VAS night:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-3.12, 0.12) <u>VAS rest:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.40 95% CI: (-2.16, 1.36) <u>WOMAC total:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -6.70 95% CI: (-17.09, 3.69) <u>Clinically significant on Lequesne index:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.79 95% CI: (0.59, 1.06)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Rogers, 2012 ⁴³	Total n = 33 Mean Age: 70 Arm 1, Mean Age: 71.2(10.9) BMI: 30.8 Arm 2, Mean Age: 70.7(10.7) BMI: 28.9 Arm 3, Mean Age: 70.8(6.5) BMI: 28.2 Arm 4, Mean Age: 68.8(10.1) BMI: 29.2 Female: 60% Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: bilateral 70%, unilateral 30% Subtype: NR Diagnosis: ACR Analgesic Use: Yes, All participants were advised to continue usual care as prescribed by their physicians, including any use of pain medication, but not to take up any lower extremity exercise program other than the prescribed intervention	Diagnosis of osteoarthritis of the knee Duration of Symptoms: >=1 month Minimum Age: 50 Ambulatory ACR: NA WOMAC function: >=17	Concomitant medical problems that prevent participation Prior surgery on one or both knees Injected hyaluronic acid in the past or during the past prior 4 weeks month(s) Injected corticosteroids in the prior prior 4 weeks month(s) Physical Therapy or Rehab or exercise in the previous 6 months month(s) Rheumaic disease other than OA Unresolved balance or neurological disorder Major knee trauma, hip or knee arthroplasty, hip or ankly instability or excessive weakness	Arm 1: Control n = 8 Duration: 8 weeks Co-Intervention: Application of intert skin lotion to knees once daily Arm 2: Agility-type exercise n = 8 Dose: 30-40 minutes Frequency: 3 times per week Duration: 8 weeks Co-Intervention: 30-second stic stretches per session Arm 3: Strength/resistance n = 8 Dose: 15 repetitions Frequency: 3 times per week Duration: 8 weeks Co-Intervention: 30-second stic stretches per session Arm 4: Agility- type plus strength/resistance n = 9 Dose: Comparable to individual intervention groups Frequency: 3 times per week Duration: 8 weeks	<u>WOMAC function:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.87 95% CI: (-13.22, 1.48) Comparator: Arm 3 vs Arm 1 , MD : -9.62 95% CI: (-19.04, -0.20) Comparator: Arm 4 vs Arm 1 , MD : -11.98 95% CI: (-19.15, -4.81) <u>WOMAC pain:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.13 95% CI: (-5.86, -0.40) Comparator: Arm 3 vs Arm 1 , MD : -3.75 95% CI: (-6.39, -1.11) Comparator: Arm 4 vs Arm 1 , MD : -3.00 95% CI: (-5.45, -0.55) <u>WOMAC total:</u> Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-19.79, 1.79) Comparator: Arm 3 vs Arm 1 , MD : -13.62 95% CI: (-26.37, -0.87) Comparator: Arm 4 vs Arm 1 , MD : -15.26 95% CI: (-25.16, -5.36)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Rosedale, 2014⁵²</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Health care setting: Academic physical therapy clinic/department</p> <p>Single Site</p>	<p>Total n = 158</p> <p>Mean Age: 65</p> <p>Arm 1, Mean Age: 64(11) BMI: 30.7(5.3)</p> <p>Arm 2, Mean Age: 64(9) BMI: 32(8.9)</p> <p>Arm 3, Mean Age: 68(10) BMI: 30.6(5.4)</p> <p>Female: 56%</p> <p>Living Situation: Community Dwelling</p> <p>Subtype: NR</p> <p>Diagnosis: Radiological confirmation, not otherwise described</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: > 4 months</p> <p>On knee replacement waiting lists</p> <p>radiologic: NR</p>	<p>Inability to attend exercise-based physiotherapy 2&3 times/week</p> <p>Neurological conditions affecting lower extremities</p> <p>Unable to understand English or provide informed consent</p>	<p>Arm 1: Control n = 59 Duration: NA</p> <p>Arm 2: Land-based exercise, generic n = 59 Dose: 20 minutes Frequency: 4-6 sessions per 2 weeks Duration: 2 weeks</p> <p>Arm 3: Land-based exercise, patient-tailored n = 40 Dose: 20 minutes Frequency: 4-6 sessions per 2 weeks Duration: 2 weeks</p>	<p><u>KOOS pain:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-15.28, -4.72)</p> <p><u>KOOS function:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-14.28, -3.72)</p> <p><u>P4 pain scale:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.00 95% CI: (-5.84, -0.16)</p> <p><u>Number with improvements in KOOS function score greater than MDC:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , RR : 0.71 95% CI: (0.39, 1.30)</p> <p><u>Number with improvements in KOOS pain score greater than MDC:</u></p> <p>Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , RR : 0.77 95% CI: (0.45, 1.33)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Sattari, 2011 ⁸⁴	Total n = 60	Diagnosis of osteoarthritis of the knee	Prior surgery on one or both knees	Arm 1: Control group n = 20 Placebo/Control with co-intervention (see below) Dose: NA Frequency: NA Duration: 9 months Method of Blinding: Evaluated by a blind examiner Co-Intervention: Conservative management included activity modification, heating agents at home, straight leg rising and isometric quadriceps home exercises and analgesics when needed	<u>VAS pain:</u> Follow-Up Time: 9 months : Comparator: Arm 2 vs Arm 1 , MD : -1.60 95% CI: (-2.31, -0.89) Comparator: Arm 3 vs Arm 1 , MD : -2.80 95% CI: (-3.58, -2.02)
Study design: RCT	Total # of knees = NR	Minimum Age: 35	Surgery knee limb in prior NR month(s)	Arm 2: Orthotics/orthoses/shoe inserts n = 20 Dose: all the time Frequency: all the time Duration: 9 months Method of Blinding: Evaluated by a blind examiner Co-Intervention: Conservative management included activity modification, heating agents at home, straight leg rising and isometric quadriceps home exercises and analgesics when needed	
Trial name: None	Mean Age: 48 years	Maximum Age:65	Whole knee degenerative joint disease	Arm 3: Knee brace n = 20 Dose: Wear it on and off every 2-3 hours for the first week and then put it on as long as possible during the day and take it off at nights Frequency: Daily Duration: 9 months Method of Blinding: Evaluated by a blind examiner Co-Intervention: Conservative management included activity modification, heating agents at home, straight leg rising and isometric quadriceps home exercises and analgesics when needed	
Study Location: Iran	Arm 1, Mean Age: NR BMI: NR	Genu varum based on radiographic evidence	Symptomatic patellofemoral pain syndrome		
Health care setting: Hospital-outpatient	Arm 2, Mean Age: NR BMI: NR	Complaint of knee pain	Heumatoid arthriti		
Multiple Sites: 3	Arm 3, Mean Age: NR BMI: NR	K-L: 3&4	BMI greater than 30		
	Female: 63%		Any superimposed hip or ankle problems		
	Racial/Ethnic Distribution: NR				
	Living Situation: NR				
	Location of OA: NR				
	Subtype: Medial 100%				
	Diagnosis: K-L: 3&4				
	Analgesic Use: Yes, When needed				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Sawitzke, 2010 ²⁷	Total n = 662	Diagnosis of osteoarthritis of the knee	Concomitant medical problems that prevent participation	Arm 1: Placebo n = 131 Placebo/Capsules Frequency: Once daily Duration: 24 months Method of Blinding: Double placebo	<u>WOMAC function:</u> Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : 9.56 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : 36.64 95% CI: (NC, NC) Comparator: Arm 4 vs Arm 1 , MD : 54.41 95% CI: (NC, NC) Comparator: Arm 5 vs Arm 1 , MD : -15.82 95% CI: (NC, NC)
Study design: RCT	Age Range: >=40	Duration of Symptoms: 6 months	Prior surgery on one or both knees	Arm 2: Glucosamine n = 134 Dose: 500 mg Frequency: 3 times daily Duration: 24 months Method of Blinding: Double dummy	<u>WOMAC pain:</u> Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : -4.84 95% CI: (NC, NC) Comparator: Arm 3 vs Arm 1 , MD : 11.50 95% CI: (NC, NC) Comparator: Arm 4 vs Arm 1 , MD : 1.04 95% CI: (NC, NC) Comparator: Arm 5 vs Arm 1 , MD : -13.54 95% CI: (NC, NC)
Trial name: GAIT	Arm 1, Mean Age: 56.9 (9.8) BMI: 25.5	Minimum Age: 40	Prior acute injury to the knee	Arm 3: Chondroitin n = 126 Dose: 400 mg Frequency: 3 times daily Duration: 24 months Method of Blinding: Double dummy	
Study Location: US	Arm 2, Mean Age: 56.7 (10.5) BMI: 27.6	K-L: 2&3	Predominant patellofemoral disease	Arm 4: Glucosamine and Chondroitin n = 129 Dose: 500mg and 400 mg Frequency: 3 times daily Duration: 24 months Method of Blinding: Double dummy	
Health care setting: NR	Arm 3, Mean Age: 56.3 (8.8) BMI: 30.2	WOMAC: 125 to 400 mm		Arm 5: Celecoxib n = 142 Dose: 200 mg Frequency: Once daily Duration: 24 months Method of Blinding: Double dummy	
Multiple Sites: 9	Arm 4, Mean Age: 56.7 (10.7) BMI: 27.1	American Rheumatism Association functional class: 1-3			
	Arm 5, Mean Age: 57.6 (10.6) BMI: 25.4				
	Female: 67.5%				
	Racial/Ethnic Distribution: NR				
	Living Situation: NR				
	Location of OA: NR				
	Subtype: Tibiofemoral 100%				
	Diagnosis: K-L: 2&3				
	Analgesic Use: Yes, <= 4000 mg of acetaminophen (Tylenol, McNeil) daily				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Simao, 2012⁷⁸</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Academic exercise physiology lab</p> <p>Single Site</p>	<p>Total n = 31</p> <p>Mean Age: 72</p> <p>Arm 1, Mean Age: 71(5.3) BMI: 26.7(2.4)</p> <p>Arm 2, Mean Age: 75(7.4) BMI: 27.4(9.7)</p> <p>Arm 3, Mean Age: 69(3.7) BMI: 29.8(2.53)</p> <p>Female: 86%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: most days of previous month</p> <p>Minimum Age: 60</p> <p>Osteophytes</p> <p>Synovial fluid typical of OA</p> <p>Crepitus</p> <p>Morning stiffness 30 minutes or less</p> <p>ACR: NA</p> <p>K-L: 2</p>	<p>Injected corticosteroids in the prior at least 2 months month(s)</p> <p>Prior acute injury to the knee</p> <p>Physical Therapy or Rehab or exercise in the previous 3 months month(s)</p> <p>Use of any assistive walking device</p> <p>The absence of the minimum clinical and cognitive conditions for performing physical activities</p> <p>Orthopedic disease; neurologic, respiratory, or acute cardiac issues that prevented the performance of the required exercises; vestibular disorders; immunosuppression or immunodeficiency; lack of sphincter control (anal and bladder); or cognitive deficits</p>	<p>Arm 1: Control n = 11 Dose: NA Frequency: NA Duration: NA</p> <p>Arm 2: Vibrating platform n = 10 Dose: NR Frequency: 3 sessions per week Duration: 12 weeks</p> <p>Arm 3: Strength training n = 10 Dose: NR Frequency: 3 sessions per week Duration: 12 weeks</p>	<p><u>6 min walk:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 3 , MD : -27.40 95% CI: (-84.05, 29.25)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 3 , MD : -122.50 95% CI: (-551.90, 306.90)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 3 , MD : 25.00 95% CI: (-93.83, 143.83)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Somers, 2012 ¹⁰⁹	Total n = 232	Diagnosis of osteoarthritis of the knee	Concomitant medical problems that prevent participation	Arm 1: Standard care n = 51	BMI:
Study design: RCT	Age Range: >=18	Duration of Symptoms: >=6 months	Concomitant or prior use of other meds	Placebo/Standard care Duration: 6 months Method of Blinding: Unblinded	Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-0.91, 0.51)
Trial name: OA Life	Arm 1, Mean Age: 57.94 (10.09) BMI: 34.1 (32.8–35.4)	Minimum Age: 18	Current use of exercise/weight loss program	Arm 2: Pain coping skills training (PCST) n = 60 Dose: 60 minutes per session Frequency: Weekly / biweekly (first/last 12 weeks) Duration: 6 months Method of Blinding: Unblinded	Comparator: Arm 3 vs Arm 1 , MD : -0.60 95% CI: (-1.24, 0.04)
Study Location: US	Arm 2, Mean Age: 58.13 (11.25) BMI: 34.4 (33.3–35.5)	No other joints affected by OA	Other arthritic disorder	Arm 3: Behavioral weight management (BWM) n = 59 Dose: 60 minutes per session + 3 90 minute exercise sessions per week for first 12 weeks Frequency: Weekly / biweekly (first/last 12 weeks) Duration: 6 months Method of Blinding: Unblinded	Comparator: Arm 4 vs Arm 1 , MD : -1.80 95% CI: (-2.44, -1.16)
Health care setting: NR	Arm 3, Mean Age: 58.27 (11.02) BMI: 33.5 (32.4–34.7)	BMI>=25, =<42		Arm 4: PCST + BWM n = 62 Dose: 120 minutes per session + 3 90 minutes exercise sessions per week Frequency: Weekly / biweekly (first/last 12 weeks) Duration: 6 months Method of Blinding: Unblinded Co-Intervention: PCST or BWM	WOMAC activity: Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-7.32, 2.72)
Single Site	Arm 4, Mean Age: 57.47 (9.43) BMI: 34.1 (33.0–35.2)	Provider considers OAK a condition that most contributes to limitations			Comparator: Arm 3 vs Arm 1 , MD : -1.50 95% CI: (-6.46, 3.46)
	Female: 79	Ability to read/speak English			Comparator: Arm 4 vs Arm 1 , MD : -12.40 95% CI: (-17.29, -7.51)
	Racial/Ethnic Distribution: 38% Nonwhite, 62% White	ACR			WOMAC pain: Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-8.80, 1.80)
	Living Situation: Community Dwelling	K-L: 1-4			Comparator: Arm 3 vs Arm 1 , MD : -2.50 95% CI: (-7.67, 2.67)
	Location of OA: NR				Comparator: Arm 4 vs Arm 1 , MD : -10.80 95% CI: (-15.77, -5.83)
	Subtype: NR				Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-8.80, 1.80)
	Diagnosis: K-L: 1-4, ACR				Comparator: Arm 3 vs Arm 1 , MD : -2.50 95% CI: (-7.67, 2.67)
	Analgesic Use: Yes				Comparator: Arm 4 vs Arm 1 , MD : -10.80 95% CI: (-15.77, -5.83)
					Weight (lbs): Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-3.59, 4.19)
					Comparator: Arm 3 vs Arm 1 , MD : -4.20 95% CI: (-7.95, -0.45)
					Comparator: Arm 4 vs Arm 1 , MD : -10.30 95% CI: (-13.92, -6.68)
					Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-3.59, 4.19)
					Comparator: Arm 3 vs Arm 1 , MD : -4.20 95% CI: (-7.95, -0.45)
					Comparator: Arm 4 vs Arm 1 , MD : -10.30 95% CI: (-13.92, -6.68)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Stambolova, 2015³²</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Bulgaria</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 191</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Analgesic Use: Yes</p>	<p>Inclusion : NR</p>	<p>Exclusion : NR</p>	<p>Arm 1: Placebo n = 98 Placebo/Not otherwise described Frequency: Placebo once daily + physiotherapy 30 days a year Duration: 3 years Co-Intervention: Physiotherapy</p> <p>Arm 2: Glucosamine n = 93 Dose: 1500 mg Frequency: GS once daily, 4 months a year; Physiotherapy 30 days a year Duration: 3 years Co-Intervention: Physiotherapy</p>	<p><u>Change in VAS pain:</u></p> <p>Follow-Up Time: 3 years : Comparator: Arm 2 vs Arm 1 , MD : -4.60 95% CI: (NC, NC)</p>
<p>Stefanik, 2015¹¹⁴</p> <p>Study design: Single arm trial</p> <p>Trial name: None</p> <p>Study Location: US</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 23</p> <p>Age Range: 25-60</p> <p>Arm 1, Mean Age: 45.7 (8.2) BMI: 41.6 (3.4)</p> <p>Female: 86%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Analgesic Use: Yes</p>	<p>Duration of Symptoms: Most days of the month</p> <p>Minimum Age: 25</p> <p>Maximum Age:59</p> <p>BMI >=35</p> <p>Approved for bariatric surgery</p>	<p>Exclusion : NR</p>	<p>Arm 1: Weight loss n = 23</p>	<p><u>VAS Pain:</u></p> <p>Follow-Up Time: post surgery : Comparator: pre-post , MD : 5.10 95% CI: (NC, NC)</p> <p><u>WOMAC Pain:</u></p> <p>Follow-Up Time: post surgery : Comparator: pre-post , MD : 27.80 95% CI: (NC, NC)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Toda, 2006 ²⁰	Total n = 61	Diagnosis of osteoarthritis of the knee	Surgery knee limb in prior month(s)	Arm 1: Traditional shoe insert n = 32	<u>Lequesne index:</u>
Study design: RCT	Age Range: 63.1-66.4	ACR	Injected corticosteroids in the prior 1 month(s)	Placebo/Traditional shoe inserts Duration: 6 months	Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-5.45, 0.85)
Trial name: None	Arm 1, Mean Age: 66.4 BMI: 25.00	Standing FTA: >176 degrees	Prior acute injury to the knee	Arm 2: Wedge strapped insole n = 29	Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-4.23, 1.23)
Study Location: Japan	Arm 2, Mean Age: 63.1 BMI: 24.58		Prior experience with the intervention of interest	Duration: 6 months	
Health care setting: Orthopedic Rheumatology Clinic	Female: 100%		Steinbrocker 4		
Single Site	Racial/Ethnic Distribution: Asian 100%		Greater or similar reduction in the lateral than the medial femorotibial joint space width		
	Living Situation: NR		Bilateral OA, hip OA, ankle OA		
	Location of OA: NR		Hallux rigidus, valgus deformity of the midfoot, other symptomatic deformities of the foot, advanced arthroplasty of the hindfoot		
	Subtype: Medial 100%				
	Diagnosis: ACR				
	Analgesic Use: Yes, Lornoxicam (NSAID) 4mg twice daily				

