Systematic video analysis of ACL injuries in professional male football (soccer): injury mechanisms, situational patterns and biomechanics study on 134 consecutive cases

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ABSTRACT

Background A few small studies have reported on the mechanisms of ACL injury in professional male football. **Aim** To describe the mechanisms, situational patterns and biomechanics (kinematics) of ACL injuries in professional male football matches.

Methods We identified 148 consecutive ACL injuries across 10 seasons of professional Italian football. 134 (90%) injury videos were analysed for mechanism and situational pattern, while biomechanical analysis was possible in 107 cases. Three independent reviewers evaluated each video. ACL injury epidemiology (month), timing within the match and pitch location at the time of injury were also reported.

Results 59 (44%) injuries were non-contact, 59 (44%) were indirect contact and 16 (12%) were direct contact. Players were frequently perturbed immediately prior to injury. We identified four main situational patterns for players who suffered a non-contact or an indirect contact injury: (1) pressing and tackling (n=55); (2) tackled (n=24); (3) regaining balance after kicking (n=19); and (4) landing from a jump (n=8). Knee valgus loading (n=83, 81%) was the dominant injury pattern across all four of these situational patterns (86%, 86%, 67% and 50%, respectively). 62% of the injuries occurred in the first half of the matches (p < 0.01). Injuries peaked at the beginning of the season (September-October) and were also higher at the end of the season (March–May). Conclusions 88% of ACL injuries occurred without direct knee contact, but indirect contact injuries were as frequent as non-contact injuries, underlying the importance of mechanical perturbation. The most common situational patterns were pressing, being tackled and kicking.

INTRODUCTION

ACL injury is a severe and concerning health issue among professional football players that causes long lay-off time.¹ Despite improved knowledge on ACL injuries and injury prevention, the rate of injuries in professional football is not declining.¹ Each team of 25 players can expect one ACL injury every 2 years.² Even if 95%–100% of professional footballers return to play (RTP),^{1 3} the risk of subsequent knee injury,^{4 5} early onset of knee osteoarthritis⁶ and reduced career length^{7 8} are serious concerns.

Understanding the situations and mechanisms which lead to ACL injuries is crucial to effectively

design specific exercise programmes to reduce their incidence. Several systematic video analysis studies of ACL injuries have been published across different sports.⁹⁻¹⁶ With regard to football, three additional studies have been published in the past 5 years.^{17–19} However, limitations in the study design, such as lack of systematic assessment¹⁹ and the limited number of cases with more than 30% dropout rate,¹⁸ could not provide conclusive evidence on the mechanisms of ACL injury in football.

In addition, there are gaps which need to be systematically addressed. First is the lack of focus on the perturbation type injury, which is found to be important in American football.¹¹ Second is the lack of research detailing the biomechanical factors of ACL injuries in football, particularly concerning the role of the trunk. Finally, there is little research detailing the distribution of ACL injuries across the season, as well as within the match and on the pitch location.

As such, the purpose of this study was to describe on a large cohort of professional football players the mechanisms, situational patterns and biomechanics related to ACL injury. A further purpose was to document the distribution of ACL injuries across the match, season and pitch location.

METHODS

Injury identification and video extraction

A systematic search of online database resources was performed across 10 seasons (from 2008/2009 to 2018/2019, until December 2018) to identify ACL injuries occurring during matches in players of Italian first (Serie A) and second (Serie B) division professional football teams.

To identify ACL injuries, each season and team rosters were extracted from online databases (legaseriea.it; legab.it) and single team websites. Then, each player was searched on Transfermarkt.de (Transfermarkt, Hamburg, Germany) for details on injury history. This methodology has been recently validated for identification of injuries in professional football²⁰ and was also adopted by two very recent studies on RTP after ACL injury⁸ and hip surgery²¹ in professional football.

Second, the same systematic single-player approach was used in additional data sources to look for other possible injuries which may have been missed, including national (eg, www.gazzetta. it; www.corrieredellosport.it) and local media.

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/ bjsports-2019-101247).

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Accepted 4 May 2020 Published Online First 19 June 2020

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To cite: Della Villa F, Buckthorpe M, Grassi A, et al. Br J Sports Med 2020;54:1423–1432.



Finally, injuries were included only when we were able to track an official communication with the medical staff of the team stating the nature of the injury (complete ACL injury) suffered by the player. Through similar methods (public available sources), ACL reconstructions underwent by all players were also tracked.

Videos of matches were obtained from an online digital platform (wyscout.com; Wyscout, Genova, Italy) (n=127). When the video was not available, a second digital platform was searched (paninidigital.com; Panini Digital, Digital Soccer Project, Modena, Italy) (n=7). Videos were then processed on a digital cloud (paninidigitalcloud.com) and downloaded to a personal computer.

Match video processing was done with a cloud available tool (Digital Log, Digital Soccer Project). Each video of ACL injury was cut to approximately 12–15 s prior to and 3–5 s post the estimated injury frame (IF) in order to accurately evaluate the playing situation that preceded the injury and the mechanism of injury.

Video evaluation

The videos were independently evaluated by three different reviewers (FDV, AG, MB) according to two predetermined checklists (online supplementary table 1 and table 2). All reviewers are involved in sports medicine and orthopaedic rehabilitation practice (MD, MD and PhD).

Each video of ACL injury was downloaded on the personal computer and opened with an available software online, Kinovea (KinoveaInk), and analysed through an evaluation flow.

Each reviewer evaluated the original video to define the injurious situation, defensive or offensive, which was then categorised based on ball possession and specific playing situation. Then, a series of views were used to determine the injury mechanism and situational pattern (see table 1 for explanation of the terms). Three categories of injury mechanism were used: (1) non-contact, defined as an injury occurring without any contact (at the knee or any other level) prior to or at IF; (2) indirect contact, defined as an injury resulting from an external force applied to the footballer, but not directly to the injured knee; and (3) direct contact, defined as an external force directly applied to the injured knee.²² Situational patterning was done only in cases of non-contact or indirect contact mechanisms. Based on previous findings we considered the estimation of IF as initial contact (IC) plus 40 ms.¹²23

Subsequently, the reviewers met for a 2-day comprehensive discussion about the main injury mechanism and situational patterns. If no complete agreement was reached between reviewers, problems were solved with a collegiate decision, as in previous research.^{14 18} Consensus agreement on all the items, including IC and IF, was reached during the meeting. Prior to the meeting, the intraclass correlation index for the IC between the reviewers was 0.99.

Biomechanical analysis (kinematics)

Biomechanical/kinematic analysis was performed on non-contact and indirect contact injuries when a frontal and/or sagittal view of sufficient quality was available. The analysis was performed to estimate intersegmental relationship and joint angles according to frontal and sagittal plane alignment at IC and IF. When more than one view was available, composite videos were created by manual synchronisation using visual clues (eg, initial ground contact).¹⁴ Three videos had five camera views, 10 had four, 54 had three, 48 had two and 19 had one.

Sagittal plane angles were estimated using a custom-made software (GPEM Screen Editor, GPEM, Genova, Italy) to the nearest 5° at IC and estimated IF.

Trunk tilt was also estimated to the nearest 5° on the frontal plane at IC and IF, while the remaining frontal and coronal plane estimated joint positions were categorised according to the appearance at IC and IF.

Foot strike was evaluated according to a previous methodology¹⁸ and after foot contact to the ground at IC and IF. The items that have been evaluated are listed in online supplementary table 2.

Seasonal, match and field distribution

For each available injury video, a list of data regarding the seasonal, match and field distribution were gathered through systematic web revision and analysis of videos in relation to the position of the injured player. We considered (1) month of ACL injury, (2) phase of the game when the ACL injury occurred (minute and half), (3) number of minutes played by the ACL-injured athlete and (4) field location according to a customised version of an already published division of the pitch.²² Player localisation at the time of ACL injury was gathered according to the field lines. The football pitch was divided as indicated in online supplementary table 1 and further divided into 11 different zones. The field zone dimensions in square metres were calculated considering the official FIFA football field size (105 by 70 m) (see online supplementary material).

Patient and public involvement

The results of the study will be shared with publicly available resources (eg, newspaper) to inform the audience with regard to treatment for ACL injuries.

Equity, diversity and inclusion

Football is played by millions of women around the world, and the *British Journal of Sports Medicine* encourages research that includes gender-based analysis. The methodology that we used was not applicable to women's football. Alternative approaches should be used to fill this gap and our group is going towards this direction.

Table 1 Terms, defin	itions and their use within this manuscript to describe ACL injuries in football (valid for team sports)
Term	Definition and use
Injury mechanism	This term describes the ACL injury causation, referring to player-to-player interaction that led to the injury. Three categories have been used: (1) non- contact, (2) indirect contact and (3) direct contact.
Situational pattern	This term describes the situation leading to ACL injuries. The patterns can be divided into defensive and offensive situations. This is the situation and not just the action, in that it considers the action interacting with the environment (eg, pressing pattern).
Biomechanics of injury	This term refers to the kinematics or intersegmental body segment relationships at initial contact and suspected injury frame on the frontal and sagittal planes.

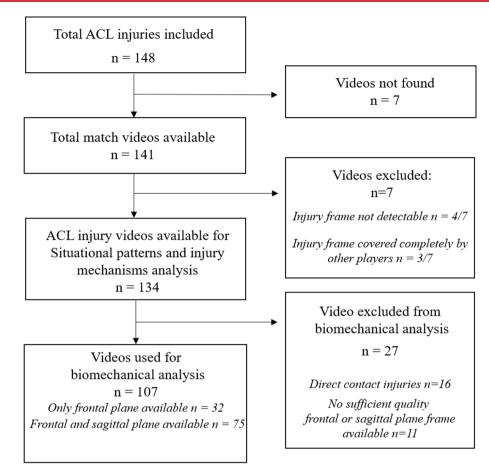


Figure 1 Detailed flow chart of the study.

Ethical considerations

All the videos we accessed are publicly available, data were treated confidentially, no personal player information was accessed and therefore ethical permission was not required.¹⁴

Statistical analysis

Continuous variables are presented as mean (\pm SD) or median (range) as appropriate according to the distribution of variables. Discrete variables were presented as absolute numbers and as percentage of the total number of observations. The proportion test was used to explore possible differences in the distribution of ACL injuries between match halves. An a priori statistically significant level of p<0.05 was used. Microsoft Excel 2016 (Microsoft, USA) and Stata V.12 were used for analyses.

RESULTS

One hundred and forty-eight ACL injuries were tracked and included. Of these, 75 and 55 occurred during the Serie B and A matches, while 10, 6 and 2 injuries occurred during international, Italian cup and friendly competitions, respectively. There were 89 (60%) injuries to the right and 58 (39%) injuries to the left ACL (1 injury was unidentifiable), with 128 primary, 9 contralateral native and 11 previously reconstructed knee (ACL graft injuries) ACL injuries.

Injury mechanism analysis

Video footage was available and identifiable for situational pattern and injury mechanism analysis in 134 cases (90%). Detailed study flow is presented in figure 1. Most injuries (121 cases; 90%) involved loading of the injured leg, with single limb

loading on the ground frequently observed (94 cases; 70%). We categorised 59 (44%) non-contact, 59 (44%) indirect contact and 16 (12%) direct contact injuries (see table 2 for injury mechanism analysis).

