OPEN ACCESS

Diagnosis, prevention and treatment of common lower extremity muscle injuries in sport – grading the evidence: a statement paper commissioned by the Danish Society of Sports Physical Therapy (DSSF)

Lasse Ishøi [1], Kasper Krommes,[1] Rasmus Skov Husted,[2,3] Carsten B Juhl,[4] Kristian Thorborg [1,2]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bjsports-2019-101228).

[1]Department of Orthopedic Surgery, Copenhagen University Hospital, Amager-Hvidovre, Sports Orthopedic Research Center - Copenhagen (SORC-C), Hvidovre, Denmark
[2]Department of Orthopedic Surgery and Physical Therapy, Physical Medicine & Rehabilitation Research – Copenhagen (PMR-C), Copenhagen University Hospital, Hvidovre, Denmark
[3]Clinical Research Centre, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark
[4]Research Unit of Musculoskeletal Function and Physiotherapy, Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark

Correspondence to
Lasse Ishøi, Department of Orthopedic Surgery, Copenhagen University Hospital, Amager-Hvidovre, Sports Orthopedic Research Center - Copenhagen (SORC-C), Hvidovre 2650, Denmark; lasse.ishoei@regionh.dk

Accepted 30 December 2019
Published Online First 14 January 2020

To cite: Ishøi L, Krommes K, Husted RS, *et al*. *Br J Sports Med* 2020;**54**:528–539.

ABSTRACT

This statement summarises and appraises the evidence on diagnosis, prevention and treatment of the most common lower extremity muscle injuries in sport. We systematically searched electronic databases, and included studies based on the highest available evidence. Subsequently, we evaluated the quality of evidence using the Grading of Recommendations Assessment, Development and Evaluation framework, grading the quality of evidence from high to very low. Most clinical tests showed very low to low diagnostic effectiveness. For hamstring injury prevention, programmes that included the Nordic hamstring exercise resulted in a hamstring injury risk reduction when compared with usual care (medium to large effect size; moderate to high quality of evidence). For prevention of groin injuries, both the FIFA 11+programme and the Copenhagen adductor strengthening programme resulted in a groin injury risk reduction compared with usual care (medium effect size; low to moderate quality of evidence). For the treatment of hamstring injuries, lengthening hamstring exercises showed the fastest return to play with a lower reinjury rate compared with conventional hamstring exercises (large effect size; very low to low quality of evidence). Platelet-rich plasma had no effect on time to return-to-play and reinjury risk (trivial effect size; moderate quality of evidence) after a hamstring injury compared with placebo or rehabilitation. At this point, most outcomes for diagnosis, prevention and treatment were graded as very low to moderate quality of evidence, indicating that further high-quality research is likely to have an important impact on the confidence in the effect estimates.

INTRODUCTION

Lower extremity muscle injuries are frequent in sports involving explosive actions such as high-speed running, jumping, change of direction and kicking.[1] In professional football, muscle injuries constitute up to half of all injuries,[1] and in sports, such as American football,[2] Australian football,[3] rugby,[4] basketball[5] and track and field,[6] the incidence is also high. The majority of muscle injuries in football occur during non-contact situations,[7] classified as 'indirect muscle injuries' or 'muscle strains'.[8 9] These are typically thought to occur in the muscle-tendon junction[8] when the force applied exceeds the tissue capacity.[10]

In football, muscle strain injuries constitute up to 31% of all injuries, and up to 37% of players experience absence from training and/or match play during a season due to a muscle injury.[1 7] Besides from significant financial costs at the professional level,[11] the high injury burden of muscle injuries[12] also have substantial implications on player availability, potentially affecting team performance.[13] Up to 92% of all muscle strain injuries encountered in football are located in the hamstrings (37%), adductors (23%), rectus femoris/quadriceps (19%) and calf muscles (13%),[7] with hamstring strain injuries also being the most common diagnosis in sports such as Australian football[3] and track and field.[6]

The fact that incidence of muscle strain injury has remained constant during the last decades in football[12] and Australian football[3] with slightly increased incidence for hamstring[14] and calf muscle strains,[3] highlights the ongoing challenge of muscle strain injuries in sport. Thus, to aid management of common muscle injuries in sport, the aim of this statement, commissioned by the Danish Society of Sports Physical Therapy, was to provide an overview of the existing literature. We identify, evaluate and grade the quality of evidence concerning the diagnostic effectiveness of clinical tests and the effect of preventive and treatment strategies for the most common lower limb muscle injuries including hamstring, adductor, rectus femoris/quadriceps and calf muscle injuries.

METHODS

This statement is divided into four sections: (1) hamstring, (2) adductor, (3) rectus femoris/quadriceps and (4) calf muscle strain injuries, and it includes three domains in each section: (1) diagnosis, (2) prevention and (3) treatment. We did not include studies solely reporting on non-acute problems, and/or clear traumatic injuries such as total muscle ruptures, avulsion injuries and muscle contusions.[8] A systematic search was employed to identify literature for the three domains in each section, with inclusion of studies based on the highest level of available evidence.[15] Data were synthesised and the quality of evidence were evaluated using the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) working group.[16]

Search

Twelve systematic searches covering diagnosis, prevention and treatment for each of the four sections (1: hamstring, 2: adductor, 3: rectus femoris/quadriceps and 4: calf) were conducted in MEDLINE (via PubMed), CENTRAL and Embase (via Ovid) during July 2018 and updated in September 2019.[17] No restrictions were applied concerning year of publication, however, only publications in English were included. We searched individual text words in title and abstract supplemented with Medical Subject Headings (MeSH) terms. We combined anatomical region of interest (eg, 'Groin (MeSH)' OR 'adductor' OR 'groin') AND type of injury (eg, 'Athletic Injury (MeSH)' OR 'Strains and Sprains (MeSH)' OR 'strain*' OR 'injur*' OR 're-injur*' OR 'reinjur*') AND outcome for diagnosis and treatment domains (eg, 'Diagnosis (MeSH)' OR 'exam*' and 'Return To Sport' OR 'full training,' respectively) or intervention for prevention domains (eg, 'Primary Prevention (MeSHs)' OR 'Reduc*'). If studies from one search was deemed relevant for one of the other 11 searches, the study was included as literature identified from other sources. In addition, reference lists of the included trials and relevant systematic reviews were scanned for relevant references. A flow chart of searches (see online supplementary file 1) and the complete search strategy for all searches and databases (see online supplementary file 2) is available as supplementary.

Selection

Three authors (LI, KK, RSH) screened records ordered from the most recent to the oldest records, using the Rayyan system (http://rayyan.qcri.org).[18] With 12 sets of search results, two authors screened 8 sets each, and thus all searches were screened independently by two authors. For all domains we included studies based on the highest level of available evidence.[15] For the diagnosis domain, we initially screened for systematic reviews and diagnostic cohort studies as these represent the highest starting point for the GRADE assessment.[16] Thus, for diagnosis, we intended to include systematic reviews of diagnostic studies supplemented with additional diagnostic cohort studies.[15] We aimed for studies that compared clinical tests to either ultrasonography or magnetic resonance imaging as the diagnostic reference standard. For the prevention and treatment domains, we initially screened for systematic reviews and randomised controlled trials (RCTs) as these represent the highest starting point for the GRADE assessment.[16] If no systematic reviews and/or RCTs were identified, we screened for observational studies. Thus, for prevention and treatment, we intended to include systematic reviews on RCTs supplemented with additional RCTs, or secondly observation studies if no systematic reviews or RCTs were identified.[15] For the prevention domain, we aimed for studies that assessed the risk of injury using a definition of injury based on time loss,[19] problems[20] or medical attention.[21] For the treatment domain, we aimed for studies that investigated the effect of treatment on risk of reinjuries and/or time to return-to-play, defined as completion of treatment,[22 23] criteria passed[24–27] or self-reported completion of a full training session or match play.[28–30] Studies that investigated the effect of treatment and/or prevention, but did not data extraction of individual muscle injuries were not included.

Appraisal

Two authors assessed risk of bias (LI and KK) of individual studies, as required for the GRADE framework[31] and in line with Cochrane procedures. [16] Therefore, tools assessing risk of bias rather than the study quality was chosen,[32] and thus we used The Cochrane Collaboration's risk of bias assessment tool (version 1) for RCTs,[33] QUADAS-2 tool for diagnostic studies[34] and Scottish Intercollegiate Guidelines Network Methodology Checklist 3 for cohort studies.[35] Details of each tool can be found in online supplementary file 4. Furthermore, two authors assessed risk of bias (RSH and CBJ) in systematic reviews using the ROBIS assessment tool.[36] Agreement was reached by consensus. If a systematic review included a risk of bias assessment of individual studies using one of the assessment tools stated above, no further risk of bias assessment was conducted for these individual studies. However, if these tools were not used, or if risk of bias was conflicting between two or more systematic reviews, we reassessed all risk of bias domains in the specific individual studies as part of this statement. The risk of bias assessments for systematic reviews and individual studies can be found in supplementary material (see online supplementary file 3; Table 1–11).

Data synthesis

Two authors assessed the quality of evidence (LI and KK) for each outcome relating to diagnostic tests (eg, effectiveness), prevention (eg, risk of injury) and treatment (eg, time to return-to-play) according to the approach from the GRADE working group.[16] Agreement was reached by consensus. The quality of evidence was graded as: (1) high, indicating that further research is unlikely to change the confidence in the estimate of effect, (2) moderate, indicating that further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate, (3) low, indicating that further research is very likely have an important impact on the confidence in the estimate of effect and is likely to change the estimate or (4) very low, indicating high uncertainty about the estimate.[16] The starting quality of evidence was rated as 'high' when data was based on either RCTs for treatment and prevention purposes or rated as 'low' when based on observational studies.[16] For diagnostic purposes, the starting quality of evidence was rated as high when based on cohort studies (prospective or cross-sectional).[16] Subsequently, the quality of evidence could be downgraded one or two levels (eg, from high to moderate) for each of the following five domains of the GRADE approach: Study limitations (ie, serious risk of bias such as lack of blinding of outcome assessor or other concerns determined to influence the study result),[31] inconsistency (ie, the heterogeneity of the results across studies if more than one study was included for the specific outcome),[37] indirectness (ie, poor generalisability of the findings to the target population, eg, use groin injuries vs acute adductor injuries for prevention, and/or use of a clinically irrelevant outcome in relation to the question, eg, 'time to end of treatment' for 'time to return-to-play' outcomes),[38] imprecision of the estimates (ie, wide CIs)[39] and the risk of publication bias.[40] Furthermore, the level of evidence for cohort studies could be upgraded due to a large effect, a dose–response relationship or if no effect was found and all plausible confounding factors identified in the study could be expected to increase the effect.[16] An overview of the risk of bias and grading is provided as supplementary material (see online supplementary file 3; Table 1–11).

Diagnostic tests

The diagnostic effectiveness of clinical tests was estimated from positive (LR+) and negative (LR−) likelihood ratios, and express the change in probability of the patient having the injury.[41 42] A LR+ >1 increases the post-test probability of a diagnosis following a positive test, while a LR− <1 decreases

the post-test probability of a diagnosis following a negative test. The diagnostic effectiveness of a positive and negative test was classified based on current guidelines as: very low (LR+: 1 to 2; LR−: 0.5 to 1), low (LR+: >2 to 5; LR−: 0.2 to <0.5), moderate (LR+: >5 to 10; LR−: 0.1 to <0.2); high (LR+: >10; LR−: <0.1).[41]

Prevention and treatment

Review Manager V.5.3 (The Nordic Cochrane Centre, Copenhagen) was used to calculate risk ratio and standardised effect sizes (Hedges' g) if not available through published meta-analyses or individual RCT's, to allow for consistency of interpretation across studies. Thus, if a meta-analysis did not report standardised effect size for continuous variables or risk ratio for dichotomised variables, we re-ran the analysis, if possible, using a random-effect model, unless otherwise stated in the original meta-analysis.[43] Heterogeneity in study results was calculated using the I^2 statistic, which is a measure to indicate the consistency of results across studies, from 0% (no inconsistency) to 100% (maximal inconsistency).[44] For continuous variables, for example, time to return-to-play, the effect of treatment was based on the standardised between-group difference calculated as Hedges' g and assessed as trivial ($g<0.2$), small ($g\geq0.2$), medium ($g\geq0.5$) and large ($g\geq0.8$).[45] For dichotomised variables (eg, risk of reinjury for treatment or risk of injury for prevention), the effect of treatment and prevention was based on the magnitude of the risk reduction following the intervention calculated as: Risk Ratio $(RR) = \frac{a/(a+b)}{c/(c+d)}$, where a is the number of injuries in the intervention group, b is the number without injuries in the intervention group, c is the number of injuries in the control group and d is the number without injuries in the control group.[46] The magnitude of effect was inspired by the risk ratios proposed by Bahr [47] for sample size calculations in sports injury prevention, and thus reflects arbitrary cut off values. Since these values were originally presented to study the magnitude of risk factors, that is a higher risk, we calculated the inverse values as 1/RR to determine the preventive effect and assessed the magnitude as trivial (RR >0.78), small (0.78≥ RR >0.61), medium (0.61≥ RR >0.47) and large (RR ≤0.47).[47]

RESULTS

In total 44 studies were included. For a detailed overview of included studies, including risk of bias assessment, GRADE and which individual studies are contained in systematic reviews, we refer to online supplementary file 3.

Hamstring injuries

Domain 1: diagnostic tests

In total 7081 studies were identified in the literature search. One systematic review[48] and three cohort studies were included.[49–51] No meta-analysis of diagnostic effectiveness was available from previous literature[48] or conducted as part of this statement. Based on one prospective study, where diagnostic effectiveness was calculated by the authors of this statement,[51] and two diagnostic studies,[49 50] the *'Taking off shoe test'* showed high diagnostic effectiveness, with perfect agreement between clinical testing and ultrasonography (n=140) (very low quality of evidence; table 1).[50] However, since no false positives were observed in Zeren and Oztekin[50] this precludes calculation of LR+ for tests in that study. All other tests displayed very low to low diagnostic effectiveness (LR+: 0.95 to 1.50; LR−: 0.37 to 0.96) in predicting a positive or negative MRI (n=58 to 180) (moderate to high quality of evidence)[49 51] (table 1).