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Trombini-Souza, 2013⁹³</p> <p>Study design: Conference abstract</p> <p>Trial name: None</p> <p>Study Location: NR</p> <p>Health care setting: NR</p> <p>Site size: NR</p>	<p>Total n = 28</p> <p>Total # of knees = NR</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: NR BMI: NR</p> <p>Arm 2, Mean Age: NR BMI: NR</p> <p>Female: 100%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: K-L: 2&3</p> <p>Analgesic Use: Yes, Paracetamol was permitted, dose unclear</p>	<p>Diagnosis of osteoarthritis of the knee: K-L: 2&3</p>	<p>Physical therapy during the study duration</p>	<p>Arm 1: Control n = 12 Placebo/Control, did not wear similar shoes Dose: NR Frequency: NR Duration: 6 months Method of Blinding: NR Co-Intervention: NR</p> <p>Arm 2: Orthotics/orthoses/shoe inserts n = 16 Dose: NA Frequency: At least 6 hours daily Duration: 6 months Method of Blinding: NR Co-Intervention: NR</p>	<p><u>WOMAC function:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 37.00 95% CI: (NC, NC)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 44.00 95% CI: (NC, NC)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Trombini-Souza, 2015⁹⁴</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Brazil</p> <p>Health care setting: Academic rheumatology clinic/department, Physical Therapy Department</p> <p>Single Site</p>	<p>Total n = 56</p> <p>Age Range: 60-80</p> <p>Arm 1, Mean Age: 66 (4)</p> <p>Arm 2, Mean Age: 66 (5)</p> <p>Female: 100</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: Medial 100%</p> <p>Diagnosis: K-L: 2&3, ACR</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 60</p> <p>Maximum Age:79</p> <p>Ambulatory</p> <p>Able to sign Consent</p> <p>ACR</p> <p>K-L: 2&3</p> <p>VAS: 3-8</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 month(s)</p> <p>Concomitant or prior use of other meds</p> <p>Injected hyaluronic acid in the past or during the past 6 month(s)</p> <p>Injected corticosteroids in the prior 3 month(s)</p> <p>No leg length discrepancy greater than 1 cm</p> <p>Currently not using the Moleca® or similar shoes for more than 25 hours/week</p>	<p>Arm 1: Waitlist control n = 28 Placebo/Waitlist Duration: 6 months Method of Blinding: Unblinded</p> <p>Arm 2: Orthotic shoe n = 28 Dose: 6 hr/day Frequency: Daily Duration: 6 months Method of Blinding: Unblinded</p>	<p><u>6 min walk (meter):</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 11.00 95% CI: (-31.81, 9.81)</p> <p><u>Lequesne index:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -4.20 95% CI: (-6.29, -2.11)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -43.80 95% CI: (NC, NC)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -38.60 95% CI: (NC, NC)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Tsai, 2013³⁶</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: US</p> <p>Health care setting: NR</p> <p>Multiple Sites: 8</p>	<p>Total n = 55</p> <p>Age Range: >=60</p> <p>Arm 1, Mean Age: 78.93 (8.30) Arm 2, Mean Age: 78.89 (6.91)</p> <p>Female: 72.7%</p> <p>Racial/Ethnic Distribution: Caucasian 92.7%, 7.3% Other</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: A diagnosis of knee OA based on medical history reviewed with elders or family members/staff and confirmed by a health care provider</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 60</p> <p>Ambulatory</p> <p>Able to sign Consent</p> <p>Mild, moderate or subtle cognitive impairment</p> <p>Ability to speak English</p> <p>MD's/NP's permission to participate</p> <p>Verbal Descriptive Scale (VDS): >=2</p> <p>estern Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Score: 3+</p>	<p>Concomitant medical problems that prevent participation</p> <p>Surgery knee limb in prior 6 month(s)</p> <p>Physical Therapy or Rehab or exercise in the previous 1 month(s)</p> <p>Fractures in last 6 months</p> <p>Falls in last 3 months</p> <p>Vertigo in last month</p>	<p>Arm 1: Attention Control n = 27</p> <p>Placebo/Attention control</p> <p>Dose: 20-40 minutes (increasing over treatment period)</p> <p>Frequency: 3 sessions/week</p> <p>Duration: 20 weeks</p> <p>Method of Blinding: Unblinded</p> <p>Arm 2: Tai Chi n = 28</p> <p>Dose: 20-40 minutes (increasing over treatment period)</p> <p>Frequency: 3 sessions/week</p> <p>Duration: 20 weeks</p> <p>Method of Blinding: Unblinded</p>	<p><u>GUG:</u></p> <p>Follow-Up Time: 21 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.15 95% CI: (-0.07, 2.37)</p> <p>Follow-Up Time: 9 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.54 95% CI: (0.32, 2.76)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 21 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.58 95% CI: (-2.76, -0.40)</p> <p>Follow-Up Time: 9 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.14 95% CI: (-2.34, 0.06)</p> <p><u>WOMAC physical:</u></p> <p>Follow-Up Time: 21 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.52 95% CI: (-9.70, -1.34)</p> <p>Follow-Up Time: 9 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.54 95% CI: (-9.72, -1.36)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Wallace, 2006 ⁸⁹ Study design: RCT Trial name: None Study Location: US Health care setting: Academic sport science department Single Site	Total n = 39 Arm 1, Mean Age: 61.0 ± 9.2 BMI: 27.9 ± 4.2 Arm 2, Mean Age: 60.8 ± 9.8 BMI: 28.7 ± 3.7 Racial/Ethnic Distribution: NR Living Situation: Community Dwelling Location of OA: NR Subtype: Medial tibiofemoral 100% Diagnosis: K-L: mean 3.2 Analgesic Use: Yes, Subjects were allowed to continue all medications and other treatments as prescribed by their physicians, including over-the-counter or prescription nonsteroidal anti-inflammatory drugs (NSAIDs)	Diagnosis of osteoarthritis of the knee: physican diagnosis of medial tibiofemoral OA Minimum Age: 39 Radiographic medial knee narrowing Mild to moderage pain during walking Pain more than half the days of the month K-L: >=2	Prior experience with the intervention of interest Prior tibial osteotomy or total knee replacement Significant peripheral or central nervous system disease Clinically serious OA of the hip or ankle Requirement for an assistive device to walk	Arm 1: Orthotics n = 18 Dose: NA Frequency: NA Duration: 12 weeks Arm 2: Orthotics n = 18 Dose: NA Frequency: NA Duration: 12 weeks	<u>VAS pain during stair descent:</u> Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -19.60 95% CI: (-22.70, -16.50) <u>VAS pain while walking:</u> Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -15.10 95% CI: (-25.69, -4.51) <u>WOMAC function:</u> Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.39 95% CI: (-7.95, 3.17) <u>WOMAC pain:</u> Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.00 95% CI: (-10.56, 0.56)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Wang, 2015⁸¹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: China</p> <p>Health care setting: Academic rehabilitative medicine clinic/department</p> <p>Single Site</p>	<p>Total n = 99</p> <p>Arm 1, Mean Age: 61.5±9.1 BMI: 26.7± 1.5</p> <p>Arm 2, Mean Age: 61.2±9.6 BMI: 26.1 ± 1.2</p> <p>Female: 72%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Duration of Symptoms: at least 3 months</p> <p>Minimum Age: 40</p> <p>Maximum Age:65</p> <p>BMI≤30</p> <p>No previous knee surgeries</p> <p>ACR criteria: NA</p> <p>K-L: 2&3</p>	<p>Surgery knee limb in prior month(s)</p> <p>Any surgery in the preceding year</p> <p>Central nervous system disease, especially epilepsy and serious psychotic disorders</p> <p>History of arthritis (inflammatory or metabolic disease)</p> <p>Deep venous thrombosis in prior 24 weeks</p> <p>Severe heart or lung disease or advanced cancer</p>	<p>Arm 1: Strength/resistance training n = 50 Dose: 3 sets of 10 reps, 40 minutes per day Frequency: 5 days per week Duration: 24 weeks</p> <p>Arm 2: Whole body vibration n = 49 Dose: 30 minutes per day Frequency: 5 days per week Duration: 24 weeks Co-Intervention: quadriceps resistance exercise</p>	<p><u>6 min walk (meter):</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -77.07 95% CI: (-119.18, -34.96)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.14 95% CI: (-47.01, 40.73)</p> <p><u>Lequesne index:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.19 95% CI: (-2.30, -0.08)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.47 95% CI: (-1.59, 0.65)</p> <p><u>SF-36:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.88 95% CI: (-12.03, -5.73)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.89 95% CI: (-5.03, 1.25)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.01 95% CI: (-3.92, -2.10)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.26 95% CI: (-1.22, 0.70)</p> <p><u>VAS pain walking:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.71 95% CI: (-1.21, -0.21)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.50 95% CI: (-1.10, 0.10)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.63 95% CI: (-5.63, 0.37)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.21 95% CI: (-2.63, 3.05)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Wang, 2015 ⁸¹ -Continued					<p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.49 95% CI: (-3.53, -1.45)</p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.45 95% CI: (-1.40, 0.50)</p>
Wang, 2015 ⁷⁹ Study design: RCT Trial name: None Study Location: China Health care setting: Rehab medicine clinic Single Site	<p>Total n = 39</p> <p>Age Range: NR</p> <p>Arm 1, Mean Age: 61.5 (7.3) BMI: 26.2(2.7)</p> <p>Female: 59%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: Medial 100%</p> <p>Diagnosis: K-L: NR, ACR</p> <p>Analgesic Use: Yes</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 40</p> <p>Maximum Age:80</p> <p>Pain predominantly over medial knee</p> <p>Radial evidence of medial compartment KOA</p> <p>Medial joint space narrowing>lateral joint space narrowing</p> <p>Medial compartment osteophyte grade>lateral osteophyte grade</p> <p>K-L: >=2</p> <p>ACR</p>	<p>Concomitant medical problems that prevent participation</p> <p>Secondary or inflammatory KOA</p> <p>Ankle, hip, or foot disorders</p> <p>Chronic back pain</p> <p>Alzheimers, Parkinson's, moror neuron disorders, inability to understand procedure</p> <p>Diabetes mellitus, cardiac or respiratory insufficiency</p>	<p>Arm 1: Strength/resistance training n = 20 Dose: NR Frequency: 5 days per week Duration: 12 weeks</p> <p>Arm 2: Vibrating platform</p>	<p><u>6 min walk (meter):</u></p> <p>Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.40 95% CI: (-11.12, 4.32)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.30 95% CI: (-3.25, 0.65)</p> <p><u>VAS pain:</u></p> <p>Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.39, 0.19)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-4.78, 3.58)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (-2.17, 1.97)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Wortley, 2013⁴¹</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: US</p> <p>Health care setting: NR</p> <p>Single Site</p>	<p>Total n = 31</p> <p>Arm 1, Mean Age: 70.5 (5.0) BMI: 30.0(6.2)</p> <p>Arm 2, Mean Age: 69.5(6.7) BMI: 30.5(6.0)</p> <p>Arm 3, Mean Age: 68.1(5.3) BMI: 35.1(5.9)</p> <p>Female: 22/31</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: Community Dwelling</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: ACR</p> <p>Analgesic Use: Yes, Groups were asked not to alter their regular physical activity or pain medications during the intervention programs</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Minimum Age: 60</p> <p>Maximum Age:85</p> <p>ACR: NR</p> <p>K-L: 1-4</p>	<p>Injected hyaluronic acid in the past or during the past 3 month(s)</p> <p>Injected corticosteroids in the prior 3 month(s)</p> <p>Arthroscopic surgery within prior 3 months</p> <p>Participated in a resistance training or Tai Ji in the past 6 months</p> <p>Neurological disorders</p>	<p>Arm 1: Control n = 6 Placebo/No activity Dose: NA Frequency: NA Duration: 10 weeks</p> <p>Arm 2: Land-based exercise: strength/resistance n = 13 Dose: 5 or 10 lb. weight, 1 hour per session, two sets of eight repetitions to three sets of 12 repetitions during the first 6 weeks Frequency: 2 sessions per week Duration: 10 weeks</p> <p>Arm 3: Tai Chi n = 12 Dose: 1 hour per session Frequency: 2 sessions per week Duration: 10 weeks</p>	<p><u>6 min walk:</u></p> <p>Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : 33.40 95% CI: (-66.24, 133.04)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 75.60 95% CI: (-26.73, 177.93)</p> <p><u>TUG (s):</u></p> <p>Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.50 95% CI: (-0.85, 1.85)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 0.60 95% CI: (-0.91, 2.11)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -53.00 95% CI: (-397.56, 291.56)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : 5.00 95% CI: (-381.77, 391.77)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -86.00 95% CI: (-180.10, 8.10)</p> <p>Comparator: Arm 3 vs Arm 1 , MD : -16.00 95% CI: (-113.80, 81.80)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
<p>Yildirim, 2010⁶³</p> <p>Study design: RCT</p> <p>Trial name: None</p> <p>Study Location: Turkey</p> <p>Health care setting: Home home, Physical therapy outpatient clinic</p> <p>Site size: NR</p>	<p>Total n = 46</p> <p>Total # of knees = 80</p> <p>Age Range: 58.78</p> <p>Arm 1, Mean Age: 58.78 (SD 9.55) BMI: 29.24 (SD 3.33)</p> <p>Arm 2, Mean Age: 58.78 (SD 10.56) BMI: 30.67 (SD 5.37)</p> <p>Female: 84.8%</p> <p>Racial/Ethnic Distribution: NR</p> <p>Living Situation: NR</p> <p>Location of OA: NR</p> <p>Subtype: NR</p> <p>Diagnosis: Diagnosed with knee OA according to ACR criteria</p> <p>Analgesic Use: Yes, When recruited, patients underwent an outpatient pharmacological treatment such as NSAID and paracetamol. Patients were allowed to continue routine medication.</p>	<p>Diagnosis of osteoarthritis of the knee</p> <p>Able to sign Consent</p> <p>Literate</p> <p>ACR: Diagnosis of knee OA</p>	<p>Concomitant medical problems that prevent participation</p> <p>Prior acute injury to the knee</p> <p>Acute trauma or inflammation around the leg</p> <p>Cardiac pacemaker</p> <p>Sensitivity or allergy for heat</p> <p>Communication disorder or psychological problems</p> <p>Sensory complications, peripheral vascular diseases, tendency to haemorrhage, oedema on the knee, large scar tissue, malignancy, or deformity to attract the attention during examination or thigh OA</p>	<p>Arm 1: Control n = 23 Placebo/Control, received home visit 2 times Dose: NA Frequency: Visited 2 times Duration: 4 weeks Method of Blinding: NR Co-Intervention: Training guideline with equal information on OA, its effects and treatment based on the available literature</p> <p>Arm 2: Heat n = 23 Dose: 20 minutes Frequency: Visited 15 times Duration: 4 weeks Method of Blinding: NR Co-Intervention: Training guideline with equal information on OA, its effects and treatment based on the available literature</p>	<p><u>SF-36 pain:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 10.95 95% CI: (1.11, 20.79)</p> <p><u>SF-36 physical function:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 12.61 95% CI: (3.73, 21.49)</p> <p><u>WOMAC function:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -6.05 95% CI: (-9.65, -2.45)</p> <p><u>WOMAC pain:</u></p> <p>Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.85 95% CI: (-3.15, -0.55)</p>