Direct contact injuries

Direct contact injuries (n=16) occurred in both defensive (n=9) and offensive (n=7) playing situations, with five injuries being classified as tackling, eight tackled and three goalkeeping injuries.

Biomechanically most of the direct contact ACL injuries resulted from an external force with a knee valgus loading (n=13), combined with a posterolateral force application in one case, while the remaining three cases were hyperextension injuries, as a direct consequence of an anteriorly applied force.

Situational pattern of indirect and non-contact injuries

Four main situational patterns were identified for non-contact or indirect contact ACL injuries:

- Pressing/tackling (n=55).
- ► Tackled (n=24).
- ▶ Regaining balance after kicking (n=19).
- ► Landing from a jump (n=8).

Finally, the other 12 cases did not fall into one of the aforementioned categories. Additional details are reported in table 3.

Pressing and tackling injuries (47%) were all classified as defensive, where the player typically approached the opponent with the intention to tackle. In pressing, the player was injured during non-contact deceleration or cutting. In tackling injuries, there was typically opponent contact prior to or at estimated IF (figure 2).

Variables	Results
Weather conditions	
Precipitations	Yes (n=6)
	No (n=128)
Sunny weather	Yes (n=51)
	No (n=34)
	Night (n=49)
Playing phase before injury	Defensive (n=91)
5 51	Offensive (n=43)
Field location at injury	
Long axis of the field	Defensive third (n=50)
5	Mid-field third (n=45)
	Offensive third (n=39)
Short axis of the field	Left side corridor (n=33)
	Middle corridor (n=67)
	Right side corridor (n=34)
Player contact preceding injury	Yes (n=56)
	No (n=78)
If contact, where?	Upper body (n=41)
,,	Pelvis (n=6)
	Injured leg (n=2)
	Uninjured leg (n=7)
Player contact at IF	Direct contact (n=16)
	Indirect contact (n=31)
	Non-contact (n=87)
If indirect contact at IF, where?	Upper body (n=20)
	Pelvis (n=6)
	Injured leg (ankle) (n=1)
	Uninjured leg (n=4)
Injury classification	Direct contact (n=16)
	Indirect contact (n=59)
	Non-contact (n=59)
How many feet on the ground	One (n=94)
, <u>.</u>	Two (n=29)
	Unsure (n=10)
Leg loading at IF	Injured leg (n=121)
	Uninjured leg (n=2)
	Unsure (n=10)
Horizontal speed	Zero (n=6)
	Low (n=49)
	High (n=78)
Vertical speed	Zero (n=75)
	Low (n=49)

IF, injury frame.

Being 'tackled', the second most common situation (20%), involved a duel-type interaction between the opponent and the injured player (figure 3) either in (n=13, 54%) or out (n=11, 46%) of ball possession. There was typically a mechanical perturbation involving the upper (n=14) or lower (n=10) part of the body, without direct knee contact.

Regaining balance after kicking (16%) also involved player-toplayer contact (n=11, 58%), mostly to the upper body.

Landing from a jump (7%) was less prevalent, with six cases from heading and two in goalkeepers when landing after catching the ball. Five of these occurred during single leg landing and three during double leg landing.

 Table 3
 Indirect contact and non-contact injuries' situational pattern classification

Categories	ACL injuries
Pressing/tackling	Total, n=55 (47%)
	Pressing, n=40
	Tackling, n=15
Tackled	Total, n=24 (20%)
	Lower body, n=9
	Upper body, n=15
Regaining balance after kicking	Total, n=19 (16%)
Landing from a jump	Total, n=8 (7%)
	Heading, n=6
	Goalkeepers, n=2
Others	Total, n=12 (10%)
	Dribbling, n=2
	Cutting without the ball, n=2
	Jumping take-off, n=2
	Receiving the ball, n=2
	Controlling the ball with chest, n=1
	Regaining balance after reaching, n=1
	Kicking the ground, n=1
	Goalkeeping (side stepping), n=1

Biomechanical analysis

Biomechanical analysis was possible in 107 cases, with 75 cases having both frontal and sagittal plane images and 32 with frontal plane only. More variability in intersegmental body positioning was observed at IC, rather than at IF. All angle data are reported as median values. On the sagittal plane at IC, players displayed an upright trunk (0°), early flexed hip (35°), shallow knee flexion (17.5°) and early plantar flexed ankle with heel strike in nearly half (48%) of the cases. On the frontal plane at IC, the trunk was slightly tilted ipsilaterally (5°) either in a neutral position (34%) or rotated towards the uninjured limb (53%), an abducted hip (88%), neutral (63%) or valgus (27%) knee appearance, and an externally rotated foot (59%).

From a sagittal plane perspective at estimated IF, the trunk remained upright (0°), with similar hip flexion (37.5°), greater knee flexion (40°) and neutral ankle (0°), with planted flat foot (89%). On the frontal plane, the trunk remained tilted ipsilaterally (5°), with greater prevalence of trunk rotation towards the uninjured side (83%). The hip remained abducted in most cases (72%), with greater prevalence of knee valgus (81%) and externally rotated foot (66%). The most frequent intersegmental positioning at IF is reported in figure 4.

Knee valgus loading was frequently observed (81%), and a significant increase in hip internal rotation and/or adduction from IC to IF was seen in most (69%), while valgus collapse was uncommon (13%). Additional details are reported in tables 4 and 5.

Seasonal, match and field distribution

Seasonal distribution (n=148) demonstrated bimodal distribution, with more injuries early in the season (September–October) and a secondary peak later in the season (March–May) (figure 5).

More injuries occurred during the first (n=88, 62%) than the second (n=53, 38%) half (p<0.01). A quarter of all injuries (n=34) happened in the first 15 min of the match (figure 6A). When considering the minutes played, correcting for substitutions, 68% of ACL injuries happened in the first 45 min (figure 6B).



Figure 2 Pressing and tackling injuries. Pressing: approaching the opponent (A), initial contact (B), injury frame (C) and loss of balance (D). Tackling: approaching the opponent (E), initial contact and tackling (F), injury frame (G) and loss of balance (H).

Injuries according to pitch location (n=133) are detailed in online supplementary material.

mechanism; and (3) the distribution during the match and the season suggests a higher risk in the first part of both.

DISCUSSION

The most important findings of the present study are that (1) most ACL injuries in professional male football occur without direct contact mechanism at IF, but a large proportion occur by some form of indirect contact; (2) four main situational patterns were identified, with an under-representation of the heading

Injury mechanisms

Of the injuries, 88% occurred without direct knee contact, similar to another study (85%).¹⁸ However, 44% of ACL injuries were due to indirect contact (predominantly at the upper body or pelvis level), meaning that 56% of injuries actually involved some form of contact, leaving only 44% non-contact injuries.



Figure 3 Being tackled situational patterns. Example of injury categorised as 'being tackled' with contact on lower body part (uninjured limb): mechanical perturbation (A), initial contact (B), injury frame (C) and loss of balance (D). Being tackled on the upper part of the body: mechanical perturbation (E), initial contact (F), estimated ACL injury frame (G) and loss of balance (H).

Original research

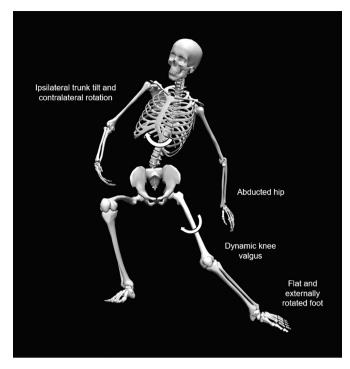


Figure 4 Frequently observed mechanism for non-contact ACL injuries during pressing situation.

Although different from Waldén *et al* (66% non-contact),¹⁸ this is identical to others (56% direct and indirect injuries).^{17 19} Given our study has adopted the largest prospectively identified

video analysis sample to date (N=134 injuries), these findings are important and likely reflect the generalised ACL injury mechanisms in professional footballers.

Situational pattern of non-contact and indirect injuries

Similar to others, two-thirds of ACL injuries involved defending,^{17 18} while pressing or attempting to tackle.

We identified four key situational patterns, three previously described¹⁸ (although with different prevalence): (1) pressing/ tackling; (2) regaining balance after kicking; (3) landing from a jump; and (4) a new situational pattern, 'tackled', accounting for 20% of all non-contact or indirect contact injuries. Contact mostly occurred prior to the injury, predominantly to the upper body. This mechanical perturbation, often coupled with a distraction immediately prior to injury, played an important role in the causation of these injuries in our cohort, and has been shown to be important in other sports, such as basketball¹³ and rugby,¹⁴ and more recently American football in which 'perturbation like scenarios' account for half of ACL injuries.¹¹ Landing from heading was under-represented in our cohort versus another (7% vs 25%),¹⁸ which may reflect differences in playing style²⁴ and/or anthropometrics.

Biomechanics

Our data support the existing literature showing ACL injuries occur generally in early knee flexion, with dynamic knee valgus loading.^{10 12 13 15 18 23} We reported a high knee loading movement pattern (knee dominant), with limited loading/motion at joints other than the knee, similar to other research.^{18 23} From IC to IF, no change in sagittal plane angles at other joints than the

Variables	Total	Pressing	Tackled	Kicking	Landing	Other
Trunk flexion IC	0 (–35, 70)	-5 (-35, 40)	5 (-20, 70)	-5 (-20, 30)	-2.5 (-15, 5)	0 (0, 20)
(+ flexion, – extension)						
Trunk flexion IF	0 (-40, 90)	-5 (-35, 50)	5 (–40, 90)	0 (–10, 50)	0 (–25, 10)	5 (0, 40)
(+ flexion, – extension)						
Hip flexion IC	35 (0, 90)	40 (5, 60)	37.5 (25, 90)	30 (0, 60)	17.5 (10, 30)	45 (10, 60)
(+ flexion, – extension)						
Hip flexion IF	37.5 (0, 90)	42.5 (5, 80)	30 (10, 90)	30 (0, 90)	17.5 (5, 45)	45 (10, 60)
(+ flexion, – extension)						
Knee flexion IC	17.5 (–5, 90)	15 (5, 90)	20 (0, 60)	20 (-5, 40)	12.5 (10, 15)	15 (10, 35)
+ flexion, – extension)						
Knee flexion IF	40 (–50, 120)	40 (–35, 120)	60 (–50, 80)	35 (–35, 60)	30 (10, 55)	45 (10, 55)
+ flexion, – extension)						
Ankle flexion IC	-10 (-55, 45)	–15 (–30, 15)	-5 (-30, 45)	–15 (–55, 15)	-5 (-45, 0)	-10 (-25, 0)
+ dorsiflexion, – plantar flexion)						
Ankle flexion IF	0 (-40, 45)	-10 (-40, 20)	15 (–30, 45)	0 (–40, 25)	10 (10, 20)	10 (0, 15)
+ dorsiflexion, – plantar flexion)						
oot strike at IC						
Heel	51 (48%)	29 (57%)	15 (68%)	5 (31%)	0 (0%)	2 (22%)
Flat	30 (28%)	15 (30%)	3 (14%)	7 (44%)	2 (25%)	3 (33%)
Тое	15 (14%)	3 (6%)	2 (9%)	4 (25%)	5 (62.5%)	1 (11%)
Unsure	10 (9%)	4 (8%)	2 (9%)	0 (0%)	1 (12.5%)	3 (33%)
Foot strike at IF						
Heel	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Flat	94 (89%)	45 (88%)	20 (91%)	16 (100%)	6 (75%)	7 (78%)
Тое	2 (2%)	2 (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unsure	10 (9%)	4 (8%)	2 (9%)	0 (0%)	2 (25%)	2 (22%)

