

Appendix

Appendix 1 Search strategies.....	2
Appendix 2 Results of re-analysis.....	4
Appendix 3 Results of Inconsistency.....	6
Appendix 4 Conventional meta-analyses results	7
Appendix 5 Network Diagram.....	10
Appendix 6 Table of GRADE.....	11
Appendix 7 Comparison-adjusted funnel plot for each outcome from the network meta-analysis	16

Appendix 1 Search strategies

Search strategies for randomized controlled trials Pubmed

1. (((((((("Osteoarthritis, Knee"[Mesh]) OR Knee Osteoarthritis[Title/Abstract]) OR Knee Osteoarthritis[Title/Abstract]) OR Osteoarthritis of Knee[Title/Abstract]) OR Osteoarthritis of the Knee[Title/Abstract]))) AND (((((((((((("Physical Therapy Modalities"[Mesh]) OR (Modalities, Physical Therapy[Title/Abstract])) OR (Modality, Physical Therapy[Title/Abstract])) OR (Physical Therapy Modality[Title/Abstract])) OR (Physiotherapy (Techniques)[Title/Abstract]) OR (Physiotherapies (Techniques)[Title/Abstract]) OR (Physical Therapy Techniques[Title/Abstract]) OR (Physical Therapy Technique[Title/Abstract]) OR (Techniques, Physical Therapy[Title/Abstract]) OR (Group Physiotherapy[Title/Abstract]) OR (Group Physiotherapies[Title/Abstract]) OR (Physiotherapies, Group[Title/Abstract]) OR (Physiotherapy, Group[Title/Abstract]) OR (Neurological Physiotherapy[Title/Abstract]) OR (Physiotherapy, Neurological[Title/Abstract])) OR (Neurophysiotherapy[Title/Abstract])
 2. (((((((("Osteoarthritis, Knee"[Mesh]) OR Knee Osteoarthritis[Title/Abstract]) OR Knee Osteoarthritis[Title/Abstract]) OR Osteoarthritis of Knee[Title/Abstract]) OR Osteoarthritis of the Knee[Title/Abstract]))) AND (((("Orthopedic Equipment"[Mesh]) OR(Equipment,Orthopedic[Title/Abstract]))OR(Equipments,
1. ('physiotherapy'/exp OR 'physical therapy':ab,ti OR 'physical therapy (speciality)':ab,ti OR 'physical therapy (specialty)':ab,ti OR 'physical therapy modalities ':ab,ti OR 'physical therapy service':ab,ti OR 'physical therapy speciality':ab,ti OR 'physical therapy specialty ':ab,ti OR 'physical treatment':ab,ti OR ' physio therapy ':ab,ti OR 'physical therapy techniques':ab,ti OR 'physical treatment':ab,ti OR 'physiotherapy department':ab,ti OR 'therapy, physical':ab,ti) AND ('knee osteoarthritis'/exp OR 'arthrosis, knee':ab,ti OR 'femorotibial arthrosis':ab,ti OR 'gonarthrosis':ab,ti OR 'knee arthrosis':ab,ti OR 'knee joint arthrosis':ab,ti OR 'knee joint osteoarthritis':ab,ti OR 'knee osteo-arthritis':ab,ti OR 'knee osteo-arthritis':ab,ti OR 'knee osteoarthritis':ab,ti OR 'osteoarthritis, knee':ab,ti OR 'osteoarthrosis, knee':ab,ti)
 2. ('orthosis'/exp OR 'device, orthotic':ab,ti OR 'devices, orthotic':ab,ti OR 'orthesis':ab,ti OR 'orthoepedic support device':ab,ti OR 'orthopedic support device':ab,ti OR 'orthoses':ab,ti OR 'orthotic device (physical object)':ab,ti OR 'orthotic devices':ab,ti) AND ('knee osteoarthritis'/exp OR 'arthrosis, knee':ab,ti OR 'femorotibial arthrosis':ab,ti OR 'gonarthrosis':ab,ti OR 'knee arthrosis':ab,ti OR 'knee joint arthrosis':ab,ti OR 'knee joint osteoarthritis':ab,ti OR 'knee osteo-arthritis':ab,ti OR 'knee osteo-arthritis':ab,ti OR 'knee osteoarthritis':ab,ti OR 'osteoarthritis, knee':ab,ti OR 'osteoarthrosis, knee':ab,ti)

Web of Science

1. AB=(physical therapy OR physiotherapy OR physio therapy OR physical treatment OR physiotherapy department OR physical therapy techniques)
2. TI=(physical therapy OR physiotherapy OR physio therapy OR physical treatment OR physiotherapy department OR physical therapy techniques)
3. AB=(orthosis OR device OR orthosis OR orthoses OR orthopaedic support device OR orthotic device)
4. TI=(orthosis OR device OR orthosis OR orthoses OR orthopaedic support device OR orthotic device)
5. #4 OR #3 OR #2 OR #1
6. AB=(knee osteoarthritis OR femorotibial arthrosis OR gonarthrosis OR knee arthrosis OR knee osteo-arthritis OR knee osteoarthritis OR osteoarthritis)
7. TI=(knee osteoarthritis OR femorotibial arthrosis OR gonarthrosis OR knee arthrosis OR knee osteo-arthritis OR knee osteoarthritis OR osteoarthritis)
8. #6 OR #7
9. #8 AND #5

