

## Culvenor et al., ACL and meniscal injury rehabilitation

**Appendix: web extra material**

<b>Appendix 1.</b> Systematic search strategy .....	page 2
<b>Appendix 2.</b> ROBIS risk of bias domains.....	page 9
<b>Appendix 3.</b> Algorithm specifically developed to assign GRADE levels of evidence.....	page 10
<b>Appendix 4.</b> Heatmaps displaying the overlap of individual trials that evaluated interventions included in more than one systematic review .....	page 11
<b>Appendix 5.</b> GRADE levels of evidence for overviews of systematic reviews.....	page 12

**Appendix 1. Systematic search strategy****MEDLINE (OVID)**

1. Athletic Injuries/ or Rupture/ or "Sprains and Strains"/
2. Anterior Cruciate Ligament/ or Menisci, Tibial/
3. 1 and 2
4. Anterior Cruciate Ligament Injuries/ or Tibial Meniscus Injuries/
5. 3 or 4
6. (menisc\* adj3 (resect\* or injur\* or tear\* or repair\* or reconstruct\* or shav\* or surg\* or rupture\*)).tw,kf.
7. ((ACL\* or anterior cruciate ligament\*) adj4 (injur\* or tear\* or sprain\* or strain\* or rupture\* or reconstruct\* or surg\* or repair\*)).tw,kf.
8. Meniscectomy/
9. Anterior Cruciate Ligament Reconstruction/
10. meniscectom\*.tw,kf.
11. or/6-10
12. Arthroscopy/
13. arthroscop\*.tw,kf.
14. 12 or 13
15. (ACL\* or anterior cruciate ligament\* or menisc\*).tw,kf.
16. 2 or 15
17. 14 and 16
18. 5 or 11 or 17
19. (rehabilitat\* or physiotherapy or physical therapy or exercis\* or physical activity or (resistance adj4 train\*) or (strength adj4 train\*) or (muscle adj4 strength\*) or (muscle adj4 train\*) or (weight adj4 lifting) or stretch\* or manual therapy or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobilisation or kinesio\* or acupuncture or orthos\$ or orthotics or brace or splint or tape or taping or (tai adj2 chi) or (tai adj2 ji)).tw,kf
20. ((ultrasound or ultrason\*) and (treatment or therapy or intervention)).tw,kf.
21. ((cardiovascul\* adj2 (train\* or exercis\*)) or (aerob\* adj2 exercise\*) or (physical adj2 fitness) or (physical adj2 activit\*) or (high adj2 intensity adj2 interval adj2 train\*) or run\* or walk\* or jog\* or crossfit or danc\*).tw,kf.
22. Rehabilitation/ or Physiotherapy/ or Exercise/ or Exercise Therapy/ or Exercise Movement Techniques/ or Physical Activity/ or Resistance Training/ or Muscle Strength/ or Closed Kinetic Chain Exercise/ or Open Kinetic Chain Exercise/ or Isokinetic Exercise/ or Isometric Exercise/ or Muscle Stretching/ or Massage/ or Cryotherapy/ or Electrotherapy/ or Hydrotherapy/ or Mobilization/ or Joint Mobilization/ or Kinesiotherapy/ or Acupuncture/ or Conservative Treatment/ or Ultrasound Therapy/ or Athletic Tape/
23. or/19-22
24. systematic review/ or meta analysis/ or practice guideline/
25. (systematic review or meta-analysis or guideline).tw,kf.
26. 24 or 25

**EMBASE (OVID)**

1. sport injury/ or joint dislocation/ or rupture/ or sprain/
2. anterior cruciate ligament/ or knee meniscus/
3. 1 and 2
4. anterior cruciate ligament injury/ or anterior cruciate ligament rupture/
5. knee meniscus rupture/
6. or/3-5
7. (menisc\* adj3 (resect\* or injur\* or tear\* or rupture\* or repair\* or reconstruct\* or shav\* or surg\*)).tw,kw.
8. ((ACL\* or anterior cruciate ligament\*) adj4 (injur\* or tear\* or sprain\* or rupture\* or reconstruct\* or surg\* or repair\*)).tw,kw.
9. meniscectomy/
10. meniscectom\*.tw,kw.
11. anterior cruciate ligament reconstruction/
12. or/7-11
13. knee arthroscopy/ or arthroscopy/
14. arthroscop\*.tw,kw.
15. or/13-14
16. (ACL\* or anterior cruciate ligament\* or menisc\*).tw,kw.
17. 2 or 16
18. 15 and 17
19. 6 or 12 or 18
20. (rehabilitat\* or physiotherapy or physical therapy or exercis\* or physical activity or (resistance adj4 train\*) or (strength adj4 train\*) or (muscle adj4 strength\*) or (muscle adj4 train\*) or (weight adj4 lifting) or stretch\* or manual therapy or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobilisation or kinesio\* or acupuncture or orthos\$ or orthotics or brace or splint or tape or taping or (tai adj2 chi) or (tai adj2 ji)).tw,kw.
21. ((ultrasound or ultrason\*) and (treatment or therapy or intervention)).tw,kw.
22. ((cardiovascul\* adj2 (train\* or exercis\*)) or (aerob\* adj2 exercise\*) or (physical adj2 fitness) or (physical adj2 activit\*) or (high adj2 intensity adj2 interval adj2 train\*) or run\* or walk\* or jog\* or crossfit or danc\*).tw,kw.
23. rehabilitation/ or athletic rehabilitation/ or physiotherapy/ or exercise/ or aerobic exercise/ or aquatic exercise/ or closed kinetic chain exercise/ or isometric exercise/ or muscle exercise/ or dynamic exercise/ or isokinetic exercise/ or isotonic exercise/ or leg exercise/ or kinesiotherapy/ or physical activity/ or resistance training/ or muscle strength/ or training/ or stretching exercise/ or muscle stretching/ or stretching/ or massage/ or cryotherapy/ or electrotherapy/ or hydrotherapy/ or mobilization/ or joint mobilization/ or acupuncture/ or conservative treatment/ or ultrasound therapy/ or athletic tape/
24. open kinetic chain exercise/ or high frequency electrotherapy/ or low frequency electrotherapy/
25. or/20-24
26. systematic review/ or meta analysis/ or practice guideline/
27. (systematic review or meta-analysis or guideline).tw,kw.
28. 26 or 27
29. 19 and 25 and 28