Domain 2: prevention

In total 2468 studies were identified in the literature search. Three systematic reviews[52–54] and 12 RCT's was included.[21 55–65] A systematic review and meta-analysis performed by van Dyk *et al* (2019) showed a medium and significant risk reduction (RR: 0.55, 95% CI 0.34 to 0.89; I^2=67.0%) of hamstring injuries in football players in interventions including the Nordic hamstring exercise versus usual care (n=5362) (moderate quality of evidence).[53] A systematic review and meta-analysis by Goode *et al* (2015) showed a medium but non-significant risk reduction (RR: 0.59, 95% CI 0.24 to 1.44; I^2=69.6%) of mixed eccentric hamstring exercises versus usual care on hamstring injuries in football players (n=1229) (low quality of evidence).[52] A systematic review and meta-analysis by Thorborg *et al* (2017) showed a large and significant risk reduction (RR: 0.39, 95% CI 0.24 to 0.64; I^2=0.0%) of the FIFA 11+programme versus usual care on hamstring injuries in football players (n=3417) (moderate quality of evidence).[54] Since the meta-analysis from van Dyk *et al* (2019) only assessed the effect of interventions that included the Nordic Hamstring exercise, a post hoc meta-analyses, as part of the present statement paper, was performed to investigate the isolated effect of the Nordic hamstring exercise protocol.[66] Thus, data from Petersen *et al*[56] and van der Horst *et al*[57] was pooled. Based on this, the Nordic hamstring exercise protocol showed a large and significant risk reduction (RR: 0.35, 95% CI 0.22 to 0.54; I^2=0.0%) compared with usual care on hamstring injuries in football (n=1521) (high quality of evidence).[56 57] Data from individual studies[62–65] are presented in table 2.

Domain 3: treatment

In total 978 studies were identified in the literature search. One systematic review[67] and 11 RCT's were included.[22–30 68 69]

Return to play

A systematic review by Pas *et al* (2015) performed two meta-analyses with time to return to play as outcome.[67] First, the effect of lengthening hamstring exercises versus conventional exercises was estimated as HR,[67] thus we re-ran the analysis to report Hedges' g for consistency across studies. Based on this, lengthening hamstring exercises showed a large and significant effect versus conventional hamstring exercises (Hedges' g=1.23, 95% CI 0.85 to 1.60; I^2=0.0%) on return to play in elite football[28] and track and field[29] (n=131) (low quality of evidence). Second, platelet-rich plasma showed a trivial and non-significant effect versus control interventions (placebo saline[27 68] or rehabilitation[25 26]) (HR=1.03, 95% CI 0.87 to 1.22; I^2=75.0%)[67] on return to play in athletes (n=154) (moderate quality of evidence). No additional RCTs could be added to the meta-analysis by Pas *et al*[67] due to heterogeneous interventions. Data from individual studies[22–24 30 69] are presented in table 3.

Reinjuries

A systematic review by Pas *et al* from 2015 performed two meta-analyses with risk of reinjuries as outcome.[67] First, lengthening hamstring exercises showed a large but non-significant risk reduction (RR: 0.25, 95% CI 0.03 to 2.20; I^2=0.0%) versus conventional hamstring exercises[67] at 12-month follow-up in elite football[28] and track and field athletes[29] (n=131) (very low quality of evidence). Second, platelet-rich plasma showed a trivial and non-significant risk reduction (RR: 0.88, 95% CI

Table 1 Hamstring injury diagnosis: effectiveness of clinical tests and grading the quality of evidence

		Diagnostic effectiveness		
Clinical tests	**Likelihood ratio, (95% CI)**	**High**	**Moderate**	**Low/very low**
MRI used as reference standard				
Pain on trunk flexion[51]	LR+=1.48 (1.12 to 1.97)			Moderate quality of evidence
	LR−=0.37 (0.22 to 0.63)			Moderate quality of evidence
Pain on active knee flexion[51]	LR+=1.50 (0.91 to 2.49)			High quality of evidence
	LR−=0.78 (0.78 to 1.01)			High quality of evidence
Painful passive straight leg raise[51]	LR+=1.33 (1.04 to 1.70)			Moderate quality of evidence
	LR−=0.42 (0.23 to 0.74)			Moderate quality of evidence
Painful active knee extension[51]	LR+=1.33 (1.02 to 1.72)			Moderate quality of evidence
	LR−=0.48 (0.28 to 0.81)			Moderate quality of evidence
Painful resisted knee flexion 90°[51]	LR+=1.18 (0.99 to 1.41)			Moderate quality of evidence
	LR−=0.40 (0.19 to 0.87)			Moderate quality of evidence
Painful resisted knee flexion 30°[51]	LR+=1.13 (0.94 to 1.36)			Moderate quality of evidence
	LR−=0.55 (0.27 to 1.13)			Moderate quality of evidence
Active slump[51]	LR+=1.16 (0.59 to 2.28)			Moderate quality of evidence
	LR−=0.96 (0.79 to 1.16)			Moderate quality of evidence
Composite test*[49]	LR+=0.95 (0.89 to 1.02)			Moderate quality of evidence
	LR−=NA			
US used as reference standard				
Taking off shoe test[50]	LR+=NA			
	LR−=0.00	Very low quality of evidence		
Resisted range of motion test[50]	LR+=NA			
	LR−=0.39 (0.32 to 0.48)			Very low quality of evidence
Passive range of motion test[50]	LR+=NA			
	LR−=0.43 (0.35 to 0.52)			Very low quality of evidence
Active range of motion test[50]	LR+=NA			
	LR−=0.45 (0.38 to 0.54)			Very low quality of evidence

*Passive straight leg raise, active knee extension, manual muscle testing, active slump; MRI; The diagnostic effectiveness of the positive (LR+) and negative (LR−) likelihood ratios are classified individually as: very low (LR+: 1 to 2; LR−: 0.5 to 1), low (LR+: >2 to 5; LR−: 0.2 to <0.5), moderate (LR+: >5 to 10; LR−: 0.1 to <0.2); high (LR+: >10; LR−: <0.1). NA (non-applicable); diagnositc effectiveness unknown

NA, non-applicable; US, ultrasonography.

0.45 to 1.71; I^2=0.0%) versus control interventions (placebo saline[27 68] or rehabilitation[25 67] at 6 and 12-month follow-up in athletes (n=129) (moderate quality of evidence). No additional RCTs was added to the existing meta-analysis[67] due to heterogeneous interventions. Data from individual studies[24 30] are presented in table 3.

Adductor injuries

Domain 1: diagnostic tests

In total 6832 studies were identified in the literature search. Two cohort studies[70 71] were identified, however, due to duplication of data between these studies, only the study focusing on

Table 2 Hamstring injury prevention: effect and grading the quality of evidence

		Effect size			
Outcomes	**RR (95% CI)**	**Large**	**Medium**	**Small**	**Trivial**
Risk of injury					
Meta-analyses					
Interventions including the Nordic hamstring exercise versus usual care*; n=5362, male/female football[53]	0.55 (0.34 to 0.89); I^2=67.0%		Moderate quality of evidence		
Mixed eccentric hamstring training versus usual care based*; n=1229, male football[52]	0.59 (0.24 to 1.44); I^2=69.6%		Low quality of evidence		
FIFA 11+ programme versus usual care;* n=3417, male/female football[54]	0.39 (0.24 to 0.64); I^2=0.0%	Moderate quality of evidence			
Nordic hamstring exercise protocol versus usual care;* n=1521, male football[56 57]	0.35 (0.22 to 0.54); I^2=0.0%	High quality of evidence			
Individual studies					
Bounding exercise programme versus usual care; n=400, male football[63]	0.89 (0.55 to 1.44)				Moderate quality of evidence
FIFA 11+ programme performed pre-football and post-football versus FIFA 11+ performed pre-football; n=280, male football[62]	0.21 (0.05 to 0.95)	Very low quality of evidence			
Modified FIFA 11+ with rescheduling of Part 2 versus standard FIFA 11+; n=806, male football[64]	0.86 (0.59 to 1.25)				Moderate quality of evidence
Balance board training versus usual care; n=140, female football[65]	0.18 (0.02 to 1.42)	Very low quality of evidence			

*Based on pooled data from meta-analysis. RR (risk ratio); I^2 (heterogeneity in study results); The preventive effect is assessed as RR assessed as trivial (RR >0.78), small (0.78≥ RR >0.61), medium (0.61≥ RR >0.47) and large (RR ≤0.47).[47]

Table 3 Hamstring rehabilitation after injury: effect and grading the quality of evidence

		Effect size			
Outcomes		**Large**	**Medium**	**Small**	**Trivial**
Time to return-to-play					
Meta-analyses	**Hedges' g (95% CI)**				
Lengthening hamstring exercises versus conventional hamstring exercises*; n=131, male football and track and field athletes[67]	1.23 (0.85 to 1.60); I^2=0.0%	Low quality of evidence			
	HR (95% CI)				
Platelet-rich plasma versus placebo or rehabilitation*; n=154, various athletes[67]	1.03 (0.87 to 1.22); I^2=75.0%				Moderate quality of evidence
Individual studies	**Hedges' *g* (95% CI)**				
Lengthening hamstring exercises versus a criteria-based algorithm; n=48, male football[30]	0.23 (–0.34 to 0.80)			Low quality of evidence	
Hamstring stretching four times per day versus hamstring stretching one time per day; n=80, track and field athletes[22]	2.31 (1.75 to 2.88)	Very low quality of evidence			
Agility and trunk stabilisation versus hamstring stretching and strengthening; n=24, various athletes[24]	0.75 (–0.08 to 1.58)		Very low quality of evidence		
Running and eccentric hamstring strengthening versus agility and trunk stabilisation; n=29, various athletes[23]	0.39 (–0.42 to 1.20)			Very low quality of evidence	
	HR (95% CI)				
Pain-threshold (≤4 on the 0 to 10 NRS) versus pain-free (0 on the 0 to 10 NRS) rehabilitation; n=37, male/female[69]	0.75 (0.40 to 1.40)			Low quality of evidence	
Reinjuries					
Meta-analyses	**RR (95 % CI)**				
Lengthening hamstring exercises versus conventional hamstring exercises*; n=131, male football and track and field athletes[67]	0.25 (0.03 to 2.20); I^2=0.0%	Very low quality of evidence			
Platelet-rich plasma versus placebo or rehabilitation at 6–12 month follow-up*; n=129, various athletes[67]	0.88 (0.45 to 1.71); I^2=0.0%				Moderate quality of evidence
Individual studies					
Criteria-based algorithm versus lengthening hamstring exercises at 6 month follow-up, n=48, male football[30]	0.17 (0.02 to 1.28)	Low quality of evidence			
Agility and trunk stabilisation versus hamstring stretching and strengthening at 12 months follow-up, n=24, various athletes[24]	0.10 (0.01 to 0.70)	Very low quality of evidence			
	HR (95 % CI)				
Pain-threshold (≤4 on the 0 to 10 NRS) versus pain-free (0 on the 0 to 10 NRS) rehabilitation at 6 month follow-up; n=37, male/female[69]	1.05 (0.14 to 7.47)				Low quality of evidence

*Based on pooled data from meta-analysis. RR (Risk ratio); HR; I^2 (Heterogeneity in study results); NRS (Numeric Rating Scale); the effect of treatment regarding return to play is assessed by Hedges' *g* as trivial (*g*<0.2), small (*g*≥0.2), medium (*g*≥0.5) and large (*g*≥0.8).[39] The effect of treatment on reinjuries is assessed as risk ratio as trivial (RR >0.78), small (0.78≥ RR >0.61), medium (0.61≥ RR >0.47) and large (RR ≤0.47).[47]

Table 4 Adductor injury diagnosis: effectiveness of clinical tests and grading the quality of evidence

Clinical tests	Likelihood ratio, (95% CI)	Diagnostic effectiveness		
		High	Moderate	Low/very low
MRI used as reference standard				
Adductor palpation (adductor longus, gracilis, pectineus)[71]	LR+=2.23 (1.51 to 3.29)			Moderate quality of evidence
	LR−=0.08 (0.02 to 0.31)	Low quality of evidence		
Squeeze 0°[71]	LR+=3.13 (1.75 to 5.59)			Low quality of evidence
	LR−=0.26 (0.14 to 0.48)			Moderate quality of evidence
Squeeze 45°[71]	LR+=1.81 (1.13 to 2.92)			Moderate quality of evidence
	LR−=0.52 (0.33 to 0.81)			Moderate quality of evidence
Resisted outer range adduction[71]	LR+=3.30 (1.85 to 5.87)			Low quality of evidence
	LR−=0.20 (0.10 to 0.41)			Moderate quality of evidence
Passive adductor stretching[71]	LR+=3.04 (1.51 to 6.14)			Low quality of evidence
	LR−=0.49 (0.34 to 0.71)			Moderate quality of evidence
Flexion abduction external rotation test[71]	LR+=1.45 (0.81 to 2.60)			Moderate quality of evidence
	LR−=0.79 (0.59 to 1.06)			Moderate quality of evidence

MRI; the diagnostic effectiveness of the positive (LR+) and negative (LR−) likelihood ratios are classified individually as: very low (LR+: 1 to 2; LR−: 0.5 to 1), low (LR+: >2 to 5; LR−: 0.2 to <0.5), moderate (LR+: >5 to 10; LR−: 0.1 to <0.2); high (LR+: >10; LR−: <0.1).[37]

diagnostic effectiveness was included (n=81).[71] Adductor palpation showed high diagnostic effectiveness in predicting a negative MRI (LR−: 0.08) (low quality of evidence).[71] For the remaining tests (see table 4), very low to low diagnostic effectiveness (LR+: 1.45 to 3.30; LR−: 0.20 to 0.79) were observed in predicting a positive or negative MRI (low to moderate quality of evidence).