 Table 5
 Frontal and transverse plane metrics of non-contact or indirect contact ACL injuries, stratified according to main situational patterns (data on 107 cases)

Variables	Total	Pressing	Tackled	Kicking	Landing	Other
Trunk tilt IC	5 (–35, 35)	10 (–5, 30)	10 (-10, 20)	0 (–35, 30)	7.5 (–5, 35)	-2.5 (-15, 20)
(+ ipsilateral, – contralateral)						
Trunk tilt IF	5 (–20, 50)	17.5 (–5, 90)	10 (–15, 35)	0 (–20, 50)	0 (–15, 40)	-2.5 (-15, 10)
(+ ipsilateral, – contralateral)						
Trunk rotation IC						
Towards injured	6 (6%)	4 (8%)	1 (4%)	1 (7%)	0 (0%)	0 (0%)
Neutral	35 (34%)	14 (28%)	7 (32%)	6 (40%)	2 (25%)	6 (75%)
Towards uninjured	55 (53%)	28 (56%)	11 (50%)	8 (53%)	6 (75%)	2 (25%)
Unsure	7 (7%)	4 (8%)	3 (14%)	0 (0%)	0 (0%)	0 (0%)
Trunk rotation IF						
Towards injured	5 (5%)	4 (8%)	1 (4,3)	0 (0%)	0 (0%)	0 (0%)
Neutral	8 (8%)	2 (4%)	1 (4,3%)	3 (20%)	1 (12.5%)	1 (12.5%)
Towards uninjured	86 (83%)	40 (80%)	20 (87%)	12 (80%)	7 (87.5%)	7 (87.5%)
Unsure	5 (5%)	4 (8%)	1 (4,3%)	0 (0%)	0 (0%)	0 (0%)
Frontal plane hip alignment IC						
Abduction	91 (88%)	46 (92%)	18 (82%)	13 (87%)	7 (87.5%)	7 (87.5%)
Neutral	7 (7%)	2 (4%)	2 (9%)	1 (7%)	1 (12.5%)	1 (12.5%)
Adduction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unsure	5 (5%)	2 (4%)	2 (9%)	1 (7%)	0 (0%)	0 (0%)
Frontal plane hip alignment IF		. ,	, <i>,</i>	. ,	, ,	. ,
Abduction	74 (72%)	39 (78%)	15 (68%)	11 (73%)	6 (75%)	3 (37.5%)
Neutral	15 (15%)	5 (10%)	2 (9%)	3 (20%)	2 (25%)	3 (37.5%)
Adduction	8 (8%)	3 (6%)	3 (14%)	0 (0%)	0 (0%)	2 (25%)
Unsure	6 (6%)	3 (6%)	2 (9%)	1 (7%)	0 (0%)	0 (0%)
Frontal plane knee alignment IC						
Valgus	28 (27%)	13 (26%)	8 (35%)	3 (20%)	2 (25%)	2 (25%)
Neutral	66 (63%)	32 (64%)	12 (52%)	10 (67%)	6 (75%)	6 (75%)
Varus	2 (2%)	0 (0%)	1 (4%)	1 (7%)	0 (0%)	0 (0%)
Unsure	8 (8%)	5 (10%)	2 (9%)	1 (7%)	0 (0%)	0 (0%)
Frontal plane knee alignment IF		. ,	, <i>,</i>	. ,	, ,	. ,
Valgus	83 (81%)	43 (86%)	19 (86.4%)	10 (67%)	4 (50%)	7 (87.5%)
Neutral	9 (9%)	3 (6%)	1 (4.5%)	2 (13%)	3 (37.5%)	0 (0%)
Varus	4 (4%)	1 (2%)	1 (4.5%)	1 (7%)	1 (12.5%)	0 (0%)
Unsure	7 (7%)	3 (6%)	1 (4.5%)	2 (13%)	0 (0%)	1 (12.5%)
Foot position IC		. ,	. ,	. ,	. ,	. ,
External	61 (59%)	30 (60%)	13 (59%)	11 (73%)	2 (25%)	5 (62.5%)
Neutral	18 (17%)	11 (22%)	2 (9%)	1 (7%)	4 (50%)	0 (0%)
Internal	5 (5%)	1 (2%)	2 (9%)	1 (7%)	0 (0%)	1 (12.5%)
Unsure	19 (18%)	8 (16%)	5 (23%)	2 (13%)	2 (25%)	2 (25%)
Foot position IF						
External	68 (66%)	34 (68%)	15 (68%)	11 (73%)	4 (50%)	4 (50%)
Neutral	10 (10%)	7 (14%)	0 (0%)	1 (7%)	2 (25%)	0 (0%)
Internal	6 (6%)	2 (4%)	2 (9%)	1 (7%)	1 (0%)	1 (12.5%)
Unsure	19 (18%)	7 (14%)	5 (23%)	2 (13%)	2 (25%)	3 (37.5%)
Significant hip IR/ADD from IC to I	,					
Yes	71 (69%)	36 (72%)	16 (73%)	10 (67%)	3 (37.5%)	6 (75%)
No	20 (19%)	6 (12%)	4 (18%)	3 (20%)	5 (62.5%)	2 (25%)
Unsure	12 (12%)	8 (16%)	2 (9%)	2 (13%)	0 (0%)	0 (0%)
Valgus collapse?	x • · /	(/	<u> </u>	(·-··)		
Yes	13 (13%)	7 (14%)	4 (18%)	1 (7%)	0 (0%)	1 (12.5%)
No	86 (83%)	41 (82%)	18 (82%)	13 (87%)	7 (87.5%)	7 (87.5%)
	- (/-/		(, . , . ,		(2.1.2.70)	(37.13 /0)

Four injuries had incomplete biomechanical data on the frontal plane.

ADD, adduction; IC, initial contact; IF, injury frame; IR, internal rotation.

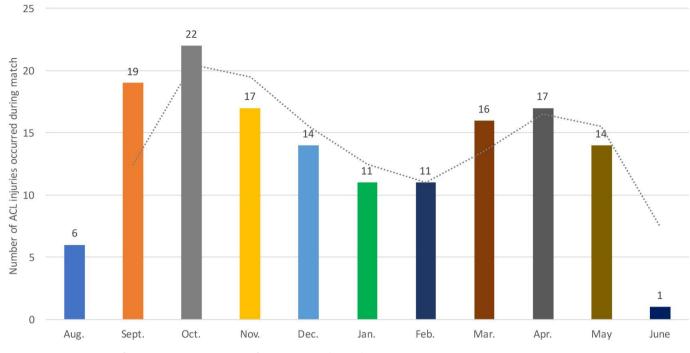


Figure 5 Distribution of ACL injuries throughout the football season (n=148). Bimodal distribution is noted. The dotted line is the moving average of ACL injuries per month.

knee occurred, with an average 22.5° increase in knee flexion. This is similar to Waldén *et al*,¹⁸ although we reported higher knee flexion angles at IF (40° vs 30°), and in almost perfect agreement with Koga et al, who found near identical increases in knee flexion from IC to estimated IF frame 40 ms later (+24°), using the model-based image-matching technique.¹² ACL injuries typically occur with around three to four times body mass (2000–3000 N) vertically directed ground reaction force.¹² In this sagittal plane scenario, these forces would likely be preferentially focused on the knee, predisposing it to injury.

This preferential knee loading strategy was accompanied by altered frontal and transverse plane motions, thought to be essential in ACL injury.²⁵ Knee valgus and valgus-type loading from IC to IF were found, similar to what previous authors have found.¹⁸²³ Similarly, hip abduction motion was common,¹⁸²³ with a significant increase in hip internal rotation and/or adduction (medial thigh motion) from IC to IF in most (69%) cases. This common increase in frontal plane motion is likely due to the high external knee abduction moment, determined by hip abduction^{26 27} on a laterally orientated and planted foot posi-tion outside the base of support.^{26 28} Although we observed an average ipsilateral trunk tilt in the frontal plane for all ACL injuries (5° at IC and IF), this appears more important for pressingtype ACL injuries, where we found a 10° ipsilateral trunk lean at IC, increasing to 17.5° at IF. A lateral trunk lean may increase ACL loading as a result of a lateral shift in centre mass, achieving a resultant vector line lateral to the knee joint and causing a knee abduction moment.27

Seasonal, match and field distribution

The higher proportion of ACL injuries occurring during the first part of the season (September–October) and the secondary peak (March–May) compared with the winter months (January–February) is similar to other research.¹⁹ This is likely indicative of sunny/hot weather and hard/dry fields, which are thought to increase risk of injury.^{29 30} Similar to previous findings

(95%–97%),¹⁸ ¹⁹ most injuries occurred without rain (96%). Rain is more apparent in late autumn and winter months in Italy. This seasonal injury pattern could also relate to a lack of preparedness at the start of season and cumulative fatigue at the end of the season. Additionally, higher exposure during these months cannot be excluded.

The higher prevalence of ACL injuries in the first half suggests accumulating fatigue throughout the match is not a key risk factor for injury.^{31 32} It is likely that factors other than fatigue may be more relevant to ACL injuries, which are more specific to the first half. These may include differences in playing actions, particularly intense engagements in the opening period of the match.³³ The fact that a quarter of ACL injuries happen in the first 15 min of match may also suggest an inadequate neuromuscular readiness of fresh, unfatigued players.

The field distribution of ACL injuries is consistent with the higher proportion of defensive injuries¹⁷ and shows a higher proportion of injuries on the wings, similar to another study.¹⁹ This is likely due to a higher proportion of duels and deceleration-type tasks occurring in these areas.

Methodological considerations

The main strengths of our study are (1) its sample size, which is the largest to date in a systematic video analysis study of ACL injuries; (2) the consecutive nature of the 134 injuries analysed; (3) the consistent biomechanical analysis of three independent viewers using measurement tools; and (4) the presentation of field, match and seasonal distribution data, which have never been presented before in a consecutive series. The weaknesses of the study lie in the methodology used to identify ACL injuries, different from the gold standard of prospective studies with frequent contact with the teams, and the use of video analysis with assessment of kinematics using videos and tools, as opposed to the gold standard model-based image-matching technique.³⁴ However, the video analysis method is valid³⁴ and consistently adopted in

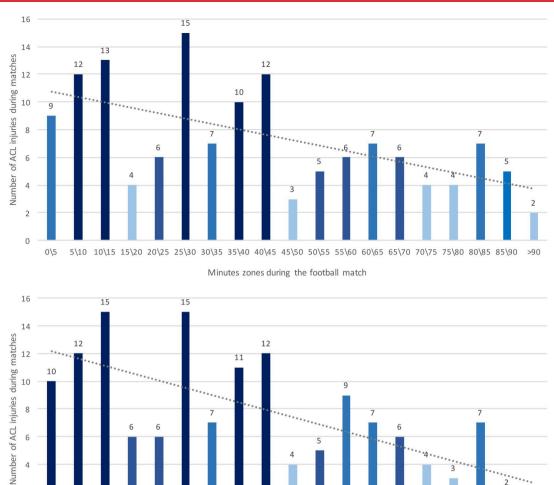


Figure 6 Distribution of ACL injuries throughout the match. A decrease in the number of ACL injuries is noted across the game. Dotted lines represents the linear tendencies of distribution of ACL injury during the match (A) and according to effective playing time (B).