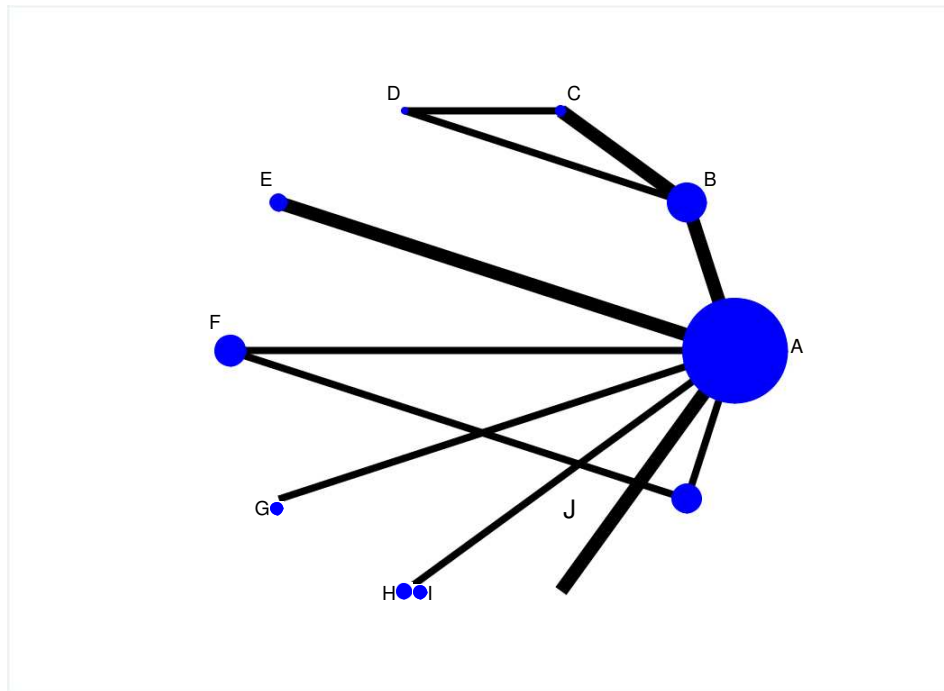
1. (MeSH descriptor: [Physical Therapy Modalities] explode all trees OR (Neurological Physiotherapy):ti,ab,kw OR (Physiotherapy, Neurological):ti,ab,kw OR (Neurophysiotherapy):ti,ab,kw OR (Techniques, Physical Therapy):ti,ab,kw OR (Physiotherapies (Techniques)):ti,ab,kw OR (Physical Therapy Techniques):ti,ab,kw OR (Physiotherapy (Techniques)):ti,ab,kw OR (Modality, Physical Therapy):ti,ab,kw OR (Physical Therapy Modality):ti,ab,kw OR (Physical Therapy Technique):ti,ab,kw OR (Modalities, Physical Therapy):ti,ab,kw OR (Group Physiotherapies):ti,ab,kw OR (Physiotherapy, Group):ti,ab,kw OR (Group Physiotherapy):ti,ab,kw OR (Physiotherapies, Group):ti,ab,kw) AND ((Osteoarthritis of Knee):ti,ab,kw OR (Knee Osteoarthritis):ti,ab,kw OR (Knee Osteoarthritis):ti,ab,kw OR (Osteoarthritis of the Knee):ti,ab,kw) OR MeSH descriptor: [Osteoarthritis, Knee] explode all trees)
2. (MeSH descriptor: [Orthopedic Equipment] explode all trees OR (Orthopedic Equipments):ti,ab,kw OR (Equipment, Orthopedic):ti,ab,kw OR (Equipments, Orthopedic):ti,ab,kw) AND ((Osteoarthritis of Knee):ti,ab,kw OR (Knee Osteoarthritis):ti,ab,kw OR (Knee Osteoarthritis):ti,ab,kw OR (Osteoarthritis of the Knee):ti,ab,kw) OR MeSH descriptor: [Osteoarthritis, Knee] explode all trees)