Domain 2: prevention

In total 1566 studies were identified in the literature search. Two systematic reviews[54 72] and 13 RCTs were included.[21 58 60 62 64 65 73–79] None of the studies specifically reported on acute adductor injuries. A systematic review by Esteve *et al* (2015) performed three meta-analyses with risk of groin injuries as outcome.[72] First, mixed groin prevention programmes showed a trivial and non-significant risk reduction (RR: 0.81, 95% CI 0.60 to 1.09; I^2=7.0%) versus usual care on groin injuries in football (n=4191) (low quality of evidence).[72] Second, specific adductor strength training showed a trivial and non-significant risk reduction (RR: 0.80, 95% CI 0.53 to 1.22; I^2=3.0%) versus usual care on groin injuries in football (n=1067) (low quality of evidence).[72] Third, the FIFA 11+ programme showed a small but non-significant risk reduction (RR: 0.64, 95% CI 0.27 to 1.49; I^2=59.0%) versus usual care on groin injuries in football (n=2476) (very low quality of evidence).[72] Furthermore, a systematic review and meta-analysis by Thorborg *et al* (2017) investigating the effect of the FIFA 11+ programme in football showed a medium and significant risk reduction (RR: 0.58, 95% CI 0.40 to 0.84; I^2=8.0%) versus usual care on groin injuries in football (n=3417) (low level of evidence).[54] No additional RCTs were added to the existing meta-analyses[54 72] due to heterogeneous interventions, populations and injury definitions (eg, groin injuries vs groin problems as used in Haroy *et al*[73]). However, two additional studies on the preventive effect of the FIFA 11+ programme in mixed sports and basketball were pooled in a post hoc meta-analysis.[78 79] Based on this, the FIFA 11+ programme showed a medium but non-significant risk reduction (RR: 0.58, 95% CI 0.06 to 5.93; I^2=62.0%) versus usual care on groin injuries in mixed sports (n=3732) (very low quality of evidence). Data from individual studies are presented in table 5.

Domain 3: treatment

In total 217 studies were identified in the literature search; however, no studies on the effect of treatment of groin injury could be included.

Rectus femoris/quadriceps injuries

Domain 1: diagnostic tests

In total 8729 studies were identified in the literature search. Two cohort studies[70 71] were eligible, however, due to duplication of data between these studies, only the study focusing on diagnostic effectiveness was included (n=81 athletes).[71] Proximal rectus femoris palpation showed high diagnostic effectiveness when positive (LR+: 11.20) and negative (LR−: 0.00) in predicting a positive or negative rectus femoris injury on MRI (low to moderate quality of evidence).[71] Furthermore, resisted knee extension showed high diagnostic effectiveness when negative (LR−: 0.00) in ruling out a rectus femoris injury on MRI (moderate quality of evidence). For the remaining tests (see table 6), very low to moderate diagnostic effectiveness (LR+: 1.45 to 5.47; LR−: 0.15 to 0.55) were observed (low to moderate quality of evidence).[71]

Domain 2: prevention

In total 3002 studies were identified in the literature search. No systematic reviews and five RCTs were included.[21 60 62 64 65] As part of this statement data from Soligard *et al*[60] and Silvers-Granelli *et al*[21] was pooled post hoc, as this analysis was not available in the existing literature. Based on this, the FIFA 11+ programme showed a small and not significant effect versus usual care (RR: 0.73, 95% CI 0.48 to 1.12; I^2=0.0%) in reducing anterior thigh injuries in football (n=3417) (low quality of evidence).[21 60] Data from individual studies[62 64 65] are presented in table 7.

Domain 3: treatment

In total 484 studies were identified in the search. No systematic reviews or RCT's were included. One study (case-series) was included with a total of 18 Australian rules football players.[80] A two-phase criteria-based intervention with increasing running and kicking intensity led to a return to full training at a mean of 13 days (range: 2 to 43) with no reinjuries during an unreported time-frame (very low quality of evidence).[80]

Table 5 Groin injury prevention: effect and grading the quality of evidence

Outcomes		Effect size			
		Large	Medium	Small	Trivial
Risk of injury					
Meta-analyses	**RR (95% CI)**				
Mixed groin prevention programmes versus usual care*; n=4191, male/female football[72]	0.81 (0.60 to 1.09); I^2=7.0%				Low quality of evidence
Specific adductor strength training versus usual care*; n=1067, male football[72]	0.80 (0.53 to 1.22); I^2=3.0%				Low quality of evidence
FIFA 11+ programme versus usual care*; n=2476, male/female football[72]	0.64 (0.27 to 1.49); I^2=59.0%			Very low quality of evidence	
FIFA 11+ programme versus to usual care*; n=3417, male/female football[54]	0.58 (0.40 to 0.84); I^2=8.0%		Low quality of evidence		
FIFA 11+ programme versus usual care*; n=3732, male/female from mixed sports[78 79]	0.58 (0.06 to 5.93); I^2=62.0%		Very low quality of evidence		
Individual studies	**OR (95% CI)**				
Adductor strengthening programme versus usual care; n=486, male football[73]	0.59 (0.40 to 0.86)		Moderate quality of evidence		
	RR (95% CI)				
FIFA 11+ programme performed pre-football and post-football versus FIFA 11+ performed pre-football; n=280, male football[62]	0.16 (0.02 to 1.29)	Very low quality of evidence			
Modified FIFA 11+ with rescheduling of Part 2 versus standard FIFA 11+; n=806, male football[64]	1.19 (0.81 to 1.76)				Moderate quality of evidence

*Based on pooled data from meta-analysis. RR (risk ratio) ORs; I^2 (heterogeneity in study results); the preventive effect is assessed as RR assessed as trivial (RR >0.78), small (0.78≥ RR >0.61), medium (0.61≥ RR >0.47) and large (RR ≤0.47).[47]

Calf injuries

Domain 1: diagnostic tests

In total 5410 studies were identified in the search; however, no studies were included.

Domain 2: prevention

In total 2944 studies were identified in the search. No systematic reviews or RCTs were identified. One prospective cohort study could be included (n=24).[81] A soccer-specific balance programme performed during five half-seasons were superior to a 6-month control period with a medium effect size (rate ratio: 0.57; 95% CI not reported) on reducing gastrocnemius injuries in football (very low quality of evidence).[81]

Domain 3: treatment

In total 91 studies were identified in the search. No systematic reviews or RCTs were identified. Three studies (two case-series and one retrospective observational) were included with a total number of 825 subjects.[82–84] Very low quality of evidence was observed for a multimodal treatment consisting of passive treatment modalities and progressive

Table 6 Rectus femoris/quadriceps injury diagnosis: effectiveness of clinical tests and grading the quality of evidence

Clinical tests	Likelihood ratio (95% CI)	Diagnostic effectiveness		
		High	Moderate	Low/very low
MRI used as reference standard				
Rectus femoris palpation[71]	LR+=11.20 (4.85 to 25.86)	Low quality of evidence		
	LR−=0	Moderate quality of evidence		
Resisted hip flexion at 0°[71]	LR+=1.45 (0.90 to 2.32)			Moderate quality of evidence
	LR−=0.55 (0.15 to 1.79)			Low quality of evidence
Resisted hip flexion at 90°[71]	LR+=2.47 (1.41 to 4.34)			Moderate quality of evidence
	LR−=0.36 (0.11 to 1.21)			Low quality of evidence
Resisted hip flexion (modified Thomas test position)[71]	LR+=2.36 (1.53 to 3.66)			Moderate quality of evidence
	LR−=0.20 (0.03 to 1.27)		Low quality of evidence	
Resisted knee extension (modified Thomas test position)[71]	LR+=4.17 (2.54 to 6.82)			Moderate quality of evidence
	LR−=0	Moderate quality of evidence		
Passive hip extension (modified Thomas test position)[71]	LR+=2.70 (1.50 to 4.86)			Moderate quality of evidence
	LR−=0.35 (0.10 to 1.17)			Low quality of evidence
Passive knee flexion (modified Thomas test position)[71]	LR+=5.47 (2.75 to 10.87)		Low quality of evidence	
	LR−=0.15 (0.02 to 0.94)		Low quality of evidence	

MRI; the diagnostic effectiveness of the positive (LR+) and negative (LR−) likelihood ratios are classified individually as: very low (LR+: 1 to 2; LR−: 0.5 to 1), low (LR+: >2 to 5; LR−: 0.2 to <0.5), moderate (LR+: >5 to 10; LR−: 0.1 to <0.2); high (LR+: >10; LR−: <0.1).[37]

Table 7 Quadriceps/anterior thigh injuries injury prevention: effect and grading the quality of evidence

Outcomes	RR (95% CI)	Effect size			
		Large	Medium	Small	Trivial
Risk of injury					
Meta-analyses					
FIFA 11+ programme versus usual care; n=3417, male/female football*[21 60]	0.73 (0.48 to 1.12); I^2=0.0%			Low quality of evidence	
Individual studies					
FIFA 11+ programme performed pre-football and post-football versus to FIFA 11+ performed pre-football; n=280, male football[62]	0.16 (0.02 to 1.35)	Very low quality of evidence			
Modified FIFA 11+ with rescheduling of Part 2 versus standard FIFA 11+; n=806, male football[64]	1.95 (1.11 to 3.43)				High quality of evidence
Balance board training versus usual care; n=140, female football[65]	3.76 (0.16 to 90.77)				Very low level of evidence

*Based on pooled data from meta-analysis. RR (risk ratio); I^2 (heterogeneity in study results); the preventive effect is assessed as RR assessed as trivial (RR >0.78), small (0.78≥ RR >0.61), medium (0.61≥ RR >0.47) and large (RR ≤0.47).[47]

exercises, which led to an average treatment time of 9 days (range: not reported) in one study[82] and a 1 year reinjury rate of 6.8% (95% CI not reported) in another study.[84] Furthermore, platelet-rich plasma and rehabilitation showed a large and significant effect versus rehabilitation alone (Hedges' g=1.78, 95% CI 1.19 to 2.37) on return to previous sport activity (very low quality of evidence).[83]

DISCUSSION

The following sections discuss the statements for each type of injury and domain including the limitations in the existing literature.

Hamstring injuries

Domain 1: diagnostic tests

Based on the existing literature, conducted mostly in male football players,[49–51] very low to low diagnostic effectiveness was observed for most clinical tests. This means that the shift in pre-test to post-test probability, and thus the change in the certainty of an injury or not, was minimal for most tests. For example, in Wangensteen *et al*[51] the certainty of an MRI-defined hamstring injury was 78% (pre-test probability) before clinical testing, and this changed to 80% to 84% for a positive test and to 59% to 73% for a negative test (moderate to high quality of evidence).[51] In practice, this means that 59% to 73% of players will still have a hamstring injury following a negative test, and thus commonly used tests, such as pain during strength testing and/or stretching of the hamstring muscles, seems to provide limited value in ruling in or out a hamstring injury. This, notion is confirmed by Schneider-Kolsky *et al*,[49] who observed no shift in pre-test to post-test probability (67% to 67%) following a cluster of tests (moderate quality of evidence).[51] The only test with high diagnostic effectiveness was the *'Taking off shoe test,'* which showed perfect agreement with ultrasound when positive, which means that a negative test is highly effective at ruling out a hamstring injury.[50] However, the study was associated with serious risk of bias due to lack of blinding, which results in very low quality of evidence for this test.[50] The limited diagnostic effectiveness of most tests may be explained by inclusion of athletes with acute onset of posterior thigh pain during sport[49 51] or a verified hamstring injury on ultrasonography,[50] that is a high pre-test probability of a hamstring strain injury. Thus, if a clear medical history, such as self-reported onset of acute posterior thigh pain during sport, is present it is questionable whether pain on stretching and/or contraction provide additional value in the clinical setting when diagnosing hamstring strain injuries, despite being considered important by most experts.[85]

Domain 2: prevention

Several interventions for prevention of hamstring muscle injuries have been investigated, with most included subjects being male football players, with one study conducted in Australian football[55] and one study in female football players.[59] The highest quality of evidence for a preventive effect on hamstring injuries was observed for interventions including the Nordic hamstring exercise (moderate quality of evidence),[53] the FIFA 11+ intervention (moderate quality of evidence)[54] and the isolated 10-week Nordic hamstring exercise protocol (high quality of evidence).[56 57] These interventions resulted in a significant 45% to 65% lower risk of injury. These findings are partly in line with prevention practices utilised in elite football. In a survey of 44 elite clubs 66% reported using the Nordic hamstring exercise as a preventive strategy,[86] however, most elite clubs (>80%) are non-compliant to the 10-week Nordic hamstring exercise protocol,[87] making the preventive effect of the exercise questionable in real-life settings.[52] Similarly, in professional youth football teams the FIFA 11+ intervention was only performed fully in 12% of training sessions across a season.[88] These observations, regarding low compliance, could likely explain the continuous rise in hamstring strain injuries in elite football.[14 21 52] We also found moderate quality of evidence for a trivial non-significant effect of a comprehensive bounding programme involving plyometric and running drills directed towards the injury mechanisms during high-speed running.[63]

In summary, hamstring training, in form of the Nordic hamstring exercise, may be essential for prevention of hamstring injuries, where improvements in eccentric strength,[66 89] fatigue resistance[90 91] and alterations in muscle morphology and architecture,[89 92] collagen expression at the myotendinous junctions[93] and angle of peak torque[94] are suggested mechanisms of effect.