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Zegels, 2013 ³⁵	Total n = 352 Study design: RCT Trial name: None Study Location: Belgium, France, Switzerland Health care setting: Hospital-outpatient Multiple Sites: 10	Diagnosis of osteoarthritis of the knee: ACR Minimum Age: 45 VAS: >=40mm Lequesne index: >=7	Concomitant medical problems that prevent participation Surgery knee limb in prior 3 month(s) Pending surgery Concomitant or prior use of other meds Injected hyaluronic acid in the past or during the past 6 month(s) Prior experience with the intervention of interest Genu varum or valgum >8 degrees Arthritis and metabolic arthropathies, Paget's illness Pregnancy	Arm 1: Placebo n = 117 Placebo/Matching sachets and capsules Frequency: Sachet once daily, capsule three times daily Duration: 3 months Method of Blinding: Double dummy Arm 2: Chondroitin n = 117 Dose: 1200 mg Frequency: Once daily Duration: 3 months Method of Blinding: Double dummy Arm 3: Chondroitin n = 119 Dose: 400 mg Frequency: 3 times daily Duration: 3 months Method of Blinding: Double dummy	<u>Lequesne function:</u> Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-3.11, -0.69) Comparator: Arm 3 vs Arm 1 , MD : -2.20 95% CI: (-3.37, -1.03) <u>VAS pain:</u> Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -7.70 95% CI: (-14.43, -0.97) Comparator: Arm 3 vs Arm 1 , MD : -8.30 95% CI: (-15.20, -1.40)

Study	Participants	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Relevant Outcomes Reported
Zhang, 2012 ¹⁰¹	Total n = 36	Diagnosis of osteoarthritis of the knee	Concomitant medical problems that prevent participation	Arm 1: Usual care n = 21	<u>WOMAC function:</u>
Study design: RCT	Age Range: 50-70	Duration of Symptoms: 6 months	Injected corticosteroids in the prior 2 month(s)	Placebo/Usual care Duration: 12 weeks Method of Blinding: Unblinded	Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.88 95% CI: (-10.58, 6.82)
Trial name: None	Arm 1, Mean Age: 59.86 (4.91) BMI: 28.46 (4.05)	Minimum Age: 50	Prior experience with the intervention of interest	Arm 2: Acupressure n = 15	Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.40 95% CI: (-12.56, 5.76)
Study Location: US	Arm 2, Mean Age: 63.47 (2.64) BMI: 28.89 (4.16)	Maximum Age:69	Knee or hip replacement	Dose: 30 minutes Frequency: 5 times a week; 2 training session and 1 conclusion session	<u>WOMAC pain:</u>
Health care setting: NR	Female: 100	Otherwise Healthy	Current treatment of acupuncture for knee pain	Duration: 12 weeks Method of Blinding: Unblinded	Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.08 95% CI: (-2.36, 2.52)
Site size: NR	Racial/Ethnic Distribution: NR	Able to sign Consent	Autoimmune dis ease that caused joint pain such as rheumatoid arthritis and lupus		Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.15 95% CI: (-3.45, 1.15)
	Living Situation: NR	Female	Severe unstable chronic illness or terminal dis ease		<u>WOMAC total:</u>
	Location of OA: NR	BMI<=35			Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.74 95% CI: (-15.65, 8.17)
	Subtype: NR	Health good to satisfactory			Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.51 95% CI: (-16.97, 5.95)
	Analgesic Use: Yes, Stable use in previous month	Pain in the knee in the preceding 2 weeks _3/10 on a Likert pain scale from 1–10,			
		Stable treatment with nonsteroidal anti inflammatory drugs and analgesics in the previous month, (9) if receiving glucosamine, a stable dose for the past 2 months,			
		Unspecified diagnosis of OAK			
		Mild/moderate symptoms of OAK: Most days last month			

Appendix D. Data Abstraction Tools

- 1. Data abstraction tool**
- 2. Modified Cochrane Risk of Bias tool**
- 3. Modified Newcastle-Ottawa Quality Assessment Scale**
- 4. McHarms Tool**

1. Data Abstraction Tool

Does this article report on additional outcomes or followup or post-hoc analysis of a study reported in a separate article?

- Yes (specify ID or reference)
- No

[Clear Response](#)

If this is a follow-up to a study reported in another article, then what is the follow-up time for this article?
[Please do not state the follow-up time for the original article]

If this is part of a named trial or study, please specify the name?

- CAROT
- GAIT
- IDEA
- OAI
- LEGS
- OA Life
- impact-p
- Healthy weight for life
- LIGHT
- Osteoarthritis Chronic CAre Program (OACCP)
- MOVES
- Osteoarthritis of the Knee Self- Management Program
- Osteoarthritis Before and After Bariatric Surgery (OABS) Study
- Physical Activity, Inflammation, and Body Composition Trial

[Permanently add an answer to this question](#)

Do you need another article to complete this form?

- Yes (stop until Aneesa links the article; specify reference number)
- No

[Clear Response](#)

Study Design

- Systematic review or meta-analysis (skip to intervention) **(STOP)**
- Randomized controlled
- Weight loss single arm trial
- Observational cohort or case series for weight loss, self-managed care, or adverse events
- Single arm trial NOT for weight loss **(STOP)**
- Conference abstract
- Controlled Clinical Trial **(STOP)**

[Clear Response](#)

Location(s):

- Canada
- China
- Germany
- Iran
- Korea
- Russia
- Turkey
- USA

- Not Reported
- Other (specify)

Health care Setting:

- Academic orthopedic surgery clinic/department
- Academic rheumatology clinic/department
- Aquatic center
- Gym-self managed
- Home
- Home-pool
- Hospital-inpatient
- Hospital-outpatient
- Physical therapy outpatient clinic
- Primary care practice
- Rehab/skilled nursing facility
- Other
- Not Reported

Is this a single center or multicenter study?

- Single center
- Multicenter study [speciy how many sites]
- NR

[Clear Response](#)

Participants (living situation):

- Community dwelling
 - Institutionalized
 - Hospitalized
 - Rehab-inpatient
 - Not Reported
-

Participants (race/ethnicity):

Average the number and put % after
For other, please indicate as "20% Korean"

- % African American
 - % Asian
 - % Caucasian
 - % Hispanic
 - % Latino
 - Other 1 (specify race and %)
 - Other 2 (specify race and %)
 - Other 3 (specify race and %)
 - Other 4 (specify race and %)
 - Other 5 (specify race and %)
 - NR
-

Participants:

Average the number and put % after

- Age range: ___ to ___ (specify range)
- Number of participants enrolled (specify number)
- Number of knees if analyzed that way (specify)

% female (specify %)

Location of OA [if % specified, record]:

Bilateral knee OA [specify %, if given]

Unilateral knee OA [specify %, if given]

Not reported

Subtype location [if % specified, record]

Medial [specify %, if given]

Lateral [specify %, if given]

Patellofemoral [specify %, if given]

Tibiofemoral [specify %, if given]

Other (specify type and %)

Not Reported

Diagnosis

Kellgren-Lawrence stages, (specify number: e.g., III-IV)

Other severity measure (e.g., mild-to-moderate)

Other criteria (e.g., ACR)

Were participants allowed to continue use of analgesics?

Yes

No

NR

[Clear Response](#)

Inclusion criteria for participation in the study:

- Diagnosis of osteoarthritis of the knee (specify diagnostic modality and cutoff scores, if relevant)
- Duration of symptoms
- Age \geq ___ (specify inclusion of age)
- Age $<$ ___ (specify inclusion of age)
- Ambulatory
- Otherwise healthy
- Able to sign consent/no mental or cognitive problems
- Other 1 (specify)
- Other 2 (specify)
- Other 3 (specify)
- Other 4 (specify)
- Other 5 (specify)
- Not Reported

Exclusion criteria for the study:

- Concomitant medical problems that prevent participation
- Prior surgery on one or both knees
- Surgery on the knee/limb in the prior ___ months (specify how many months)
- Pending surgery on the knee
- Concomitant or prior use of other medication
- Injected hyaluronic acid in the past or during the past ___ months (specify how many months)
- Analgesic use in the previous ___ months (specify how many months)
- Injected corticosteroids in the prior ___ months (specify how many months)

- Prior acute injury to knee
 - Continued use of analgesics
 - Physical therapy or rehab or exercise in the previous ___ months (specify how many months)
 - Prior experience with the intervention of interest
 - Other 1 (specify)
 - Other 2 (specify)
 - Other 3 (specify)
 - Other 4 (specify)
 - Other 5 (specify)
 - Not Reported
-

Arms

How many arms are there?

- 1
- 2
- 3
- 4
- 5
- 6

Funding:

- Government
- Private foundation
- Manufacturer
- Other funding (specify)



NR

Did the authors have any conflict of interest?



The article reported that some or all of the authors had conflict of interest (such as employment by, or consultation for, the manufacturer of the intervention)



The article stated that authors had no conflict of interest



The article did not mention author conflict of interest

[Clear Response](#)

2. Modified Cochrane Risk of Bias tool

Cochrane Risk of Bias Tool

Selection Bias

1. Was the allocation sequence adequately generated (e.g., rand number table, computer-generated randomization)

There is a LOW RISK OF BIAS if the investigators describe a random component in the sequence generation process such as: referring to a random number table, using a computer random number generator, coin tossing, shuffling cards or envelopes, throwing dice, drawing of lots. There is a HIGH RISK OF BIAS if the investigators describe a non-random component in the sequence generation process, such as: sequence generated by odd or even date of birth, date (or day) of admission, hospital or clinic record number; or allocation by judgement of the clinician, preference of the participant, results of a laboratory test or a series of tests, or availability of the intervention. IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- Low risk (yes)
- High risk (no)
- Unclear

[Clear Response](#)

High risk notes



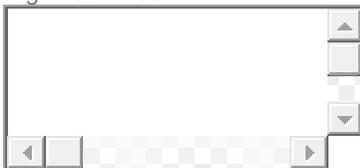
2. Was ALLOCATION adequately concealed (prior to assignment)?

There is a LOW RISK OF BIAS if the participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance; or sequentially numbered, opaque, sealed envelopes. There is a HIGH RISK OF BIAS if participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; or other explicitly unconcealed procedures. IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- Low risk
- High risk
- Unclear

[Clear Response](#)

High risk notes



Performance bias

3. Were PARTICIPANTS or THE HEALTH CARE PROVIDER who administered the intervention adequately BLINDED?

There is a LOW RISK OF BIAS if blinding of participants was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.

- Low risk
- High risk
- Unclear

[Clear Response](#)

High risk notes



Detection Bias

4. Were OUTCOME ASSESSORS adequately BLINDED?

There is LOW RISK OF BIAS if the blinding of the outcome assessment was ensured and it was unlikely that the blinding could have been broken; or if there was no or incomplete blinding, but the outcome is unlikely to be influenced by lack of blinding (ie, lab tests--lipids--inherently low risk of bias, but not blood pressure).

- Low risk
- High risk
- Unclear

[Clear Response](#)

High risk notes



Attrition bias

5. Incomplete outcome data (ATTRITION BIAS) due to amount, nature or handling of incomplete outcome data

There is a LOW RISK OF BIAS if there were no missing outcome data; reasons for missing outcome data were unlikely to be related to the true outcome; missing outcome data were balanced in numbers, with similar reasons for missing data across groups (****The percentage of withdrawals and drop-outs should not exceed 20% for short-term follow-up [≤ 1 year] and 30% for long-term follow-up [> 1 year]****). IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- Low risk
- High risk
- Unclear

[Clear Response](#)

High risk notes

Reporting bias

6. Is there evidence of **SELECTIVE OUTCOME REPORTING** bias?

Were the potential outcomes prespecified by the researchers? Are all prespecified outcomes reported? The authors can refer to a published protocol or to another study. Select high risk if they list outcomes for which they report no data, do not refer to another article for that outcome, or don't mention a published (posted) protocol, OR if they say they used something like the WOMAC but report only the outcome for, say, pain or function.

- Low risk
- High risk
- Unclear

[Clear Response](#)

Notes

Other bias

7. INTENTION-TO-TREAT analysis? (Yes/No)

YES if they state ITT and methods used were actually ITT, or ****all**** participants were analyzed in the group to which they were allocated by randomization (no cross-over). IF NO ITT, EXPLAIN IN NOTES.

- Yes
- No
- Unclear

[Clear Response](#)

Notes

8. Group **SIMILARITY AT BASELINE** (****GENERAL****)

There is **LOW RISK OF BIAS** if groups are similar at baseline for demographic and other factors (e.g, BMI, baseline pain). Also **LOW** risk of bias if any baseline differences were adjusted for in all relevant analyses. IF **HIGH RISK OF BIAS**, EXPLAIN IN NOTES.

- Low risk
- High risk

- Unclear

[Clear Response](#)

Notes



9. Was there incomplete adherence/COMPLIANCE with interventions across groups?

There is LOW RISK OF BIAS if compliance with the interventions was acceptable ($\geq 80\%$ across intervention duration), based on the reported actual compliance compared to protocol or increased biomarker levels were reported during or at the end of the intervention. There is HIGH RISK OF BIAS if compliance was low ($< 80\%$). There is UNCLEAR RISK OF BIAS if these data were not reported.

- Low risk
- High risk
- Unclear

[Clear Response](#)

Notes



10. Additional Bias: Did authors report a power calculation and did they achieve adequate n?

- Yes
- No

3. Modified Newcastle-Ottawa Quality Assessment Scale

Selection

1) Representativeness of the exposed cohort

- a) truly representative of the average pregnant women and children in the community
- b) somewhat representative of the average pregnant women and children in the community
- c) selected group of users eg nurses, volunteers
- d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

- a) drawn from the same community as the exposed cohort
- b) drawn from a different source
- c) no description of the derivation of the non exposed cohort
- d) N/A

3) Ascertainment of exposure

- a) secure record (eg surgical records)
- b) structured interview
- c) written self report
- d) no description

4) Demonstration that outcome of interest was not present at start of study (if relevant, which will almost never be the case) or author's statement that a valid outcome measure was chosen.

- a) yes
- b) no

[Clear Response](#)

Comparability

1) Comparability of cohorts on the basis of the design or analysis

If the authors describe factors for which they adjusted or noted that cohorts were matched on important factors and listed the factors, count that as a "yes."

- a) study controls for _____ (select the most important factor)
- b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

- a) independent blind assessment
- b) record linkage
- c) self report
- d) no description

2) Was follow-up long enough for outcomes to occur (e.g., 5 years or older for asthma; for other outcomes, if the authors say why they chose a particular followup time, definitely select "yes"; otherwise use your own judgment.

- a) yes (select an adequate follow up period for outcome of interest)
- b) no

[Clear Response](#)

3) Adequacy of follow up of cohorts

- a) complete follow up - all subjects accounted for
- b) subjects lost to follow up unlikely to introduce bias - >80% retention for ≤ 1 year followup; >30% retention for 1-5 years followup; >40% retention for 6-10 years followup; >50% retention for 11-18 years followup; or description provided of those lost)
- c) follow up rate < 80% (select an adequate %) and no description of those lost
- d) no statement

4. McHarms Tool

1. Were the harms PRE-DEFINED using standardized or precise definitions?

Harms can be defined as the totality of adverse consequences of an intervention or therapy. Harms are the opposite of benefits, against which they are directly compared. The balance between the benefit(s) and harm(s) of an intervention (i.e. drug or surgery) is ideally used to determine its efficacy or effectiveness.

Pre-defined indicates that the harms that were expected are explicitly defined prior to the collection of these expected events. For example, if bleeding is listed as a harmful event, the criteria by which they determine the bleeding (i.e. body location, type, or amount of blood loss that counts as an event, etc) should be specified.

Standardized classification of harms can be derived from any of the following:

- 1) reference to standard terminology or classifications of harms from a recognized external organization(s)(such as government regulatory or health agencies. Examples of standardized terminology for harms includes, WHO-ART, MEDra, HTA report on the Measurement and Monitoring of Surgical Adverse Events)
- 2) previously explicitly defined classifications of harms in the literature, or
- 3) based on pre-specified clinical criteria, or
- 4) pre-specified laboratory test (may not need to have a specific cut-off level specified in all cases)

In some instances only some of the harms identified in a study will be precisely defined. In this case, there must be some judgement.

- Yes
- No
- Unclear

[Clear Response](#)

2. Was the mode of harms collection specified as ACTIVE?

Active ascertainment of harms indicates that participants are asked about the occurrence of specific harms in structured questionnaires or interviews or pre-defined laboratory or diagnostic tests and usually performed at pre-specified time intervals.

Passive ascertainment of harms indicates that study participants spontaneously report (on their own initiatives) or are allowed to report harmful events not probed with active ascertainment.

- Yes
- No
- Unclear

[Clear Response](#)

3. Was the potential occurrence of harmful events collected at pre-specified intervals; for example, the occurrence of post-operative complications were evaluated on a daily basis within 30 days of the surgery?

- Yes
- No

Unclear

[Clear Response](#)

4. Did the author(s) specify the NUMBER for each TYPE of harmful event for each study group?

For example, the study reported 3 types of harmful events (nausea, vomiting, and bleeding); for each of these events the frequency was reported for each study group.