**CINAHL (Ebsco)**

1. (MH "Athletic Injuries+") or (MH "Rupture") or (MH "Sprains and Strains")
2. (MH "Anterior Cruciate Ligament") or (MH "Menisci, Tibial")
3. S1 AND S2
4. (MH "Anterior Cruciate Ligament Injuries") or (MH "Meniscal Injuries")
5. S3 OR S4
6. TI ((menisc\* N3 (resect\* or injur\* or tear\* or rupture\* or repair\* or reconstruct\* or shav\* or surg\*))) OR AB ((menisc\* N3 (resect\* or injur\* or tear\* or rupture\* or repair\* or reconstruct\* or shav\* or surg\*)))
7. TI (((ACL\* or anterior cruciate ligament\*) N4 (injur\* or tear\* or sprain\* or rupture\* or reconstruct\* or surg\* or repair\* or rupture\*))) OR AB (((ACL\* or anterior cruciate ligament\*) N4 (injur\* or tear\* or sprain\* or rupture\* or reconstruct\* or surg\* or repair\* or rupture\*)))
8. (MH "Meniscectomy")
9. (MH "Anterior Cruciate Ligament Reconstruction")
10. TI meniscectom\* OR AB meniscectom\*
11. S6 OR S7 OR S8 OR S9 OR S10
12. (MH "Arthroscopy")
13. TI arthroscop\* OR AB arthroscop\*
14. S12 OR S13
15. TI ((ACL\* or anterior cruciate ligament\* or menisc\* ) OR AB ((ACL\* or anterior cruciate ligament\* or menisc\*)))
16. S2 OR S15
17. S14 AND S16
18. S5 OR S11 OR S17
19. TI (rehabilitat\* or physiotherapy or "physical therapy" or exercis\* or "physical activity" or ("resistance N4 train\*") or ("strength N4 train\*") or ("muscle N4 strength\*") or ("muscle N4 train\*") or ("weight N4 lifting") or stretch\* or "manual therapy" or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobili?ation or kinesio\* or acupuncture or orthos?s or orthotics or brace or splint or tape or taping or ("tai N2 chi") or ("tai N2 ji")) OR AB (rehabilitat\* or physiotherapy or "physical therapy" or exercis\* or "physical activity" or ("resistance N4 train\*") or ("strength N4 train\*") or ("muscle N4 strength\*") or ("muscle N4 train\*") or ("weight N4 lifting") or stretch\* or "manual therapy" or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobili?ation or kinesio\* or acupuncture or orthos?s or orthotics or brace or splint or tape or taping or ("tai N2 chi") or ("tai N2 ji"))
20. TI (((ultrasound or ultrason\*) and (treatment or therapy or intervention))) OR AB (((ultrasound or ultrason\*) and (treatment or therapy or intervention)))
21. TI ( ("cardiovascul\* N2 (train\* or exercis\*") or ("aerob\* N2 exercise\*") or ("physical N2 fitness") or ("physical N2 activit\*") or ("high N2 intensity N2 interval N2 train\*") or run\* or walk\* or jog\* or crossfit or danc\* ) OR AB (((("cardiovascul\* N2 (train\* or exercis\*") or ("aerob\* N2 exercise\*") or ("physical N2 fitness") or ("physical N2 activit\*") or ("high N2 intensity N2 interval N2 train\*") or run\* or walk\* or jog\* or crossfit or danc\* )
22. (MH "Rehabilitation+" or (MH "Rehabilitation, Athletic) or (MH "Physical Therapy+") or (MH "Exercise+") or (MH "Resistance Training") or (MH "Therapeutic Exercise+) or (MH "Group Exercise") or (MH "Sport Specific Training") or (MH "Open Kinetic Chain Exercises) or (MH "Closed Kinetic Chain Exercises") or (MH "Physical Activity) or (MH "Muscle Strengthening+) or (MH "Isokinetic Exercises) or (MH "Isometric Exercises") or (MH "Stretching") or (MH "Plyometrics") OR (MH "Massage+") or (MH "Sports Massage") or (MH "Deep Tissue Massage") or (MH "Cryotherapy") or (MH "Heat-Cold Application") or (MH "Electrotherapy+") or (MH "Joint Mobilization") or (MH "Hydrotherapy+") or (MH "Aquatic Exercises") or (MH "Acupuncture+") or (MH "Dry Needling") or (MH "Manual Therapy+") or (MH "Athletic Tape")
23. S19 OR S20 OR S21 OR S22

## Culvenor et al., ACL and meniscal injury rehabilitation

24. (MH "Systematic Review") or (MH "Meta Analysis") or (MH "Practice Guidelines")
25. TI (systematic review or meta-analysis or guideline) OR AB (systematic review or meta-analysis or guideline)
26. S24 OR S25
27. S18 AND S23 AND S26