MEDLINE

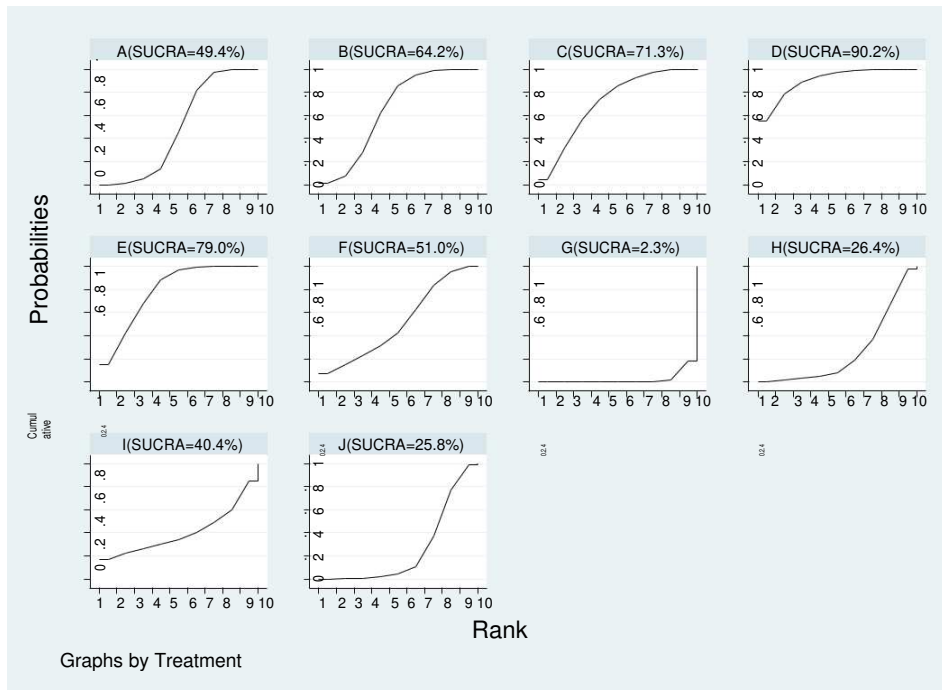
1. (knee osteoarthritis) OR (femorotibial arthrosis) OR (gonarthrosis) OR (knee arthrosis) OR (knee osteo-arthritis) OR (knee osteoarthritis) OR (osteoarthritis)
2. (physical therapy) OR (physiotherapy) OR (physio therapy) OR (physical treatment) OR (physiotherapy department) OR (physical therapy techniques)
3. (orthotic devices) OR (Orthopedic Equipment) OR (orthosis) OR (device) OR (orthosis) OR (orthoses) OR (orthopaedic support device)
4. #2 OR #3

5. #1 AND #4

Appendix 2 Results of re-analysis

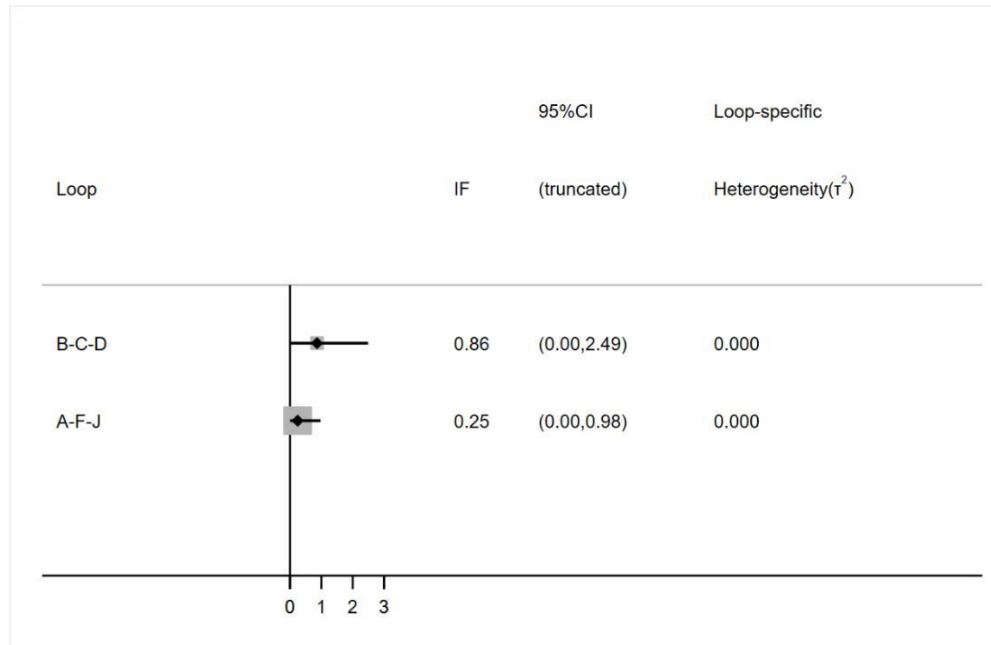


eFigure 1. Structure of network formed by interventions and their direct comparisons on First peak KAM (re-analysis). A= Control condition; B= Lateral Wedge Insole; C= Knee Brace; D= Lateral Wedge Insole+ Knee Brace; E= Gait retraining; F= Quadriceps strengthening; G= Variable-stiffness shoe; H= Hip strengthening; I= Lower limb exercise; J= Neuromuscular exercise.