Domain 3: treatment

Several interventions for treatment of hamstring injuries have been investigated, including targeted hamstring exercises and running,[23 28–30 69] stretching,[22 24] agility and trunk exercises[23 24] and injection therapy.[25–27] The majority of included subjects were male football players[25 27 28 30 68] or track and field athletes.[22 26 29] For the outcome measure *'time to return-to-play,'*

large heterogeneity in the outcome definitions (eg, criteria-based vs self-reported vs medical clearance) preclude any clear recommendations of a superior rehabilitation strategy for return to play. However, rehabilitation programmes with a focus on progressive targeted eccentric hamstring exercises supplemented with progressive running drills seems to result in the shortest return-to-play times with an associated low reinjury risk.[28–30 69] Thus, lengthening hamstring exercises showed significant faster return to play and no reinjuries compared with conventional exercises in elite football players[28] and track and field athletes.[29] However, in a recent study, lengthening hamstring exercises showed a substantial higher reinjury rate of 25% compared with a multifactorial criteria-based programme with a reinjury rate of 4% with only small, and non-significant, differences in return-to-play time.[30] Interestingly, the return-to-play times were markedly faster in the latter study, suggesting that longer return-to-play times may decrease risk of reinjury.[10 95 96] It should however be noted, that due to the small absolute number of reinjuries in the above studies the effect of the interventions on reinjury risk is associated with substantial imprecision of the estimate leading to a downgrade of the evidence.[39]

Finally, moderate quality of evidence was observed for a trivial, non-significant, effect of platelet-rich plasma on time to return-to-play and reinjury risk.[67]

Adductor injuries

Domain 1: diagnostic tests

Based on one study concerning primarily male football players,[71] high diagnostic effectiveness was observed for a negative adductor palpation test in ruling out a diagnosis of a MRI-verified adductor injury. Accordingly, Serner *et al* (2016) observed that 57% of athletes presented with an MRI-defined acute adductor injury (pre-test probability) but after negative palpation test the probability of injury decreased to 9%.[71] Thus, the clinician can be fairly certain that no adductor injury is present if the athlete reports no pain on palpation. The test was downgraded to low quality of evidence due to indirectness (clinical value of a negative or positive test unknown)[38] and imprecision (wide CIs).[39] Additionally, potential important clinical implications for diagnosis were also observed for pain during the squeeze test, outer range isometric adduction and passive adductor stretch, with shifts in pre-test to post-test probability from 57% to 80% to 81% for a positive test.[71] Thus, these tests could be used to rule-in an adductor injury, although a positive test is still associated with uncertainty; that is one out of five athletes with a positive test do not have an adductor injury on MRI. Currently, no evidence is available concerning potential implications for return-to-play prognosis, and therefore all tests were downgraded due to indirectness (clinical value of a negative or positive test unknown).[38]

Domain 2: prevention

Several interventions for prevention of groin injuries have been investigated primarily in football including both males and females,[54 72 73] however, no RCT's have specifically reported on adductor strain injuries. Thus, the quality of evidence for all studies/outcomes have been downgraded due to indirectness.[38] The highest quality of evidence for a preventive effect was observed for an adductor strengthening programme consisting of the Copenhagen adduction exercise[97] performed at different levels of intensity (moderate quality of evidence).[73] The outcome measure in the study was the Oslo Sports Trauma Research Center Overuse Injury Questionnaire,[20] which captures all problems rather than only time-loss injuries. Thus, the risk reduction of 41% following the adductor strengthening programme encompass all groin problems from delayed onset muscle soreness to more severe injuries, hence the preventive effect specifically on acute adductor strain injures is uncertain.[73] The FIFA 11+ programme also showed a medium risk reduction of 42% in football players and is a viable option for prevention of groin injuries.[54] The preventive effect of an adductor strengthening programme[98] indicates the importance to focus on hip adduction strength gains for prevention.[97 99] These findings are partly in line with prevention practices of groin injuries in football, with a recent survey of 64 professional youth academies demonstrating focus on adductor strengthening, although only few academies specifically performed the Copenhagen adduction exercise.[100]

Domain 3: treatment

No studies were identified for treatment of acute adductor injuries, which is remarkable since acute adductor injuries are considered a common muscle injury in football.[7] However, based on current literature concerning long-standing adductor-related pain, an exercise-based approach with a large focus on strengthening the adductor muscles has been recommended.[101]

Rectus femoris/quadriceps injuries

Domain 1: diagnostic tests

One study including primarily male football players was included.[71] However, it should be noted that this study only included athletes with acute onset of groin pain, and thus only encompass proximal rectus femoris injuries.[71] High diagnostic effectiveness was observed for proximal rectus femoris palpation in predicting a rectus femoris injury in MRI-positive cases, that is cases are only included if they had positive MRI. The test showed a substantial shift in pre-test to post-test probability from 13% to 62% for a positive test and from 13% to 0% for a negative test.[71] Although the test showed high diagnostic effectiveness, the post-test probability of 62% suggest that a positive test is still associated with large uncertainties in the diagnosis; that is one out of three athletes with a positive palpation test do not have an injury.[71] Conversely, the clinician can be fairly certain that no injury is present if the athlete report no pain on palpation. Currently, no evidence is available concerning potential implications for return-to-play prognosis, and thus all tests were downgraded due to indirectness (clinical value of a negative or positive test unknown).[38]

Domain 2: prevention

The highest quality of evidence for a preventive effect was observed for the FIFA 11+ programme compared with usual care, which resulted in a 27% lower risk (non-significant) of quadriceps/anterior thigh injuries (low quality of evidence).[21 60] Since the FIFA 11+ programme improve hip and knee strength,[102] the preventive effect could result from this. It should, however, be noted that anterior thigh injuries may encompass different injury locations, and thus the effect on rectus femoris injuries is uncertain. Furthermore, none of the included studies investigated the preventive effect on rectus femoris/quadriceps injuries as the primary outcome measure.

Domain 3: treatment

Limited literature was found to guide treatment of rectus femoris/quadriceps injuries. Thus, a single small case-series in male Australian rules football observed no reinjuries after a two-phase criteria-based intervention with increasing running and kicking intensity (very low quality of evidence).[80] It should,

however, be noted that assessment of reinjury rate was not the purpose of the study, and thus these findings should be treated with caution.

Calf injuries

Despite calf muscle injuries being prevalent in football[3 7] very limited literature was found to guide diagnosis, treatment and prevention. Thus, very low quality of evidence was observed for both a multimodal treatment approach, consisting of passive therapy, stretching and strengthening[82 84] or platelet-rich plasma for treatment[83] and a soccer-specific balance programme in elite female football players for prevention.[81]

Limitations and methodological considerations

The current statement is not without limitations. First, risk of bias assessments of individual studies were not conducted by the authors of this statement, if an assessment was already available as part of a systematic review. This was chosen a priori in acknowledgement of the original study findings; however, this introduces several risk of bias rater teams, and potential rating discrepancies may exist due to differences in interpretation of risk of bias domains. However, since GRADE represents an overall assessment encompassing several domains, and thus does not rely only on risk of bias,[16] potential minor discrepancies in the risk of bias assessments are unlikely to change the quality of evidence provided in the present study. Second, for evaluating the effect of treatment and prevention, we have reported estimates and compared interventions using effect sizes, rather than using absolute measures (eg, days to return to play). This approach was chosen to allow standardised comparisons across studies and to account for the different definitions of return to play (eg, criteria-based, self-reported or medical clearance) or number reinjuries (self-reported, imaging-defined, length of follow-up). Third, the cut off values used to estimate the magnitude of a preventive effect are based on arbitrary values proposed to aid sample size calculations for risk factor studies in sports injury research.[47] Finally, post hoc meta-analyses were performed on existing literature if the results were not available in published meta-analyses, and if the post hoc analysis was deemed to add clinical value. Since post hoc analyses increase the risk of false positive findings these should be interpreted with caution.[103]

What is already known

- Lower extremity muscle strain injuries are very common in multidirectional sports.
- The quality of evidence related to diagnosis, prevention and treatment for the most common muscle injuries (hamstring, adductor, calf, rectus femoris/quadriceps) have not been investigated.

What are the new findings

- Most clinical tests for acute muscle injuries show very low to low diagnostic effectiveness.
- Hamstring and groin injuries can be reduced 40% to 65% using specific exercise interventions.
- Lengthening hamstring exercises show fastest return to play and lower reinjury rate compared with conventional exercises, and platelet-rich plasma offers no additional effect to current rehabilitation.
- Most outcomes were graded as very low to moderate quality of evidence, thus further high-quality research is likely to have an important impact on the confidence in the effect estimates.

CONCLUSION

We have graded the quality of evidence concerning diagnosis, prevention and treatment of the most common muscle injuries and provide a comprehensive and up-to-date summary of the best available evidence. Most clinical tests showed very low to low diagnostic effectiveness. For hamstring injury prevention, programmes that included the Nordic hamstring exercise resulted in a risk reduction of 45% to 65% when compared with usual care. For prevention of groin injuries, both the FIFA 11+ programme and the Copenhagen adductor strengthening programme resulted in risk reduction of 41% when compared with usual care. For treatment of hamstring injuries, lengthening hamstring exercises showed fastest return to play with a lower reinjury rate when compared with conventional hamstring exercises. Platelet-rich plasma had no effect on time to return-to-play and reinjury risk after a hamstring injury when compared with placebo or rehabilitation. Most outcomes for all muscle injuries and domains were graded as very low to moderate quality of evidence, indicating that further high-quality research is likely to have an important impact on the confidence in the effect estimates. At this point, research on diagnosis, prevention and treatment of muscle injuries primarily concerns hamstring muscle injuries, with only limited research on quadriceps, adductor and calf muscle injuries. Furthermore, muscle injury prevention research is mainly conducted in football, whereas muscle injury treatment research is conducted across different sports.

Twitter Lasse Ishøi @Lasselshoei, Kasper Krommes @krommes, Rasmus Skov Husted @Husted_RS, Carsten B Juhl @BoghJuhl and Kristian Thorborg @KThorborg

Acknowledgements We would like to acknowledge the Danish Society of Sports Physical Therapy (DSSF) for initiating this project.

Contributors The paper has been commissioned by the Danish Society of Sports Physical Therapy (DSSF). All authors are part of the association, and has contributed substantially to the work.

Funding The Danish Society of Sports Physical Therapy initiated the project and provided financial support to authors (LI, KK, RSH).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

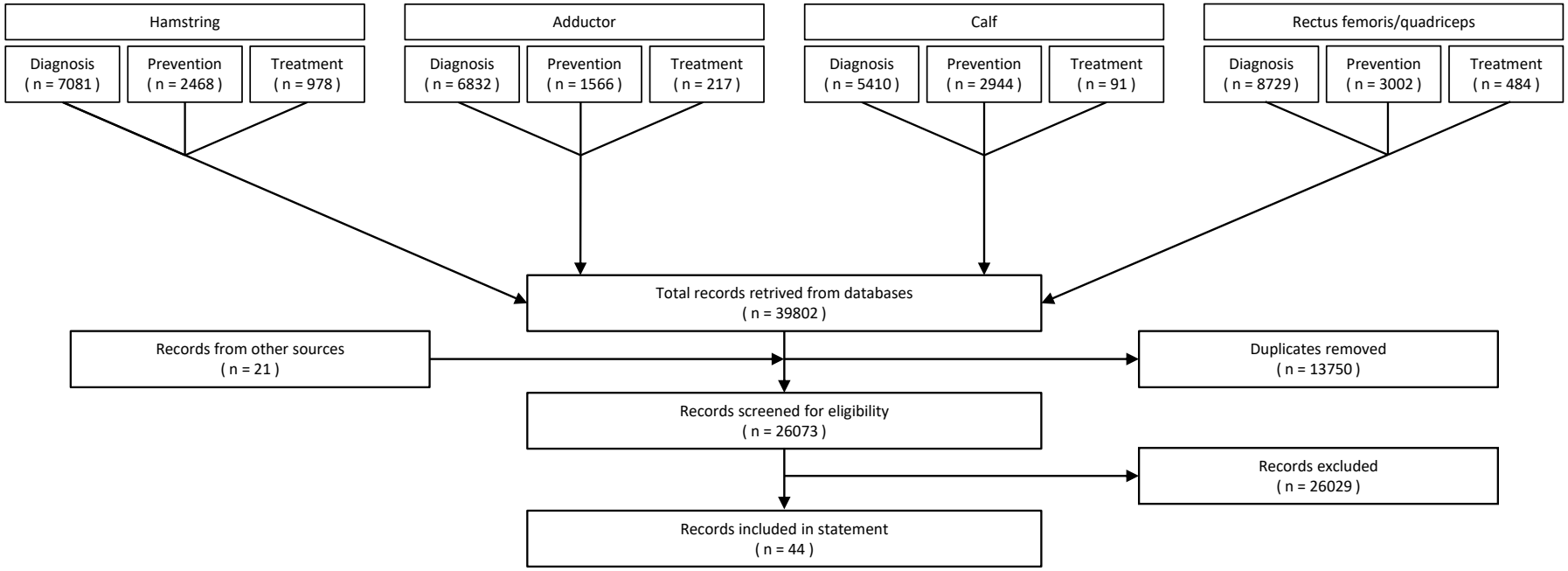
ORCID iDs
Lasse Ishøi http://orcid.org/0000-0002-2716-6567
Kristian Thorborg http://orcid.org/0000-0001-9102-4515

REFERENCES

1 Ekstrand J, Hagglund M, Walden M. Injury incidence and injury patterns in professional football: the UEFA injury study. *Br J Sports Med* 2011;45:553–8.
2 Brophy RH, Wright RW, Powell JW, *et al*. Injuries to kickers in American football: the National football League experience. *Am J Sports Med* 2010;38:1166–73.
3 Orchard JW, Seward H, Orchard JJ. Results of 2 decades of injury surveillance and public release of data in the Australian football League. *Am J Sports Med* 2013;41:734–41.
4 Williams S, Trewartha G, Kemp S, *et al*. A Meta-Analysis of Injuries in Senior Men's Professional Rugby Union. *Sports Med* 2013;43:1043–55.
5 Borowski LA, Yard EE, Fields SK, *et al*. The epidemiology of US high school Basketball injuries, 2005–2007. *Am J Sports Med* 2008;36:2328–35.