**SPORTdiscus (Ebsco)**

1. DE "SPORTS injuries" or DE "SPRAINS"
2. DE "ANTERIOR cruciate ligament" or DE "MENISCUS (Anatomy)"
3. S1 OR S2
4. DE "ANTERIOR cruciate ligament injuries" or DE "MENISCUS injuries"
5. S3 OR S4
6. TI ( ( (menisc\* N3 (resect\* or injur\* or tear\* or rupture\* or repair\* or reconstruct\* or shav\* or surg\*)) ) OR AB ( ( (menisc\* N3 (resect\* or injur\* or tear\* or rupture\* or repair\* or reconstruct\* or shav\* or surg\*)) ) OR KW ( ( (menisc\* N3 (resect\* or injur\* or tear\* or rupture\* or repair\* or reconstruct\* or shav\* or surg\*)) ) )
7. TI ( ((ACL\* or anterior cruciate ligament\*) N4 (injur\* or tear\* or sprain\* or rupture\* or reconstruct\* or surg\* or repair\* or rupture\*)) ) OR AB ( ((ACL\* or anterior cruciate ligament\*) N4 (injur\* or tear\* or sprain\* or rupture\* or reconstruct\* or surg\* or repair\* or rupture\*)) ) OR KW ( ((ACL\* or anterior cruciate ligament\*) N4 (injur\* or tear\* or sprain\* or rupture\* or reconstruct\* or surg\* or repair\* or rupture\*)) )
8. TI meniscectom\* OR AB meniscectom\* OR KW meniscectom\*
9. DE "ANTERIOR cruciate ligament surgery"
10. S5 OR S6 OR S7 OR S8 OR S9
11. DE "ARTHROSCOPY"
12. TI arthroscop\* OR AB arthroscop\* OR KW arthroscop\*
13. S11 OR S12
14. TI ( (ACL\* or anterior cruciate ligament\* or menisc\*) ) OR AB ( (ACL\* or anterior cruciate ligament\* or menisc\*) ) OR KW ( (ACL\* or anterior cruciate ligament\* or menisc\*) )
15. S2 OR S14
16. S13 AND S15
17. S5 OR S10 OR S16
18. TI ( rehabilitat\* or physiotherapy or "physical therapy" or exercis\* or "physical activity" or ("resistance N4 train\*") or ("strength N4 train\*") or ("muscle N4 strength\*") or ("muscle N4 train\*") or ("weight N4 lifting") or stretch\* or "manual therapy" or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobili?ation or kinesio\* or acupuncture or orthos?s or orthotics or brace or splint or tape or taping or ("tai N2 chi") or ("tai N2 ji") ) OR AB ( rehabilitat\* or physiotherapy or "physical therapy" or exercis\* or "physical activity" or ("resistance N4 train\*") or ("strength N4 train\*") or ("muscle N4 strength\*") or ("muscle N4 train\*") or ("weight N4 lifting") or stretch\* or "manual therapy" or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobili?ation or kinesio\* or acupuncture or orthos?s or orthotics or brace or splint or tape or taping or ("tai N2 chi") or ("tai N2 ji") ) OR KW ( rehabilitat\* or physiotherapy or "physical therapy" or exercis\* or "physical activity" or ("resistance N4 train\*") or ("strength N4 train\*") or ("muscle N4 strength\*") or ("muscle N4 train\*") or ("weight N4 lifting") or stretch\* or "manual therapy" or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobili?ation or kinesio\* or acupuncture or orthos?s or orthotics or brace or splint or tape or taping or ("tai N2 chi") or ("tai N2 ji") )
19. TI ( ((ultrasound or ultrason\*) and (treatment or therapy or intervention)) ) OR AB ( ((ultrasound or ultrason\*) and (treatment or therapy or intervention)) ) OR KW ( ((ultrasound or ultrason\*) and (treatment or therapy or intervention)) )
20. TI ( ( ("cardiovascul\* N2 (train\* or exercis\*") ) or ("aerob\* N2 exercise\*") or ("physical N2 fitness") or ("physical N2 activit\*") or ("high N2 intensity N2 interval N2 train\*") or run\* or walk\* or jog\* or crossfit or danc\* ) ) OR AB ( ( ("cardiovascul\* N2 (train\* or exercis\*") ) or ("aerob\* N2 exercise\*") or ("physical N2 fitness") or ("physical N2 activit\*") or ("high N2 intensity N2 interval N2 train\*") or run\* or walk\* or jog\* or crossfit or danc\* ) ) OR KW ( ( ("cardiovascul\* N2 (train\* or exercis\*") ) or ("aerob\* N2 exercise\*") or ("physical N2 fitness") or ("physical N2 activit\*") or ("high N2 intensity N2 interval N2 train\*") or run\* or walk\* or jog\* or crossfit or danc\* ) )

## Culvenor et al., ACL and meniscal injury rehabilitation

21. DE "REHABILITATION" or DE "SPORTS physical therapy" or DE "PHYSICAL therapy" or DE "EXERCISE" or DE "ISOMETRIC exercise" or DE "EXERCISE therapy" or DE "ISOTONIC exercise" or DE "ISOKINETIC exercise" or DE "PHYSICAL activity" or DE "MOVEMENT therapy" or DE "MECHANOTHERAPY" or DE "WEIGHT training" or DE "RESISTANCE training" or DE "STRENGTH training" or DE "MUSCLE strength" or DE "FUNCTIONAL training" or DE "STRETCH (Physiology)" or DE "MASSAGE" or DE "MASSAGE therapy" or DE "SPORTS massage" or DE "REFLEXOTHERAPY" or DE "ORTHOPEDIC braces" or DE "COLD therapy" or DE "ELECTROTHERAPEUTICS" or DE "HYDROTHERAPY" or DE "SWIMMING therapy" or DE "ATHLETIC tape" or DE "KINESIOLOGY" or DE "ACUPUNCTURE"
22. S18 OR S19 OR S20 OR S21
23. TI (systematic review or meta-analysis or guideline) OR AB (systematic review or meta-analysis or guideline) OR KW (systematic review or meta-analysis or guideline)
24. S17 AND S22 AND S23