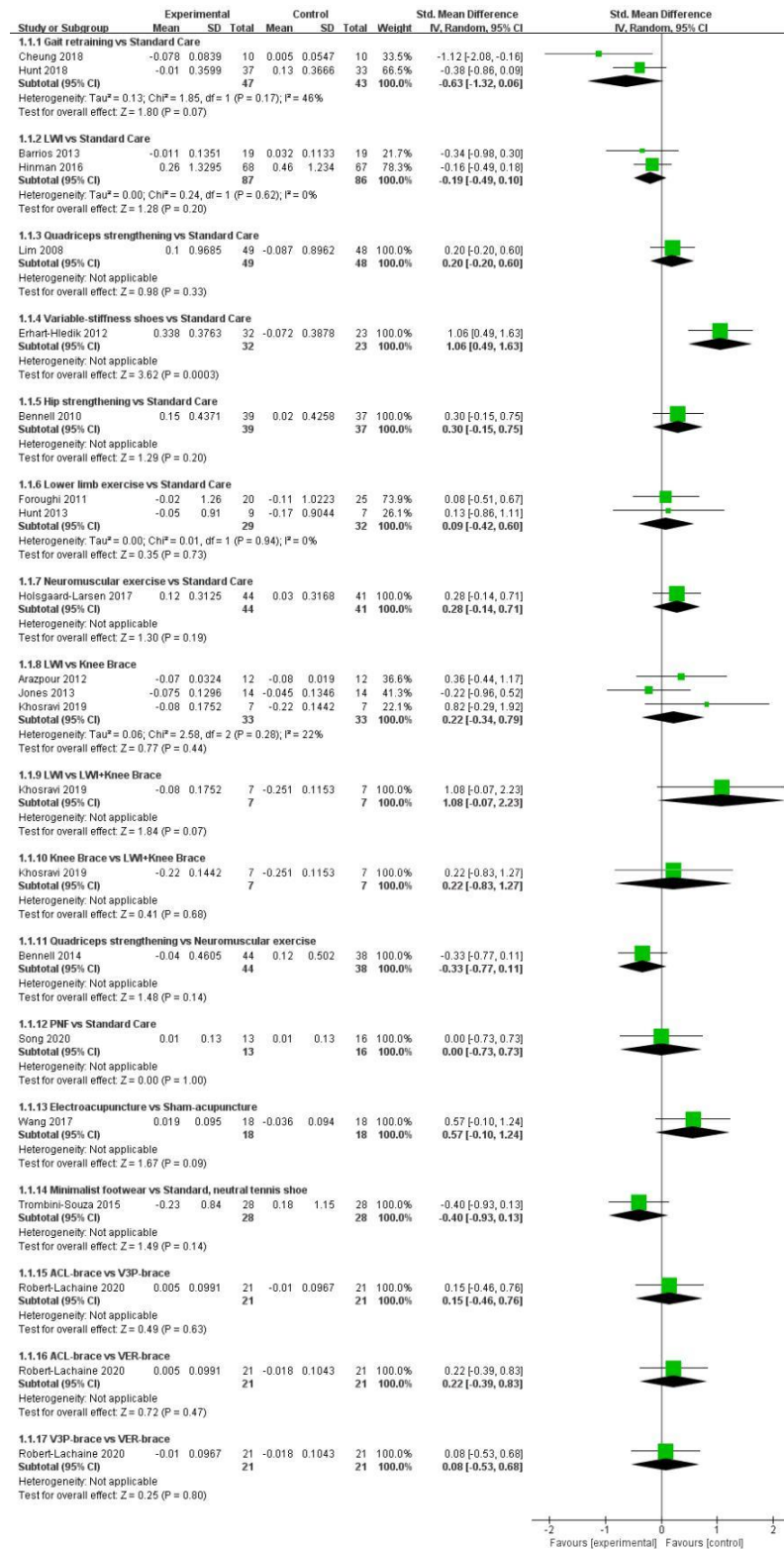
eFigure 2. Rankings for effects on First peak KAM (re-analysis). Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on. A= Control condition; B= Lateral Wedge Insole; C= Knee Brace; D= Lateral Wedge Insole+ Knee Brace; E= Gait retraining; F= Quadriceps strengthening; G= Variable-stiffness shoe; H= Hip strengthening; I= Lower limb exercise; J= Neuromuscular exercise.

Appendix 3 Results of Inconsistency

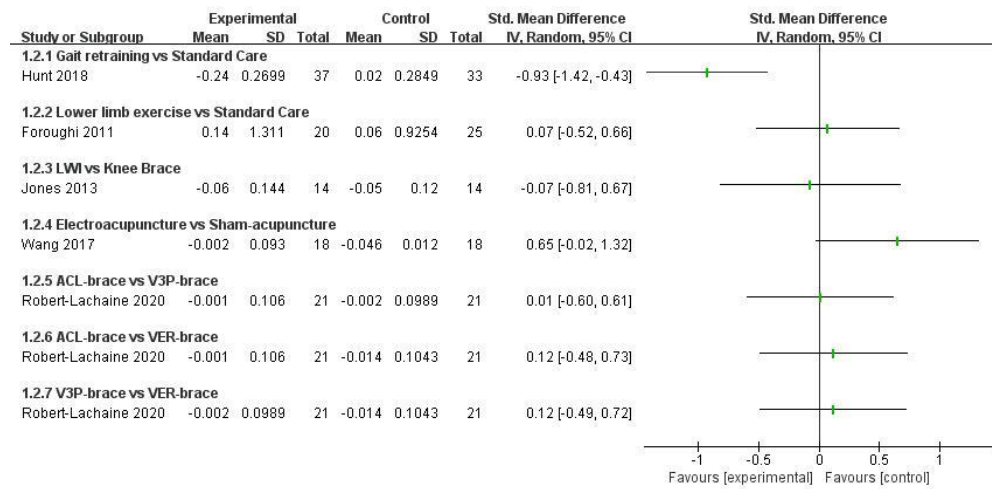


eFigure 1. Inconsistency for triangular loops in First peak KAM.