Yes

No

Unclear

[Clear Response](#)

5. Was the TOTAL NUMBER of participants affected by harms specified for each study arm?

Yes

No

Unclear

[Clear Response](#)

6. If the study reported that there were no serious AE's reported did they define serious AEs?

Yes

No

Unclear

N/A

[Clear Response](#)

Appendix E. Strength of Evidence

Table E1: Strength of Evidence

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
KQ 1 Platelet-rich plasma							
Short-term pain (KOOS, WOMAC)	2 RCTs	Single or dual injections vs. saline: MD -5.22 Single injection PRP vs. paracetamol: no difference	6/10, 2/10	Inconsistent	Direct	imprecise	Insufficient evidence
Short-term function	1 RCT	Single or dual injections vs. saline: MD -15.56	6/10	NA	Direct	Not reported	Insufficient evidence
Short-term WOMAC total	1 RCT	Single or dual injections vs. saline: MD -21.42	6/10	NA	Direct	Not reported	Insufficient evidence
Medium-term pain	2 RCTs	Single injection: MD-2.45(-3.12, -1.78), MD -14.00 (11.56, -16.44) Multiple injections vs. saline: MD -2.07 (2.81, -1.33), MD-23.40 (-19.66, -27.14)	6/10, 8/10	Consistent	Direct	Precise	Low for a positive effect of PRP on medium term pain
	1 RCT	Dual injections vs. TAU: no differences	3/10	NA	Direct	Precise	Insufficient evidence
	1 RCT	Single injection vs. paracetamol KOOS pain significantly improved (p=0.0008)	2/10	NA	Direct	imprecise	Insufficient evidence
Medium-term function	1 RCT	Injection vs. saline: MD -19.38	6/10	NA	Direct	Not reported	Insufficient evidence
	1 RCT	Injection vs. TAU: no differences	3/10	NA	Direct		
Medium term WOMAC total	1 RCT	Single or dual injections vs. saline: MD -25.91, -22.61	6/10	NA	Direct	Not reported	Low for a positive effect of PRP on global quality of life and functioning measures
Medium term SF-36 physical domain	1 RCT	Injection vs. TAU MD -1.00	3/10	NA	Direct	Not reported	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
Medium term EQ-5d	1 RCT	1 injection vs. saline: MD -14.00 (-16.44, -11.56) 3 injections: -23.40, (-27.14, -19.66)	8/10	NA	Direct	Precise	
Long-term pain	0						Insufficient evidence
Long-term function	0						Insufficient evidence
Long-term other	0						Insufficient evidence
Glucosamine plus chondroitin							
Medium term pain	2 RCTs		3,8/10	Consistent	Direct	Precise	Low for an effect of glucosamine-chondroitin on medium-term pain(2 studies: one head to head and one open)
	1 RCT (n=603)	WOMAC, VAS: no difference glucosamine sulfate-chondroitin celecoxib in non-inferiority trial and response met MCID	8/10	N/A	Direct	Precise	
		WOMAC MD -1.59(-2.31, -0.87); VAS MD-2.08 (-2.40, -1.76)	3/10	N/A	Direct	Precise	
Medium term function	2 RCTs		3,8/10	Consistent	Direct	Precise	Low for an effect of glucosamine-chondroitin on medium term function
	1 RCT (n=603)	WOMAC function: no difference from celecoxib control (both achieved MCII)	8/10	N/A	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
	1 RCT	WOMAC function Lequesne function MD -3.86(-6.16, -1.56) and Lequesne (MD -2.56(-3.35, -1.77))	3/10		Direct	Precise	
Medium-term other outcomes	2 RCTs		3, 8/10	Consistent	Direct	N/R	Low for an effect of glucosamine-chondroitin on medium-term WOMAC stiffness
	1 RCT (n=603)	No difference in WOMAC stiffness or EQ-5D from celecoxib control	8/10	N/A			
		Significant improvement in WOMAC stiffness cf controls	3/10	N/A	Direct	Precise	
Long-term pain	3 RCTs		3, 10, 10/10	Inconsistent	Direct	Precise	Low for no effect of glucosamine-sulfate on long-term pain
		GAIT Trial 12 months (n=) WOMAC pain did not differ between glucosamine-chondroitin and celecoxib: improvement not sustained	10/10	N/A	Direct	Precise	
		WOMAC pain MD -3.10 (-3.69, -2.51); VAS pain MD -1.70 (-1.99, -1.41) compared with control	3/10	N/A	Direct	Precise	
		LEGS trial (n=605)	10/10	N/A	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		no effect of glucosamine-sulfate and chondroitin on pain at 1 and 2 years					
Long-term function	3 RCTs		3, 10, 10/10	Inconsistent	Direct	Precise	Low for no effect of glucosamine on long-term function
	1 RCT	GAIT Trial: WOMAC function did not differ between groups	10/10				
	1 RCT	WOMAC function: MD -7.90(-10.06, -5.74) and Lequesne scores MD -3.20(-3.86, -2.54) compared with control	3/10				
	1 RCT	LEGS trial no effects of glucosamine-chondroitin on function at 1-2 years	10/10				
Long-term other outcomes							
	1 RCT	Significant effect on long-term WOMAC stiffness	3/10	N/A	Direct	N/A	Insufficient evidence
	1 RCT	LEGS trial showed no effect compared with placebo on long-term SF-12 physical domain	10/10	N/A	Direct	Precise	Insufficient evidence
<i>Glucosamine</i>							
Short-term pain	0 RCTs						Insufficient evidence
Short-term function	0 RCTs						Insufficient evidence
Short-term other	0 RCTs						Insufficient evidence
Medium-term pain	0 RCTs						Insufficient

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
							evidence
Medium-term function	0 RCTs						Insufficient evidence
Medium-term other	0 RCTs						Insufficient evidence
Long-term pain	3 RCTs		2, 10, 10/10	Inconsistent	Direct	Precise	Insufficient evidence
		GAIT Trial No difference in improvement in WOMAC pain or in likelihood of achieving 20% improvement in pain scores vs. celecoxib	10/10	N/A	Direct	Precise	
		LEGS study: no differences in WOMAC pain versus placebo	10/10				
		(n=190) Bulgarian Glucosamine-sulfate study VAS pain increased less over 3 years in the glucosamine group vs. control	2/10 (abstract)				
Long-term function	3 RCTs		2, 10, 10/10	Inconsistent	Direct	Precise	Insufficient evidence
		GAIT Trial: WOMAC function scores did not differ between glucosamine and celecoxib	10/10	N/A	Direct	Precise	
		LEGS Trial: WOMAC function scores did not differ between glucosamine and placebo	10/10	N/A	Direct	Precise	
		Bulgarian study: Lequesne scores	2/10	N/A	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		significantly improved in glucosamine group vs. placebo					
Long-term other outcomes	1 RCT	GAIT trial: likelihood of achieving 20% improvement in OMERACT-OARSI scores same for glucosamine vs. celecoxib	10/10				Insufficient evidence
	1 RCT	LEGS Trial SF-12 physical domain score improvement showed no difference vs. placebo	10/10				Insufficient evidence
	2 pooled RCTs	Risk for undergoing TKR decreased by more than 50% with glucosamine supplementation vs. placebo	9/10				Insufficient evidence
<i>Chondroitin-sulfate</i>							
Short-term pain	1 RCT	Zegels trial: 2 dosing strategies vs. placebo (n=353) VAS pain: no differences between doses or vs. placebo	10/10	Consistent	Direct	Precise	Low for no effect of chondroitin on short-term pain
Short-term function	1 RCT	Zegels trial: significant improvement in Lequesne scores vs. placebo (p=0.003)	10/10	Consistent	Direct	Precise	Low for no effect of chondroitin on short-term function
Short-term other	0 RCTs						
Medium-term pain	2 RCTs		9,10/10	Consistent	Direct	Precise	Low for an effect of chondroitin on medium-term pain
		Zegels trial: VAS pain significantly	10/10				

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		improved by both dosing strategies vs. placebo: MD -7.70 (-14.43, -0.97) and MD -8.30(CI -15.20, -1.40)					
		STOPP trial (n=622) VAS and WOMAC % responders significantly greater for chondroitin vs. placebo (RR 0.44(0.23, 0.85 and RR 0.83(0.68, 1.02)	9/10				
Medium-term function	2 RCTs		9, 10/10	Inconsistent	Direct	Precise	Insufficient evidence
		Zegels trial: significant improvement in Lequesne scores vs. placebo for both dosing strategies:	10/10	N/A	Direct	Precise	
		STOPP Trial found no difference in WOMAC function vs. placebo	9/10	N/A	Direct	Precise	
Medium-term other	0 RCTs						
Long-term pain	3 RCTs		9, 10, 10/10	Consistent	Direct	Precise	Moderate for no long-term effect of chondroitin sulfate on pain
		STOPP Trial showed no difference in VAS or WOMAC pain vs. placebo	9/10	N/A	Direct	Precise	
		GAIT Trial showed no significant change in WOMAC pain vs. placebo and no	10/10	N/A	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		difference in clinically meaningful response					
		LEGS Trial showed no difference in WOMAC pain scores vs. placebo	10/10	N/A	Direct	Precise	
Long-term function	2 RCTs		10,10/10	Consistent	Direct	Precise	Low for no significant effect of chondroitin on long-term function
		GAIT Trial showed no significant improvement in WOMAC function vs. placebo	10/10	N/A	Direct	Precise	
		LEGS Trial showed no significant improvement in WOMAC function vs. placebo	10/10	N/A	Direct	Precise	
Long-term other	1 RCT	STOPP Trial showed no significant between-group difference in analgesic use	9/10	N/A	Direct	Precise	Insufficient evidence
Strength/resistance Training							
Short-term pain	5 RCTs	5 pooled RCTs (n=160) SMD -0.40 (95% CI -1.22, 0.42)	1-8/10	Inconsistent	Direct	Precise	Low for no effect of strength training on short-term pain
Short-term function	5 RCTs	5 pooled RCTs SMD -0.34 (95% CI -0.95, 0.28)	1-8/10	Inconsistent	Direct	Precise	Low for no effect of strength training on short-term function
Short-term other							
	3 RCTs	WOMAC total Significant between-group differences	4, 5, 8/10	Consistent	Direct	Precise	Moderate for short-term effect of strength

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
							training on WOMAC total
	2 RCTs	TUG	1/10, 8/10	Inconsistent	Direct	Precise	Insufficient evidence
	2 RCTs	SF-36	5,8/10	Consistent	Direct	Precise	Low for a short-term effect on quality of life
	1 RCT	6-minute walk	1/10	N/A	Direct	Precise	Insufficient evidence
Medium-term pain	2 RCTs	No improvements in pain when combined with PCST vs. PCST alone or when compared with other active controls	5, 10/10	Consistent	Direct	Precise	Insufficient evidence
Medium-term function	2 RCTs	Improved function when combined with PCST vs. PCST alone but no effect on WOMAC function in 2 nd RCT	5, 10/10	Inconsistent	Direct	Precise	Insufficient evidence
Medium-term other	1 RCT	No effect on SF-36 physical domain	5/10	N/A	Direct	Precise	Insufficient evidence
Long-term pain	1 RCT	Significant improvements in VAS pain: MD -8.4 (-0.3, -16.6) and WOMAC pain: MD -1.2, (-0.1, -2.4)	10/10	N/A	Direct	Precise	Insufficient evidence
Long-term function	1 RCT	Significant improvement in WOMAC function with strength+ PCST vs. PCST alone MD -5.5(-1.6, -9.3)	10/10	N/A	Direct	Precise	Insufficient evidence
Agility Training							
Short-term pain	3 RCTs		1, 5, 9/10	Inconsistent but consistent vs. passive controls	Direct	Precise	Low for an effect on short-term pain
	1 RCT	WOMAC pain	5/10	N/A	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		significantly improved vs sham control (MD -3.13, 95% CI, -5.86, -0.40)					
	1 RCT	NRS pain: no difference in % responders between agility+ strength-training vs. strength alone (MCID 15%)	9/10	N/A	Direct	Precise	
	1 RCT	VAS pain significantly improved vs. no-intervention control (MD -4.00, 95% CI -5.32, -2.68)	1/10	N/A	Direct	Precise	
Short-term function	3 RCTs		5,5, 9/10	Inconsistent	Direct	Precise	Low for an effect on short-term function
	2 RCTs	WOMAC function: no improvement vs. sham control or vs. strength training (% responders 66% vs. 63% based on MCID of 12%)	5/10	N/A	Direct	Precise	
	1 RCT	Lequesne function: no improvement vs. education control (both exceeded the MCID of 1%)	5/10	N/A	Direct	Precise	
Short-term other	1 RCT	TUG improved vs. education group (MD -2.05, 95% CI -3.12, -0.98)	5/10	N/A	Direct	Precise	Insufficient evidence
	1 RCT	6-minute walk improved vs. education control (MD -50.40, 95% CI -	5/10	N/A	Direct	Precise	Insufficient evidence

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		94.26, -6.54)					
	1 RCT	WOMAC total not improved vs. strength training	9/10	N/A	Direct	Precise	Insufficient evidence
Medium-term pain	2 RCTs	NRS: no significant difference in pain KOOS pain: significant improvement vs. no-attention control	2/10, 9/10	Inconsistent	Direct	Precise	Insufficient evidence
Medium term function	1 RCT	WOMAC function: no difference vs. strength training	9/10	N/A	Direct	Precise	Insufficient evidence
Medium-term other	1 RCT	TUG no improvement vs. strength training	9/10	N/A		Precise	Insufficient evidence
	1 RCT	Walking speed improved for water-based agility training but not land-based agility training vs. control	3/10	N/A		Precise	Insufficient evidence
Long-term pain	2 RCTs		7,9/10	Consistent	Direct	Precise	Low for improvement in long-term pain (or comparable improvement with other exercise interventions)
	1 RCT	No between-group differences in NRS pain vs. standard exercise (n=183)	7/10	N/A		Precise	
	1 RCT	No between group differences in NRS pain vs strength training but % responders exceeded that for controls (based on MCID of	9/10	N/A		Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		12%)					
Long-term function	2 RCTs	No between group differences in WOMAC function vs. other exercise programs	7,9/10	Consistent		Precise	Low for improvement in long-term function (or comparable improvement with other exercise interventions)
Long-term other	1 RCT	Total WOMAC showed no difference vs. standard exercise	7/10	N/A			Insufficient evidence
Aerobic Exercise							
Short-term pain, function, other outcomes	0 RCTs						Insufficient evidence function, or other outcomes
Medium-term pain, function, other outcomes	0 RCTs						Insufficient evidence
Long-term pain	1 RCT	No significant between-group differences in WOMAC pain vs. educational control	4/10				Insufficient evidence
Long-term function	1 RCT	No significant between-group differences in WOMAC function vs. educational control	4/10				Insufficient evidence
Long-term other	1 RCT	No significant between-group differences in WOMAC total scores, SF-36 functional domain scores, TUG scores, or 6-minute walk distances vs. educational control	4/10				Insufficient evidence

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
Exercise, not specified							
Medium-term pain	1 RCT	KOOS and P4 pain scores significantly improved over non-exercise control scores (KOOS 0-100 scale MD -10.00, 95% CI -15.28, -4.72 and P4 pain scores (0-40: MD -3.00, 95% CI -5.84, -0.16) (n=180)	8/10	N/A		Precise	Insufficient evidence
Medium-term function	1 RCT	Significant improvement in KOOS function scores over non-exercise control (0-100 scale: MD -9.00, 95% CI -14.28, -3.72)	8/10	N/A		Precise	Insufficient evidence
Long-term pain	2 RCTs	Improvement in VAS pain with longer exercise program vs. shorter in one study but no improvement in another study	7, 9/10	Inconsistent	Direct	Precise	Insufficient evidence
	1 RCT	Significant improvement in VAS pain scores with booster exercise sessions compared with no booster sessions (1-10mm scale: MD -2.00, 95% CI -3.84, -0.16) (n=75)	7/10				
	1 RCT	CAROT trial showed no difference in VAS pain among weight loss program participants who	9/10				

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		received exercise program vs. no exercise (n=192)					
Long-term function	1 RCT	CAROT trial showed no difference in KOOS function scores between exercisers and non-exercisers (n=192)	9/10	N/A		Precise	Insufficient evidence
Long-term other	2 RCTS						Insufficient evidence
		No difference in 6-minute walk distances in exercisers vs. non exercisers (n=192)	9/10	N/A		Precise	
		No difference in SF-36 physical domain scores in exercisers vs. non-exercisers (n=192)	9/10	N/A		Precise	
		Significant between-group difference in WOMAC total scores favoring the booster session group					
Tai Chi							
Short-term pain	2 RCTs	No between-group differences in WOMAC pain vs. resistance training, TAU, or education	1,4/10	Consistent	Direct	Precise	Very low for no effect of tai chi on short-term pain
Short-term function	2 RCTs		1,4/10	Inconsistent	Direct	Precise	Insufficient evidence
	1 RCT	No between-group differences vs. resistance training or TAU	1/10	N/A	Direct	Precise	
	1 RCT	Significant between-group difference in WOMAC function for	4/10	N/A			