**COCHRANE Library**

1. Athletic Injuries [MeSH] or Rupture [MeSH] or "Sprains and Strains" [MeSH]
2. Anterior Cruciate Ligament [MeSH] or Menisci, Tibial [MeSH] or Meniscus [MeSH]
3. 1 and 2
4. Anterior Cruciate Ligament Injuries [MeSH] or Tibial Meniscus Injuries [MeSH]
5. 3 or 4
6. menisc\*.ti,ab,kw
7. (ACL\* or anterior cruciate ligament\*).ti,ab,kw
8. Meniscectomy [MeSH]
9. Anterior Cruciate Ligament Reconstruction [MeSH]
10. 6 or 7 or 8 or 9
11. Arthroscopy [MeSH]
12. arthroscop\*.ti,ab,kw
13. 11 or 12
14. (ACL\* or anterior cruciate ligament\* or menisc\*).ti,ab,kw
15. 2 or 14
16. 13 and 15
17. 5 or 10 or 16
18. (rehabilitat\* or physiotherapy or physical therapy or exercis\* or physical activity or strength\* or train\* or weight\* or stretch\* or manual therapy or neuromuscular or cryotherapy or electrostim\* or hydrotherapy or mobilisation or kinesio\* or acupuncture or orthosis or orthoses or orthotics or brace or splint or tape or taping or tai).ti,ab,kw
19. ((ultrasound or ultrason\*) and (treatment or therapy or intervention)).ti,ab,kw
20. (run\* or walk\* or jog\* or crossfit or danc\*).ti,ab,kw
21. Rehabilitation [MeSH] or Exercise [MeSH] or Exercise Therapy [MeSH] or Exercise Movement Techniques [MeSH] or Resistance Training [MeSH] or Muscle Strength [MeSH] or Isometric Contraction [MeSH] or Muscle Stretching Exercises [MeSH] or Massage [MeSH] or Cryotherapy [MeSH] or Electric Stimulation Therapy [MeSH] or Hydrotherapy [MeSH] or Acupuncture [MeSH] or Conservative Treatment [MeSH] or Athletic Tape [MeSH]
22. 18 or 19 or 20 or 21
23. 17 and 22
24. Limit 23 to Cochrane Reviews



## Culvenor et al., ACL and meniscal injury rehabilitation

**Appendix 2.** ROBIS risk of bias domains and questions rated as high, low or unclear risk of bias**Domain 1: Study Eligibility Criteria**

- 1.1 Did the review adhere to pre-defined objectives and eligibility criteria?
- 1.2 Were the eligibility criteria appropriate for the review question?
- 1.3 Were eligibility criteria unambiguous?  
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g., date, sample size, study quality, outcomes measured)?
- 1.4 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g., publication status or format, language, availability of data)?
- 1.5

Overall Concerns

**Domain 2: Identification and selection of studies**

- 2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?
- 2.2 Were methods additional to database searching used to identify relevant reports?  
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?
- 2.3
- 2.4 Were restrictions based on date, publication format, or language appropriate?
- 2.5 Were efforts made to minimise error in selection of studies?

Overall Concerns

**Domain 3: Data collection and study appraisal**

- 3.1 Were efforts made to minimise error in data collection?  
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?
- 3.2
- 3.3 Were all relevant study results collected for use in the synthesis?
- 3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria?
- 3.5 Were efforts made to minimise error in risk of bias assessment?

Overall Concerns

**Domain 4: Synthesis and Findings**

- 4.1 Did the synthesis include all studies that it should?
- 4.2 Were all pre-defined analyses reported or departures explained?  
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?
- 4.3
- 4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis?
- 4.5 Were the findings robust, e.g., as demonstrated through funnel plot or sensitivity analyses?
- 4.6 Were biases in primary studies minimal or addressed in the synthesis?

Overall Concerns

**Risk of Bias In the Review**

- 5.1 Did the interpretation of findings address all of the concerns identified in Domains 1 to 4?
- 5.2 Was the relevance of identified studies to the review's research question appropriately considered?
- 5.3 Did the reviewers avoid emphasizing results on the basis of their statistical significance?

Overall Concerns

## Culvenor et al., ACL and meniscal injury rehabilitation

**Appendix 3. Algorithm specifically developed to assign GRADE levels of evidence for overviews.**

(From Pollock A, Farmer SE, Brady MC, Langhorne P, Mead GE, Mehrholz J, et al. An algorithm was developed to assign GRADE levels of evidence to comparisons within systematic reviews. *J Clin Epidemiol.* 2016;70:106-10)

Area assessed	Imprecision	Risk of bias (trial)	Inconsistency	Risk of bias (review)
Method of assessment	Number of participants within pooled analysis	Proportion of participants included in the pooled analysis judged to have low ROB for randomisation and observer blinding*	Heterogeneity, assessed by $I^2$ statistic	Responses to ROBIS domains 1-4
No downgrade (no serious limitations)	$\geq 200$	$\geq 75\%$ of participants have low ROB	$I^2 \leq 75\%$	4/4 are all low ROB
Downgrade 1 level (serious limitations)	100-199	$< 75\%$ of participants have low ROB	$I^2 > 75\%$	3/4 are low ROB
Downgrade 2 levels (very serious limitations)	1-99			$< 3/4$ are low ROB
Notes		If ROB for individual trials was not reported within the review, we were conservative and assumed that less than 75% of studies had low ROB.	If only one trial contributed to analysis, no downgrade; if $I^2$ not reported, assumed to be greater than 75%.	