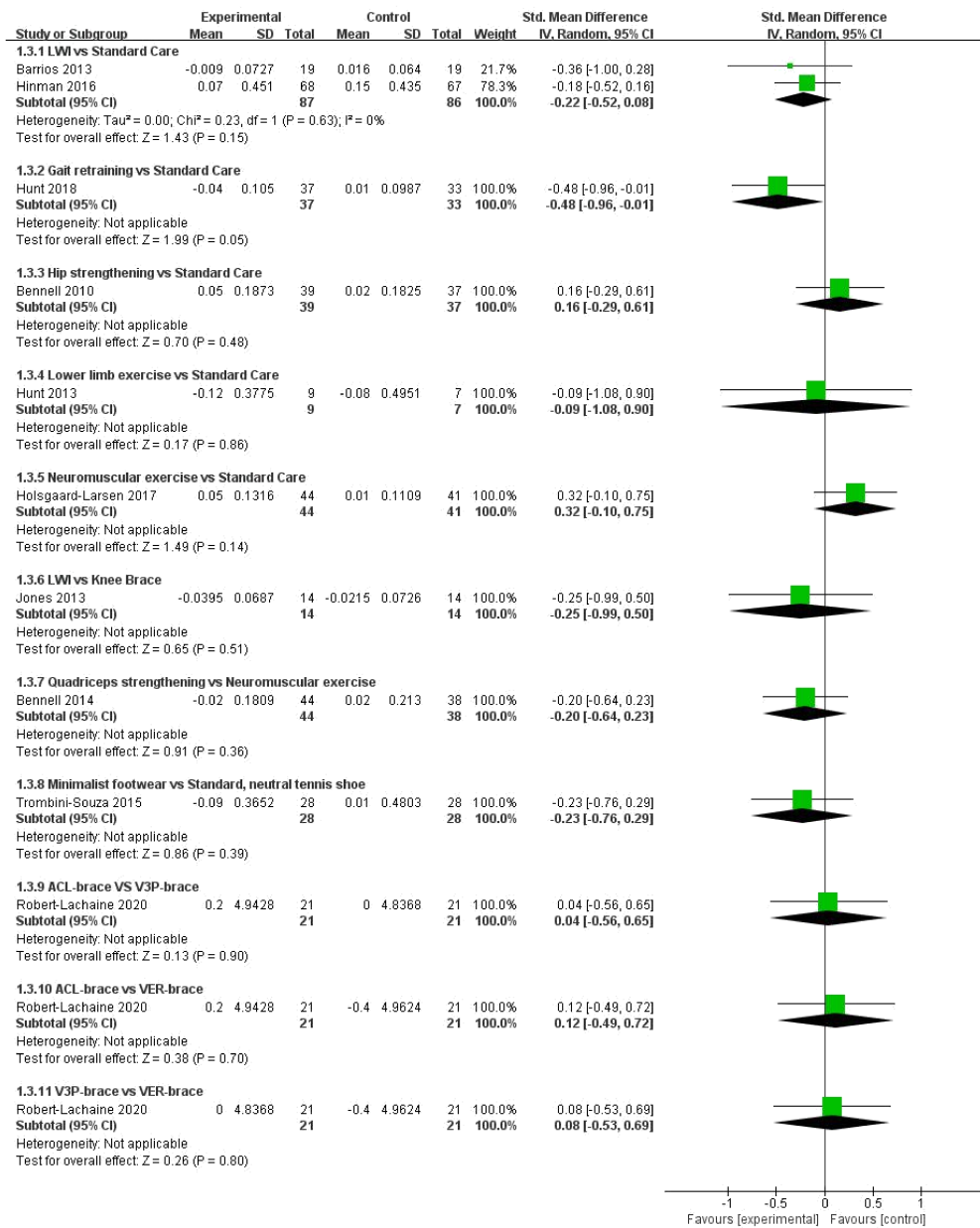
Appendix 4 Conventional meta-analyses results



eFigure 1a. Conventional meta-analysis of treatment effects on First peak KAM.