6 Alonso JM, Junge A, Renström P, *et al*. Sports injuries surveillance during the 2007 IAAF world athletics Championships. *Clin J Sport Med Off J Can Acad Sport Med* 2009;19:26–32.
7 Ekstrand J, Hägglund M, Waldén M. Epidemiology of muscle injuries in professional football (soccer). *Am J Sports Med* 2011;39:1226–32.
8 Mueller-Wohlfahrt H-W, Haensel L, Mithoefer K, *et al*. Terminology and classification of muscle injuries in sport: the Munich consensus statement. *Br J Sports Med* 2013;47:342–50.
9 Ueblacker P, Müller-Wohlfahrt H-W, Ekstrand J. Epidemiological and clinical outcome comparison of indirect ('strain') versus direct ('contusion') anterior and posterior thigh muscle injuries in male elite football players: UEFA Elite League study of 2287 thigh injuries (2001–2013). *Br J Sports Med* 2015;49:1461–5.
10 Järvinen TAH, Järvinen TLN, Kääriäinen M, *et al*. Muscle injuries: biology and treatment. *Am J Sports Med* 2005;33:745–64.
11 Hickey J, Shield AJ, Williams MD, *et al*. The financial cost of hamstring strain injuries in the Australian football League. *Br J Sports Med* 2014;48:729–30.
12 Ekstrand J, Hägglund M, Kristenson K, *et al*. Fewer ligament injuries but no preventive effect on muscle injuries and severe injuries: an 11-year follow-up of the UEFA champions League injury study. *Br J Sports Med* 2013;47:732–7.
13 Hägglund M, Waldén M, Magnusson H, *et al*. Injuries affect team performance negatively in professional football: an 11-year follow-up of the UEFA champions League injury study. *Br J Sports Med* 2013;47:738–42.
14 Ekstrand J, Waldén M, Hägglund M. Hamstring injuries have increased by 4% annually in men's professional football, since 2001: a 13-year longitudinal analysis of the UEFA Elite Club injury study. *Br J Sports Med* 2016;50:731–7.
15 Howick J, Chalmers I, Glasziou P, *et al*. *Explanation of the 2011 Oxford centre for evidence-based medicine (OCEBM) levels of evidence (background document)*. Oxford Centre for Evidence-Based Medicine.
16 Schünemann H, Brożek J, Guyatt G, *et al*. *Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach*, 2013.
17 Aagaard T, Lund H, Juhl C. Optimizing literature search in systematic reviews – are Medline, EMBASE and central enough for identifying effect studies within the area of musculoskeletal disorders? *BMC Med Res Methodol* 2016;16.
18 Rayyan—a web and mobile app for systematic reviews | systematic reviews | full text. Available: https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-016-0384-4 [Accessed 24 Sep 2019].
19 Fuller CW, Ekstrand J, Junge A, *et al*. Consensus statement on injury definitions and data collection procedures in studies of football (soccer) injuries. *Br J Sports Med* 2006;40:193–201.
20 Clarsen B, Myklebust G, Bahr R. Development and validation of a new method for the registration of overuse injuries in sports injury epidemiology: the Oslo sports trauma research centre (OSTRC) overuse injury questionnaire. *Br J Sports Med* 2013;47:495–502.
21 Silvers-Granelli H, Mandelbaum B, Adeniji O, *et al*. Efficacy of the FIFA 11+ injury prevention program in the collegiate male soccer player. *Am J Sports Med* 2015;43:2628–37.
22 Malliaropoulos N, Papalexandris S, Papalada A, *et al*. The role of stretching in rehabilitation of hamstring injuries: 80 athletes follow-up. *Med Sci Sports Exerc* 2004;36:756–9.
23 Silder A, Sherry MA, Sanfilippo J, *et al*. Clinical and morphological changes following 2 rehabilitation programs for acute hamstring strain injuries: a randomized clinical trial. *J Orthop Sports Phys Ther* 2013;43:284–99.
24 Sherry MA, Best TM. A comparison of 2 rehabilitation programs in the treatment of acute hamstring strains. *J Orthop Sports Phys Ther* 2004;34:116–25.
25 Hamilton B, Tol JL, Almusa E, *et al*. Platelet-rich plasma does not enhance return to play in hamstring injuries: a randomised controlled trial. *Br J Sports Med* 2015;49:943–50.
26 A Hamid MS, Mohamed Ali MR, Yusof A, *et al*. Platelet-rich plasma injections for the treatment of hamstring injuries: a randomized controlled trial. *Am J Sports Med* 2014;42:2410–8.
27 Reurink G, Goudswaard GJ, Moen MH, *et al*. Platelet-rich plasma injections in acute muscle injury. *N Engl J Med* 2014;370:2546–7.
28 Askling CM, Tengvar M, Thorstensson A. Acute hamstring injuries in Swedish elite football: a prospective randomised controlled clinical trial comparing two rehabilitation protocols. *Br J Sports Med* 2013;47:953–9.
29 Askling CM, Tengvar M, Tarassova O, *et al*. Acute hamstring injuries in Swedish elite sprinters and jumpers: a prospective randomised controlled clinical trial comparing two rehabilitation protocols. *Br J Sports Med* 2014;48:532–9.
30 Mendiguchia J, Martinez-Ruiz E, Edouard P, *et al*. A multifactorial, Criteria-based progressive algorithm for hamstring injury treatment. *Med Sci Sports Exerc* 2017;49:1482–92.
31 Guyatt GH, Oxman AD, Vist G, *et al*. GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). *J Clin Epidemiol* 2011;64:407–15.
32 Boutron I, Ravaud P. Classification systems to improve assessment of risk of bias. *J Clin Epidemiol* 2012;65:236–8.
33 Higgins JPT, Altman DG, Gøtzsche PC, *et al*. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
34 Whiting PF, Rutjes AWS, Westwood ME, *et al*. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529–36.
35 Scottish Intercollegiate guidelines network (SIGN) checklist for cohort studies. Available: https://www.sign.ac.uk/checklists-and-notes.html [Accessed 24 Apr 2019].
36 ROBIS: A new tool to assess risk of bias in systematic reviews was developed. - PubMed - NCBI. Available: https://www.ncbi.nlm.nih.gov/pubmed/26092286 [Accessed 12 Sep 2019].
37 Guyatt GH, Oxman AD, Kunz R, *et al*. GRADE guidelines: 7. Rating the quality of evidence—inconsistency. *J Clin Epidemiol* 2011;64:1294–302.
38 Guyatt GH, Oxman AD, Kunz R, *et al*. GRADE guidelines: 8. Rating the quality of evidence—indirectness. *J Clin Epidemiol* 2011;64:1303–10.
39 Guyatt GH, Oxman AD, Kunz R, *et al*. GRADE guidelines 6. Rating the quality of evidence—imprecision. *J Clin Epidemiol* 2011;64:1283–93.
40 Guyatt GH, Oxman AD, Montori V, *et al*. GRADE guidelines: 5. Rating the quality of evidence—publication bias. *J Clin Epidemiol* 2011;64:1277–82.
41 Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The evidence-based medicine Working group. *JAMA* 1994;271:703–7.
42 McGee S, Ratios SL. Simplifying likelihood ratios. *J Gen Intern Med* 2002;17:647–50.
43 Greenland S, Robins JM. Estimation of a common effect parameter from sparse follow-up data. *Biometrics* 1985;41:55–68.
44 Higgins JPT*et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
45 Cohen J. A power primer. *Psychol Bull* 1992;112:155–9.
46 Altman DG. *Practical Statistics for Medical Research*. CRC Press, 1990.
47 Bahr R. Risk factors for sports injuries - a methodological approach. *Br J Sports Med* 2003;37:384–92.
48 Reiman MP, Loudon JK, Goode AP. Diagnostic accuracy of clinical tests for assessment of hamstring injury: a systematic review. *J Orthop Sports Phys Ther* 2013;43:222–31.
49 Schneider-Kolsky ME, Hoving JL, Warren P, *et al*. A comparison between clinical assessment and magnetic resonance imaging of acute hamstring injuries. *Am J Sports Med* 2006;34:1008–15.
50 Zeren B, Oztekin HH. A new self-diagnostic test for biceps femoris muscle strains. *Clin J Sport Med* 2006;16:166–9.
51 Wangensteen A, Almusa E, Boukarroum S, *et al*. MRI does not add value over and above patient history and clinical examination in predicting time to return to sport after acute hamstring injuries: a prospective cohort of 180 male athletes. *Br J Sports Med* 2015;49:1579–87.
52 Goode AP, Reiman MP, Harris L, *et al*. Eccentric training for prevention of hamstring injuries may depend on intervention compliance: a systematic review and meta-analysis. *Br J Sports Med* 2015;49:349–56.
53 van DN, Behan FP, Whiteley R. Including the Nordic hamstring exercise in injury prevention programmes halves the rate of hamstring injuries: a systematic review and meta-analysis of 8459 athletes. *Br J Sports Med* 2019:bjsp orts-2018-100045.
54 Thorborg K, Krommes KK, Esteve E, *et al*. Effect of specific exercise-based football injury prevention programmes on the overall injury rate in football: a systematic review and meta-analysis of the FIFA 11 and 11+ programmes. *Br J Sports Med* 2017;51:562–71.
55 Gabbe BJ, Branson R, Bennell KL. A pilot randomised controlled trial of eccentric exercise to prevent hamstring injuries in community-level Australian football. *J Sci Med Sport* 2006;9:103–9.
56 Petersen J, Thorborg K, Nielsen MB, *et al*. Preventive effect of eccentric training on acute hamstring injuries in men's soccer: a cluster-randomized controlled trial. *Am J Sports Med* 2011;39:2296–303.
57 van der Horst N, Smits D-W, Petersen J, *et al*. The preventive effect of the nordic hamstring exercise on hamstring injuries in amateur soccer players: a randomized controlled trial. *Am J Sports Med* 2015;43:1316–23.
58 Engebretsen AH, Myklebust G, Holme I, *et al*. Prevention of injuries among male soccer players: a prospective, randomized intervention study targeting players with previous injuries or reduced function. *Am J Sports Med* 2008;36:1052–60.
59 del Ama Espinosa G, Pöyhönen T, Aramendi JF, *et al*. Effects of an eccentric training programme on hamstring strain injuries in women football players. *Biomed Hum Kinet* 2015;7.
60 Soligard T, Myklebust G, Steffen K, *et al*. Comprehensive warm-up programme to prevent injuries in young female footballers: cluster randomised controlled trial. *BMJ* 2008;337:a2469.
61 Askling C, Karlsson J, Thorstensson A. Hamstring injury occurrence in elite soccer players after preseason strength training with eccentric overload. *Scand J Med Sci Sports* 2003;13:244–50.
62 Al Attar WSA, Soomro N, Pappas E, *et al*. Adding a post-training FIFA 11+ exercise program to the pre-training FIFA 11+ injury prevention program reduces injury rates among male amateur soccer players: a cluster-randomised trial. *J Physiother* 2017;63:235–42.

63 van de Hoef PA, Brink MS, Huisstede BMA, *et al*. Does a bounding exercise program prevent hamstring injuries in adult male soccer players? - A cluster-RCT. *Scand J Med Sci Sports* 2019;29:515–23.
64 Whalan M, Lovell R, Steele JR, *et al*. Rescheduling Part 2 of the 11+ reduces injury burden and increases compliance in semi-professional football. *Scand J Med Sci Sports* 2019;29:1941–51.
65 Söderman K, Werner S, Pietilä T, *et al*. Balance board training: prevention of traumatic injuries of the lower extremities in female soccer players? A prospective randomized intervention study. *Knee Surg Sports Traumatol Arthrosc* 2000;8:356–63.
66 Mjolsnes R, Arnason A, osthagen T, *et al*. A 10-week randomized trial comparing eccentric vs. concentric hamstring strength training in well-trained soccer players. *Scand J Med Sci Sports* 2004;14:311–7.
67 Pas HI, Reurink G, Tol JL, *et al*. Efficacy of rehabilitation (lengthening) exercises, platelet-rich plasma injections, and other conservative interventions in acute hamstring injuries: an updated systematic review and meta-analysis. *Br J Sports Med* 2015;49:1197–205.
68 Reurink G, Goudswaard GJ, Moen MH, *et al*. Rationale, secondary outcome scores and 1-year follow-up of a randomised trial of platelet-rich plasma injections in acute hamstring muscle injury: the Dutch hamstring injection therapy study. *Br J Sports Med* 2015;49:1206–12.
69 Hickey JT, Timmins RG, Maniar N, *et al*. Pain-Free versus Pain-Threshold rehabilitation following acute hamstring strain injury: a randomized controlled trial. *J Orthop Sports Phys Ther* 2019:1–35.
70 Serner A, Tol JL, Jomaah N, *et al*. Diagnosis of acute groin injuries: a prospective study of 110 athletes. *Am J Sports Med* 2015;43:1857–64.
71 Serner A, Weir A, Tol JL, *et al*. Can standardised clinical examination of athletes with acute groin injuries predict the presence and location of MRI findings? *Br J Sports Med* 2016;50:1541–7.
72 Esteve E, Rathleff MS, Bagur-Calafat C, *et al*. Prevention of groin injuries in sports: a systematic review with meta-analysis of randomised controlled trials. *Br J Sports Med* 2015;49:785–91.
73 Haroy J, Clarsen B, Wiger EG, *et al*. The adductor strengthening programme prevents groin problems among male football players: a cluster-randomised controlled trial. *Br J Sports Med*.
74 Hölmich P, Larsen K, Krogsgaard K, *et al*. Exercise program for prevention of groin pain in football players: a cluster-randomized trial. *Scand J Med Sci Sports* 2010;20:814–21.
75 van Beijsterveldt AMC, van de Port IGL, Krist MR, *et al*. Effectiveness of an injury prevention programme for adult male amateur soccer players: a cluster-randomised controlled trial. *Br J Sports Med* 2012;46:1114–8.
76 Steffen K, Myklebust G, Olsen OE, *et al*. Preventing injuries in female youth football - a cluster-randomized controlled trial. *Scand J Med Sci Sports* 2008;18:605–14.
77 Arnason A, Engebretsen L, Bahr R. No effect of a video-based awareness program on the rate of soccer injuries. *Am J Sports Med* 2005;33:77–84.
78 Longo UG, Loppini M, Berton A, *et al*. The FIFA 11+ program is effective in preventing injuries in elite male basketball players: a cluster randomized controlled trial. *Am J Sports Med* 2012;40:996–1005.
79 Slauterbeck JR, Choquette R, Tourville TW, *et al*. Implementation of the FIFA 11+ injury prevention program by high school athletic teams did not reduce lower extremity injuries: a cluster randomized controlled trial. *Am J Sports Med* 2019;0363546519873270.
80 Cross TM, Gibbs N, Houang MT, *et al*. Acute quadriceps muscle strains: magnetic resonance imaging features and prognosis. *Am J Sports Med* 2004;32:710–9.
81 Kraemer R, Knobloch K. A soccer-specific balance training program for hamstring muscle and Patellar and Achilles tendon injuries: an intervention study in premier League female soccer. *Am J Sports Med* 2009;37:1384–93.
82 Millar AP. Strains of the posterior calf musculature ("tennis leg"). *Am J Sports Med* 1979;7:172–4.
83 Borrione P, Fossati C, Pereira MT, *et al*. The use of platelet-rich plasma (PRP) in the treatment of gastrocnemius strains: a retrospective observational study. *Platelets* 2018;29:596–601.
84 Pedret C, Rodas G, Balius R, *et al*. Return to play after soleus muscle injuries. *Orthop J Sports Med* 2015;3:232596711559580.
85 Kerkhoffs GMMJ, van Es N, Wieldraaijer T, *et al*. Diagnosis and prognosis of acute hamstring injuries in athletes. *Knee Surg Sports Traumatol Arthrosc* 2013;21:500–9.
86 McCall A, Carling C, Nedelec M, *et al*. Risk factors, testing and preventative strategies for non-contact injuries in professional football: current perceptions and practices of 44 teams from various premier leagues. *Br J Sports Med* 2014;48:1352–7.
87 Bahr R, Thorborg K, Ekstrand J. Evidence-Based hamstring injury prevention is not adopted by the majority of champions League or Norwegian premier League football teams: the Nordic hamstring survey. *Br J Sports Med* 2015;49:1466–71.
88 O'Brien J, Young W, Finch CF. The use and modification of injury prevention exercises by professional youth soccer teams. *Scand J Med Sci Sports* 2017;27:1337–46.
89 Timmins RG, Bourne MN, Shield AJ, *et al*. Short biceps femoris fascicles and eccentric knee flexor weakness increase the risk of hamstring injury in elite football (soccer): a prospective cohort study. *Br J Sports Med* 2016;50:1524–35.
90 Ishøi L, Hölmich P, Aagaard P, *et al*. Effects of the Nordic hamstring exercise on sprint capacity in male football players: a randomized controlled trial. *J Sports Sci* 2018;36:1663–72.
91 Small K, McNaughton L, Greig M, *et al*. Effect of timing of eccentric hamstring strengthening exercises during soccer training: implications for muscle fatigability. *J Strength Cond Res* 2009;23:1077–83.
92 Bourne MN, Duhig SJ, Timmins RG, *et al*. Impact of the Nordic hamstring and hip extension exercises on hamstring architecture and morphology: implications for injury prevention. *Br J Sports Med* 2017;51:469–77.
93 Jakobsen JR, Mackey AL, Knudsen AB, *et al*. Composition and adaptation of human myotendinous junction and neighboring muscle fibers to heavy resistance training. *Scand J Med Sci Sports* 2017;27:1547–59.
94 Timmins RG, Shield AJ, Williams MD, *et al*. Is there evidence to support the use of the angle of peak torque as a marker of hamstring injury and Re-Injury risk? *Sports Med* 2016;46:7–13.
95 Thorborg K. Why hamstring eccentrics are hamstring essentials. *Br J Sports Med* 2012;46:463–5.
96 Wangensteen A, Tol JL, Witvrouw E, *et al*. Hamstring Reinjuries occur at the same location and early after return to sport: a descriptive study of MRI-Confirmed Reinjuries. *Am J Sports Med* 2016;44:2112–21.
97 Ishøi L, Sørensen CN, Kaae NM, *et al*. Large eccentric strength increase using the Copenhagen adduction exercise in football: a randomized controlled trial. *Scand J Med Sci Sports* 2016;26:1334–42.
98 Serner A, Jakobsen MD, Andersen LL, *et al*. EMG evaluation of hip adduction exercises for soccer players: implications for exercise selection in prevention and treatment of groin injuries. *Br J Sports Med* 2014;48:1108–14.
99 Haroy J, Thorborg K, Serner A, *et al*. Including the Copenhagen adduction exercise in the FIFA 11+ provides missing eccentric hip adduction strength effect in male soccer players: a randomized controlled trial. *Am J Sports Med* 2017;363546517720194.
100 Light N, Smith N, Delahunt E, *et al*. Hip and groin injury management in English youth football: a survey of 64 professional academies. *Sci Med Footb* 2018;2:133–40.
101 Serner A, van Eijck CH, Beumer BR, *et al*. Study quality on groin injury management remains low: a systematic review on treatment of groin pain in athletes. *Br J Sports Med* 2015;49:813.
102 Daneshjoo A, Rahnama N, Mokhtar AH, *et al*. Effectiveness of injury prevention programs on developing quadriceps and Hamstrings strength of young male professional soccer players. *J Hum Kinet* 2013;39:115–25.
103 Bandholm T, Christensen R, Thorborg K, *et al*. Preparing for what the reporting checklists will not tell you: the prepare trial guide for planning clinical research to avoid research waste. *Br J Sports Med* 2017;51:1494–501.