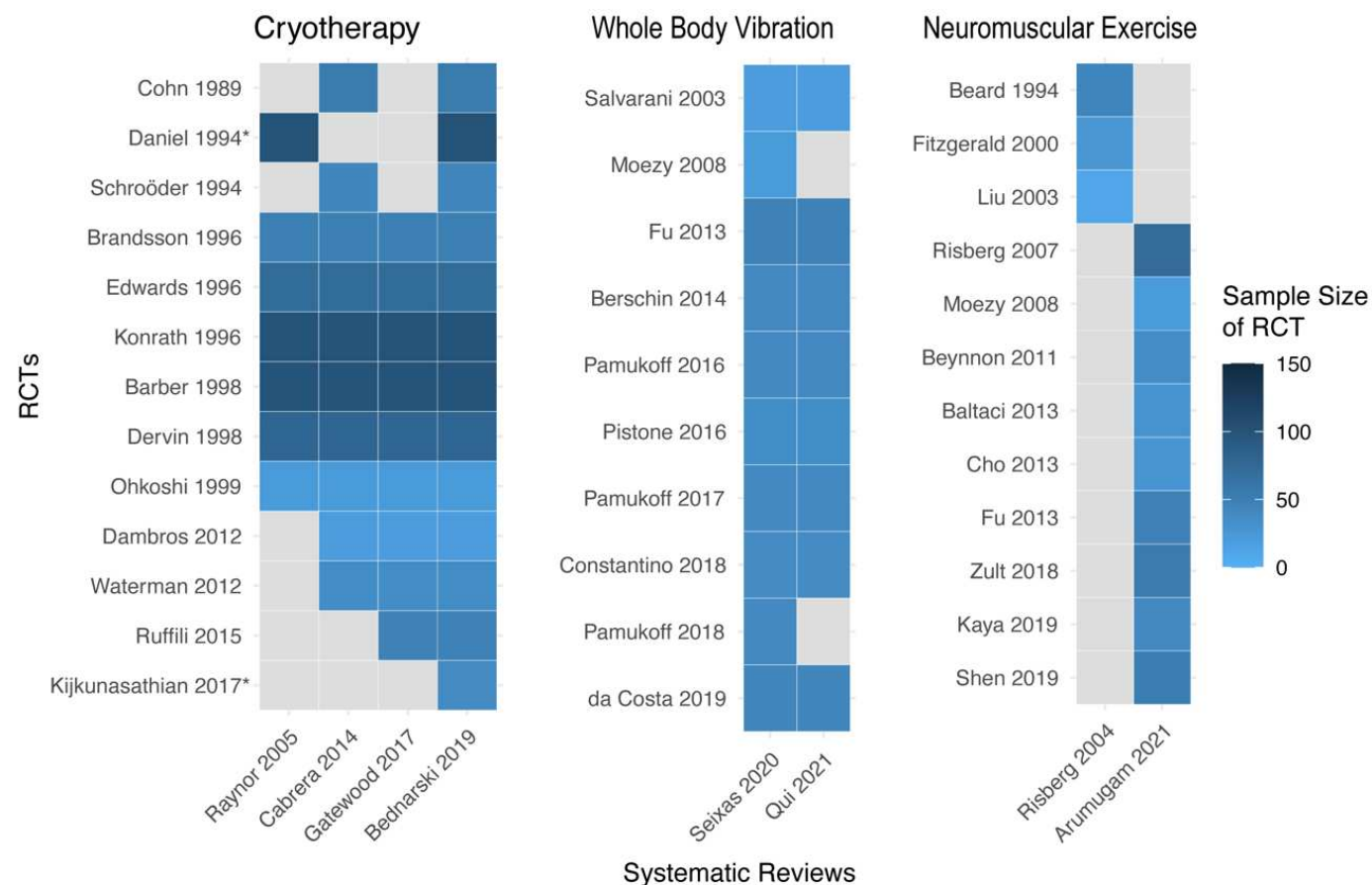
Formula for applying GRADE level of evidence from number of downgrades determined using the algorithm

GRADE certainty of evidence	Number of downgrades (derived from objective assessment)
High	0 downgrade
Moderate	1 or 2 downgrades
Low	3 or 4 downgrades
Very low	5 or 6 downgrades

\* Method of randomisation and concealed allocation were both considered as part of the randomisation criteria

Culvenor et al., ACL and meniscal injury rehabilitation

**Appendix 4.** Heatmaps displaying the overlap of individual trials that evaluated interventions included in more than one systematic review (with very-low to low certainty evidence). Includes all eligible systematic reviews, irrespective of whether they were included or excluded from data synthesis. Grey boxes indicate that an RCT was not included in the respective systematic reviews. \*indicates that an RCT was not included in our data synthesis because the systematic reviews that assessed it were excluded from our data synthesis due to high risk of bias.