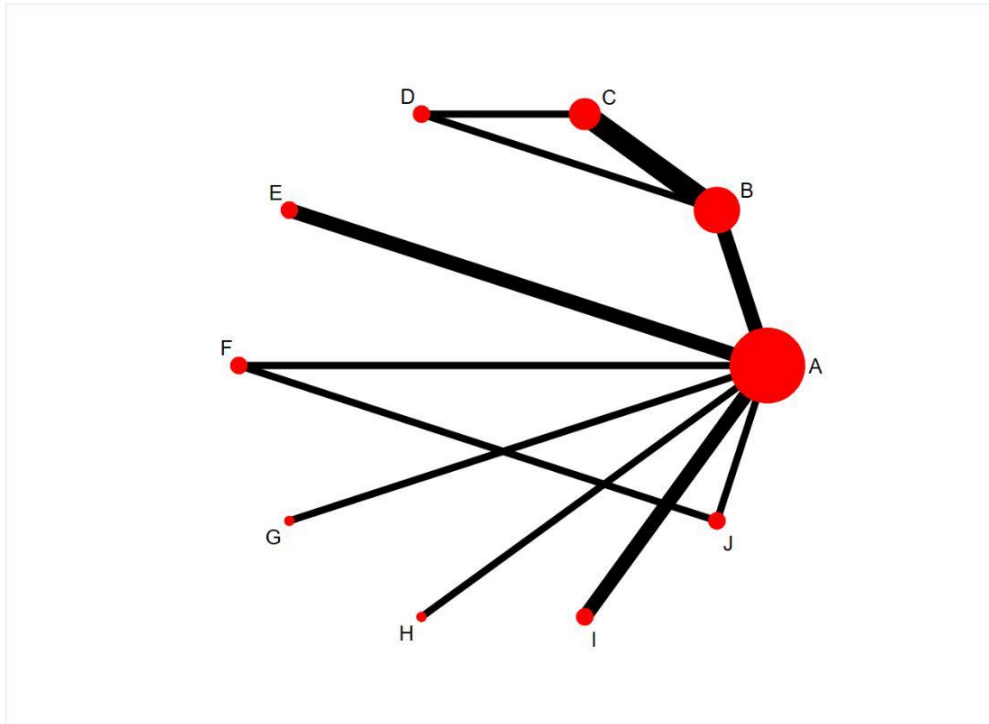


eFigure 1b. Conventional meta-analysis of treatment effects on Second peak KAM.



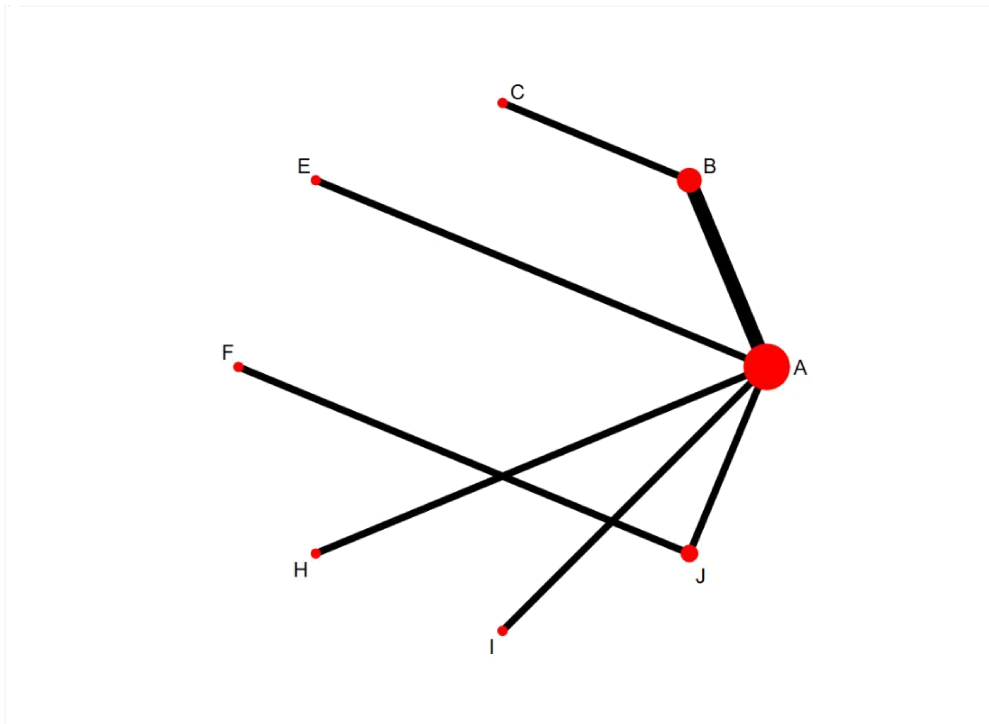
eFigure 1c. Conventional meta-analysis of treatment effects on KAAI.

Appendix 5 Network Diagram



eFigure 1a. Structure of network formed by interventions and their direct comparisons (First peak KAM). A= Control condition; B= Lateral Wedge Insole; C= Knee Brace; D= Lateral Wedge Insole+ Knee Brace; E= Gait retraining; F= Quadriceps strengthening; G= Variable-stiffness shoe; H= Hip strengthening; I= Lower limb exercise; J= Neuromuscular exercise.

Footnote: Width of the lines is proportional to the number of trials comparing every pair of treatments. Size of every circle is proportional to the number of randomly assigned participants (ie, sample size).



eFigure 1b. Structure of network formed by interventions and their direct comparisons (KAAI). A= Control condition; B= Lateral Wedge Insole; C= Knee Brace; E= Gait retraining; F= Quadriceps strengthening; H= Hip strengthening; I= Lower limb exercise; J= Neuromuscular exercise.

Footnote: Width of the lines is proportional to the number of trials comparing every pair of treatments. Size of every circle is proportional to the number of randomly assigned participants (ie, sample size).

Appendix 6 Table of GRADE

Based on all the above information, we GRADEd each network estimate according to the following criteria:

- 1) Study limitations: We downgraded by one level when the contributions from low RoB comparisons were less than 30% and contributions from moderate RoB comparisons were 70% or greater. And we downgraded by two level when the contributions from low RoB comparisons were more than 30%.
- 2) Imprecision: We considered a clinically meaningful threshold for CI to be 0 and did not

downgrade the estimate if the upper limit is below 0; or if the lower limit is above 0.