Minutes of effective gameplay

35\40 40\45

What are the findings?

8

6

4

2

0 0\5

- Indirect contact injuries are equally as prevalent as noncontact injuries in professional Italian male football.
- Four main situational patterns were present: (1) pressing/ tackling, (2) tackled, (3) regaining balance after kicking and (4) landing from a jump.

5\10 10\15 15\20 20\25 25\30 30\35

- ACL injuries from landing after heading are underrepresented in Italian professional male footballers.
- ACL injuries are more prevalent at the start of the match (first half) than at the end of the match (second half).

How might it impact on clinical practice in the future?

- ▶ There is a need for a greater focus on indirect contact ACL injuries and the role of perturbation in prevention and rehabilitation after ACL injury.
- Fatigue over the course of match play appears not to be a major risk factor for ACL injuries in professional male football.

many previously studies.^{9-11 13-19} An additional limitation of our study was the exclusion of training injuries, which could potentially interfere with the overall presentation of ACL injuries in professional football.

75\80 80/85 85/90

0

>90

CONCLUSIONS

45\50 50\55 55\60 60\65 65\70 70\75

Most ACL injuries occur without direct knee contact in professional football, but nearly half occur via indirect contact mechanisms. While the defensive 'pressing/tackling' type was the most common situational pattern observed, we also described the offensive or duel 'tackled' situation. This information may be useful for a better comprehension of potential situations that may be considered in primary reduction and secondary reduction (rehabilitation) setting.

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Acknowledgements The authors thank Dr Ing Stefano Di Paolo for helping with figure 4. The authors also thank Dr Federico Ferri and Sky Sport Italia for the kind collaboration in providing the access and permission to use of figure 2 and figure 3 frames.

Contributors FDV. MB and AG contributed to the ideation of the study. AN and FT supported the data collection. FDV, MB and AG undertook the video analysis. FDV,

Original research

MB, AG, AN, FT, SZ and SDV provided intellectual contribution to the writing and drafting of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All the videos we accessed are publicly available, data were treated confidentially, and no personal player information was accessed, and therefore ethical permission was not required. Injured players' privacy was respected and no personal information has been published.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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Primary surgery versus primary rehabilitation for treating anterior cruciate ligament injuries: a living systematic review and meta-analysis

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ABSTRACT

Objective Compare the effectiveness of primarily surgical versus primarily rehabilitative management for anterior cruciate ligament (ACL) rupture.

Design Living systematic review and meta-analysis. **Data sources** Six databases, six trial registries and prior systematic reviews. Forward and backward citation tracking was employed.

Eligibility criteria Randomised controlled trials that compared primary reconstructive surgery and primary rehabilitative treatment with or without optional reconstructive surgery.

Data synthesis Bayesian random effects meta-analysis with empirical priors for the OR and standardised mean difference and 95% credible intervals (Crl), Cochrane RoB2, and the Grading of Recommendations Assessment, Development and Evaluation approach to judge the certainty of evidence.

Results Of 9514 records, 9 reports of three studies (320 participants in total) were included. No clinically important differences were observed at any follow-up for self-reported knee function (low to very low certainty of evidence). For radiological knee osteoarthritis, we found no effect at very low certainty of evidence in the long term (OR (95% Crl): 1.45 (0.30 to 5.17), two studies). Meniscal damage showed no effect at low certainty of evidence (OR: 0.85 (95% CI 0.45 to 1.62); one study) in the long term. No differences were observed between treatments for any other secondary outcome. Three ongoing randomised controlled trials were identified. **Conclusions** There is low to very low certainty of evidence that primary rehabilitation with optional surgical reconstruction results in similar outcome measures as early surgical reconstruction for ACL rupture. The findings challenge a historical paradigm that anatomic instability should be addressed with primary surgical stabilisation to provide optimal outcomes. PROSPERO registration number CRD42021256537.

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi. org/10.1136/bjsports-2021-105359).

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Accepted 4 August 2022 Published Online First 29 August 2022

Check for updates

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To cite: Sauere	essig T,
Braun T, Steglic	
et al. Br J Sport	s Med
2022;56:1241	-1251.

INTRODUCTION

Anterior cruciate ligament (ACL) injury is one of the most common and serious knee injuries, with an annual incidence of 0.03% in the general population and 0.15–3.67% in professional athletes.^{1–3} ACL injuries are associated with marked individual^{4–12} and socioeconomic burden^{13–16}; optimising recovery is pertinent. The patient and/or clinician stand point determines the outcome of interest.¹⁷ This may be prevention of joint osteoarthritis and

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ There is uncertainty whether early surgical reconstruction or rehabilitation with optional surgical reconstruction of ACL rupture yields better functional and clinical outcomes.
- ⇒ Observational studies do not offer clear information whether early surgical reconstruction or primary rehabilitation with optional surgical reconstruction leads to better outcomes.

WHAT THIS STUDY ADDS

- ⇒ Through systematic review and meta-analysis, we found primary rehabilitation with optional surgical reconstruction results in similar patientreported outcomes for ACL rupture as early surgical reconstruction.
- ⇒ Primary rehabilitation with optional surgical reconstruction showed a positive trend for better radiological knee osteoarthritis outcomes, albeit with very low certainty of evidence. Early surgical reconstruction showed a positive trend for better meniscal outcomes, but with a low certainty of evidence.
- ⇒ This 'living' systematic review will update on a yearly basis as the evidence develops.

HOW MIGHT THIS STUDY AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Current treatment recommendations and guidelines regarding ACL patients without serious concomitant injuries should be revised to a 'stepped care approach' with a primarily rehabilitation focused treatment approach as first line treatment.
- ⇒ Randomised controlled trials with longer follow-ups are necessary to reach firm conclusions about the development of adverse outcomes, such as posttraumatic joint damage. Recent advancements in ACL surgical techniques need to be tested in high-quality randomised controlled trials.

secondary meniscal damage, return to sport rate and time to return, athletic performance, improvement of quality of life and cost-effectiveness as all have their relevance and this spectrum needs to be considered in clinical practice and research.



There has been debate on whether management should be primarily surgical (ie, surgical reconstruction soon after injury) versus primarily rehabilitative (with the option of later reconstruction in the case of persistent instability).^{17–20} To date, this debate has not been informed by high-quality systematic review. Accordingly, the quality of evidence in the underlying randomised controlled trials (RCTs) available to previous reviews of the topic^{21–25} could not document a superiority of one approach versus another. Furthermore, new RCT data will come to light over time to add to the evidence base for specific outcomes and subgroups. Living systematic reviews²⁶ are a relevant methodological approach for when one can expect the evidence based for a spectrum of outcomes to mature over time.

The aim of this living systematic review is to examine the comparative effectiveness of primarily surgical versus primarily rehabilitative treatment strategy after ACL rupture. To comprehensively capture the multidimensional facets of this question, we consider patient-reported outcome measures and other outcome measures in different individual, social and economic dimensions.

METHODS

This review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines^{27 28} and was prospectively registered in PROSPERO. Data and statistical code are found in an online repository (https://doi.org/10.17605/OSF.IO/Q69UV).

Patient involvement

There was no patient or public involvement in creating this systematic review.

Administration, dissemination and updating the living systematic review

This review is hosted on the website of the Hochschule für Gesundheit (University of Applied Sciences), Bochum, Germany. We plan to update this living systematic review every year for a minimum of 6 years. We will screen the literature every year to identify new data that may alter our conclusions and recommendations. When new data become available, we will update the analysis and present the updated findings at the website of the Hochschule für Gesundheit (University of Applied Sciences), Bochum, Germany (https://bit.ly/3ogGYIe).

Search strategy

An electronic database search of MEDLINE, EMBASE, CINAHL, Web of Science Core Collection, CENTRAL, SPORTDiscus was conducted (online supplemental appendix 1). Searches were performed from their inception to June 2022. The search terms were identified after preliminary searches of the literature and by comparing them against a previous systematic review.²¹ No language or any other restrictions were applied to the database searches.

Unpublished and ongoing studies were searched via the US National Institutes of Health (https://clinicaltrials.gov/), EU Clinical Trial Register (https://www.clinicaltrialsregister.eu/), DRKS—German Clinical Trials Register (https://www.drks.de), ISRCTN registry (https://www.isrctn.com/), Australian New Zealand Clinical Trials Registry (https://www.anzctr.org.au) and the Netherlands Trial Register (https://www.trialregister.nl/).

A search for prior systematic reviews published was completed via the Cochrane Database of Systematic Reviews (search terms: 'anterior cruciate ligament'; limits: none) and GoogleScholar (search terms: 'anterior cruciate ligament' 'systematic review; limits: first 10 pages). Forward and backward citation tracking of included articles was performed (TS and TB). Two independent reviewers (NS and TB) evaluated all trials against prespecified inclusion/exclusion criteria based on title/abstract and subsequently full text. Disagreements were settled through discussion among the reviewers (NS and TB). A third reviewer (TS) adjudicated any disagreement.

Inclusion and exclusion criteria

Inclusion criteria followed the Participants, Interventions, Comparators, Outcomes, Study design framework.²⁷ Participants were those with ACL rupture of any age. We excluded studies that included patients with inflammatory arthropathy or end-stage osteoarthritis (grade 4 Kellgren and Lawrence)²⁹ as well as studies that focused on the management of ACL injuries with unstable longitudinal meniscus tears. Interventions were reconstructive surgery of the ACL with any method of reconstruction or type of reconstruction technique. Comparators were any type of rehabilitation (eg, physiotherapy, exercise training, bracing, education) with or without optional delayed reconstruction of the ACL. Primary outcome measures were selfreported knee function, radiological osteoarthritis and meniscal injuries at all follow-ups. Secondary outcomes were adverse events, health-related quality of life, return to activity or level of sports participation, functional assessments, knee stability and objective measures of muscle strength. Study designs were required to be parallel randomised (individual, cross-over or cluster design) controlled trials (RCTs). Quasi-RCTs and non-RCTs were excluded given they do not offer an unbiased estimate of the effect size.³⁰

Data extraction

Study information was extracted independently by two authors (NS and TS), with disagreement settled via discussion. If disagreement could not be settled, a third adjudicator (JZ) decided. Reviewers were not blinded to information regarding the authors, journal or outcomes for each article reviewed. The following information was extracted: author, year, journal, funding, conflict of interest, study type, sample size, age, sex, type of intervention, body mass index, sports participation while injured, setting, description of intervention and comparator, follow-up time points and outcome measure scores. We used the following categories to characterise the different follow-up time points: short-term (≤ 1 year), medium-term (>1-3 years) and long-term (>3 years). If multiple follow-ups existed within each timeframe, we extracted the follow-up closest to 1 year for short term, 3 years for intermediate term and 10 years for long term. When two time points were equally close to these follow-ups, we extracted the one that was furthest from baseline. Data for the main results were extracted either as mean and SD (post-treatment) or the number of events (n) and non-events (N) where applicable. If a study report did not report relevant data for extraction, the corresponding author was contacted on two occasions over a 2-week period.