Hamstring
Diagnosis (n = 7081)
Prevention (n = 2468)
Treatment (n = 978)
Adductor
Diagnosis (n = 6832)
Prevention (n = 1566)
Treatment (n = 217)
Calf
Diagnosis (n = 5410)
Prevention (n = 2944)
Treatment (n = 91)
Rectus femoris/quadriceps
Diagnosis (n = 8729)
Prevention (n = 3002)
Treatment (n = 484)
Total records retrived from databases (n = 39802)
Records from other sources (n = 21)
Duplicates removed (n = 13750)
Records screened for eligibility (n = 26073)
Records excluded (n = 26029)
Records included in statement (n = 44)

Overview of Risk of Bias tools used in "*Diagnosis, prevention, and treatment of common lower extremity muscle injuries in sport – Grading the evidence: a statement paper commissioned by the Danish Society of Sports Physical Therapy (DSSF)"*

QUADAS-2 tool
The tool was originally based on data of the methodological literature on diagnostic test assessment, and a review on the existing quality assessment tools to identify all possible relevant items and their evidence-based. Through a four-round Delphi process, 11 experts agreed on the items to include.[1] The QUADAS was evaluated by asking reviewers a range of questions about its use and performance, and assessed overall agreement.[2] The interrater reliability of QUADAS items was found to be poor, with a study reporting 47-90% agreement (mean 69%) and of -0.28 – 0.58 κ (mean 0.22).[3] The new QUADAS-2 has since been developed with new distinct domains; 'Patient Selection', 'Index Test', 'Reference Standard', and 'Flow and Timing',[4] which is recommended in the GRADE handbook.[5]

SIGN (Scottish intercollegiate guideline network) checklist
The SIGN 3 checklist developed by the network consists of 14 items and is closely aligned to procedures in the Cochrane handbook and the GRADE handbook.[6] No studies have investigated the validity or reliability of the checklist.

ROBIS
The ROBIS tool was developed in accordance with evidence-based standards, similar to the approach for the QUADAS-2 tool.[7–9] Properties of reliability of the ROBIS tool are comparable to the AMSTAR quality assessment tool.[10,11]

RoB
The tool to assess risk of bias in RCTs was developed from the Cochrane group, to be used when assessing risk of bias for studies included in systematic reviews.[12] The reliability of the 5 different domains ranges from 0.79 to 0.05 κ.[13]

References

1 Whiting P, Rutjes AWS, Reitsma JB, *et al.* The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003;**3**:25. doi:10.1186/1471-2288-3-25

2 Whiting PF, Weswood ME, Rutjes AWS, *et al.* Evaluation of QUADAS, a tool for the quality assessment of diagnostic accuracy studies. *BMC Med Res Methodol* 2006;**6**:9. doi:10.1186/1471-2288-6-9

3 Hollingworth W, Medina LS, Lenkinski RE, *et al.* Interrater reliability in assessing quality of diagnostic accuracy studies using the QUADAS tool. A preliminary assessment. *Acad Radiol* 2006;**13**:803–10. doi:10.1016/j.acra.2006.03.008

4 Whiting PF, Rutjes AWS, Westwood ME, *et al.* QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;**155**:529–36. doi:10.7326/0003-4819-155-8-201110180-00009

5 Schünemann H, Brożek J, Guyatt G, *et al.* Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. 2013.

6 Scottish Intercollegiate Guidelines Network (SIGN) checklist for cohort studies. https://www.sign.ac.uk/checklists-and-notes.html (accessed 24 Apr 2019).

7 Whiting P, Savović J, Higgins JPT, *et al.* ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol* 2016;**69**:225–34. doi:10.1016/j.jclinepi.2015.06.005

8 Moher D, Schulz KF, Simera I, *et al.* Guidance for developers of health research reporting guidelines. *PLoS Med* 2010;**7**:e1000217. doi:10.1371/journal.pmed.1000217

9 Banzi R, Cinquini M, Gonzalez-Lorenzo M, *et al.* Quality assessment versus risk of bias in systematic reviews: AMSTAR and ROBIS had similar reliability but differed in their construct and applicability. *J Clin Epidemiol* 2018;**99**:24–32. doi:10.1016/j.jclinepi.2018.02.024

10 Pieper D, Puljak L, González-Lorenzo M, *et al.* Minor differences were found between AMSTAR 2 and ROBIS in the assessment of systematic reviews including both randomized and nonrandomized studies. *J Clin Epidemiol* 2019;**108**:26–33. doi:10.1016/j.jclinepi.2018.12.004

11 Lorenz RC, Matthias K, Pieper D, *et al.* A psychometric study found AMSTAR 2 to be a valid and moderately reliable appraisal tool. *J Clin Epidemiol* 2019;**114**:133–40. doi:10.1016/j.jclinepi.2019.05.028

12 Higgins JPT, Altman DG, Gøtzsche PC, *et al.* The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;**343**:d5928. doi:10.1136/bmj.d5928

13 Hartling L, Hamm MP, Milne A, *et al.* Testing the risk of bias tool showed low reliability between individual reviewers and across consensus assessments of reviewer pairs. *J Clin Epidemiol* 2013;**66**:973–81. doi:10.1016/j.jclinepi.2012.07.005

Table 1. Risk of bias assessment and GRADE of clinical tests for diagnosing hamstring injuries.

Diagnosis				QUADAS 2 Items*											GRADE (outcome level)						
Hamstring injuries																					
Index test	Reference standard	Study	Likelihood ratio	1	2	3	4	5	6	7	8	9	10	11	Study design	Risk of bias	Indirectness	Inconsistency	Imprecise evidence	Publication bias	Downgrade **
Aktiv slump	MRI	Wangensteen et al. (1)	LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	?	✓	?	↓
			LR-																✓		↓
Pain during SLR	MRI		LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	?	✓	?	↓
			LR-																✓		↓
Pai during 90deg R KF	MRI		LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	?	✓	?	↓
			LR-																✓		↓
Pai during 30deg R KF	MRI		LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	?	✓	?	↓
			LR-																✓		↓
Pain during active KF	MRI		LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	?	↔
			LR-																✓		↔
Pain during active KE	MRI		LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	?	✓	?	↓
			LR-																✓		↓
Pain during trunk F	MRI		LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	?	✓	?	↓
			LR-																✓		↓
Taking off shoe	US	Zeren et al. (2)	LR+: N/A	×	✓	?	×	✓	✓	×	×	✓	?	?	✓	××	×	?	N/A	?	N/A
			LR-																?		↓↓↓
Resisted range of motion test	US		LR+: N/A	×	✓	?	×	✓	✓	×	×	✓	?	?	✓	××	×	?	N/A	?	N/A
			LR-																✓		↓↓↓
Passive range of motion test	US		LR+: N/A	×	✓	?	×	✓	✓	×	×	✓	?	?	✓	××	×	?	N/A	?	N/A
			LR-																✓		↓↓↓
Active range of motion test	US		LR+: N/A	×	✓	?	×	✓	✓	×	×	✓	?	?	✓	××	×	?	N/A	?	N/A
			LR-																✓		↓↓↓
Composit	MRI	Schneider-Kolsky et al. (3)	LR+	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR-: N/A																N/A		N/A

Abbreviations: MRI (magnetic resonance imaging); US (ultrasound); LR+ (Positive likelihood ratio); LR- (negative likelihood ratio); N/A (not applicable)

*Item 1: Was a consecutive or random sample of patients enrolled? Item 2: Was a case-control design avoided? Item 3: Did the study avoid inappropriate exclusions? Item 4: Were the index test results interpreted without knowledge of the results of the reference standard? Item 5: If a threshold was used, was it pre-specified? Item 6: Is the reference standard likely to correctly classify the target condition? Item 7: Were the reference standard results interpreted without knowledge of the results of the index test? Item 8: Was there an appropriate interval between index test(s) and reference standard? Item 9: Did all patients receive a reference standard? Item 10: Did patients receive the same reference standard? Item 11: Were all patients included in the analysis?

Quadas 2 risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 2. Risk of bias assessment and GRADE of clinical tests for diagnosing adductor injuries.

Diagnosis				QUADAS Items											GRADE (outcome level)						
Adductor injuries																					
Index test	Reference standard	Study	Likelihood ratio	1	2	3	4	5	6	7	8	9	10	11	Study design	Risk of bias	Indirectness	Inconsistency	Imprecise evidence	Publication bias	Downgrade**
Palpation	MRI	Serner et al. (4)	LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																×		↓↓
Squeeze 0°	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	×	?	↓↓
			LR -																✓		↓
Squeeze 45°	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																		
Isometric adduction (outer range)	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	×	?	↓↓
			LR -																✓		↓
Adductor stretching	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	×	?	↓↓
			LR -																✓		↓
Flexion Abduction External Rotation (FABER)	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																		

Abbreviations: MRI (magnetic resonance imaging); LR+ (Positive likelihood ratio); LR- (negative likelihood ratio).

*Item 1: Was a consecutive or random sample of patients enrolled? Item 2: Was a case-control design avoided? Item 3: Did the study avoid inappropriate exclusions? Item 4: Were the index test results interpreted without knowledge of the results of the reference standard? Item 5: If a threshold was used, was it pre-specified? Item 6: Is the reference standard likely to correctly classify the target condition? Item 7: Were the reference standard results interpreted without knowledge of the results of the index test? Item 8: Was there an appropriate interval between index test(s) and reference standard? Item 9: Did all patients receive a reference standard? Item 10: Did patients receive the same reference standard? Item 11: Were all patients included in the analysis?

Quadas 2 risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 3. Risk of bias assessment and GRADE of clinical tests for diagnosing rectus femoris injuries.

Diagnosis				QUADAS Items											GRADE (outcome level)						
Rectus femoris injuries																					
Index test	Reference standard	Study	Likelihood ratio	1	2	3	4	5	6	7	8	9	10	11	Study design	Risk of bias	Indirectness	Inconsistency	Imprecise evidence	Publication bias	Downgrade **
Palpation	MRI	Serner et al. (4)	LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	×	?	↓↓
			LR -																?		↓
Isometric hip flexion 0°	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																×		↓↓
Isometric hip flexion 90°	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																×		↓↓
Isometric hip flexion (modified Thomas Test)	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																×		↓↓
Isometric knee extension (modified Thomas Test)	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																?		↓
Hip extension (stretching; modified Thomas Test)	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	✓	?	↓
			LR -																×		↓↓
Knee flexion (stretching; modified Thomas Test)	MRI		LR +	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	✓	✓	×	?	×	?	↓↓
			LR -																×		↓↓

Abbreviations: MRI (magnetic resonance imaging); LR+ (Positive likelihood ratio); LR- (negative likelihood ratio).