- 3) Inconsistency: We rated two concepts, heterogeneity and incoherence (inconsistency), in this domain. For heterogeneity, we did not downgrade any network estimate for heterogeneity, because we looked at the common tau and found that it is low. For inconsistency, we looked at the results of inconsistency (Appendix 2), where we have not downgraded for imprecision.
- 4) Indirectness: We have assured transitivity in our network by limiting the included studies to patients with knee osteoarthritis. Evaluation of transitivity for singly-connected nodes is unclear, so we downgraded such nodes for indirectness.
- 5) Publication bias: The comparison-adjusted funnel plot (Appendix 5) did not suggest presence of overall publication bias. We managed to retrieve supplementary and unpublished information included in the available systematic reviews and network meta-analyses, and we are confident that we have all available information that is possible to capture from clinical trial registries. Although we cannot completely rule out the possibility that some research is still missing, we still believe that the project does not need to be downgraded.

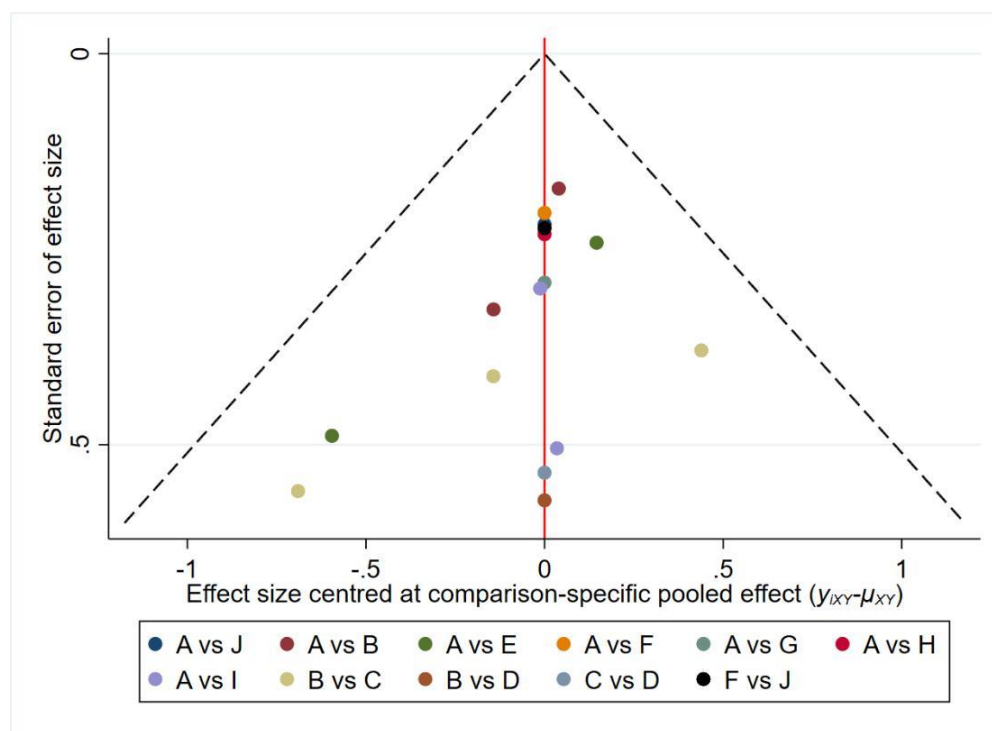
Comparison	Nature of the Evidence	GRADE	Downgrading due to
AB: Control Condition vs LWI	Mixed	LOW	Study limitations; Imprecision
AC: Control Condition vs Knee Brace	Indirect	LOW	Study limitations; Imprecision
AD: Control Condition vs LWI+Knee Brace	Indirect	LOW	Study limitations; Imprecision
AE: Control Condition vs Gait Retraining	Mixed	VERY LOW	Study limitations; Indirectness
AF: Control Condition vs Quadriceps Strengthening	Mixed	VERY LOW	Study limitations; Imprecision
AG: Control Condition vs Variable-Stiffness Shoes	Mixed	VERY LOW	Study limitations; Indirectness;
AH: Control Condition vs Hip Strengthening	Mixed	VERY LOW	Study limitations; Indirectness; Imprecision

AI: Control Condition vs Lower Limb Exercise	Mixed	VERY LOW	Study limitations; Indirectness; Imprecision
AJ: Control Condition vs Neuromuscular Exercise	Mixed	MODERATE	Study limitations
BC: LWI vs Knee Brace	Mixed	VERY LOW	Study limitations; Imprecision
BD: LWI vs LWI+Knee Brace	Mixed	VERY LOW	Study limitations; Imprecision
BE: LWI vs Gait Retraining	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
BF: LWI vs Quadriceps Strengthening	Indirect	LOW	Study limitations; Imprecision
BG: LWI vs Variable-Stiffness Shoes	Indirect	LOW	Study limitations; Indirectness
BH: LWI vs Hip Strengthening	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
BI: LWI vs Lower Limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
BJ: LWI vs Neuromuscular Exercise	Indirect	MODERATE	Study limitations
CD: Knee Brace vs LWI+Knee Brace	Mixed	VERY LOW	Study limitations; Imprecision
CE: Knee Brace vs Gait Retraining	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
CF: Knee Brace vs Quadriceps Strengthening	Indirect	LOW	Study limitations; Imprecision
CG: Knee Brace vs Variable-Stiffness Shoes	Indirect	LOW	Study limitations; Indirectness
CH: Knee Brace vs Hip Strengthening	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
CI: Knee Brace vs Lower Limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
CJ: Knee Brace vs Neuromuscular Exercise	Indirect	MODERATE	Study limitations
DE: LWI+Knee Brace vs Gait	Indirect	VERY LOW	Study limitations; Indirectness;