Risk of bias assessment and GRADE

Risk of bias (RoB) was assessed via the Cochrane Risk of Bias Tool V.2.0.³¹ An overall RoB judgement was made for one subjective outcome (patient-reported knee score) and one objective outcome (meniscal surgery or radiological confirmed knee osteoarthritis). Assessment of RoB was based on results of the last follow-up time point of the individual study. Two

Review

independent assessors (MH and TS) performed the assessment. Disagreements were resolved through discussion or by a third reviewer (JZ).

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess the certainty of evidence (online supplemental appendix 4).^{32 33} Indirectness was judged by the approach by Schüneman.⁵ RoB was graded the following way: down grade 1 level: 50% high RoB and down grade 2 levels if 75% high RoB. We used the criteria from Confidence in Network Meta-Analysis (CINeMA)⁴ to evaluate imprecision, inconsistency and publication bias. We chose these criteria because the use of CIs, prediction intervals (PI) and a 'region of equivalence' provide a more clinically informative and robust approach to heterogeneity.^{32 33} Notably, CINeMA is not restricted to network meta-analysis and overcomes a number of the limitations of other approaches, such as, for example, the assessment of inconsistency: many authors rely solely on an I² value to assess heterogeneity, yet this is incorrect .³⁴ The assessment of publication bias based solely on statistical techniques or assessment of funnel plots is another fallacy that is still often done.^{32 35} For the imprecision and inconsistency, we downgraded by one level if there were some concerns and two levels if there were major concerns. Indirectness was downgraded by one level if deemed serious and two levels if deemed very serious. We downgraded one level if publication bias was suspected. As-treated-comparisons started with a rating of 'low' as we deemed this data as observational and not as randomised.³² The evaluation of all ratings started at a high level of certainty given guidelines for meta-analyses, including RCTs only. Two authors (TS and MH) performed the GRADE assessment.

Statistical analysis

For data analysis, we created two categories of comparators: (early) reconstructive surgery of the ACL with postoperative rehabilitation ('early surgery') and rehabilitation with or without elective reconstructive surgery of the ACL ('primary rehabilitation'). We also analysed the 'as treated' (ie, per protocol) data in three groups: 'early surgery', 'delayed surgery' and 'non-operative'. If more than one outcome measure was reported for each type of outcome in the same study, only one was considered for further analysis. We prioritised scales if they measured the primary outcome in the trial to maximise statistical power. Data transformations are described in online supplemental appendix 5.

Effect size measures were standardised mean difference (SMD)³² or mean difference for continuous outcomes and OR with corresponding 95% shortest credible intervals (CrI) for meta analyses or 95% frequentist CIs for dichotomous outcomes.³⁶ SMD effect size was interpreted as: small (0.2), medium (0.5) or large (0.8).³⁷ We used the International Knee Documentation Committee questionnaire (IKDC) for patient-reported knee scores as a measure of the minimally clinically important difference (MCID). We used the following values for the follow-up time points³⁸: short- (MCID: 16.7 points), medium term (MCID: 17.0 points), long term (MCID: 17.0 points). Backtransformation of SMDs was performed to a common scale.³² We also backtransformed the OR by using the median comparator group risk as the assumed comparator risk.³² We also created synthetic effect sizes for all available time points to compute a summary measure for all time points combined if permissible by the data.³⁹ We performed our analysis with a correlational value of $\rho = 0.5$ and sensitivity analysis with $\rho = (0.6, 0.7)$.

For meta-analysis, we used pairwise Bayesian random effects meta-analysis. Bayesian meta-analysis can be more efficient than frequentist methods if the number of studies is small (≤ 5 studies) and heterogeneity is present.^{40–43} This is the case if empirical prior distributions for variance of the true effects (τ^2) are available, as this allows a better estimation of τ^2 when few studies are available.⁴³ Prespecified prior distributions are described in online supplemental appendix 5. As treated data were analysed via Bayesian random effects network meta-analysis . For estimation details, please see online supplemental appendix 5.

Publication bias and small study effects were assessed statistically via funnel plots if at least 10 studies were included in the meta-analysis.⁴⁴ Non-statistical assessment of publication bias was performed as described by our GRADE criteria (online supplemental appendix 4). Pending the number of available studies (≥ 10 trials required for meta-regression), we performed subgroup analysis based on prespecified covariates.³⁹ We performed sensitivity analysis for all prior distributions and for self-reported return to activity (long term), as the latter was reported in both studies with medians.⁴⁵ All calculations and graphics were performed with the R statistical computing environment,⁴⁶ and the R packages Meta,⁴⁷ Bayesmeta,⁴⁸ Metafor,⁴⁹ Netmeta,⁵⁰ metamedian and gemtc.⁵¹

RESULTS

We identified 9514 reports through database searching and manual search of reference lists of relevant literature reviews. After removing duplicates and screening titles and abstracts of all remaining unique reports, 104 full-text reports were assessed for eligibility. We included three studies^{52–54} with nine study reports (figure 1).^{52–60} Literature sources and reasons for exclusion of ineligible studies/reports are reported in online supplemental appendix 2.

Unpublished and ongoing trials

We identified three ongoing trials potentially relevant for this review.^{13 61 62} We provide further information concerning these trials in online supplemental appendix 3.

Study characteristics

The characteristics of the three included studies are shown in table 1. Sample size ranged from 32 to 167 participants (mean: n=106; total: n=320). Mean (SD) age of all participants was 29.5 (7.05) years, whereas body mass index was 24.4 (3.4) kg/m² based on two studies.^{53 54} On average, 93% injured their ACL while performing their chosen sport. This result is based on two studies.^{53 54} All trials employed active rehabilitation. One trial⁵⁴ employed evidence-based, progressive rehabilitation, one trial⁵³ based its rehabilitation on Dutch rehabilitation guidelines and one trial used⁵² a progressive rehabilitation programme.

RoB and GRADE assessment

Two study outcomes were rated as low RoB overall. The other study outcomes were either rated with some concerns or a high RoB overall (online supplemental appendix 6). The certainty of the evidence was rated for meta-analytic outcomes as low or very low overall and as high to very low for individual study outcomes (online supplemental appendices 7 and 8). Main reasons for downgrading the evidence were RoB, inconsistency and imprecision. We did not grade down due to publication bias in accordance to our prespecified criteria. Indirectness was not

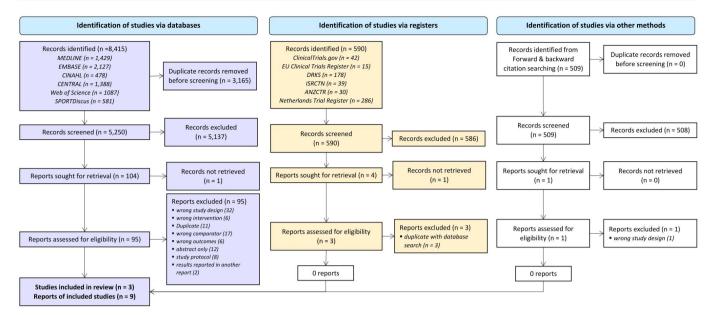


Figure 1 PRISMA flowchart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

downgraded as this review followed strict population, intervention, comparator and outcome eligibility criteria.

Data handling and synthesis

Three reports (two studies)⁵³⁻⁵⁵ only reported precision of the estimates as 95% CIs, which we converted to SD with established formulae. Two studies^{52.54} reported return to activity data as median (IQR), which we transformed to mean (SD). Two reports (one study)^{54.55} reported primary outcomes as mean difference (95% CI). The authors of the study provided the data for this outcome. The authors of one report⁵⁶ confirmed our queries regarding sample size. All outcomes are reported for meta-analytic summaries and individual study outcomes in tables 2 and 3 and figures 2–4. The secondary outcome muscle strength could not be assessed as this was not reported in any trial. All data, calculated effect sizes and as-treated analyses are reported in online supplemental appendices 9, 10 and 12.

Self-reported knee function

Three studies with four reports⁵²⁻⁵⁵ were included. Metaanalysis was performed for short-term,^{53 54} medium-term^{53 54} and long-term follow-up.^{52 55} In the short-term (SMD: -0.25; 95% CrI -0.84 to 0.36; 95% PI -1.25 to 0.76; two studies; n=288; GRADE: low) and medium-term (SMD: -0.10; 95%) CrI -0.59 to 0.41; 95% PI -0.91 to 0.72; two studies; n=288; GRADE: low) showed no statistical difference between the two groups with low certainty of evidence. Estimated raw mean difference was -4.21 (95% CrI -14.27 to 6.07) and -2.65 (95% CrI -15.94 to 10.89) points on the IKDC scale (0-100 points), which did not reach clinical meaningfulness (MCID: 16.7 points and 17 points). For long-term follow-up (SMD: -0.21; 95% CrI -1.49 to 0.81; 95% PI -2.28 to 1.58; two studies; n=152; GRADE: very low), there was no statistical between group difference for self-reported knee function with very low certainty of evidence. Estimated raw mean difference was -0.96 (95% CrI -5.79 to 3.95) points on the IKDC scale, which did not reach clinical meaningfulness (MCID: 17 points). Sensitivity analyses using as-treated data for the non-operative control group from Frobell et al⁵⁵ revealed similar effects (online supplemental appendix 12). Analysis of all time points combined

yielded also no difference between groups with low certainty of evidence (SMD: -0.27; 95% CrI -0.84 to 0.21; 95% PI -1.29 to 0.66; three studies; n=309; GRADE: low). The estimated raw mean difference was -5.07 (95% CrI -15.70 to 3.99) points on the IKDC scale and was not clinical meaningful (MCID: 17 points).

Meniscal injury

Only one report examined this outcome.⁶³

Results from single studies

One study report⁶³ reported on development of new (or worsening) meniscal damage after baseline or index surgery via MRI. Early surgery showed no effect compared with primary rehabilitation at long-term follow-up (OR: 0.85; 95% CI 0.45 to 1.62; GRADE: low) with a low level of certainty.

Radiological knee osteoarthritis

Two studies^{52 55} were included. We estimated no statistical effect at long-term follow-up (OR: 1.45; 95% CrI 0.30 to 5.17; 95% PI 0.18 to 10; two studies; n=152; GRADE: very low) with a very low level of certainty. Transformation of the OR into a risk difference with an assumed prevalence of 25% in the rehabilitation group gives a number fewer than 1000 of -72 (95% CrI (144 to -384)) at a very low level of certainty. Assuming that 250 (25%) patients of 1000 patients develop knee osteoarthritis (OA) after being treated with primary rehabilitation then 72 more patients (322 patients) treated with early surgery will develop knee osteoarthritis with a 95% CrI (144 patients less, 384 patients more) with a very low level of certainty. Sensitivity analyses using as-treated data for the non-operative control group from Frobell *et al*⁵⁵ revealed similar effects (online supplemental appendix 12).