Culvenor et al., ACL and meniscal injury rehabilitation

## Appendix 5. Results from algorithm adapted to assign GRADE certainty of evidence for overviews of systematic reviews#

Intervention, Study	Outcome	No. of studies	No. of participants	% of participants in pooled analysis with low ROB for randomisation and observer blinding	I <sup>2</sup>	No. of "Low ROB" responses to ROBIS domains 1-4§	No. of downgrades	GRADE certainty of evidence	Direction of effect <sup>¶</sup>	
Neuromuscular electrical stimulation	Hauger 2018	Quadriceps strength (meta-analysis)	6	311	3	55	4	-1	Moderate	Favours NMES – SMD: 0.73 (0.29, 1.16)
		Quadriceps strength (other)	4	195	0	NR	4	-3	Low	Favours NMES
		Self-reported function	3	194	0	NR	4	-3	Low	No effect/favours NMES
		Physical function	2	151	0	NR	4	-3	Low	Favours NMES
	Kim 2010	Quadriceps strength	7	195	0#	NR	2	-5	Very low	No effect/favours NMES
		Self-reported function	1	43	0#	NR <sup>^</sup>	2	-5	Very low	Favours NMES
		Physical function	1	20	0#	NR <sup>^</sup>	2	-5	Very low	No effect
	Gatewood 2017	Quadriceps strength	6	381	34	NR	1	-4	Low	No effect/favours NMES
		Self-reported function	2	174	75	NR	1	-4	Low	Favours NMES
		Physical function	2	151	87	NR	1	-4	Low	Favours NMES
		Laxity	2	151	87	NR	1	-4	Low	No effect
		Pain	1	43	0	NR <sup>^</sup>	1	-5	Very low	No effect
		Quadriceps size	1	10	0	NR <sup>^</sup>	1	-5	Very low	No effect
		Subcutaneous fat volume	1	10	0	NR <sup>^</sup>	1	-5	Very low	No effect
Risberg 2004	Quadriceps strength	10	355	NR	NR	1	-4	Low	Favours NMES	
	Quadriceps size	3	71	NR	NR	1	-6	Very low	Favours NMES	
Open kinetic chain exercises†	Perriman 2018	Laxity: short-term	2	102	100	56	3	-2	Moderate	No effect – MD: 0.47 (-0.48, 1.42)€
		Laxity: medium-term	2	91	100	0	3	-3	Low	No effect – MD: 0.57 (-0.06, 1.21)€
		Laxity: long-term	2	91	100	18	3	-3	Low	No effect – MD: 0.33 (-0.36, 1.03)€
		Laxity: very long-term	3	132	100	86	3	-3	Low	No effect – MD: 0.18 (-1.68, 2.04)€
		Quadriceps strength: short-term	2	102	100	0	3	-2	Moderate	No effect – SMD: 0.27 (-0.12, 0.67)€
		Quadriceps strength: medium-term	2	91	100	12	3	-3	Low	No effect – SMD: -0.06 (-0.51, 0.38)€
		Quadriceps strength: long-term	2	91	100	0	3	-3	Low	No effect – SMD: -0.16 (-0.57, 0.26)€
		Self-reported function: short-term	3	130	33	0	3	-3	Low	No effect – SMD: 0.09 (-0.25, 0.44)€
		Self-reported function: medium-term	2	93	50	87	3	-5	Very Low	No effect – SMD: 0.50 (-0.69, 1.70)€
		Self-reported function: very long-term	2	117	100	0	3	-2	Moderate	No effect – SMD: 0.24 (-0.12, 0.61)€
		Physical function	3	116	33	NR	3	-4	Low	No effect
		Adverse events	4	259	75	NR	3	-2	Moderate	No effect

## Culvenor et al., ACL and meniscal injury rehabilitation

Intervention, Study	Outcome	No. of studies	No. of participants	% of participants in pooled analysis with low ROB for randomisation and observer blinding	I <sup>2</sup>	No. of "Low ROB" responses to ROBIS domains 1-4§	No. of downgrades	GRADE certainty of evidence	Direction of effect	
Open kinetic chain exercises† (cont.)	Jewiss 2017	Self-reported function (Lysholm)	2	133	0	0	2	-4	Low	No effect – MD: -1.03 (-13.02, 10.95)€
		Self-reported function (Hughston)	2	86	0	0	2	-4	Low	No effect – MD: -1.29 (-12.02, 9.43)€
		Patellofemoral pain	3	198	0	NR	2	-5	Very Low	No effect/favours closed kinetic chain
		Quadriceps strength	2	79	0	NR	2	-6	Very Low	No effect/favours open kinetic chain
		Laxity	2	85	0	NR	2	-6	Very Low	No effect
		Range of motion	1	58	0	NR <sup>^</sup>	2	-5	Very Low	Favours closed kinetic chain
	Risberg 2004	Laxity	2	80	NR	NR	1	-6	Very Low	No effect/favours closed kinetic chain
		Pain	2	140	NR	NR	1	-5	Very Low	No effect/favours closed kinetic chain
		Strength	2	87	NR	NR	1	-6	Very Low	No effect/favours closed kinetic chain
Structured in-person rehabilitation‡	Gamble 2021	Self-reported function: short-term	3	114	0	0	4	-2	Moderate	No effect – MD: -1.24 (-6.09, 3.61)‡
		Self-reported function: medium-term	4	149	0	33	4	-2	Moderate	No effect – MD: 1.80 (-0.91, 4.50)‡
		Self-reported function: long-term	3	114	0	84	4	-3	Low	No effect – MD: -0.92 (-3.73, 1.88)‡
		Tegner: short-term	1	40	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 0.50 (-0.35, 1.35)‡
		Tegner: medium-term	3	96	0	0	4	-3	Low	No effect – MD: 0.52 (-0.01, 1.04)‡
		Tegner: long-term	2	77	0	78	4	-4	Low	No effect – MD: 0.91 (-1.04, 2.86)‡
		Quadriceps strength: short-term	3	190	0	0	4	-2	Moderate	No effect – MD: -0.56 (-4.98, 3.86)‡
		Quadriceps strength: medium-term	2	59	0	0	4	-3	Low	No effect – MD: 4.58 (-3.53, 12.70)‡
		Quadriceps strength: long-term	1	40	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 3.20 (-9.26, 15.66)‡
		Quadriceps strength: very long-term	1	88	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 7.00 (-2.33, 16.33)‡
		Hamstring strength: short-term	3	190	0	0	4	-2	Moderate	No effect – MD: -0.03 (-3.98, 3.91)‡
		Hamstring strength: medium-term	2	59	0	21	4	-3	Low	No effect – MD: 6.31 (-0.81, 13.42)‡
		Hamstring strength: long-term	1	40	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 5.10 (-9.91, 20.11)‡
		Hamstring strength: very long-term	1	88	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: -1.10 (-7.66, 5.46)‡
		Flexion range of motion: short-term	2	182	0	91	4	-3	Low	No effect – SMD: 0.03 (-1.06, 1.13)‡
		Flexion range of motion: medium-term	2	90	0	35	4	-3	Low	No effect – SMD: -0.31 (-0.84, 0.23)‡
		Flexion range of motion: long-term	1	37	0	NR <sup>^</sup>	4	-3	Low	No effect – SMD: 0.00 (-0.67, 0.67)‡
		Flexion range of motion: very long-term	1	88	0	NR <sup>^</sup>	4	-3	Low	No effect – SMD: 0.20 (-0.22, 0.62)‡
		Extension range of motion: short-term	1	129	0	NR <sup>^</sup>	4	-2	Moderate	Favours home-based rehabilitation – MD: -1.00 (-1.81, -0.19)‡
		Extension range of motion: medium-term	1	37	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 0.00 (-1.99, 1.99)‡
		Extension range of motion: long-term	1	37	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 0.00 (-2.02, 2.02)‡
Extension range of motion: very long-term	1	88	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 1.00 (-0.09, 2.09)‡		
Laxity: short-term	2	150	0	42	4	-2	Moderate	No effect – MD: -0.91 (-3.02, 1.19)‡		
Laxity: medium-term	1	19	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: -2.50 (-5.75, 0.75)‡		
Laxity: long-term	1	37	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 0.00 (-1.71, 1.71)‡		