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		tai chi vs. education (MD -5.54 95% CI - 9.72, -1.36) and for TUG (MD -1.54, 95% CI -0.32, -2.76)					
Short-term other	1 RCT	Significant between-group difference in TUG for tai chi vs. education (MD -1.54, 95% CI -0.32, -2.76) but not for sit-to stand or WOMAC stiffness	4/10	N/A			Insufficient evidence
Medium pain	1 RCT	Significant between-group differences in WOMAC pain vs. education (MD -1.58, 95% CI -2.76, -0.40)	4/10	N/A			Insufficient evidence
Medium function	1 RCT	Significant between-group difference in WOMAC function (MD -5.52, 95% CI - 9.70, -1.34)	4/10	N/A			Insufficient evidence
Long term pain, function, or other	0 RCTs						Insufficient evidence
Yoga							
Short-term pain	1 RCT	Significant between-group difference in WOMAC pain vs. waitlist control (MD - 2.50, 95% CI -4.36, - 0.64)	7/10	N/A	Direct	Precise	Insufficient evidence
Short-term function	1 RCT	No significant between-group differences in WOMAC function	7/10	N/A			Insufficient evidence
Medium-term pain or function	0 RCTs						Insufficient evidence
Long-term pain or function	0 RCTs						Insufficient evidence
Ultrasound/heat/							

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
infrared							
Short-term pain	3 RCTs						
	1 RCT U/S	Comparable improvement in WOMAC or VAS pain with pulsed and continuous U/S vs. exercise alone	3/10	N/A		Precise	Insufficient evidence
	1 RCT heat	Significant improvement in WOMAC pain with heat vs. pharmacotherapy (0-20 point scale MD - 1.85, 95% CI -3.15, -0.55)	3/10	N/A		Precise	Insufficient evidence
	1 RCT infrared	No effect of infrared vs. control on KOOS pain	9/10	N/A		Precise	Insufficient evidence
Short-term function	2 RCTs						Insufficient evidence
	1 RCT U/S	No significant effect of pulsed or continuous U/S vs. exercise alone on WOMAC function	3/10	N/A		Precise	Insufficient evidence
	1 RCT heat	Significant improvement in WOMAC function with heat vs. pharmacotherapy(0-68 point scale: (MD - 6.05, 95% CI -9.65, -2.45)	3/10	N/A		Precise	Insufficient evidence
Short-term other	2 RCTs						Insufficient evidence
	1 RCT heat	NO significant effect on WOMAC stiffness or on the SF-36 physical function	3/10				Insufficient evidence

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		domain					
	1 RCT U/S	No between group differences (pulsed vs. continuous U/S vs. exercise) in WOMAC total					Insufficient evidence
Long-term pain	1 RCT	No significant between-group differences in WOMAC or VAS pain between pulsed U/S, continuous U/S, or sham U/S	7/10	N/A		Precise	Insufficient evidence
Long-term function	1 RCT	No significant between-group differences in WOMAC function between pulsed U/S, continuous U/S, or sham U/S	7/10	N/A		Precise	Insufficient evidence
Balneotherapy and Mud Therapy							
<i>Balneotherapy</i>							
Short-term pain, function, other outcomes	0 RCTs						Insufficient evidence for any short-term effects of balneotherapy
Medium-term pain	2 RCTs			Inconsistent			Insufficient evidence for medium-term effects of balneotherapy on pain
	1 RCT	Significant between-group differences in VAS and WOMAC pain scores favoring mineral baths over usual care (VAS pain scores 0-100mm: MD-42.50, 95% CI -	6/10	N/A		Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		53.67, -31.33 and WOMAC pain scores MD -25.70, 95% CI -34.06, -17.34)					
	1 RCT	Significant between group differences in VAS pain scores at rest (MD -16.00, 95% CI -26.68, -5.32) and on exertion (MD -16.60, 95% CI -25.79, -7.41) vs. those who bathed in tap water; no difference in WOMAC pain scores	7/10	Inconsistent		Precise	
Medium-term function	2 RCTs		6,7/10	Consistent	Direct	Precise	Low for a medium-term effect of balneotherapy on overall function
		Significant between-group differences in WOMAC function scores (MD -37.47, 95% CI -46.61, -28.33) and Lequesne scores (MD -7.50, 95% CI -9.57, -5.43)	6/10	Consistent	Direct	Precise	
		significant between-group differences in WOMAC function in the balneotherapy group vs. the control group (MD -8.10, 95% CI -15.82, -0.38)	7/10	N/A	Direct	Precise	
Medium-term other	2 RCTs		6,7/10	Consistent for QoL			Insufficient evidence for medium-term effects of balneotherapy on

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
							QoL or stiffness
		significant between-group differences for the SF-36 functional domain (MD -32.60, 95% CI -49.62, -15.58)	6/10	N/A		Precise	
		Significant between-group differences in EQ-5D (P<0.05)	7/10	N/A		N/R	
		No between-group differences in WOMAC stiffness	7/10	N/A		Precise	
Long-term pain, function, other	0 RCTs						Insufficient evidence for long-term effects of balneotherapy on pain, function, other outcomes
<i>Mud baths or mud therapy</i>							
Short-term pain	1 RCT	No between group differences in WOMAC pain for mud pack vs. placebo	4/10				Insufficient evidence for short-term effects of mud packs on pain
Short-term function	1 RCT	No between group differences in WOMAC function for mud pack vs. placebo	4/10				Insufficient evidence for short-term effects of mud packs on function
Short-term other	1 RCT	Significant between-group difference in WOMAC stiffness for mud pack vs. placebo (p<0.05)	4/10				Insufficient evidence for short-term effects of mud packs on stiffness
Medium-term pain	1 RCT	Significant between-group difference in VAS pain scores for mud bath and pack vs. usual care (0-100	7/10				Insufficient evidence for an effect of mud baths on medium-term pain

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		point scale: MD -15.00, 95% CI -25.63, -4.37)					
Medium-term function	1 RCT	Significant between-group difference in WOMAC function scores for mud bath and pack vs. usual care (0-100 point scale: MD -10.00, -15.00, -5.00)	7/10				Insufficient evidence for an effect of mud baths on medium-term function
Medium-term other	1 RCT	Significant between-group difference in WOMAC stiffness scores for mud bath and pack vs. usual care	7/10				Insufficient evidence for an effect of mud baths on medium-term stiffness
	1 RCT	No significant between-group difference in SF-12 or EQ-5D for mud bath and pack vs. usual care	7/10				Insufficient evidence for a lack of effect of mud baths on medium-term QoL
Long-term pain	1 RCT	No significant between-group difference in pain for mud bath and pack vs. usual care	7/10				Insufficient evidence for long-term effect of mud baths on pain
Long-term function	1 RCT	No significant between-group difference in function for mud bath and pack vs. usual care	7/10				Insufficient evidence for long-term effect of mud baths on function
Long-term other	1 RCT	No significant between-group difference in stiffness, SF-12, EQ-5D for mud bath and pack vs. usual care	7/10				Insufficient evidence for long-term effect of mud baths on QoL and stiffness
Manual Therapy							

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
Short-term pain	3 pooled RCTs	No significant effect of manual therapy (administered by a therapist or by patients themselves) on short-term WOMAC pain (SMD -0.57, 95% CI -1.60, 0.45) (n=244)	4,6,7/10	Inconsistent	Direct	Precise	Low for no effect of manual therapy on short-term pain
	3 unpooled RCTs	No between-group differences in VAS pain (two studies), or in KOOS pain	1, 5, 8/10	Consistent	Direct	Precise	
Short-term function	3 RCTs			Inconsistent	Direct	Precise	Low for no effect of manual therapy on short-term function
	2 RCTs	No significant between-group differences in WOMAC function	4,6/10	N/A		Precise	
	1 RCT	Significant improvements in WOMAC function in three massage groups (MD -11.40, 95% CI -20.90, -1.90) (MD -14.60, 95% CI -24.50, -4.70) (MD -15.40, 95% CI -26.48, -4.32) but not in a fourth	7/10	N/A		Precise	
Short-term other	4 RCTs	No significant between-group differences in WOMAC total scores reported in 3 RCTs and in two treatment arms of the 4 th RCT but significant effects in the two remaining	4, 6, 7, 8/10	Inconsistent	Direct	Precise	Low for no short-term effect of manual therapy on WOMAC total

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		arms					
Medium-term pain	4 RCTs		3, 4, 7, 8/10	Inconsistent	Direct	N/R	Insufficient evidence for no effect of manual therapy on medium-term pain
	1 RCT	Significant between group difference in WOMAC pain for self-massage vs. waiting list controls	3/10	N/A	Direct	N/R	
	3 RCTs	No significant between-group differences in WOMAC or VAS pain	4, 7, 8/10	N/A	Direct	Precise	
Medium-term function	3 RCTs		3, 4, 7/10	Inconsistent	Direct	N/R	Insufficient evidence for no effect of manual therapy on medium-term function
	2 RCTs	No significant between-group differences in WOMAC function	4, 7/10	N/A	Direct	Precise	
	1 RCT	Significant between-group differences in function favoring self-massage vs. wait list controls	3/10	N/A	Direct	N/R	
Medium-term other	3 RCTs		3, 4, 7/10	Inconsistent	Direct	N/R	Insufficient evidence for no effect of manual therapy on other medium term outcomes
	2 RCTs	No between-group differences in	4,7/10	N/A	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		WOMAC total scores					
	1 RCT	Significant between group difference in WOMAC total scores	3/10	N/A	Direct	N/R	
Long-term pain	1 RCT	Significant between group difference vs. exercise alone (MD -2.30, 95% CI -4.07, -0.53)	7/10	N/A	Direct	Precise	Insufficient evidence for an effect of manual therapy on long-term pain
Pulsed Electromagnetic Field							
Short-term Pain	2 RCTs	Significant between-group difference in VAS pain vs. sham control (MD -1.92, 95% CI -2.35, -1.49) in one study but no significant between group difference in WOMAC or VAS pain in another study as part of a multicomponent intervention	6/10	Inconsistent	Direct	Precise	Insufficient evidence for an effect of PEMF on short-term pain
Short-term function and other outcomes	0 RCTs						Insufficient evidence for short-term effect on function or other outcomes
Medium-term pain, function, and other outcomes	0 RCTs						Insufficient evidence for medium-term effect on pain, function, or other outcomes
Long-term pain, function, and other outcomes	0 RCTs						Insufficient evidence for long-term effect on pain, function, or other outcomes
Transcutaneous Electrical Nerve Stimulation (TENS)							

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
Short-term pain	3 RCTs	Significant between-group difference on WOMAC pain vs. sham control 6 (Pooled SMD -0.38, 95% CI -0.6, -0.14) (n=343)	6, 8, 10/10	Inconsistent	Direct	Precise	Moderate for short-term effect of TENS on pain
Short-term function	2 RCTs	No between-group differences in WOMAC function but a higher % of TENS recipients had MCII than sham recipients in one study	8, 10/10	Consistent	Direct	Precise	Insufficient
Short-term other outcomes	2 RCTs	No between group difference in WOMAC total	6, 10/10	Consistent	Direct	Precise	Insufficient evidence for no effect of TENS on short-term WOMAC total
Medium-term pain	2 RCTs	No between-group differences in VAS or WOMAC pain	8,10/10	Consistent	Direct	Precise	Low for no effect of TENS on medium-term pain
Medium-term function	2 RCTs	No between-group differences in WOMAC function	8,10/10	Consistent	Direct	Precise	Low for no effect of TENS on medium-term function
Medium-term other	1 RCT	No between-group difference in WOMAC total	10/10	N/A	Direct	Precise	Insufficient evidence for no effect of TENS on WOMAC total
Long-term pain, function, and other	0 RCTs						Insufficient evidence for effects of TENS on long-term pain, function, or other outcomes
Neuromuscular Electrical Stimulation (NMES)							
Short-term pain	4 RCTs	Significant between-	5, 9, 8, 5	Inconsistent	Direct	Precise	Insufficient

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		group differences in 2 of 4 RCTs showed significant between-group differences for VAS and NRS pain scores (MD -1.70, 95% CI -2.98, -0.42; MD -1.44, 95% CI -2.65, -0.23) with no difference in 2 others					evidence for an effect of NMES on short-term pain
Short-term function	3 RCTs	2 RCTs showed no between-group differences in WOMAC function; 1 RCT showed significant between-group differences in Lequesne scores (MD -2.81, 95% CI -4.53, -1.09)	5, 9, 8/10	Inconsistent	Direct	Precise	Insufficient evidence for short-term effects of NMES on function
Medium-term pain	2 RCTs	No between-group differences in WOMAC pain in 1 RCT but persistent differences in another RCT (MD -1.90, 95% CI -3.25, -0.55)	5,6/10	Inconsistent	Direct	Precise	Insufficient evidence for medium-term effect of NMES on pain
Medium-term function	1 RCT	No between-group differences in WOMAC function	5/10	N/A	Direct	Precise	Insufficient evidence for medium-term effect of NMES on function
Long-term pain, function, and other	0 RCTs						Insufficient evidence for long-term effects of NMES
Whole-body Vibration(WBV)							
Short-term pain	2 RCTs	1 RCT showed a significant between-	1, 9/10	Inconsistent	Direct	Precise	Insufficient evidence for an

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		group difference in NRS pain (MD -2.00, 95% CI -3.77, -0.23; a 2 nd RCT showed no significant between-group differences in WOMAC or VAS pain					effect of WBV on short-term pain
Short-term function	1 RCT	No significant between-group difference in WOMAC function for WBV plus strength training vs. strength training alone	9/10	N/A	Direct	Precise	Insufficient evidence for an effect of WBV on short-term function
Short-term other	2 RCTs	No between-group differences in WOMAC total for WBV plus home exercise vs. home exercise alone; no differences in 6-minute walk distance, TUG, or SF-36	1, 9/10	N/A	Direct	Precise	Insufficient evidence for no effect of WBV on short-term overall improvement, other performance, or QoL
Medium-term pain	4 RCTs	Pooled analysis showed no significant between-group difference in WOMAC pain (SMD -0.20, 95% CI -1.12, 0.71 (n=193))	4, 7, 8, 9/10	Inconsistent	Direct	Precise	Low for no medium-term effect of WBV on pain
Medium-term function	4 RCTs	Pooled analysis showed a small but significant between-group difference in WOMAC function (SMD -0.26, 95% CI -0.45, -0.06)(n=193)	4, 7, 8, 9/10	Inconsistent	Direct	Precise	Low for an effect of WBV on medium-term function
Medium-term other							

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
	4 RCTs	No significant pooled between-group difference in 6-minute walk distances (SMD -28.16, 95% CI -75.45, 19.13) (n=204)	4,7,9,9/10	Inconsistent	Direct	Imprecise	Low for a medium-term effect on walking speed
	4 RCTs	No consistent between-group differences in WOMAC total, WOMAC stiffness, TUG	4, 7, 9, 9	Inconsistent	Direct	Precise	Insufficient evidence for effect of WBV on other outcomes
Long-term pain, function, other outcomes	0 RCTs						Insufficient evidence for a long-term effect of WBV on pain, function, other outcomes
Braces and Orthoses							
<i>Braces</i>							
Short-term pain	1 RCT	Significant between-group difference in VAS pain (0-10 cm MD -1.30, 95% CI -2.01, -0.59)	7/10	N/A	Direct	Precise	Insufficient evidence for an effect of braces on short-term pain
Short-term function and other outcomes	0 RCTs						Insufficient evidence for short-term effects of braces on function or other outcomes
Medium-term pain	1 RCT	Significant between group difference in VAS pain (0-10cm MD -2.30, no variance reported)	3/10	N/A	Direct	N/R	Very low for medium-term effect of braces on pain
Medium-term function and other outcomes	0 RCTs						Insufficient evidence for

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
							medium-term effect of braces on other outcomes
Long-term pain	1 RCT	Significant between-group differences in VAS pain (0-10cm, MD -2.80, 95% CI -3.58, -2.02)	3/10	N/A	Direct	Precise	Insufficient evidence for long-term effect of braces on pain
Long-term function and other outcomes	0 RCTs						Insufficient evidence for long-term effect of braces on function or other outcomes
<i>Orthoses</i>							
Short-term pain	4 RCTs	3 of 4 RCTs showed significant between-group differences in at least one measure of VAS pain (no pooling possible); 1 of 2 RCTs showed a significant between-group difference in WOMAC pain	2, 4, 7, 8/10	Inconsistent	Direct	Precise	Insufficient evidence for an effect of orthoses on short-term pain
Short-term function	3 RCTs	1 of 3 RCTs showed significant between-group differences in function; one that showed no difference did report MCII in 100% of insole users.	2, 7, 8/10	Inconsistent	Direct	Precise	Insufficient evidence for a short-term effect on function
Short-term other	3 RCTs	Pooled outcomes of 3 RCTs showed no significant between group difference in WOMAC total (SMD -0.37, 95% CI -1.26, 0.53)(n=125)	2, 7, 8/10	Inconsistent	Direct	Precise	Low for no effect of orthotics on short-term overall improvement