Retraining			Imprecision
DF: LWI+Knee Brace vs Quadriceps	Indirect	LOW	Study limitations; Imprecision
Strengthening			
DG: LWI+Knee Brace vs Variable-Stiffness Shoes	Indirect	VERY LOW	Study limitations; Indirectness
DH: LWI+Knee Brace vs Hip	Indirect	LOW	Study limitations; Indirectness
Strengthening			
DI: LWI+Knee Brace vs Lower Limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
DJ: LWI+Knee Brace vs Neuromuscular Exercise	Indirect	MODERATE	Study limitations
EF: Gait Retraining vs Quadriceps	Indirect	VERY LOW	Study limitations; Indirectness
Strengthening			
EG: Gait Retraining vs Variable-Stiffness Shoes	Indirect	VERY LOW	Study limitations; Indirectness
EH: Gait Retraining vs Hip	Indirect	LOW	Study limitations; Indirectness
Strengthening			
EI: Gait Retraining vs Lower limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
EJ: Gait Retraining vs Neuromuscular Exercise	Indirect	LOW	Study limitations; Indirectness
FG: Quadriceps Strengthening vs Variable-Stiffness Shoes	Indirect	VERY LOW	Study limitations; Indirectness
FH: Quadriceps Strengthening vs Hip	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
Strengthening			
FI: Quadriceps Strengthening vs Lower Limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
FJ: Quadriceps Strengthening vs Neuromuscular Exercise	Mixed	LOW	Study limitations; Imprecision

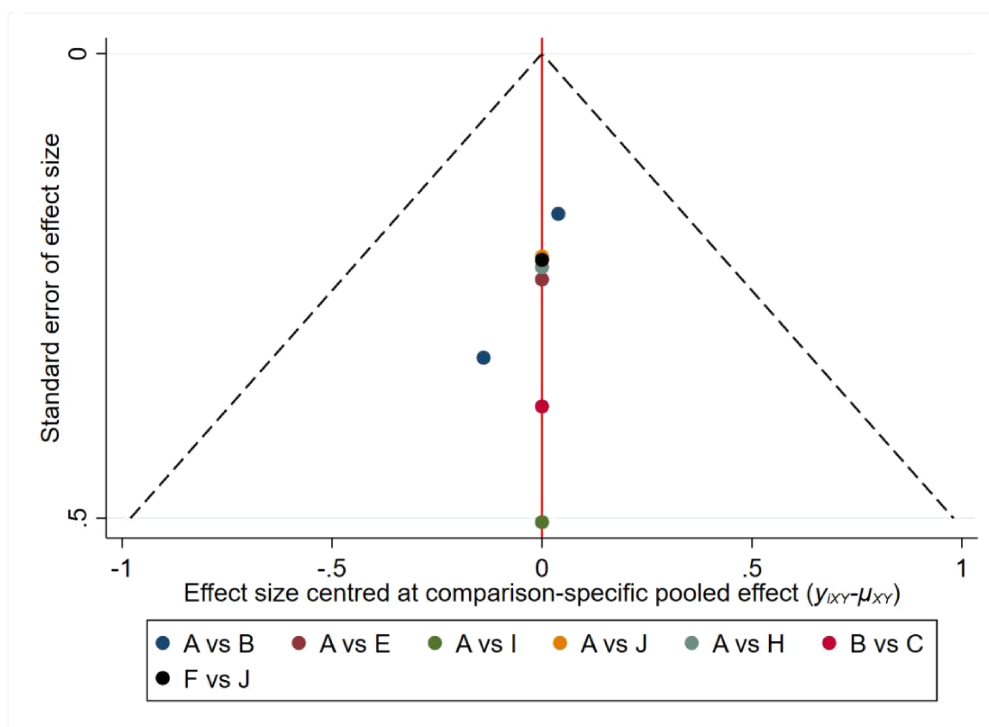
GH: Variable-Stiffness Shoes vs Hip Strengthening	Indirect	LOW	Study limitations; Indirectness
GI: Variable-Stiffness Shoes vs Lower Limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness
GJ: Variable-Stiffness Shoes vs Neuromuscular Exercise	Indirect	LOW	Study limitations; Indirectness
HI: Hip Strengthening vs Lower Limb Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
HJ: Hip Strengthening vs Neuromuscular Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision
IJ: Lower Limb Exercise vs Neuromuscular Exercise	Indirect	VERY LOW	Study limitations; Indirectness; Imprecision

Appendix 7 Comparison-adjusted funnel plot for each outcome from the network meta-analysis



eFigure 1a. Comparison-adjusted funnel plot for First peak KAM.

A= Control condition; B= Lateral Wedge Insole; C= Knee Brace; D= Lateral Wedge Insole+ Knee Brace; E= Gait retraining; F= Quadriceps strengthening; G= Variable-stiffness shoe; H= Hip strengthening; I= Lower limb exercise; J= Neuromuscular exercise.



eFigure 1b. Comparison-adjusted funnel plot for KAAI.

A= Control condition; B= Lateral Wedge Insole; C= Knee Brace; E= Gait retraining; F= Quadriceps strengthening; H= Hip strengthening; I= Lower limb exercise; J= Neuromuscular exercise.