Health-related quality of life

Two studies^{53 54} were included. We estimated no effect for early surgery compared with primary rehabilitation at medium-term follow-up (SMD: -0.40; 95% CrI -0.88 to 0.09; 95% PI -1.18 to 0.40; two studies; n=288; GRADE: low) with a low

Study type I	Inclusion criteria	Inclusion criteria Exclusion criteria	Patients (INT/ CON) at baseline	Mean age (SD) (INT/ CON)	Sex F (INT/ CON)	BMI kg/m ² mean (SD) INT/CON)	Participating in sports_while injured n (%)	INT type	CON type	Primary end point	Other follow-ups	Primary outcome(s)	Secondary outcomes
	Age: 18–35 years. Recent totational to previously uninjured knee within 4 preceding weeks. Act. insufficiency by dinical exam (positive pixof shift and/or positive tachmant est, 5–9 points on injury, complete injury, complete injury, complete injury, complete area, nomal read, nor schophytes grade 1 or of schophytes	Earlier major knee injury to the index knee, prevoux knee surgery optrovices knees urgery anthroscopy) to index knee arthroscopy) to index knee arthroscopy to index injury or oMCL injury grade III in index knee, injury to contra-lateral ligament compak with seasesment, bijury to the lateral/postenolateral ligament compak with seases arthroscop dignificanty increased Laxity, total collateral ligament compak in the lateral/postenolateral ligament to putue arthroscop and searchage lesion on MRL unstable elesion on MRL unstable biotompture of MCU cLC on MRL, pregnancy, of DVT, grental systemic disase, systemic disase, systemic steroids	62/59	26.3 (5.1)/25.5 (4.7)	12/20	244 (3.2)/238 (2.6)	62(100)/ 57(97)	Progressive, supervised goals for ROM, muscle goals for ROM, muscle hurction, and functional performance (four phases) are early ACL reconstruction (within that ACL reconstruction (within phase surgeons, conce of procedure depended on surgeons preference(parella performed as needed.	Progressive, supervised rehabilitation with and function, and functional and functional phases) the same surgeons if certain orieria were met (served instability caused by ACL insufficiency and positive priord instability caused by ACL insufficiency instability caused by ACL insufficiency instability caused by ACL insufficiency instability test)	24 m	3 m, 6 m, 12 m, 24 m, 60 m	KOOS (without ADL scale)	SF-36, TAS, knee stability (Lachman test, proof shift test; KT1000 arthrometry), adverse events meniscal surgery, and radiographic subgroup with KOOS-ADL Score-44 KOOS-ADL Score-44
RCT T T T T T T T T T T T T T T T T T T	Age 18–65 years, matter (within 2 matter initial trauma), complete phany ACL upture (confirmed by MRI and clinical willingness of patient to be randomised,	History of injury to ACL of the contralateral knee, presence of another disorder affecting the activity of the lower limb, disorder bucket handle lesion of the mericus with extension deficit, insufficient command of the Ducch language,	85/82	31.2 (10.3/) 31.4 (10.7)	36/31	243 (3.7)/25 (4.1)	76 (89.4)/ 71 (86.6)	Early ACL reconstruction (within 6 w after andomisation), surgens chose their preferred technique and gaft and decided if more intraarticular surgery was mecesary all surgeons had a minimum of 10 years experience, e-bhyliscal threapy e-bhyliscal threapy e-bhyliscal threapy achieved.	Referral to reprovised reprovised reprovised physical therapist for physical therapist for physical therapist and ACL guidelines, after a minimum of 3 m patients after a minimum of 3 m patients physical the option for reconstruction of ACL if instability per was not reached.	24 m	3 m, 6 m, 9 m, 12 m	IKDC	KOOS, TAS, Satisfaction (five point likent scale), serious adverse events

Interface Runsies (000000000000000000000000000000000000	Tahla 1	Tahla 1 Continued													
Num Num <th></th>															
2016 Rel toto, toto shared, control shared shar	Study			Exclusion criteria	at at	Mean age (SD) (INT/ CON)	Sex F (INT/ CON)	BMI kg/m ² mean (SD) INT/CON)		INT type	CON type		Other follow-ups	Primary outcome(s)	Secondary outcomes
	T soukas et a p ²		Isolated ACL Invirse, BMM<30, no previous major injury or surgery to the knee, patents completed the final follow-up successfully.			29 (5.1)/ 32.3 (4.7)	17 (0)/15 (0)	NEWR	NRVR	ACL reconstruction, media mine interval between the initial injury and beginning of treatment 6w (range 4-8, ACL reconstruction via hamstring autograth peropon, +rehabilitation as CON group	Rehabilitation, between the initial between the initial injury and beginning w (range 4-8), passive kines 4-8), passive kines 4-8, passive kines 4	Median 120 m 120-132 m)	Median 120 m (range 120–132 m)	undear	IKDC, knee stability (57N, 89N, 134N), knee osteoarthrifids, adverse events

	ity of Evidence (G	паре арр					-	
Outcome (follow- up time point)	Studies included in meta-analysis	Total N	Intervention	Control	Effect size (95% Crl)	95% prediction interval*	Raw mean difference†/risk difference‡ (95% Crl)	Certainty rating
Primary outcomes								
Self-reported knee function§ (Short-term)	Frobell <i>et al⁵⁴,</i> Reijman <i>et al⁵³</i>	288	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.25, (-0.84 to 0.36)	(-1.25 to 0.76)	-4.21, (-14.27 to 6.07) IKDC (0-100)	Low¶
Self-reported knee function§ (Medium-term)	Frobell <i>et al⁵⁴,</i> Reijman <i>et al⁵³</i>	288	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.10, (-0.59 to 0.41)	(-0.91 to 0.72)	-2.65, (-15.94 to 10.89) IKDC (0-100)	Low¶
Self-reported knee function§ (Long-term)	Frobell <i>et al⁵⁵,</i> Tsoukas <i>et al⁵²</i>	152	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.21, (-1.49 to 0.81)	(-2.28 to 1.58)	-0.96, (-5.79 to 3.95) IKDC (0-100)	Very low¶**
Self-reported knee function§ (All time points combined)	Frobell <i>et al⁵⁴,</i> Reijman <i>et al⁵³,</i> Tsoukas <i>et al⁵²</i>	309	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.27 (-0.84 to 0.21)	(-1.29 to 0.66)	-5.07, (-15.70 to 3.99) IKDC (0-100)	Low¶
Radiological knee osteoarthritis (Long-term)	Frobell <i>et al⁵⁵,</i> Tsoukas <i>et al⁵²</i>	152	Early reconstruction	Rehabilitation+optional reconstruction*	OR 1.45, (0.30 to 5.17)	(0.18 to 10.0)	—72 per 1000 patients, (144 to —384)	Very low¶**††
Secondary outcomes								
Health-related quality of life‡‡ (Medium-term)	Frobell <i>et al.⁵⁴,</i> Reijman <i>et al(⁵³</i>	288	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.40, (-0.88 to 0.09)	(-1.18 to 0.40)	-5.91, (-13.05 to 1.32) SF-36 mental health score (0-100)	Low¶
Health-related quality of life‡‡ (All time points combined)	Frobell <i>et al⁵⁴,</i> Reijman <i>et al⁵³</i>	288	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.35 (-0.87 to 0.16)	(–1.20 to 0.50)	-5.01, (-12.37 to 2.34) SF-36 mental health score (0-100)	Low¶
Self-reported return to activity§§ (Medium-term)	Frobell <i>et al⁵⁴,</i> Reijman <i>et al⁵³</i>	288	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.10, (-0.57 to 0.38)	(-0.87 to 0.68)	–0.31, (–1.80 to 1.19) Tegner Scale (0–10)	Very low¶††
Self-reported return to activity§§ (Long-term)	Frobell <i>et al⁵⁵,</i> Tsoukas <i>et al⁵²</i>	152	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.22, (-0.92 to 0.39)	(-1.32 to 0.77)	–0.75, (–2.92 to 1.23) Tegner Scale (0–10)	Very low¶**††
Self-reported return to activity§§ (All time points combined)	Frobell <i>et al⁵⁴,</i> Reijman <i>et al⁵³,</i> Tsoukas <i>et al⁵²</i>	309	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.21, (-0.57 to 0.13)	(-0.82 to 0.37)	–0.72, (–1.92, 0.42) Tegner Scale (0–10)	Very low¶††
Adverse event – graft rupture	Frobell <i>et al</i> ⁵⁴ , Reijman <i>et al</i> ⁵³	288	Early reconstruction	Rehabilitation+optional reconstruction	OR 2.3, (0.4 to 12.4)	(0.3 to 20)	-26 per 1000 patients,	Very low¶††

Table 2 Certainty of Evidence (GRADE approach) of meta-analytic outcomes

Negative standardised mean differences indicate the effect favoured the intervention.

*The prediction interval indicates the heterogeneity in the data and the range of potential values that could be possible in future studies.

*Raw data estimate was done by multiplying the SMD and associated 95% credible interval estimates by the available pooled SD from studies included in the review. *Raw data estimate used the median comparator baseline risk of included studies.

§International Knee Documentation Committee (IKDC Questionnaire) (Reijman et al. and Tsoukas et al.), Knee Injury and Osteoarthritis Outcome Score (KOOS) (Frobell et al) ¶Certainty rated down for inconsistency.

**Certainty rated down for risk of bias.

†+Certainty rated down for imprecision, e: certainty rated down for publication.

‡‡SF-36 (mental subscale) (Frobell et al), KOOS subscale Quality of Life (Reijman et al).

§§Tegner Scale (Frobell et al. and Tsoukas et al), Lysholm Scale (Reijman et al).

DR, delayed reconstruction; ER, early reconstruction; NA, not applicable; NO, non-operative.

level of certainty. The converted raw mean difference of -5.91 (95% CrI -13.05 to 1.32) points on the SF-36 (mental health score, 0–100 points) was likely not clinically meaningful (≥ 10 points).⁶⁴ Analysis of all time points combined gave evidence

of no effect (SMD: -0.35; 95% CrI -0.87 to 0.16; 95% PI -1.20 to 0.50; two studies; n=288; GRADE: low) with a low level of certainty. The converted raw mean difference of -5.01 (95% CrI -12.37 to 2.34) points on the SF-36 (mental health

(12, -186)