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
Medium-term pain	3 RCTs	Pooled outcomes of 3 RCTs showed no significant between group difference in WOMAC (SMD -0.4, 95% CI -1.35, 0.56)(n=131)	2, 2, 8/10	Inconsistent	Direct	Precise	Low for no effect of orthoses on medium-term pain
Medium-term function	4 RCTs	3 of 4 RCTs reported no between-group differences in function (2 Lequesne, 1 WOMAC) and 1 reported a significant between-group difference in WOMAC function (MD -10.06, 95% CI -19.68, -0.44)	2, 2, 4, 8/10	Inconsistent	Direct	Precise	Insufficient evidence for no effect of orthoses on medium-term function
Long-term pain	2 RCTs	1 RCT found no between-group differences in WOMAC pain and 1 RCT found a significant difference in VAS pain	3, 9/10	Inconsistent	Direct	Precise	Insufficient evidence for an effect of orthoses on long-term pain
Long-term function	2 RCTs	No between-group differences in Lequesne (1 RCT) or WOMAC (1 RCT) function	4, 9/10	Consistent	Direct	Precise	Insufficient evidence for no effect of orthoses on long-term function
Long term other	0 RCTs						Insufficient evidence for no effect of orthoses on other long-term outcomes
<i>Custom Shoes</i>	5 RCTs						
Short-term pain, function, other outcomes	0 RCTs						
Medium-term pain	2 RCTs	1 RCT reported a significant between	6, 9/10	Inconsistent	Direct	N/R	Insufficient evidence for an

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		group difference, and another RCT reported no significant difference in WOMAC pain scores					effect of minimalist footwear on medium-term pain
Medium-term function	1 RCT	Significant between-group difference reported in WOMAC and Lequesne function scores	9/10	Consistent	Direct	N/R	Insufficient evidence for an effect of minimalist footwear on medium-term function
Medium-term other	2 RCTs	No significant between-group differences in WOMAC total or walking distance	6, 9/10	Consistent	Direct	Imprecise	Insufficient evidence for an effect of minimalist footwear on other medium-term outcomes
Long-term pain	1 RCT	No significant between-group difference in WOMAC pain	8/10	N/A	Direct	N/R	Insufficient evidence for an effect of minimalist footwear on long-term pain
Long-term function and other outcomes	0 RCTs						Insufficient evidence for an effect of minimalist footwear on other long-term outcomes
<i>Cane</i>							
Short-term pain	1 RCT	Significant between-group difference in VAS pain (0-10cm: MD -2.11, 95% CI -2.83, -1.39)	9/10	N/A	Direct	Precise	Insufficient evidence for effect of cane use on short-term pain
Short-term function	1 RCT	Significant between-group difference in	9/10	N/A	Direct	Precise	Insufficient evidence for

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		Lequesne function (MD -2.34, 95% CI -4.34, -0.72)					effect of cane use on short-term function
Short-term other	1 RCT	Significant between-group difference in SF-36 physical domain (0-100: MD -9.06, 95% CI -17.81, -0.31) but not WOMAC total	9/10	N/A	Direct	Precise	Insufficient evidence for effect of cane use on other short-term outcomes
Medium- and long-term pain, function, other outcomes	0 RCTs						Insufficient evidence for effect of cane use on medium and long-term outcomes
Weight-loss							
Short-term pain	1 RCT and 1 single-arm trial						Insufficient evidence for short-term effect of weight loss on pain
	1 RCT	Significant improvement in VAS pain with weight loss across 3 intervention arms (diet+ exercise, exercise, and diet only) but not proportional to actual weight loss	2/10	Inconsistent	Direct	Precise	
	1 single-arm trial	Significant improvement in KOOS pain with weight loss (MD 5, 95% CI 0.3, 9.7)	?	N/A	Direct	Precise	
Short-term function	1 RCT	Significant improvement in WOMAC function, Lequesne function,	2/10	Inconsistent	Direct	Precise	Insufficient evidence

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		and proportion of individuals with improvements in function with weight loss in all treatment groups					
Short-term other outcomes	1 single-arm trial	Significant improvement in TUG (seconds: MD-1.4, 95% CI-3.0 to -0.4) and 6-minute walk from baseline with weight loss	?	Consistent	Direct	Precise	Insufficient evidence
Medium-term pain	2 RCTs, 4 single-arm trials			Inconsistent	Direct	Precise	Moderate evidence for a medium-term effect of weight loss on pain
	2 RCTs	Significant between-group difference in WOMAC pain for weight loss vs. no weight loss in 1 RCT, but weight loss associated with decreased pain in only 1 of two treatment arms in 2 nd RCT vs. control	3, 6/10	Inconsistent	Direct	Precise	
	Single-arm trials	1 single arm trial found significant decreases in pain with weight loss, and 3 (including CAROT, n=3,000) showed a significant dose-response relationship of weight loss with decreased pain	Not assessed	Consistent	Direct	Precise	
Medium-term function	2 RCTs, 4 single-						Moderate

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
	arm trials						evidence for an effect of weight loss on medium term function
	2 RCTs	Weight loss significantly associated with between-group differences in WOMAC function	3, 6/10	Consistent	Direct	Precise	
	2 cohort studies and 1 single-arm trial	Weight loss significantly associated with WOMAC and KOOS function; dose-response relationship of weight loss and KOOS function	Not rated	Consistent	Direct	Precise	
Medium-term other outcomes							Low for an effect of weight loss on other outcomes
	1 RCT	Significant between-group differences in WOMAC total function (MD -10.70, 95% CI -17.01, -4.39) and 6-minute walk distance (MD -51.00, 95% CI -96.03, -5.97)	3/10	N/A	Direct	Precise	
	2 single-arm trials and 1 cohort study	Significant associations of weight loss with improvements in WOMAC stiffness, and TUG and significant dose-response association with SF-12 physical domain					
Long-term pain	3 RCTs and 1						Low for effect of

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
	single-arm trial						weight loss on long-term pain
	3 RCTs	1 RCT showed a significant between-group difference in WOMAC pain with weight loss (, MD - 7.20, 95% CI -13.30, - 1.10); 1 RCT showed a non-significant between-group difference in WOMAC pain (between group differences in weight loss were small); and 1 RCT showed continued relationship between weight loss and decreased pain	6, 7, 7/10	Inconsistent	Direct	Precise	
	1 single-arm trial	Ongoing trial shows improvement in VAS and WOMAC pain at 1 year	Not determined	N/A	Direct	Precise	
Long-term function	2 RCTs	1 RCT reported no between-group differences in WOMAC function; 1 RCT reported between-group differences WOMAC function by weight loss	7, 7/10	Inconsistent	Direct	Precise	Insufficient evidence for a long-term effect of weight loss on function
Long-term other outcomes	2 RCTs	1 RCT reported no difference in WOMAC total scores; 1 RCT reported significant between group differences in 6-minute walk	7,7/10	Inconsistent	Direct	Imprecise for 6-minute walk	Insufficient evidence for effect of weight loss on other long-term outcomes

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		distance (MD -12.00, 95% CI -33.93, -9.93) and SF-36 physical domain scores (MD -2.70, 95% CI -4.89, -0.51)					
Home-based and Self-Management							
Short-term pain	2 RCTs						Low for an effect of short-term home-based or self-management interventions on pain
	1 RCT home-based	1 RCT reported significant between-group differences in WOMAC pain for 3 home-based interventions vs. a sham-control: Strength training alone: MD -3.75, 95% CI -6.39, -1.11; agility training alone: MD -3.13, 95% CI -5.86, -0.40; strength+agility training: MD -3.00, 95% CI -5.45, -0.55	5/10	Consistent	Direct	Precise	
	1 RCT self-management	Significant between-group difference in WOMAC pain scores (MD -1.50, 95% CI -2.33, -0.67) and the likelihood of achieving MCII (RR 0.20, 95% CI 0.08, 0.49)	8/10	Consistent	Direct	Precise	
Short-term function	2 RCTs						Insufficient evidence for short

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
							term effect of home-based or self-management on short-term function
	1 RCT home-based	Significant between-group differences in WOMAC function for combined strength+agility training (MD -11.98, 95% CI -19.15, -4.81) and strength-training (MD -9.62, 95% CI -19.04, -0.20) vs. controls but not agility alone	5/10	Inconsistent	Direct	Precise	
	1 RCT self-management	Significant between-group difference in WOMAC function (MD -5.30, 95% CI -7.24, -3.36); % achieving MCH was significantly different (RR 0.24, 99% CI 0.11, 0.51)	8/10	N/A	Direct	Precise	
Short-term other outcomes	2 RCTs		5,8/10				Insufficient evidence for effect of home-based or self-management on other short-term outcomes
		1 RCT showed significant between-group differences in WOMAC total for home-based vs. controls (except for agility alone); 1 RCT	5/10	Inconsistent	Direct	Precise	

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		showed significant between-group differences for home-based (MD -7.20, 95% CI -9.97, -4.43)					
	1 RCT	Significant between-group differences for self-management in SF-36 physical domain (MD -5.60, 95% CI -9.48, -1.72), TUG (MD -1.00, 95% CI -1.55, -0.45, and % achieving MCII for both	8/10	Consistent	Direct	Precise	
Medium-term pain	3 RCTs self-management	1 RCT found significant between-group differences in VAS pain with pain coping skills training (PCST)+strength training vs. strength training alone (0-100: MD -8.20, 95% CI -15.32, -1.08) but not WOMAC pain; an RCT that combined PCST with behavioral weight management (BWM) found a significant between-group difference in WOMAC pain for BWM+PCST vs. BWM alone	6, 8, 10/10	Inconsistent	Direct	Precise	Low for an effect of self-management on medium-term pain
Medium-term function	3 RCTs self-management	3 RCTs reported significant between group differences in WOMAC function (ST+PCST vs. ST	6, 8, 10/10	Consistent	Direct	Precise	Moderate for medium-term effect of self-management on function

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
		alone: 0-68 points, MD -3.80, 95% CI -7.06, -0.54; BWM+PCST vs. standard care: 0-100 points, MD-12.40, 95% CI -17.29, -7.51; self-management vs. wait list: MD-3.50, 95% CI -6.14, -0.86)					
Medium-term other outcomes	1 RCT	1 RCT found significant between-group differences in WOMAC total (MD -4.10, 95% CI -7.43, -0.77)	10/10	N/A	Direct	Precise	Insufficient evidence for an effect of self-management on medium-term WOMAC total
	2 RCTs	Significant between-group differences in TUG (MD -1.00, 95% CI -1.55, -0.45) and SF-36 (MD -5.70, 95% CI -10.97, -0.43) in 1 RCT but not another	8,10/10	Inconsistent	Direct	Precise	Insufficient evidence for an effect of self-management on other medium-term outcomes
Long-term pain	1 RCT	No between-group difference in WOMAC pain vs. control					Insufficient evidence for no effect of PCST on long-term effects on pain
Long-term function	1 RCT	No between-group difference in WOMAC function vs. control					Insufficient evidence for no effect of PCST on long-term effects on function
Long-term other outcomes	1 RCT	Significant between-group difference in Australian Q-6D	10/10	N/A	Direct	Precise	Insufficient evidence for long-term effect of PCST on other outcomes
Key Question 2 Adverse Events							

Intervention/Outcome	Number, design of studies (and participants if pooling)	Findings	Study limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of evidence
Non-serious adverse events	40 RCTs, 1 single arm trial	No systematic findings of non-serious AEs by intervention type, with the exception of minor GI complaints among individuals following low-calorie diets	McHarms scores low for all studies	Inconsistent	Direct	N/A	Low for a lack of systematic non-serious AEs among interventions
Serious adverse events	13 RCTs	No systematic findings of SAEs by intervention type	McHarms scores low for all studies. Only 1 study that reported “no SAEs” defined SAEs	Inconsistent	Direct	N/A	Low for a lack of systematic serious AEs among interventions

Abbreviations: BWM=behavioral weight management; CI=confidence intervals; MCID=minimum clinically important difference; MCII=minimum clinically important improvement; MD=mean difference; N/A=not applicable; NMES=neuromuscular electrical stimulation; N/R=not reported; NRS=Numeric Rating Scale; PCST=pain coping skills training; QoL=quality of life; RCT=randomized controlled trial; RoB=risk of bias; SF=short form; SMD=standardized mean difference; ST=strength training; TENS=transcutaneous electrical nerve stimulation; TUG=timed up and go; VAS=visual analog scale; WBV=whole-body vibration; WOMAC=Western Ontario McMaster Osteoarthritis Index

Appendix F. Quality of Included Studies

Table F1. Quality assessment of randomized controlled trials

Table F2. Quality assessment of studies reporting harms

Table F1. Quality assessment of randomized controlled trials (N=90 studies)

Author, year	Allocation Sequence Generated Adequately	Allocation Treatment Adequately Concealed	Participants or Healthcare Provider Adequately Blinded	Outcome Assessors Blinded	Incomplete outcome data (Attrition bias) due to amount, nature or handling of incomplete outcome data	Selective Outcome Reporting	Intention-to-treat	Group Similarity at Baseline (general)	Incomplete Adherence/Compliance with Interventions Across Groups	Additional bias: Report power calculation/achieve adequate n	Overall Risk of Bias
Abbott JH, et al, 2015 ⁵³	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	No	Moderate
Acosta-Olivo C, et al, 2014 ²⁶	Low risk	Unclear	High risk	High risk	Unclear	Unclear	Unclear	Unclear	Low risk	No	Unclear
Atamaz FC, et al, 2012 ⁷²	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Atkins DV, et al, 2013 ¹⁰⁴	Unclear	Unclear	High risk	High risk	Low risk	Unclear	No	Low risk	Unclear	Yes	Unclear
Avelar NC, et al, 2011 ⁷⁷	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear	No	High risk	Low risk	Yes	Unclear
Azlin MNN, et al, 2011 ⁹⁸	Unclear	Unclear	High risk	High risk	High risk	Unclear	No	High risk	Low risk	No	High
Barduzzi GO, et al, 2013 ⁵¹	Low risk	Low risk	High risk	Unclear	High risk	Unclear	Unclear	Unclear	Low risk	No	Unclear
Bartels EM, et al, 2014 ⁵⁵	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Bellare N, et al, 2014 ²⁹	Unclear	Unclear	High risk	Unclear	Low risk	Unclear	Unclear	Low risk	Low risk	No	Unclear
Bennell KL, et al, 2011 ⁹¹	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	High risk	Yes	Low
Bennell KL, et al, 2015 ⁴⁵	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Bliddal H, et al, 2011 ¹⁰⁸	Low risk	Low risk	Low risk	Low risk	High risk	Unclear	Unclear	Low risk	Low risk	Yes	Moderate
Brosseau L, et al, 2012 ³⁷	Low risk	Low risk	High risk	Low risk	High risk	Unclear	Unclear	Low risk	High risk	No	High
Bruce-Brand RA, et al, 2012 ⁴⁰	Low risk	Unclear	High risk	Low risk	High risk	Low risk	No	Low risk	Low risk	No	Moderate
Bruyere O, et al, 2008 ³¹	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low

Author, year	Allocation Sequence Generated Adequately	Allocation Treatment Adequately Concealed	Participants or Healthcare Provider Adequately Blinded	Outcome Assessors Blinded	Incomplete outcome data (Attrition bias) due to amount, nature or handling of incomplete outcome data	Selective Outcome Reporting	Intention-to-treat	Group Similarity at Baseline (general)	Incomplete Adherence/Compliance with Interventions Across Groups	Additional bias: Report power calculation/achieve adequate n	Overall Risk of Bias
Cakir S, et al, 2014 ⁶⁵	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk	Yes	Moderate
Callaghan MJ, et al, 2015 ⁸²	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Yes	Low risk	Unclear	Yes	Moderate
Campos GC, et al, 2015 ⁸⁸	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Unclear	Yes	Low
Carlos KP, et al, 2012 ⁶⁶	Unclear	Unclear	High risk	Low risk	Low risk	Unclear	Unclear	Low risk	Unclear	No	Unclear
Cheawthamai K, et al, 2014 ⁹⁹	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	No	Low risk	Unclear	No	Moderate
Cherian JJ, et al, 2015 ⁸³	Unclear	Unclear	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear	Yes	Unclear
Cheung C, et al, 2014 ⁵⁷	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	High risk	High risk	No	Moderate
Christensen R, et al, 2015 ⁵⁴	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Claes BEA, et al, 2015 ¹¹²	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Coleman S, et al, 2012 ¹¹⁵	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Unclear	Yes	Low
Cortes Godoy V, et al, 2014 ¹⁰⁰	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	No	Low
da Silva FS, et al, 2015 ⁴⁸	Low risk	Low risk	High risk	Low risk	High risk	Low risk	No	Low risk	Unclear	No	Moderate
Dundar U, et al, 2015 ⁷⁵	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk	No	Moderate
Dwyer L, et al, 2015 ¹⁰²	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Yes	High risk	Unclear	Yes	Moderate
Elboim-Gabyzon M, et al, 2013 ⁷⁰	Unclear	Low risk	High risk	High risk	Low risk	Unclear	No	Low risk	Low risk	Yes	Moderate
Erhart JC, et al, 2010 ⁹⁵	Low risk	Unclear	Low risk	Low risk	High risk	Unclear	No	Low risk	Low risk	Yes	Moderate