## Culvenor et al., ACL and meniscal injury rehabilitation

Intervention, Study	Outcome	No. of studies	No. of participants	% of participants in pooled analysis with low ROB for randomisation and observer blinding	I <sup>2</sup>	No. of "Low ROB" responses to ROBIS domains 1-4§	No. of downgrades	GRADE certainty of evidence	Direction of effect	
Structured in-person rehabilitation <sup>‡</sup> (cont.)	Gamble 2021 (cont.)	Laxity: very long-term	1	88	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: 0.90 (-0.03, 1.83) <sup>‡</sup>
		Physical function: short-term	1	40	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: -0.40 (-15.34, 14.54) <sup>‡</sup>
		Physical function: medium-term	2	77	0	0	4	-3	Low	No effect – MD: -0.56 (-7.18, 6.06) <sup>‡</sup>
		Physical function: long-term	2	77	0	0	4	-3	Low	No effect – MD: 0.29 (-5.74, 6.31) <sup>‡</sup>
		Quality of life: long-term	1	37	0	NR <sup>^</sup>	4	-3	Low	No effect – MD: -0.10 (-0.21, 0.01) <sup>‡</sup>
		Quality of life: very long-term	1	88	0	NR <sup>^</sup>	4	-3	Low	Favours home-based rehabilitation – MD: 10.10 (-18.10, -2.10) <sup>‡</sup>
	Risberg 2004	Strength	2	126	0	NR	1	-5	Very Low	No effect/favours in-person rehabilitation
		Range of motion	3	191	0	NR	1	-5	Very Low	No effect
		Laxity	3	117	0	NR	1	-5	Very Low	No effect
		Self-reported function	5	217	0	NR	1	-4	Low	No effect
Knee bracing	Yang 2019	Physical function	2	154	0	NR	1	-5	Very Low	No effect/favours in-person rehabilitation
		Self-reported function	4	198	0	43	3	-3	Low	No effect – SMD: -0.01 (-0.29, 0.27) <sup>£</sup>
		Laxity	6	293	0	41	3	-2	Moderate	No effect – SMD: -0.03 (-0.26, 0.27) <sup>£</sup>
		Physical function	4	249	0	0	3	-2	Moderate	No effect – SMD: 0.19 (-0.06, 0.44) <sup>£</sup>
		Tegner	4	198	0	75	3	-3	Low	No effect – SMD: 0.11 (-0.45, 0.68) <sup>£</sup>
Pain	4	164	0	66	3	-3	Low	No effect – SMD: 0.15 (-0.38, 0.68) <sup>£</sup>		
Preoperative rehabilitation	Carter 2020	Quadriceps strength	2	100	0	NR	3	-4	Low	No effect/favours preoperative rehabilitation
		Physical function	2	100	0	NR	3	-4	Low	Favours preoperative rehabilitation
		Self-reported function	1	20	0	NR <sup>^</sup>	3	-4	Low	Favours preoperative rehabilitation
		Return to sport	1	20	0	NR <sup>^</sup>	3	-4	Low	No effect
Cryotherapy	Cabrera 2014	Pain (meta-analysis) (48hours)	2	54	0	35	3	-4	Low	Favours cryotherapy – MD: -1.41 (-1.66, -1.17)
		Pain (other)	6	348	0	NR	3	-3	Low	No effect/favours cryotherapy
		Analgesic medication use	9	554	0	NR	3	-3	Low	Favours cryotherapy
		Range of motion	5	334	0	NR	3	-3	Low	No effect
		Self-reported function	2	80	0	NR	3	-5	Very Low	No effect/favours cryotherapy
		Quality of life	1	36	0	NR <sup>^</sup>	3	-4	Low	No effect
	Patient satisfaction	1	50	0	NR <sup>^</sup>	3	-4	Low	No effect/ favours cryotherapy	
	Gatewood 2017	Pain	8	422	25	NR	1	-4	Low	No effect/favours cryotherapy
		Analgesic medication use	8	503	25	NR	1	-4	Low	No effect/favours cryotherapy
		Range of motion	5	337	20	NR	1	-4	Low	No effect
Patient satisfaction		2	97	50	NR	1	-6	Very Low	No effect/favours cryotherapy	