Table 3Certainty of evidence	(GRADE approad	h) of indi	vidual study outco	nes		
Outcome (follow-up time point)	Study	Total N	Intervention	Control	Effect size (95% CI)	Certainty rating
Primary outcomes						
Meniscal injuries (Long-term)	Snoeker <i>et al⁵⁹</i>	121	Early reconstruction	Rehabilitation+optional reconstruction	OR 0.85, (0.45 to 1.62)	Low*
Secondary outcomes						
Health-related quality of life† (Long-term)	Frobell <i>et al⁵⁵</i>	120	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.14, (-0.50 to 0.21)	Low*
Self-reported return to activity‡ (Short-term)	Reijman <i>et al⁵³</i>	167	Early reconstruction	Rehabilitation+optional reconstruction	SMD -0.34, (-0.66 to -0.03)	Moderate§
Knee stability (Medium-term)	Frobell <i>et al⁵⁴</i>	121	Early reconstruction	Rehabilitation+optional reconstruction	MD -1.70, (-2.65 to -0.75)	Moderate*
knee stability (Long-term)	Tsoukas <i>et al⁵²</i>	32	Early reconstruction	Rehabilitation+optional reconstruction	MD-3.00, (-3.27 to -2.73)	Low§
Patello-femoral cartilage thickness (Medium-term)	Culvenor <i>et al⁶⁰</i>	120	Early reconstruction	Rehabilitation+optional reconstruction	MD 76.00, (10.63 to 141.37)	Moderate*
Patello-femoral cartilage thickness (Long-term)	Culvenor <i>et al⁶⁰</i>	120	Early reconstruction	Rehabilitation+optional reconstruction	MD 107.00, (17.33 to 196.67)	Moderate*
Meniscal surgeries (Long-term)	Snoeker <i>et al⁵⁹</i>	121	Early reconstruction	Rehabilitation+optional reconstruction	OR 0.88, (0.47 to 1.62)	Low*
Cost-effectiveness (Medium-term)	Eggerding <i>et al⁵⁷</i>	167	Early reconstruction	Rehabilitation+optional reconstruction	MD 0.04, (p=0.18), not cost- effective	Moderate§
Cost-effectiveness (Long-term)	Kiadaliri <i>et al⁵⁸</i>	120	Early reconstruction	Rehabilitation+optional reconstruction	MD 0.13, (-0.03, 0.29) QALY, not cost- effective	Moderate*
Leg-hop limb symmetry index (Short-term)	Flosadottir <i>et al⁵⁶</i>	89	Early reconstruction	Rehabilitation+optional reconstruction	MD 1.10, (–2.98 to 5.18)	Low*
Single leg-hop limb symmetry index (Long-term)	Flosadottir <i>et al⁵⁶</i>	89	Early reconstruction	Rehabilitation+optional reconstruction	MD 0.80, (-4.34 to 5.94)	Low*

Negative standardised mean differences indicate the effect favoured the intervention

*Certainty rated down for imprecision. †Certainty rated down for risk of bias.

#SF-36 (mental subscale) (Frobell et al)

§Lysholm Scale (Reijman et al).

score, 0–100 points) was likely not clinically meaningful (≥ 10 points).

Results from single studies

One study⁵⁵ reported no effect on health-related quality of life at long-term follow-up (SMD: -0.14; 95% CI -0.50 to 0.21; GRADE: low) with low level of certainty.

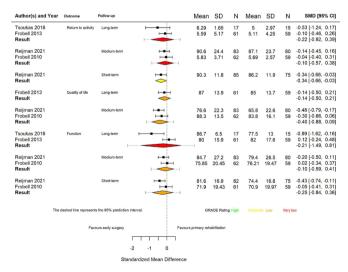


Figure 2 Overview of continuous outcomes for the comparison early surgery versus rehabilitation with optional surgery. The used software sets the limit automatically to the 95% CrIs and not the 95% prediction intervals (dashed lines). As the highest value of a 95% CrI is 0.81 it sets the positive limit to 1.0 although the prediction interval goes further than that. Crl, credible interval.

Self-reported return to activity Four reports of three studies^{52–55} were included. Meta-analysis was performed for medium-term^{53,54} and long-term follow-up for postinjury activity level at the specific follow-up time points.^{52 55} At medium-term follow-up, there was no effect (SMD: -0.10; 95% CrI -0.57 to 0.38; 95% PI -0.87 to 0.68; studies=2; n=288, GRADE: very low) with very low certainty of evidence. Raw mean difference on the Tegner Scale (0-10 points) was -0.31 (95% CrI -1.80 to 1.19) points, which was not clinically meaningful (MCID: 1 point).⁶⁵ No effect with very low certainty of evidence was also estimated for long-term follow-up (SMD: -0.22; 95% CrI -0.92 to 0.39; 95% PI -1.32 to 0.77;

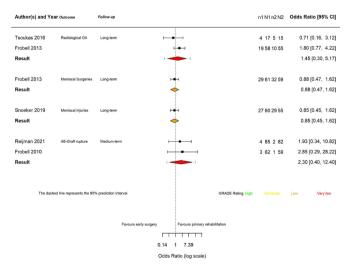
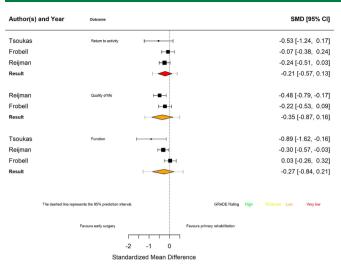
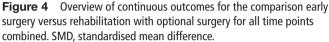


Figure 3 Overview of dichotomous outcomes for the comparison early surgery vs rehabilitation with optional surgery.

NA, not applicable





studies=2, n=152, GRADE: very low). Raw mean difference on the Tegner Scale was -0.75 (95% CrI -2.92 to 1.23) and cannot be considered clinically meaningful. Sensitivity analyses using as-treated data for the non-operative control group from Frobell et al⁵⁵ yielded no effect for early surgery in comparison to the non-operative group (SMD: -0.84; 95% CrI -2.56 to 0.87; 95% PI-3.36 to 1.67; studies=2; n=152, GRADE; very low) with a very low level of certainty. Raw mean difference on the Tegner Scale was 2.61 (95% CrI -2.67 to 7.90) and can likely be considered clinically meaningful but only with a very low degree of certainty. One should note that a sensitivity analysis with a meta-analysis of medians yielded lower values (median: 1.18, 95% CI -0.75 to 3.20) on the Tegner scale. Analysis of self-reported activity for all time points resulted in no effect (SMD: -0.21; 95% CrI -0.57 to 0.13; 95% PI -0.82 to 0.37; studies=2; n=152, GRADE: very low) between groups with a very low level of certainty. Raw mean difference on the Tegner Scale was -0.72 (95% CrI -1.92 to 0.42) and cannot be considered clinically meaningful.

Results from single studies

One study⁵³ reported no effect at short-term on return to activity (SMD: -0.34; 95% CI -0.66 to -0.03; GRADE: moderate) with a moderate level of certainty.

Meniscal surgeries

Results from single studies

One study report⁵⁵ reported on the number of patients with any meniscal surgery during the study, including those performed at baseline concomitant with index ACL reconstruction, and during follow-up up to 5 years, which showed no effect for primary surgery versus primary rehabilitation with a low level of certainty (OR: 0.88; 95% CI 0.47 to 1.62; GRADE: low). Transformation of the OR into a risk difference with an assumed prevalence of 51% in the rehabilitation group gives a number fewer than 1000 of 32 (95% CrI 181 to–119) with a low level of certainty. Assuming that 510 (51%) patients of 1000 patients develop or have a meniscal injury when undergoing primary rehabilitation then 32 less patients (478 patients) treated with early surgery will develop or have a meniscal injury with a 95%

CrI (181 patients more, 119 patients less) with a low level of certainty.

Secondary outcomes

The secondary outcomes: adverse event (graft rupture), knee stability, patellofemoral cartilage thickness, leg hop–limb symmetry index and economic resource are displayed in tables 2 and 3 and in online supplemental appendix 9.

Funding and conflict of interest

One study⁵³ was funded by a professional organisation. Another study⁵⁴ had mixed funding of private or professional and governmental organisations. One study⁵² did not report their funding source. The authors declared no conflict of interest in two studies,^{52 53} whereas one study⁵⁴ reported a conflict of interest.

Small study effects and publication bias

We did not suspect publication bias according to our criteria for GRADE. Small study effects and publication bias could not be statistically assessed because the number of studies were fewer than 10 studies.⁴⁴

Subgroup analysis and meta-regression

Subgroup analysis and meta-regression were not feasible due to the low number of studies (ie, n < 10).³²

Sensitivity analyses

We performed sensitivity analyses with different priors for the between study variance (τ^2) for meta-analytic outcomes (online supplemental appendices 12 and 13). This was done to check how sensitive the results were to different priors (prior beliefs about the distribution of τ^2) for the between study variance. The findings did not change when different priors for τ^2 were used. The meta-analysis of medians led to markedly different outcomes for self-reported return to activity for the comparison early reconstruction versus non-operative treatment in the long term. Transformed raw mean differences were 2.61, (95% CrI -2.67 to 7.90) versus 1.18, (95% CI -0.75 to 3.20) points on the Tegner scale (0–10) for the sensitivity analysis.

Protocol deviations compared with PROSPERO registration

We added a meta-analysis of medians as a sensitivity analysis and added a meta-analysis of all timepoints combined to this work. We removed the outcome treatment failure (graft rupture vs surgical reconstruction) due to recommendations made by the reviewers as a graft rupture is an obvious and 'unexpected/ unwanted' adverse event (or failure), while delayed ACL reconstruction in the rehabilitation group (in both studies) was an a priori expected and planned part of the treatment strategy.

DISCUSSION

This is the first living systematic review and meta-analysis investigating the effects of primarily surgical versus primarily rehabilitative management for ACL injuries based on RCTs. Our analysis showed that there are no clinically relevant differences in most outcomes between early surgical reconstruction and primary rehabilitation with optional reconstruction. Radiological knee osteoarthritis showed a trend to slightly favour primarily rehabilitative treatment although at very low certainty of evidence. Meniscal damage showed a favourable trend for primary surgery in the long-term but at a low level of evidence.

Improving function

From IKDC or Knee Injury and Osteoarthritis Outcome Score (KOOS) scales, a highly clinically relevant improvement in function was shown for both treatments. Regardless of treatment modality examined, more than 90% of patients achieve MCID on the KOOS scale after 2 years.⁶⁶ Furthermore, the mean values of the function scores excluding the KOOS-QoL value reach the threshold for the Patient Accepted Symptom State at the longest follow-up.^{66 67} Current evidence suggests that both early surgery and primary rehabilitation result in clinically meaningful improvements in long-term subjective knee function. Overall, our analysis showed that early ACL reconstruction did not result in improvements in function versus primary rehabilitation management with a low level of certainty.

Radiological osteoarthritis

Early reconstruction showed no protective effect on the development of post-traumatic osteoarthritis in either the primary or as-treated analysis at a very low level of certainty. Our estimates showed a trend with very low certainty of evidence, for primary rehabilitative therapy and/or delayed reconstruction to result in less cartilage loss. A result that is confirmed by Swedish ACL registry (cohort) data in a registry evaluation of 64 614 patients with ACL rupture.⁶⁸ Overall, the protective effect on the development of knee osteoarthritis of an ACL reconstruction remains a point of debate.^{10 23 25 65 69} Prior authors reported no differences in knee osteoarthritis,^{24 70} or differences in rates of osteoarthritis development, depending on the degree of osteoarthritis⁷¹ or the length of the follow-up period,⁷² but these results are only based on observational studies. Fundamentally, our findings from RCTs challenge a historical paradigm^{73–75} that anatomic instability *must* be stabilised with surgery to prevent knee osteoarthritis.

The following mechanisms may in part explain these observations: (1) increased inflammation from the surgical procedure,^{76–78} (2) failure to accurately restore the exact contact points between the tibia and femur,^{79–82} (3) kinematic differences of ACL patients, which can be interpreted as avoidance behaviour^{83–88} (4) and premature early sports participation by patients who have undergone reconstructive surgery.^{89–91} Collectively, these mechanisms highlight that the development of post-traumatic osteoarthritis is a multifactorial complex process of interacting risk factors and thus prevention of degenerative cartilage damage by surgical or conservative treatment seems neither realistic nor possible.