Author, year	Allocation Sequence Generated Adequately	Allocation Treatment Adequately Concealed	Participants or Healthcare Provider Adequately Blinded	Outcome Assessors Blinded	Incomplete outcome data (Attrition bias) due to amount, nature or handling of incomplete outcome data	Selective Outcome Reporting	Intention-to-treat	Group Similarity at Baseline (general)	Incomplete Adherence/Compliance with Interventions Across Groups	Additional bias: Report power calculation/achieve adequate n	Overall Risk of Bias
Erhart-Hledik JC, et al, 2012 ⁹⁶	Low risk	Low risk	Low risk	Low risk	High risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Fioravanti A, et al, 2012 ⁵⁸	Low risk	Unclear	High risk	Low risk	Low risk	Unclear	Yes	Unclear	Low risk	Yes	Moderate
Fioravanti A, et al, 2015 ⁶¹	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Yes	Unclear	Low risk	Yes	Moderate
Fitzgerald GK, et al, 2011 ⁵⁰	Low risk	Low risk	High risk	Low risk	High risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Foroughi N, et al, 2011 ⁴²	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	No	Low risk	Low risk	Yes	Low
Fransen M, et al, 2014 ³⁰	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Ghroubi S, et al, 2008 ¹⁰⁵	Unclear	Unclear	High risk	Unclear	Low risk	Unclear	Unclear	Low risk	Unclear	No	Unclear
Gormeli G, et al, 2015 ²⁴	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	No	Low risk	Low risk	Yes	Low
Gschiel B, et al, 2010 ⁷¹	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk	Unclear	No	Moderate
Hatef MR, et al, 2014 ⁸⁷	Unclear	Unclear	Low risk	Low risk	High risk	Unclear	No	Low risk	Low risk	No	Moderate
Henriksen M, et al, 2013 ⁴⁹	Unclear	Unclear	High risk	Low risk	Low risk	Unclear	No	Unclear	Unclear	No	Unclear
Hochberg MC, et al, 2008 ¹¹⁶	Unclear	Unclear	Unclear	Unclear	High risk	Unclear	Unclear	Low risk	Unclear	No	Unclear
Hochberg MC, et al, 2015 ²⁸	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	No	Low risk	Unclear	Yes	Low
Hsieh RL, et al, 2012 ⁶⁴	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Imoto AM, et al, 2012 ³⁹	Unclear	Unclear	High risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Moderate
Imoto AM, et al, 2013 ⁶⁹	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	High risk	Low risk	Yes	Low
Inoshi	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Author, year	Allocation Sequence Generated Adequately	Allocation Treatment Adequately Concealed	Participants or Healthcare Provider Adequately Blinded	Outcome Assessors Blinded	Incomplete outcome data (Attrition bias) due to amount, nature or handling of incomplete outcome data	Selective Outcome Reporting	Intention-to-treat	Group Similarity at Baseline (general)	Incomplete Adherence/Compliance with Interventions Across Groups	Additional bias: Report power calculation/achieve adequate n	Overall Risk of Bias
Atukorala, et al, 2016 ¹¹⁰											
Jones A, et al, 2012 ⁹⁷	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Ju SB, et al, 2015 ⁴⁷	Unclear	Unclear	High risk	Unclear	Unclear	Unclear	Unclear	Low risk	Unclear	No	Unclear
Kahan A, et al, 2009 ³⁶	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Knoop J, et al, 2013 ⁴⁶	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Koca B, et al, 2009 ⁸⁶	Unclear	Unclear	Unclear	Unclear	Low risk	Unclear	Unclear	Low risk	Unclear	No	Unclear
Kulisch A, et al, 2014 ⁵⁹	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Yes	Unclear	Low risk	Yes	Moderate
Laufer Y, et al, 2014 ⁶⁷	Unclear	Low risk	Low risk	High risk	Low risk	Low risk	No	Low risk	Low risk	No	Moderate
Mahboob N, et al, 2009 ⁶⁰	Unclear	Unclear	Low risk	Low risk	Low risk	Unclear	Yes	Unclear	Unclear	No	Unclear
Makovey J, et al, 2015 ¹¹¹	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Messier SP, et al, 2013 ¹⁰⁷	Unclear	Unclear	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Moderate
Miller GD, et al, 2006 ¹⁰⁶	Unclear	Unclear	High risk	High risk	Low risk	Unclear	No	Low risk	Low risk	No	Moderate
Mizusaki Imoto A, et al, 2013 ⁶⁸	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Nam CW, et al, 2014 ⁴⁴	Unclear	Unclear	High risk	Unclear	Low risk	Unclear	Yes	Low risk	Low risk	No	Moderate
Nelson FR, et al, 2013 ⁷⁴	Low risk	Low risk	Low risk	Low risk	High risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Oliveira AM, et al, 2012 ³⁸	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Palmer S, et al,	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low

Author, year	Allocation Sequence Generated Adequately	Allocation Treatment Adequately Concealed	Participants or Healthcare Provider Adequately Blinded	Outcome Assessors Blinded	Incomplete outcome data (Attrition bias) due to amount, nature or handling of incomplete outcome data	Selective Outcome Reporting	Intention-to-treat	Group Similarity at Baseline (general)	Incomplete Adherence/Compliance with Interventions Across Groups	Additional bias: Report power calculation/achieve adequate n	Overall Risk of Bias
2014 ⁷³											
Park YG, et al, 2013 ⁷⁶	Unclear	Unclear	High risk	Unclear	Unclear	Unclear	Unclear	Low risk	Unclear	No	Unclear
Patel S, et al, 2013 ²³	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	No	High risk	Low risk	Yes	Moderate
Perlman AI, et al, 2012 ¹⁰³	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	High risk	Low risk	No	Moderate
Rabini A, et al, 2015 ⁸⁰	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Rayegani SM, et al, 2014 ²⁵	Low risk	High risk	High risk	High risk	Low risk	Unclear	No	Unclear	Low risk	No	High
Richette P, et al, 2011 ¹¹³	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	No	N/A
Rodrigues PT, et al, 2008 ⁸⁵	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	No	Moderate
Rogers MW, et al, 2012 ⁴³	Low risk	Unclear	Low risk	High risk	High risk	Low risk	Unclear	Low risk	Low risk	No	Moderate
Rosedale R, et al, 2014 ⁵²	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Unclear	Yes	Low
Sattari S, et al, 2011 ⁸⁴	Low risk	Unclear	High risk	High risk	Low risk	Unclear	Unclear	Low risk	Unclear	No	Unclear
Sawitzke AD, et al, 2010 ²⁷	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Simao AP, et al, 2012 ⁷⁸	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	No	High risk	Low risk	Yes	Moderate
Somers TJ, et al, 2012 ¹⁰⁹	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Yes	Unclear	Unclear	Yes	Moderate
Stambolova Ivanova MP, 2015 ³²	Unclear	Unclear	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear	Unclear	No	Unclear
Stefanik J, et al, 2015 ¹¹⁴	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Toda Y, et al,	High risk	High risk	Low risk	Low risk	Low risk	Unclear	No	Low risk	Unclear	No	Moderate

Author, year	Allocation Sequence Generated Adequately	Allocation Treatment Adequately Concealed	Participants or Healthcare Provider Adequately Blinded	Outcome Assessors Blinded	Incomplete outcome data (Attrition bias) due to amount, nature or handling of incomplete outcome data	Selective Outcome Reporting	Intention-to-treat	Group Similarity at Baseline (general)	Incomplete Adherence/Compliance with Interventions Across Groups	Additional bias: Report power calculation/achieve adequate n	Overall Risk of Bias
2006 ⁹⁰											
Trombini-Souza F, et al, 2013 ⁹³	Unclear	Unclear	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear	Unclear	No	Unclear
Trombini-Souza F, et al, 2015 ⁹⁴	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Tsai PF, et al, 2013 ⁵⁶	Low risk	Unclear	Unclear	Unclear	Low risk	Unclear	Yes	Low risk	Unclear	No	Unclear
Wallace DA, 2006 ⁸⁹	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear	Unclear	Unclear	No	Unclear
Wang P, et al, 2015 ⁸¹	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Wang P, et al, 2015 ⁷⁹	Low risk	Low risk	Unclear	Low risk	Low risk	Unclear	Yes	Low risk	Low risk	Yes	Low
Wortley M, et al, 2013 ⁴¹	Unclear	Unclear	High risk	Unclear	High risk	Unclear	No	High risk	Low risk	No	High
Yildirim N, et al, 2010 ⁶³	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Yes	Unclear
Zegels B, et al, 2013 ³⁵	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Yes	Low risk	Low risk	Yes	Low
Zhang Y, et al, 2012 ¹⁰¹	Low risk	Low risk	High risk	High risk	High risk	Unclear	Yes	Low risk	Unclear	No	Moderate

Table F2. Quality assessment of studies reporting harms (N=45)

Author, year	Were the harms predefined using standardized or precise definitions?	Was the mode of harms collected specified as active?	Was the potential occurrence of harmful events collected at pre-specified intervals?	Did the author(s) specify the NUMBER for each TYPE of harmful event for each study group?	Was the TOTAL NUMBER of participants affected by harms specified for each study arm?	If the study reported that there were no serious AE's reported did they define serious AEs?
Abbott JH, et al, 2015 ⁵³	No	Unclear	Unclear	Yes	Yes	Not applicable
Atamaz FC, et al, 2012 ⁷²	Unclear	Unclear	Unclear	No	No	Not applicable
Bellare N, et al, 2014 ²⁹	No	No	No	No	No	Not applicable
Bennell KL, et al, 2011 ⁹¹	No	Yes	Yes	Yes	Yes	Not applicable
Bennell KL, et al, 2015 ⁴⁵	Yes	Yes	Unclear	Yes	Yes	Not applicable
Bliddal H, et al, 2011 ¹⁰⁸	Unclear	Unclear	Unclear	No	No	Not applicable
Callaghan MJ, et al, 2015 ⁸²	Unclear	Yes	Yes	Yes	Yes	Not applicable
Campos GC, et al, 2015 ⁸⁸	Yes	Unclear	Unclear	Yes	Yes	Not applicable
Cherian JJ, et al, 2015 ⁸³	Yes	Unclear	Unclear	No	No	Yes
Cheung C, et al, 2014 ⁵⁷	Unclear	Yes	Unclear	Yes	Yes	Not applicable
Christensen R, et al, 2015 ⁵⁴	Yes	Yes	Yes	Yes	Yes	Not applicable
Coleman S, et al, 2012 ¹¹⁵	Unclear	Unclear	Unclear	Yes	Yes	Not applicable
Dwyer L, et al, 2015 ¹⁰²	Yes	Unclear	Unclear	Yes	Yes	Not applicable
Elboim-Gabyzon M, et al, 2013 ⁷⁰	No	No	Unclear	Yes	Yes	Not applicable
Erhart JC, et al, 2010 ⁹⁵	No	No	Unclear	No	No	Not applicable
Fioravanti A, et al, 2015 ⁶¹	No	Unclear	Unclear	Yes	Yes	No
Fitzgerald GK, et al, 2011 ⁵⁰	No	Unclear	Unclear	Yes	Yes	No
Foroughi N, et al,	Yes	Yes	Yes	Yes	Yes	Not applicable

Author, year	Were the harms predefined using standardized or precise definitions?	Was the mode of harms collected specified as active?	Was the potential occurrence of harmful events collected at pre-specified intervals?	Did the author(s) specify the NUMBER for each TYPE of harmful event for each study group?	Was the TOTAL NUMBER of participants affected by harms specified for each study arm?	If the study reported that there were no serious AE's reported did they define serious AEs?
2011 ⁴²						
Fransen M, et al, 2014 ³⁰	No	Yes	Yes	No	No	Not applicable
Ghroubi S, et al, 2008 ¹⁰⁵	Unclear	No	No	Unclear	Unclear	Not applicable
Gschiel B, et al, 2010 ⁷¹	Unclear	Unclear	Unclear	Yes	Yes	Not applicable
Hochberg MC, et al, 2008 ¹¹⁶	No	Unclear	Unclear	Yes	Yes	Not applicable
Hochberg MC, et al, 2015 ²⁸	Yes	Unclear	Unclear	Yes	Yes	Not applicable
Hsieh RL, et al, 2012 ⁶⁴	No	No	Unclear	Yes	Yes	Not applicable
Imoto AM, et al, 2012 ³⁹	No	No	No	Yes	Yes	Not applicable
Imoto AM, et al, 2013 ⁶⁹	No	Unclear	Unclear	Yes	Yes	Not applicable
Kahan A, et al, 2009 ³⁶	No	Unclear	Unclear	No	Yes	Not applicable
Knoop J, et al, 2013 ⁴⁶	Yes	Unclear	Unclear	Yes	Yes	Yes
Laufer Y, et al, 2014 ⁶⁷	No	No	No	Yes	Yes	Not applicable
Messier SP, et al, 2013 ¹⁰⁷	Unclear	Unclear	Unclear	Yes	Yes	Not applicable
Mizusaki Imoto A, et al, 2013 ⁶⁸	No	Unclear	Unclear	Yes	Yes	Not applicable
Nelson FR, et al, 2013 ⁷⁴	No	Unclear	Unclear	Yes	Yes	Not applicable
Oliveira AM, et al, 2012 ³⁸	No	Unclear	Unclear	Yes	Yes	Not applicable
Park YG, et al, 2013 ⁷⁶	No	Unclear	Unclear	Yes	Yes	Not applicable
Patel S, et al, 2013 ²³	No	Unclear	Unclear	No	Yes	Not applicable
Perlman AI, et al, 2012 ¹⁰³	No	Unclear	Unclear	Yes	Yes	Not applicable

Author, year	Were the harms predefined using standardized or precise definitions?	Was the mode of harms collected specified as active?	Was the potential occurrence of harmful events collected at pre-specified intervals?	Did the author(s) specify the NUMBER for each TYPE of harmful event for each study group?	Was the TOTAL NUMBER of participants affected by harms specified for each study arm?	If the study reported that there were no serious AE's reported did they define serious AEs?
Rabini A, et al, 2015 ⁸⁰	Unclear	Unclear	Unclear	Yes	Yes	Not applicable
Rayegani SM, et al, 2014 ²⁵	No	Unclear	Unclear	Yes	Yes	Not applicable
Rodrigues PT, et al, 2008 ⁸⁵	Unclear	Unclear	Unclear	Yes	Yes	Not applicable
Sawitzke AD, et al, 2010 ²⁷	No	Yes	Yes	Yes	Unclear	Not applicable
Somers TJ, et al, 2012 ¹⁰⁹	Unclear	Unclear	Unclear	Yes	Yes	Not applicable
Wang P, et al, 2015 ⁸¹	Unclear	Yes	Yes	Yes	Yes	Not applicable
Wang P, et al, 2015 ⁷⁹	No	No	Unclear	Yes	Yes	No
Zegels B, et al, 2013 ³⁵	No	Unclear	Unclear	No	No	Not applicable
Zhang Y, et al, 2012 ¹⁰¹	Unclear	Unclear	Unclear	Yes	Yes	Not applicable

Appendix G. Policies, Guidelines, Coverage, Stakeholder Information on Interventions of Interest

Table G1. Policies, Guidelines, Coverage, Stakeholder Information on Interventions of Interest