*Item 1: Was a consecutive or random sample of patients enrolled? Item 2: Was a case-control design avoided? Item 3: Did the study avoid inappropriate exclusions? Item 4: Were the index test results interpreted without knowledge of the results of the reference standard? Item 5: If a threshold was used, was it pre-specified? Item 6: Is the reference standard likely to correctly classify the target condition? Item 7: Were the reference standard results interpreted without knowledge of the results of the index test? Item 8: Was there an appropriate interval between index test(s) and reference standard? Item 9: Did all patients receive a reference standard? Item 10: Did patients receive the same reference standard? Item 11: Were all patients included in the analysis?

Quadas 2 risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 4. Risk of bias assessment and GRADE for treatment of hamstring injuries.

Treatment Hamstring		Risk of Bias assessment Item*							Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade**
Multifactorial criteria-based algorithm vs. lengthening hamstring exercises	Mendiguchia et al. (5)	?	✗	✗	?	✓	?	✓	**Return to play**	RCT ✓	?	?	✓	✗✗	?	↓↓
									Reinjuries	RCT ✓	?	?	✓	✗✗	?	↓↓
Lengthening hamstring exercises versus to conventional hamstring exercises (6)	Askling et al. (7,8)	✗	✗	✗	✗	✓	?	?	**Return to play**	RCT ✓	✗✗	✓	✓	✓	?	↓↓
		✗	✗	✗	✗	✓	?	?	**Reinjuries**		✗✗	✓	✓	✗✗	?	↓↓↓
Running and eccentric hamstring strengthening versus agility and trunk stabilization	Silder et al. (9)	?	?	✗	?	✓	?	?	**Return to play**	RCT ✓	✗	?	✗	✗✗	?	↓↓↓
Agility and trunk stabilization vs. hamstring stretching and strengthening	Sherry et al. (10)	?	?	✗	✗	?	?	✗	**Return to play**	RCT ✓	✗✗	?	✗	✗	?	↓↓↓
									Reinjuries	RCT ✓	✗✗	?	✗	✗	?	↓↓↓
Hamstring stretching four times/day versus hamstring stretching once daily	Malliaropoulos et al. (11)	?	?	✗	?	?	?	✗	**Return to play**	RCT ✓	✗✗	?	✗	✓	?	↓↓↓
Platelet-rich plasma versus placebo or rehabilitation (6)	Reurink et al. (12)	✓	✓	✓	✓	✓	?	✓	**Return to play**	RCT ✓	✓	✗	✓	✓	?	↓
	Hamilton et al. (13)	?	?	✓	✓	✓	✗	✓								
	Hamid et al. (14)	✓	✓	✗	✓	✓	✗	✓	**Reinjuries**	RCT ✓	✓	✓	✓	✗	?	↓
Pain-threshold (≤4 on the 0-10 NRS) versus Pain-free (0 on the 0-10 NRS) rehabilitation	Hickey et al. (15)	✗	✓	✓	✓	?	?	✓	**Return to play**	RCT ✓	✓	?	✗	✗	?	↓↓
									Reinjuries		✓	?	✓	✗✗	?	↓↓

Abbreviations: RCT (randomized controlled trial)

*Item 1: Random sequence generation; Item 2: Allocation concealment; Item 3: Blinding of participants and personal; Item 4: Blinding of outcome assessor; Item 5: Incomplete outcome data; Item 6: Selective reporting; Item 7: Other sources of bias.

Risk of bias assessment: ✗ item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: ✗ = item cause for possible downgrade once; ✗✗ = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 5. Risk of bias assessment and GRADE for treatment of rectus femoris/quadriceps injuries.

Treatment Rectus femoris/quadriceps		SIGN Checklist 3*														Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade**
A two-phase criteria-based intervention	Cross et al. (16)	✓	N/A	×	N/A	?	N/A	×	×	×	?	×	N/A	?	×	Return to play	Cohort ××	×	?	×	×	?	↓↓↓
																Reinjuries	Cohort ××	×	?	✓	✓	?	↓↓↓

Abbreviations: N/A (not applicable).

*Item 1: The study addresses an appropriate and clearly focused question?; Item 2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation?; Item 3: The study indicates how many of the people asked to take part did so, in each of the groups being studied?; Item 4: The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis?; Item 5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?; Item 6: Comparison is made between full participants and those lost to follow up, by exposure status?; Item 7: The outcomes are clearly defined?; Item 8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable?; Item 9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome?; Item 10: The method of assessment of exposure is reliable?; Item 11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable?; Item 12: Exposure level or prognostic factor is assessed more than once?; Item 13: The main potential confounders are identified and taken into account in the design and analysis?; Item 14: Have confidence intervals been provided?

Risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ?= item unclear or not available, no upgrading or downgrading.

**↓↓↓=downgrade quality by three levels

Table 6. Risk of bias assessment and GRADE for treatment of calf injuries.

Treatment Calf		SIGN Checklist 3 and 4*														Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade***
Multimodal treatment program	Millar (17)	×	N/A	×	N/A	?	?	?	×	N/A	?	N/A	×	×	×	Return to play	Cohort ××	××	?	✓	?	?	↓↓↓
																Reinjuries	Cohort ××	××	?	✓	?	?	↓↓↓
Multimodal treatment program	Pedret et al. (18)	✓	N/A	×	N/A	✓	N/A	×	×	?	?	×	?	?	×	Reinjuries	Cohort ××	×	?	✓	?	?	↓↓↓
Platelet-rich plasma**	Borrione et al. (19)	×	✓	✓	?	✓	✓	✓	×	?	×	×	-	-	-	Return to play	Case-control ××	××	?	✓	✓	?	↓↓↓

Abbreviations: N/A (not applicable).

*SIGN 3: Item 1: The study addresses an appropriate and clearly focused question?; Item 2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation?; Item 3: The study indicates how many of the people asked to take part did so, in each of the groups being studied?; Item 4: The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis?; Item 5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?; Item 6: Comparison is made between full participants and those lost to follow up, by exposure status?; Item 7: The outcomes are clearly defined?; Item 8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable?; Item 9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome?; Item 10: The method of assessment of exposure is reliable?; Item 11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable?; Item 12: Exposure level or prognostic factor is assessed more than once?; Item 13: The main potential confounders are identified and taken into account in the design and analysis?; Item 14: Have confidence intervals been provided?

SIGN 4: Item 1: The study addresses an appropriate and clearly focused question?; Item 2: The cases and controls are taken from comparable populations?; Item 3: The same exclusion criteria are used for both cases and controls?; Item 4: What percentage of each group (cases and controls) participated in the study?; Item 5: Comparison is made between participants and non-participants to establish their similarities or differences?; Item 6: Cases are clearly defined and differentiated from controls?; Item 7: It is clearly established that controls are non-cases?; Item 8: Measures will have been taken to prevent knowledge of primary exposure influencing case ascertainment?; Item 9: Exposure status is measured in a standard, valid and reliable way?; Item 10: The main potential confounders are identified and taken into account in the design and analysis?; Item 11: Confidence intervals are provided.

** Risk of bias using SIGN 4

Risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ?= item unclear or not available, no upgrading or downgrading.

***↓↓↓=downgrade quality by three levels

Table 7. Risk of bias assessment and GRADE for prevention of hamstring injuries.

Prevention Hamstring		Risk of Bias assessment Item*							Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade **
Interventions including the Nordic Hamstring exercise (20)	Gabbe et al. (21)	✓	✓	×	×	✓	✓	✓	Injuries	RCT ✓	?/✓	×	✓	✓	✓	↓
	Soligard et al. (22)	?	?	×	×	×	✓	✓								
	Engebretsen et al. (23)	?	?	×	×	?	?	×								
	Petersen et al. (24)	✓	✓	×	×	✓	✓	✓								
	Del Ama Espinosa et al. (25)	✓	✓	×	×	✓	✓	✓								
	Silvers-Granelli et al. (26)	✓	?	×	×	×	?	×								
	Van der Horst et al. (27)	✓	✓	×	×	✓	✓	✓								
Mixed eccentric hamstring training (28)	Aksling et al. (29)	?	?	×	?	?	?	×	Injuries	RCT ✓	✓	×	✓	×	?	↓↓
	Gabbe et al. (21)	✓	✓	×	×	✓	✓	✓								
	Engebretsen et al. (23)	?	?	×	×	?	?	×								
	Petersen et al. (24)	✓	✓	×	×	✓	✓	✓								
FIFA 11+ (30)	Soligard et al. (22)	?	?	×	×	×	✓	✓	Injuries	RCT ✓	×	✓	✓	✓	?	↓
	Silvers-Granelli et al. (26)	✓	?	×	×	×	?	×								
Nordic Hamstring Exercise Protocol (meta-analysis performed as part of this statement)	Petersen et al. (24)	✓	✓	×	×	✓	✓	✓	Injuries	RCT ✓	✓	✓	✓	✓	?	↔
	Van der Horst et al. (27)	✓	✓	×	×	✓	✓	✓								
Bounding exercise program	Van de Hoef et al. (31)	✓	?	×	×	✓	✓	✓	Injuries	RCT ✓	✓	?	✓	×	?	↓
FIFA 11+ program pre- and post-football	Al Attar et al. (32)	✓	?	×	×	✓	✓	×	Injuries	RCT ✓	×	?	✓	××	?	↓↓↓
Modified FIFA 11+ with rescheduling of Part 2 versus standard FIFA 11+	Whalan et al. (33)	?	?	×	×	✓	?	✓	Injuries	RCT ✓	?	?	✓	×	?	↓
Balance board training	Soderman et al. (34)	?	?	×	×	✓	?	×	Injuries	RCT ✓	×	?	✓	××	?	↓↓↓

Abbreviations: RCT (randomized controlled trial)

*Item 1: Random sequence generation; Item 2: Allocation concealment; Item 3: Blinding of participants and personal; Item 4: Blinding of outcome assessor; Item 5: Incomplete outcome data; Item 6: Selective reporting; Item 7: Other sources of bias.

Risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 8. Risk of bias assessment and GRADE for prevention of groin injuries.

Prevention Adductor (Groin)		Risk of Bias assessment Item*							Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade **
Mixed groin prevention programs (35)	Arnason et al. (36)	?	?	✗	✗	?	?	✗	Injuries	RCT ✓	✗	✓	✗	✗	?	↓↓
	Beijsterveldt et al. (37)	?	?	✗	✗	✓	✗	?								
	Engebretsen et al. (23)	?	?	✗	✗	?	?	✗								
	Holmich et al. (38)	✓	✓	✗	✗	✓	?	✗								
	Soderman et al. (34)	?	?	✗	✗	✓	?	✗								
	Steffen et al. (39)	?	?	✗	✗	✓	?	✗								
Specific adductor strength training (35)	Holmich et al. (38)	✓	✓	✗	✗	✓	?	✗	Injuries	RCT ✓	✗	✓	✗	✗	?	↓↓
	Engebretsen et al. (23)	?	?	✗	✗	?	?	✗								
FIFA 11 (35)	Steffen et al. (39)	?	?	✗	✗	✓	?	✗	Injuries	RCT ✓	✗	✗	✗	✗	?	↓↓↓
	Beijsterveldt et al. (37)	?	?	✗	✗	✓	✗	?								
FIFA 11+ programme in footabll (30)	Silvers-Granelli et al. (26)	✓	?	✗	✗	✗	?	✗	Injuries	RCT ✓	✗	✓	✗	✓	?	↓↓
	Soligard et al. (22)	?	?	✗	✗	✗	✓	✓								
FIFA 11+ programme in mixed sports	Longo et al. (40)	✓	?	✗	✗	✓	✓	✓	Injuries	RCT ✓	✓	✗	✗	✗✗	?	↓↓↓
	Slauterbeck et al. (41)	✓	?	✗	✗	✓	?	✓								
Adductor strengthening program	Haroy et al. (42)	✓	?	✗	✗	✓	✓	✓	Injuries	RCT ✓	✓	?	✗	✓	?	↓
FIFA 11+ program pre- and post-football	Al Attar et al. (32)	✓	?	✗	✗	✓	✓	✗	Injuries	RCT ✓	✗	?	✗	✗✗	?	↓↓↓
Modified FIFA 11+ with rescheduling of Part 2 versus standard FIFA 11+	Whalan et al. (33)	?	?	✗	✗	✓	?	✓	Injuries	RCT ✓	?	?	✗	✓	?	↓

Abbreviations: RCT (randomized controlled trial)

*Item 1: Random sequence generation; Item 2: Allocation concealment; Item 3: Blinding of participants and personal; Item 4: Blinding of outcome assessor; Item 5: Incomplete outcome data; Item 6: Selective reporting; Item 7: Other sources of bias.

Risk of bias assessment: ✗ item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: ✗ = item cause for possible downgrade once; ✗✗ = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 9. Risk of bias assessment and GRADE for prevention of anterior thigh/quadriceps injuries.

Prevention anterior thigh/quadriceps		Risk of Bias assessment Item							Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade
FIFA 11+ (meta-analysis performed as part of this statement)	Silvers-Granelli et al. (26)	✓	?	×	×	×	?	×	Injuries	RCT ✓	×	✓	✓	×	?	↓
	Soligard et al. (22)	?	?	×	×	×	✓	✓								
FIFA 11+ program pre- and post-football	Al Attar et al. (32)	✓	?	×	×	✓	✓	×	Injuries	RCT ✓	×	?	✓	××	?	↓↓↓
Modified FIFA 11+ with rescheduling of Part 2 versus standard FIFA 11+	Whalan et al. (33)	?	?	×	×	✓	?	✓	Injuries	RCT ✓	?	?	✓	✓	?	↔
Balance board training	Soderman et al. (34)	?	?	×	×	✓	?	×	Injuries	RCT ✓	×	?	✓	××	?	↓↓↓

Abbreviations: RCT (randomized controlled trial)

*Item 1: Random sequence generation; Item 2: Allocation concealment; Item 3: Blinding of participants and personal; Item 4: Blinding of outcome assessor; Item 5: Incomplete outcome data; Item 6: Selective reporting; Item 7: Other sources of bias.

Risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ? = item unclear or not available, no upgrading or downgrading.

**↓= downgrade quality by one level; ↓↓=downgrade quality by two levels; ↓↓↓=downgrade quality by three levels; ↔=no downgrade

Table 10. Risk of bias assessment and GRADE for prevention of calf injuries.

Prevention Calf		SIGN Checklist 3*														Outcome	GRADE (outcome level)						
Interventions	Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14		Study design	Risk of bias	Inconsistency	Indirectness	Imprecise evidence	Publication bias	Downgrade**
soccer-specific balance program	Kraemer et al. (43)	✓	N/A	N/A	?	×	?	✓	×	×	✓	✓	?	?	×	Injuries	Cohort ××	×	?	✓	?	?	↓↓↓

Abbreviations: N/A (not applicable).

*SIGN 3: Item 1: The study addresses an appropriate and clearly focused question?; Item 2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation?; Item 3: The study indicates how many of the people asked to take part did so, in each of the groups being studied?; Item 4: The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis?; Item 5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?; Item 6: Comparison is made between full participants and those lost to follow up, by exposure status?; Item 7: The outcomes are clearly defined?; Item 8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable?; Item 9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome?; Item 10: The method of assessment of exposure is reliable?; Item 11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable?; Item 12: Exposure level or prognostic factor is assessed more than once?; Item 13: The main potential confounders are identified and taken into account in the design and analysis?; Item 14: Have confidence intervals been provided?

Risk of bias assessment: × item not fulfilled; ✓ = item fulfilled; ? unclear or unknown if item is fulfilled

GRADE assessments: × = item cause for possible downgrade once; ×× = item cause for possible downgrade twice; ✓= item fulfilled, no downgrading; ?= item unclear or not available, no upgrading or downgrading.

**↓↓↓=downgrade quality by three levels

ROBIS: Tool to assess risk of bias in systematic reviews

Table 11. Suggested Tabular Presentation for ROBIS Results

Review	Phase 2				Phase 3
	1. STUDY ELIGIBILITY CRITERIA	2. IDENTIFICATION AND SELECTION OF STUDIES	3. DATA COLLECTION AND STUDY APPRAISAL	4. SYNTHESIS AND FINDINGS	RISK OF BIAS IN THE REVIEW
Van Dyk 2019 (20)	☺	☹	☺	?	?
Thorborg 2017 (30)	☺	☺	☺	?	?
Esteve 2015 (35)	?	?	☺	?	?
Goode 2015 (28)	?	☺	?	?	?
Pas 2015 (6)	?	☺	☺	?	?
Rieman 2013 (44)	?	?	☺	?	?

☺ = low risk; ☹ = high risk; ? = unclear risk

REFERENCES

1. Wangensteen A, Almusa E, Boukarroum S, Farooq A, Hamilton B, Whiteley R, m.fl. MRI does not add value over and above patient history and clinical examination in predicting time to return to sport after acute hamstring injuries: a prospective cohort of 180 male athletes. Br J Sports Med. december 2015;49(24):1579–87.

2. Zeren B, Oztekin HH. A new self-diagnostic test for biceps femoris muscle strains. Clin J Sport Med. marts 2006;16(2):166–9.

3. Schneider-Kolsky ME, Hoving JL, Warren P, Connell DA. A comparison between clinical assessment and magnetic resonance imaging of acute hamstring injuries. Am J Sports Med. juni 2006;34(6):1008–15.

4. Serner A, Weir A, Tol JL, Thorborg K, Roemer F, Guermazi A, m.fl. Can standardised clinical examination of athletes with acute groin injuries predict the presence and location of MRI findings? Br J Sports Med. december 2016;50(24):1541–7.

5. Mendiguchia J, Martinez-Ruiz E, Edouard P, Morin JB, Martinez-Martinez F, Idoate F, m.fl. A Multifactorial, Criteria-based Progressive Algorithm for Hamstring Injury Treatment. Med Sci Sports Exerc. juli 2017;49(7):1482–92.

6. Pas HI, Reurink G, Tol JL, Weir A, Winters M, Moen MH. Efficacy of rehabilitation (lengthening) exercises, platelet-rich plasma injections, and other conservative interventions in acute hamstring injuries: an updated systematic review and meta-analysis. Br J Sports Med. september 2015;49(18):1197–205.

7. Askling C, Tengvar M, Tarassova O, Thorstensson A. Acute hamstring injuries in Swedish elite sprinters and jumpers: a prospective randomised controlled clinical trial comparing two rehabilitation protocols. Br J Sports Med. april 2014;48(7):532–9.

8. Askling C, Tengvar M, Thorstensson A. Acute hamstring injuries in Swedish elite football: a prospective randomised controlled clinical trial comparing two rehabilitation protocols. Br J Sports Med. oktober 2013;47(15):953–9.

9. Silder A, Sherry MA, Sanfilippo J, Tuite MJ, Hetzel SJ, Heiderscheit BC. Clinical and morphological changes following 2 rehabilitation programs for acute hamstring strain injuries: a randomized clinical trial. J Orthop Sports Phys Ther. maj 2013;43(5):284–99.

10. Sherry MA, Best TM. A comparison of 2 rehabilitation programs in the treatment of acute hamstring strains. J Orthop Sports Phys Ther. marts 2004;34(3):116–25.

11. Malliaropoulos N, Papalexandris S, Papalada A, Papacostas E. The role of stretching in rehabilitation of hamstring injuries: 80 athletes follow-up. Med Sci Sports Exerc. maj 2004;36(5):756–9.

12. Reurink G, Goudswaard GJ, Moen MH, Weir A, Verhaar JAN, Bierma-Zeinstra SMA, m.fl. Platelet-rich plasma injections in acute muscle injury. N Engl J Med. 26. juni 2014;370(26):2546–7.

13. Hamilton B, Tol JL, Almusa E, Boukarroum S, Eirale C, Farooq A, m.fl. Platelet-rich plasma does not enhance return to play in hamstring injuries: a randomised controlled trial. Br J Sports Med. juli 2015;49(14):943–50.

14. MS AH, Mohamed Ali MR, Yusof A, George J, Lee LP. Platelet-rich plasma injections for the treatment of hamstring injuries: a randomized controlled trial. Am J Sports Med. oktober 2014;42(10):2410–8.

15. Hickey JT, Timmins RG, Maniar N, Rio E, Hickey PF, Pitcher CA, m.fl. Pain-Free Versus Pain-Threshold Rehabilitation Following Acute Hamstring Strain Injury: A Randomized Controlled Trial. J Orthop Sports Phys Ther. 28. juni 2019;1–35.

16. Cross TM, Gibbs N, Houang MT, Cameron M. Acute quadriceps muscle strains: magnetic resonance imaging features and prognosis. Am J Sports Med. april 2004;32(3):710–9.

17. Millar AP. Strains of the posterior calf musculature (“tennis leg”). Am J Sports Med. maj 1979;7(3):172–4.

18. Pedret C, Rodas G, Balius R, Capdevila L, Bossy M, Vernooij RWM, m.fl. Return to Play After Soleus Muscle Injuries. Orthop J Sports Med. juli 2015;3(7):2325967115595802.

19. Borrione P, Fossati C, Pereira MT, Giannini S, Davico M, Minganti C, m.fl. The use of platelet-rich plasma (PRP) in the treatment of gastrocnemius strains: a retrospective observational study. Platelets. september 2018;29(6):596–601.

20. Dyk N van, Behan FP, Whiteley R. Including the Nordic hamstring exercise in injury prevention programmes halves the rate of hamstring injuries: a systematic review and meta-analysis of 8459 athletes. Br J Sports Med. 26. februar 2019;bjsports-2018-100045.

21. Gabbe BJ, Branson R, Bennell KL. A pilot randomised controlled trial of eccentric exercise to prevent hamstring injuries in community-level Australian Football. J Sci Med Sport. maj 2006;9(1–2):103–9.

22. Soligard T, Myklebust G, Steffen K, Holme I, Silvers H, Bizzini M, m.fl. Comprehensive warm-up programme to prevent injuries in young female footballers: cluster randomised controlled trial. BMJ. 10. december 2008;337:a2469.

23. Engebretsen AH, Myklebust G, Holme I, Engebretsen L, Bahr R. Prevention of injuries among male soccer players: a prospective, randomized intervention study targeting players with previous injuries or reduced function. Am J Sports Med. juni 2008;36(6):1052–60.

24. Petersen J, Thorborg K, Nielsen MB, Budtz-Jorgensen E, Holmich P. Preventive effect of eccentric training on acute hamstring injuries in men's soccer: a cluster-randomized controlled trial. Am J Sports Med. november 2011;39(11):2296–303.

25. Espinosa G del A, Pöyhönen T, Aramendi JF, Samaniego JC, Knörr JIE, Kyröläinen H. Effects of an eccentric training programme on hamstring strain injuries in women football players. Biomed Hum Kinet [Internet]. 25. september 2015 [henvist 2. maj 2019];7(1). Tilgængelig hos: https://content.sciendo.com/view/journals/bhk/7/1/article-bhk-2015-0019.xml.xml

26. Silvers-Granelli H, Mandelbaum B, Adeniji O, Insler S, Bizzini M, Pohlig R, m.fl. Efficacy of the FIFA 11+ Injury Prevention Program in the Collegiate Male Soccer Player. Am J Sports Med. november 2015;43(11):2628–37.

27. van der Horst N, Smits DW, Petersen J, Goedhart EA, Backx FJ. The preventive effect of the nordic hamstring exercise on hamstring injuries in amateur soccer players: a randomized controlled trial. Am J Sports Med. juni 2015;43(6):1316–23.

28. Goode AP, Reiman MP, Harris L, DeLisa L, Kauffman A, Beltramo D, m.fl. Eccentric training for prevention of hamstring injuries may depend on intervention compliance: a systematic review and meta-analysis. Br J Sports Med. marts 2015;49(6):349–56.

29. Askling C, Karlsson J, Thorstensson A. Hamstring injury occurrence in elite soccer players after preseason strength training with eccentric overload. Scand J Med Sci Sports. august 2003;13(4):244–50.

30. Thorborg K, Krommes KK, Esteve E, Clausen MB, Bartels EM, Rathleff MS. Effect of specific exercise-based football injury prevention programmes on the overall injury rate in football: a systematic review and meta-analysis of the FIFA 11 and 11+ programmes. Br J Sports Med. april 2017;51(7):562–71.

31. van de Hoef PA, Brink MS, Huisstede BMA, van Smeden M, de Vries N, Goedhart EA, m.fl. Does a bounding exercise program prevent hamstring injuries in adult male soccer players? - A cluster-RCT. Scand J Med Sci Sports. april 2019;29(4):515–23.

32. Al Attar WSA, Soomro N, Pappas E, Sinclair PJ, Sanders RH. Adding a post-training FIFA 11+ exercise program to the pre-training FIFA 11+ injury prevention program reduces injury rates among male amateur soccer players: a cluster-randomised trial. J Physiother. oktober 2017;63(4):235–42.

33. Whalan M, Lovell R, Steele JR, Sampson JA. Rescheduling Part 2 of the 11+ reduces injury burden and increases compliance in semi-professional football. Scand J Med Sci Sports. 3. august 2019;

34. Soderman K, Werner S, Pietila T, Engstrom B, Alfredson H. Balance board training: prevention of traumatic injuries of the lower extremities in female soccer players? A prospective randomized intervention study. Knee Surg Sports Traumatol Arthrosc. 2000;8(6):356–63.

35. Esteve E, Rathleff MS, Bagur-Calafat C, Urrutia G, Thorborg K. Prevention of groin injuries in sports: a systematic review with meta-analysis of randomised controlled trials. Br J Sports Med. juni 2015;49(12):785–91.

36. Arnason A, Engebretsen L, Bahr R. No effect of a video-based awareness program on the rate of soccer injuries. Am J Sports Med. januar 2005;33(1):77–84.

37. van Beijsterveldt AM, van de Port IG, Krist MR, Schmikli SL, Stubbe JH, Frederiks JE, m.fl. Effectiveness of an injury prevention programme for adult male amateur soccer players: a cluster-randomised controlled trial. Br J Sports Med. december 2012;46(16):1114–8.

38. Holmich P, Larsen K, Krogsgaard K, Gluud C. Exercise program for prevention of groin pain in football players: a cluster-randomized trial. Scand J Med Sci Sports. december 2010;20(6):814–21.

39. Steffen K, Myklebust G, Olsen OE, Holme I, Bahr R. Preventing injuries in female youth football--a cluster-randomized controlled trial. Scand J Med Sci Sports. oktober 2008;18(5):605–14.

40. Longo UG, Loppini M, Berton A, Marinozzi A, Maffulli N, Denaro V. The FIFA 11+ program is effective in preventing injuries in elite male basketball players: a cluster randomized controlled trial. Am J Sports Med. maj 2012;40(5):996–1005.

41. Slauterbeck JR, Choquette R, Tourville TW, Krug M, Mandelbaum BR, Vacek P, m.fl. Implementation of the FIFA 11+ Injury Prevention Program by High School Athletic Teams Did Not Reduce Lower Extremity Injuries: A Cluster Randomized Controlled Trial. Am J Sports Med. 17. september 2019;0363546519873270.

42. Haroy J, Clarsen B, Wiger EG, Oyen MG, Serner A, Thorborg K, m.fl. The Adductor Strengthening Programme prevents groin problems among male football players: a cluster-randomised controlled trial. Br J Sports Med [Internet]. 10. juni 2018; Tilgængelig hos: https://www.ncbi.nlm.nih.gov/pubmed/29891614

43. Kraemer R, Knobloch K. A soccer-specific balance training program for hamstring muscle and patellar and achilles tendon injuries: an intervention study in premier league female soccer. Am J Sports Med. juli 2009;37(7):1384–93.

44. Reiman MP, Loudon JK, Goode AP. Diagnostic accuracy of clinical tests for assessment of hamstring injury: a systematic review. J Orthop Sports Phys Ther. april 2013;43(4):223–31.