## Culvenor et al., ACL and meniscal injury rehabilitation

Intervention, Study		Outcome	No. of studies	No. of participants	% of participants in pooled analysis with low ROB for randomisation and observer blinding	I <sup>2</sup>	No. of "Low ROB" responses to ROBIS domains 1-4§	No. of downgrades	GRADE certainty of evidence	Direction of effect		
Psychological interventions	Coronado 2018	Self-reported function	2	159	0	NR	3	-4	Low	No effect/favours psychosocial intervention		
		Healthy-related quality of life	1	101	0	NR <sup>^</sup>	3	-3	Low	No effect		
		Pain	2	88	0	NR	3	-5	Very Low	No effect/favours psychosocial intervention		
		Psychosocial outcomes	4	210	0	NR	3	-3	Low	Favours psychosocial intervention		
		Knee laxity	1	21	0	NR <sup>^</sup>	3	-4	Low	Favours psychosocial intervention		
		Quadriceps strength	2	51	0	NR	3	-5	Very Low	No effect/favours psychosocial intervention		
Supplements	Protein	Greif 2020	Quadriceps strength	3	101	26	NR	2	-5	Very low	No effect/favours supplement use	
			Quadriceps size	2	71	37	NR	2	-6	Very low	Favours supplement use	
			Pain	2	102	0	NR	2	-5	Very low	No effect/favours supplement use	
	Creatine	Greif 2020	Self-reported function	2	102	0	NR	2	-5	Very low	No effect	
			Quadriceps strength	1	51	100	NR <sup>^</sup>	2	-4	Low	No effect	
	Vitamin E/C	Greif 2020	Self-reported function	1	51	100	NR <sup>^</sup>	2	-4	Low	No effect	
			Quadriceps strength	4	96	0	NR	2	-6	Very low	No effect	
		Testosterone	Greif 2020	Self-reported function	1	29	0	NR <sup>^</sup>	2	-5	Very low	No effect
				Quadriceps strength	1	13	100	NR <sup>^</sup>	2	-4	Low	No effect
				Self-reported function	1	13	100	NR <sup>^</sup>	2	-4	Low	No effect
Whole-body vibration	Seixas 2020	Quadriceps strength (single session)	2	84	52	NR	4	-4	Low	No effect		
		Quadriceps strength (multiple sessions)	5	180	0	NR	4	-3	Low	Favours whole-body vibration		
		Quadriceps rate of force development (single session)	2	100	0	NR	2	-5	Very low	No effect		
		Hamstring strength (multiple sessions)	4	160	0	NR	2	-5	Very low	Favours whole-body vibration		
		Physical function (multiple sessions)	1	48	0	NR <sup>^</sup>	2	-5	Very low	Favours whole-body vibration		
		Self-reported function (multiple sessions)	2	74	0	NR	2	-6	Very low	No effect/favours whole-body vibration		
		Range of motion (multiple sessions)	2	88	0	NR	2	-6	Very low	No effect		
		Joint position sense (multiple sessions)	2	71	0	NR	2	-6	Very low	No effect/favours whole-body vibration		
		Balance (multiple sessions)	3	105	0	NR	2	-5	Very low	Favours whole-body vibration		
Laxity (multiple sessions)	2	88	0	NR	2	-6	Very low	No effect				

## Culvenor et al., ACL and meniscal injury rehabilitation

Intervention, Study	Outcome	No. of studies	No. of participants	% of participants in pooled analysis with low ROB for randomisation and observer blinding	I <sup>2</sup>	No. of "Low ROB" responses to ROBIS domains 1-4§	No. of downgrades	GRADE certainty of evidence	Direction of effect	
Whole-body vibration (cont.)	Qiu 2021	Quadriceps strength (single session)	2	84	52	NR	4	-4	Low	No effect
		Quadriceps strength (multiple sessions)	5	180	0	NR	4	-3	Low	Favours whole-body vibration
		Quadriceps rate of force development (single session)	2	100	0	NR	4	-3	Low	No effect
Blood-flow restriction	Charles 2020	Quadriceps size	3	84	NR	NR	1	-6	Very low	Favours blood-flow restriction
		Thigh lean muscle mass	1	14	NR	NR <sup>^</sup>	1	-5	Very low	Favours blood-flow restriction
Neuromuscular control exercises	Risberg 2004	Quadriceps strength	1	10	NR	NR <sup>^</sup>	1	-5	Very low	Favours neuromuscular training
		Hamstring strength	1	10	NR	NR <sup>^</sup>	1	-5	Very low	Favours neuromuscular training
		Return to high-level activity	1	26	NR	NR <sup>^</sup>	1	-5	Very low	Favours neuromuscular training
	Arumugam 2021	Self-reported function	1	43	NR	NR <sup>^</sup>	1	-5	Very low	Favours neuromuscular training
		Joint position sense	7	276	48	NR	3	-3	Low	No effect/favours neuromuscular training
		Threshold to detect passive motion	2	88	100	NR	3	-4	Low	No effect/favours neuromuscular training
Continuous passive motion	Gatewood 2017	Quadriceps force control	1	55	0	NR <sup>^</sup>	3	-4	Low	No effect/favours neuromuscular training
		Range of motion	2	94	0	NR	1	-6	Very low	No effect
		Pain	1	60	0	NR <sup>^</sup>	1	-5	Very low	No effect
		Joint position sense	1	60	0	NR <sup>^</sup>	1	-5	Very low	Favours continuous active motion

# From Pollock A, Farmer SE, Brady MC, Langhorne P, Mead GE, Mehrholz J, et al. An algorithm was developed to assign GRADE levels of evidence to comparisons within systematic reviews. *J Clin Epidemiol.* 2016;70:106-10.

§ The four domains on the ROBIS tool: i) study eligibility criteria; ii) identification and selection of studies; iii) data collection and study appraisal; and iv) synthesis and findings.

\* mean of several meta-analyses

^ Effect size and 95% confidence interval provided when meta-analysis reported in the systematic review

^only one study (therefore not downgraded)

† Closed kinetic chain exercises is the comparator

¥ Home-based rehabilitation is the comparator

€ Positive values favour closed kinetic chain exercises

£ Positive values favour no brace

‡ Positive values favour structured in-person rehabilitation



## Culvenor et al., ACL and meniscal injury rehabilitation

ROB, risk of bias; ROBIS, Risk of Bias In Systematic reviews; GRADE, Grading of Recommendations Assessment, Development and Evaluation; NR, not reported; NMES, neuromuscular electrical stimulation; SMD, standardised mean difference; MD, mean difference.