Intervention	Current Guidelines	FDA Approval for Indicated Use	CMS Coverage
Glucosamine Chondroitin	ACR: Conditional recommendation <i>against</i> use AAOS: Recommendation <i>against</i> use glucosamine and chondroitin (strong)	Evidence insufficient to demonstrate reduction in risk or disease modification (2004) Unclear regarding treatment of symptoms	Not relevant (over-the-counter)
Platelet Rich Plasma	ACR: not mentioned AAOS: <i>unable</i> to recommend <i>for or against</i> growth factor injections and/or platelet rich plasma (inconclusive)	Off-label use for an FDA-approved product	CMS National Coverage Determination: covered only for certain chronic non-healing wounds
Mesenchymal Stem Cells	ACR: not mentioned AAOS: not mentioned	Not approved by the FDA	Not covered for OA National Coverage Determination for Stem Cell Transplantation: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=45&ncdver=5&NCAId=9&IsPopup=y&bc=AAAAAAgAAAA%3D%3D&
Weight loss	ACR: strongly recommends weight loss (for persons who are overweight) AAOS: suggests weight loss <i>for</i> patients with symptomatic osteoarthritis of the knee OAK and a BMI ≥ 25. (moderate)	Not searched	<p>Bariatric Surgery for the Treatment of Morbid Obesity Certain procedures for the treatment of obesity are covered for Medicare beneficiaries who have a BMI ≥35, have at least one co-morbidity related to obesity and have been previously unsuccessful with the medical treatment of obesity.</p> <p>https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=57&ncdver=5&NCAId=258&NcaName=Bariatric+Surgery+for+the+Treatment+of+Morbid+Obesity&IsPopup=y&bc=AAAAAAACAAAA%3D%3D&.</p> <p>Other Treatments for Obesity Nationally Noncovered Indications</p> <ol style="list-style-type: none"> 1. Treatments for obesity alone remain non-covered. 2. Supplemented fasting is not covered under the Medicare program as a general treatment for obesity, with certain exceptions. Where weight loss is necessary before surgery in order to ameliorate the complications posed by obesity when it coexists with pathological conditions such as cardiac and respiratory diseases, diabetes, or hypertension (and other more conservative techniques to achieve this end are not regarded as appropriate), supplemented fasting with adequate monitoring of the patient is eligible for coverage on a case-by-case basis or pursuant to a local coverage determination. The risks associated with the achievement of rapid weight loss must be carefully balanced against the risk posed by the

Intervention	Current Guidelines	FDA Approval for Indicated Use	CMS Coverage
			condition requiring surgical treatment
Physical therapy	<p>ACR: conditionally recommends receiving manual therapy in combination with supervised exercise.</p> <p>AAOS: Not found specifically on physical therapy, although there were studies presented [unless if the following: “We are unable to recommend for or against the use of physical agents (including electrotherapeutic modalities) in patients with symptomatic osteoarthritis of the knee. (inconclusive)”</p> <p>“We are unable to recommend for or against manual therapy in patients with symptomatic osteoarthritis of the knee. (inconclusive)”]</p>	Not relevant	Covered under Part B subject to certain conditions and limitations
TENS/NMES	<p>ACR: conditionally recommends instruction in use of TENS</p> <p>AAOS: found insufficient evidence supporting use of TENS</p>		Medicare Part B may cover a TENS unit for a patient who has been suffering from chronic pain for at least three months, for which other, standard pain relief methods have failed
Braces and/or orthotics (orthoses or wedges)	<p>ACR: conditionally recommends using medially directed patellar taping; wearing medially wedged insoles if a patient with OAK has lateral compartment OA, wearing laterally wedged subtalar strapped insoles if a patient with OAK have medial compartment OA; has no recommendations on wearing laterally wedged insoles and wearing knee braces.</p> <p>AAOS: cannot suggest that lateral wedge insoles be used for patients with symptomatic medial compartment osteoarthritis of the knee. (moderate)</p>	Unloader braces are approved by the FDA as medical equipment [need to check orthotics]	Medicare Part B covers medically necessary arm, leg, back, and neck braces under the durable medical equipment prefabricated orthotics benefit, subject to certain conditions and limitations. Shoes and foot orthotics are covered under certain circumstances only when criteria are met.

Appendix H. Adverse Events

Table H1. Adverse Events by treatment (number (%))

Table H1a. Platelet-rich plasma (PRP)

Reference	Type	Control	PRP 1 injection	PRP 2 injections
Patel, 2013 ²³	Pain and stiffness	0	6(22.22)	11(44.00)
	Adverse events (AEs)	0	4(14.8)	3(12)
Rayegani, 2014 ²⁵	Significant Complications	0	0	

Table H1b. Glucosamine/chondroitin

Reference	Type	Control	Glucosamine	Chondroitin	Glucosamine+chondroitin	Celecoxib
Hochberg, 2008 ¹¹⁶	Death	0	0	0	0	0
	Non-fatal myocardial infarction (MI)	0	0	0	0	0
	GI bleed	0	0	0	0	0
	Cerebrovascular accident (CVA)	0	0	0	0	1 (0.31)
	Transient ischemic attack (TIA)	0	1(0.32)	0	0	1(0.31)
	Withdrawal (w/d) due to AE	11(3.52)	9(2.84)	20(6.29)	12(3.79)	7(2.20)
Kahan, 2009 ³⁶	Good or very good tolerability	291(93)		290(94)		
	GI side effects	18(5.9)		19(6)		
	W/d due to AEs	17(5)		16(5)		
Sawitzke, 2010 ²⁷	MI	0	1(0.75)	0	2(1.55)	0
	Coronary angioplasty	1(0.76)	0	0	0	0
	Hip arthroplasty	0	0	0	0	1(0.70)
	CVA	0	0	1(0.75)	0	2(1.41)
	Abdominal wall abscess	0	0	0	0	1
	Suicide	1(0.76)	0	0	0	0
	HTN	1(0.76)	0	0	1(0.78)	0
	Palpitations	0	0	0	1	0
	TIA	0	0	0	1	0
	Serious GI bleed	0	0	0	0	0
Fransen, 2014 ³⁰	W/d due to AE	8(5.30)	8(5.26)	11(7.28)	7(4.6)	
	w/d due to blood glucose issues	1(0.66)	0	1(0.66)	0	
	W/d due to cardiac	1(0.66)	0	0	3(1.98)	
	W/d due to GI, rash	5(3.31)	4(2.63)	4(2.64)	2(1.32)	

Reference	Type	Control	Glucosamine	Chondroitin	Glucosamine+ chondroitin	Celecoxib
		Diet alone			G/C+ diet	
Bellare, 2014 ²⁹	SAE	0			0	
Hochberg, 2016 ²⁸	AEs				22(7.24)	22(7.36)

Table H1c. Chondroitin

Reference	Type	Control	1200mg Chondroitin qd/400mg tid
Zegels, 2013 ³⁵	Serious AE	2(1.7)	2(1.7)/4(3.41)
	AEs related to treatment	49(41)	31(26)/31(26)

Table H1d. Strength Training

Reference	Type	Control	Exercise
Oliveira, 2012 ³⁸	Exercise intolerance	0	2(4)
Foroughi, 2011 ⁴²	Minor AEs	1(3.57)	0
Imoto, 2012 ³⁹	Significant knee inflammation	0	2(4)

Table H1e. Agility Training

Reference	Type	Control	Exercise
Knoop, 2013 ⁴⁶	Any serious AEs	0	0
Fitzgerald, 2011 ⁵⁰	Serious AEs	0	0

Table H1f. Yoga

Reference	Type	Control	Yoga
Cheung, 2014 ⁵⁷	AEs	0	0

Table H1g. Manual Therapy

Reference	Type	Control	Exercise	Exercise + booster	Exercise + manual therapy	Exercise + booster+ manual therapy	Massage/ Acupressure
Abbott, 2015 ⁵³	Hip pain		1(5.62)	0	0	0	
	Fall on knee associated with exercise		0	0	0	1(5.62)	
Zhang, 2012 ¹⁰¹	AEs	0					0
Perlman, 2012 ¹⁰³	Any AEs	0					0(30-120- minutes per week
Dwyer, 2015 ¹⁰²	Any AEs		0		0		0

Table H1h. Infrared (IR)

Reference		Control	IR
Hsieh, 2012 ⁶⁴	AEs	0	0

Table H1i. Mud bath

Reference		Control	Mud bath
Fioravanti, 2015 ⁶¹	Mild hypotension	0	3(5.66)
	Febrile episode	0	1(1.89)
	Gastric pyrosis	3(6)	0
	Epigastralgia	2(4)	0

Table H1j. Braces

Reference		Control	Brace
Callaghan, 2015 ⁸²	Bilateral leg swelling	0	1(1.59)
Cherian, 2015 ⁸³	Severe AEs	0	0
	Minor irritation at pad placement sites	0	1(6.90)

Table H1k. Orthotics

Reference		Control	Insole
Bennell, 2011 ⁹¹	Back pain	1(1.03)	9(8.74)
	Foot pain	14(14.43)	32(31.07)
	Uncomfortable or difficulty fitting in shoes	4(4.12)	15(14.56)
	Increased knee pain	5(5.14)	2(1.94)
	Instability	1(1.03)	0
	Self-reported problems with insoles	21(21.65)	42(40.78)
Rodrigues, 2008 ⁸⁵	Mild discomfort	1(7.14)	0
Campos, 2015 ⁸⁸	Ankle pain	4(13.79)	5(17.24)

Table H1l. Minimalist Shoe

Reference		Control	Shoe
Erhart, 2010 ⁹⁵	Hip pain	1(2.56)	0
	Shoe discomfort	4(10.26)	1(2.5)
	Foot pain	2(5.13)	0
	Sciatic pain	0	1(2.5)
	Meniscectomy	2(5.2)	1(2.5)
	TKR	1(2.56)	0

Table H1m. TENS

Reference		Sham TENS	TENS
Atamaz,	Worsening of	3(8.11)	3(8.11)

2012 ⁷²	symptoms		
Gschiel, 2010 ⁷¹	AEs	0	0

Table H1n. NMES

Reference		Sham NMES	NMES
Elboim-Gabyzon, 2013 ⁷⁰	Pneumonia	1(3.03)	1(3.33)
Laufer, 2014 ⁶⁷	Adverse reaction to treatment	0	0
Imoto, 2013 ⁶⁹	Hypertensive crisis	0	1(2)
		Exercise	NMES + exercise
Mizusaki Imoto, 2013 ⁶⁸	Blood pressure spike	0	1

Table H1o. Whole Body Vibration

Reference		Control	Treated
Rabini, 2015 ⁸⁰	AEs	0	0
Wang, 2015 ⁸¹	AEs	0	0
Wang, 2015 ⁷⁹	Slight low back pain	0	1(5.62)
	Severe AEs	0	0
Park, 2013 ⁷⁶	Any AE	0	1(9.09)

Table H1p. Weight loss

Reference		Control	Exercise	Diet	Diet + exercise
Messier, 2013 ¹⁰⁷	Heart palpitations		1	0	0
	ALS		0	0	1(0.66)
	Stroke		0	0	1(0.66)
	Lung HTN		0	0	1(0.66)
	Lung infection		0	0	1(0.66)
	Cancer		1(0.66)	1(0.67)	2(1.32)
	Staph infection		0	0	1(0.66)
Ghroubi, 2008 ¹⁰⁵	Worsening knee pain	0	0	0	0
Christensen, 2015 ⁵⁴	Nausea	1(1.56)	8(12.5)	3(4.69)	
	Diarrhea	4(6.2)	6(9.38)	3(4.69)	
	Constipation	8(12.5)	7(10.94)	9(14.06)	
	Flatulence	14(21.88)	10(15.63)	19(29.69)	
	Epigastric pain	1(1.56)	7(10.94)	6(9.38)	
	Vomiting	1(1.56)	4(6.25)	3(4.69)	
	Abdominal pain	3(4.69)	4(6.25)	6(9.38)	
	Heartburn	3(4.69)	9(14.06)	3(4.69)	
	Biliary symptoms	0	4(6.25)	2(3.13)	
	Cramps	8(12.5)	7(10.93)	6(9.38)	
	Joint pain	12(18.75)	12(18.75)	15(23.44)	
	Back pain	10(15.62)	6(9.38)	11(17.19)	

Reference		Control	Exercise	Diet	Diet + exercise
	Swollen joints	11(17.19)	10(15.63)	11(17.19)	
	Sciatic pain	9(14.06)	7(10.94)	4(6.25)	
	Dizziness	8(12.5)	10(15.63)	7(10.94)	
	Headache	5(7.81)	12(18.75)	6(9.38)	
	Anxiety	2(3.13)	5(7.81)	3(4.69)	
	Sleeplessness	11(17.18)	11(17.19)	6(9.38)	
	Fatigue	12(18.75)	13(20.31)	8(12.5)	
	Mood changes	5(7.81)	13(20.31)	5(7.81)	
	Depressive tendencies	4(6.25)	5(7.81)	6(9.38)	
	Dry skin	6(9.38)	6(9.38)	4(6.25)	
	Allergic rash	4(6.25)	7(10.94)	5(7.81)	
	Redness	2(3.13)	7(10.94)	4(6.25)	
	Eczema	3(4.69)	5(7.81)	4(6.25)	
	Perianal itching	2(3.13)	11(17.2)	5(7.81)	
	Skin irritation	3(4.69)	8(12.5)	5(7.81)	
	Urticaria	1(1.56)	3(4.69)	3(4.69)	
	Cold sensitivity	6(9.38)	8(12.5)	9(14.06)	
	Influenza	2(3.13)	5(7.8)	7(10.9)	
	Hair loss	2(3.13)	7(10.9)	5(7.8)	
	Bad breath	5(7.8)	9(14.06)	6(9.38)	
	Toothache	4(6.25)	6(9.38)	4(6.25)	
Bliddal, 2011 ¹⁰⁸	Constipation			5(11.36)	
	Increased flatulence			4(9.09)	
	Dizziness			2(4.55)	
	Heightened cold sensitivity	0		2(4.55)	

Table H1q. Pain Coping Skills Training (PCST)

Reference	Type	Control	Exercise	PCST	PCST+ exercise	Weight management	PCST+ weight management
Bennell, 2015 ⁴⁵	Number reporting AEs during treatment		28(37.33)	4(5.4)	24(37.3)		
	Number AEs during treatment		38(50.67)	7(9.46)	31(42.47)		
	Increased knee pain during treatment		22(29.33)	2(2.70)	15(20.55)		
	Pain in other regions during treatment		11(14.67)	3(5.05)	11(15.07)		
	Swelling/ inflammation during treatment		2(2.67)	2(2.70)	2(2.74)		
	Increased stiffness		2(2.67)	0	3(4.11)		

Reference	Type	Control	Exercise	PCST	PCST+ exercise	Weight manage- ment	PCST+ weight manage- ment
	during treatment						
	Knee instability during treatment		1(1.33)	0	0		
	Number participants reporting AEs during followup		12(16)	4(5.41)	7(9.59)		
	Number of AEs during followup		15(20)	4(5.41)	8(10.96)		
	Increased knee pain during followup		6(8)	4(5.41)	3(4.11)		
	Pain in other regions during follow- up		7(9.33)	0	2(2.74)		
	Swelling/ inflammation during followup		2(2.67)	0	2(2.74)		
	Increased stiffness during followup		0	0	1(1.37)		
Somers, 2012 ¹⁰⁹	Fall from treadmill	0		0		0	1(1.61)

Table H1r. Self-management

Reference	Type	Control	Self- Management
Coleman, 2012 ¹¹⁵	Number with serious AEs	0	0

Appendix I. MCID cutoffs

Table I1. MCID cutoffs developed or used in a representative sample of articles

Author, Year	Condition/ Intervention /FU	Cutoffs	Notes
Eberle, 1999 PMID: 10489324	Knee OA HA injection, 6 month followup	VAS pain: 8.4mm on a 0-100 mm scale; 0.7 points on Lequesne 24-point scale	Anchor question: complaints reduced
Angst 2001 PMID:11501727	Knee or hip OA Rehabilitation, 3 month followup	WOMAC pain: 0.75 (0-10 scale) WOMAC function and total: 0.67 SF-36 physical function: 3.3 (0-100 scale)	Anchor question: current subjective health much better, slightly better, no change, slightly worse... Converted all 5 WOMAC pain item scores to a 0-10 scale and took the average) Separate values for worsening and improvement
Salaffi 2004 PMID: 15207508	Chronic musculoskeletal pain (OA knee, OA hip, AS, RA, OA hand) Not described	NRS: 15% or 1 point decrease for minimum improvement, 33% or 2 points for much better (which they regarded as clinical improvement)	Anchor: Patient global impression of change
Tubach 2005 PMID: 15208174	Knee or hip OA NSAIDs, 4 weeks	Knee: VAS pain: -19.9mm (-40.8%) WOMAC function: -9.1(-26%)	WOMAC 17 items, 5-point likert scale, total score normalized to 0-100 scale MCII Initial severity affected MCII but age, disease duration, and sex did not
Wandel 2010 PMID: 20847017	Knee or hip OA Glucosamine-chondroitin vs. placebo network MA	MCID 0.37 SD units, corresponding to 0.9cm (0-10cm VAS scale)	Median pooled SD of 2.5cm used to back transform effect sizes to 10cm VAS scale
OMERACT-OARSI responder criteria Pham 2003 PMID: 12858473	Knee or hip OA	Clinical response was defined as either 1. improvement of at least 50% in pain or function and an absolute change of at least 20 points on a scale of 0-100 in the WOMAC pain or function subscores, or 2. at least 2 of the following criteria: improvement of at least 20% and an absolute change greater than 10 points on a scale of 0-100 in the WOMAC pain score, improvement of at least 20% and an absolute change greater than 10 points (on a 0-100 scale) in the WOMAC function score, or improvement of at least 20% in the patient Global Assessment score and an absolute change >10 points on a scale of 0-100	WOMAC pain and function scales converted to single 0-100 scores.