Meniscal status and meniscal surgery

There is no statistical difference between early surgery and primary rehabilitation but with low certainty of evidence. Our analysis indicated that the observed differences were particularly due to the inferior results of the patients with delayed ACL reconstruction. Similar results with a low degree of certainty are found in the literature.¹² ²³ An early ACL reconstruction in patients with functional instability might be recommended following the 'as treated' analysis results, especially as the 'delayed surgery' group showed a less favourable meniscal situation. There is no direct RCT evidence that patients with functional instability need to be stabilised. But it is a best practice recommendation⁹² to operate on these instable patients and it was a prespecified criterion in the investigated RCT. We suggest that in the case of functional instability of the knee, a surgical reconstruction of the knee is warranted.

Improving return to activity

In the medium term and long term, patients reported no effect between groups, but the certainty of evidence for these results is very low. The effect sizes were also not clinically meaningful. Widespread expert recommendations are that athletes with a high functional demand should undergo surgical treatment.⁹²⁻⁹⁴ However, the quality of evidence for such recommendations is very low according to our results. What is not currently available is RCT-level information on an extreme high level of sports participation (Tegner Score of 10). A return to knee-loading sports, even those with high rotational loads, is also described after a treatment approach of primary rehabilitation in a larger group of patients.^{95'96} Notably, although competitive athletes are successful in returning to their sport after ACL reconstruction,⁸ many of these athletes do not reach their preinjury level of performance.⁹⁷ According to our analysis, one cannot unequivocally conclude that athletes are required to undergo early ACL reconstruction. Further RCTs need to be conducted to answer this question for an athletic population.

Patient-centred care

We observed no clinically meaningful differences between treatment approaches, and, thus, propose an individualised and patient-centred form of care. Depending on a patient's medical situation (eg, concomitant injuries such as repairable meniscal tears, relevant cartilage injuries, other higher grade ligamentous injuries),^{53 54 98} individual anatomical differences (eg, the tibial slope, femoral morphology, alignment),^{92 99 100} functional demands in daily life or sports,⁹² an individualised primary treatment strategy should be determined as a 'shared decision process'.¹⁰¹⁻¹⁰³ For many patients with ACL injuries without serious concomitant injuries, a 'stepped care approach' with a primarily rehabilitation focused treatment approach seems appropriate, especially pertaining to cost-effectiveness^{57 58} and the avoidance of surgical risks.¹⁰³ Functional instability, despite a high-quality exercise-based approach, determines the need for subsequent surgical treatment to minimise secondary joint damage.^{86'91 97 101 103 104} The task of future research will be to define valid predictors for an individual's success or failure with primary non-surgical care to enable an evidence-based clinical decision-making process. One such example is the decisionmaking and treatment algorithm based on the Delaware-Oslo ACL Cohort Study, which certainly requires confirmatory studies.^{98 104 105} Furthermore, such a stepped approach requires health systems to provide the necessary financial resource for an adequate primary rehabilitative care.^{106 107}

Limitations

This study is not without limitations. The low number of included studies still left uncertainties regarding the best approach for dealing with ACL ruptures. Furthermore, only one trial was of low RoB, which further undermined the certainty in the estimates. All RCTs included patients with complete ACL injuries, but the inclusion criteria regarding concomitant injuries were somewhat different in the individual trials. The applied surgical techniques were also different across the included trials, depending on the surgeon's preference. Furthermore, the current data do not permit conclusions in favour or against primary surgical management for professional athletes. We also did not prespecify different MCIDs for other outcomes beyond self-reported knee function. The use of MCID for interpretation of outcomes is debated because it varies based on analytic methods, study populations, type of disease, baseline status, change in values and treatments and patient demographics. It should be interpreted with caution. 38

FUTURE DIRECTIONS

RCTs with longer follow-ups are necessary to allow robust conclusions about the development of adverse outcomes, such as post-traumatic joint damage. In the context of ACL surgery, anatomic surgical techniques (eg, double-bundle technique, anteromedial femoral tunnel drilling technique), extra-articular reconstructions such as those of the anterolateral ligament or even slope-reducing tibial osteotomies have become particularly established in recent years and need to be evaluated in RCTs in the future.^{108–110} Initial reviews here show partial benefits for individual outcomes, for example, of anatomical versus non-anatomical techniques.^{111 112} The same can be said for rehabilitation programmes as a lot of these do not follow current best practice recommendations.¹¹³ Future studies will need to address how these new surgical procedures (eg, slope reducing tibial osteotomies) compare to contemporary primary rehabilitation.^{17 106}

CONCLUSION

We found very low to low certainty of evidence of no clinically relevant differences in most outcomes between early surgical reconstruction and primary rehabilitation with optional reconstruction. Early surgery showed a positive trend pertaining to a better meniscal status but with a low level of certainty of evidence. Rehabilitation with optional surgery showed a trend for an advantage regarding the avoidance of the development of radiological knee osteoarthritis. On the weight of the current evidence, indicating that early surgical ACL reconstruction is not beneficial for all patients, we propose an individualised, patientcentred form of care that discusses the potential treatment options with the patient.

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Acknowledgements We thank Dr. Clare Ardern for comments on the methodological approach in this work

Contributors Conceptualisation: TS, JZ, FD; data curation: TS, NS; formal analysis: TS; funding acquisition: NA. Investigation: TS, JZ, FD; methodology: TS, DB, TB, NS, MH; project administration: TS; resources: TS; software: TS; supervision: DB, PO, TB, WZ; validation: NA. Visualisation: TS; writing—original draft: TS, JZ, FD; writing—review and editing: all. Approved final manuscript: all.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors. No funding was received to support this work.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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Effects of a neuromuscular training program using external focus attention cues in male athletes with anterior cruciate ligament reconstruction: a randomized clinical trial

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Abstract

Background: Athletes who have undergone anterior cruciate ligament (ACL) reconstruction often exhibit persistent altered biomechanics and impaired function. Neuromuscular training programs appear to be effective for reducing high-risk landing mechanics and preventing primary ACL injuries; however, there have been few attempts to examine their effects in athletes who have undergone ACL reconstruction. The purpose of our study was to examine the effects of a neuromuscular training program that emphasizes external focus of attention cuing on biomechanics, knee proprioception, and patient-reported function in athletes who had undergone ACL reconstruction and completed conventional post-operative rehabilitation.

Methods: Twenty-four male athletes who had undergone primary, unilateral, hamstring autograft ACL reconstruction and completed conventional post-operative rehabilitation were randomly allocated to an experimental group (n = 12)who took part in an 8-week neuromuscular training program or a control group (n = 12) who continued a placebo program. The neuromuscular training program included lower extremity strengthening and plyometric exercises, balance training, and movement pattern re-training. Biomechanics during single-leg landing, knee proprioception, and patient-reported function were assessed before and after the 8-week training period.

Results: Athletes in the experimental group demonstrated increased trunk, hip, and knee flexion angles and decreased knee abduction, internal rotation angles and knee valgus during landing following the intervention. Further, the experimental group decreased their peak knee extension and abduction moments and vertical ground reaction force on landing post-intervention. International Knee Documentation Committee questionnaire (IKDC) scores increased in the experimental group following training. The control group demonstrated no changes in any variable over the same time period.

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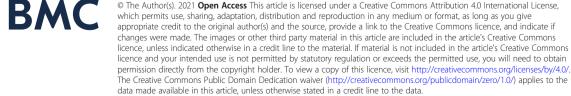
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Conclusions: Neuromuscular training with external focus of attention cueing improved landing biomechanics in patients after ACL reconstruction. Neuromuscular training programs beneficially mitigate second ACL injury risk factors and should be emphasized during and after traditional post-operative rehabilitation.

Trial registration: Current Controlled Trials using the IRCT website with ID number of, IRCT20180412039278N1 "Prospectively registered" at 21/12/2018.

Keywords: Anterior cruciate ligament reconstruction, Neuromuscular training, Rehabilitation, External focus attention

Background

Anterior cruciate ligament (ACL) injuries mostly occur during sports activities that include sudden stops, changes in direction, jumping, or landing [1]. Immediately after this injury, the athlete is confronted with multi-planar biomechanical asymmetries, loss of a season in their respective sport, a long, difficult recovery ahead, and a possible reduction in performance following a return to sport (RTS) [1, 2]. Nearly two-thirds of athletes do not return to preinjury level one year after ACL reconstruction [3]. In fact, only 65% of athletes return to the pre-injury level of sport at a mean follow-up of nearly 3.5 years despite recovering normal knee function [4]. Also, seven years after ACL reconstruction, only 36% still participated in their original sports [5]. Moreover, for those who do resume their previous level of activity, the risk of a second ACL injury to the ipsilateral or the contralateral knee due to reduced muscle strength and function may be as high as 29% [6].

Aberrant jump-landing biomechanics, particularly increased vertical ground reaction force (vGRF), decreased hip and knee flexion, and increased knee abduction and internal rotation, which collectively lead to dynamic "knee valgus", have been associated with second ACL injury risk [7, 8]. These biomechanical components of second ACL injury risk may be effectively addressed with targeted neuromuscular training prior to unrestricted sports participation [9].

Neuromuscular training programs, which incorporate lower extremity strengthening exercises, plyometric exercises, balance training, and movement pattern re-training are recommended for primary prevention of ACL injuries [9, 10]. Programs of this nature appear to reduce ACL injury rates [9] and promote safer landing mechanics in athletes without a history of ACL injury [11].

Neuromuscular training has been demonstrated to mitigate biomechanical risk factors associated with ACL injury. For example, neuromuscular training programs 1) with added feedback reduced knee valgus angles and moments [11]; 2) with verbal feedback on incorrect technique improved VGRF [12]; 3) neuromuscular improved the H/Q ratio in female athletes [11]; and 4) increased the activity of the medial hamstrings in the pre landing phase which is thought to be beneficial for stabilizing

the knee [13]. Specific to patients after ACL reconstruction, neuromuscular training has been demonstrated to significantly improved knee pain and global knee function compared with the traditional strength training. The authors also emphasized including neuromuscular training in the rehabilitation program after ACL reconstruction [14]. In addition, Shim et al., (2015) reported another benefit of neuromuscular training is that it reduces the anterior tibial displacement of the affected knee joints during standing, which, in turn, reduces ACL strain. Finally, neuromuscular training evoked higher muscle activation of the vastus medialis oblique, vastus lateralis, biceps femoris, and semitendinosus, all of which may improve functional joint stability [15].

Since the potential mechanism underlying the secondary injury is multifactorial (age, surgical procedure, and post-injury activity level [16], more focus on these factors into post-operative rehabilitation seems warranted. However, modification of these programs to emphasize an external focus of attention may be necessary to reduce risk factors of second ACL injury. Instructions that promote an internal focus of attention, which is common in rehabilitation, direct an athlete to attend to a specific aspect of their movement, whereas instructions that promote an external focus direct an athlete to attend to the effects of their movement [17]. For example, when an athlete is performing a hop for distance, they could be instructed to focus on extending their knee as rapidly as possible (internal focus) or pushing against the ground as forcefully as possible (external focus). Although the difference in these instructions appears subtle, training with an external focus has been shown to result in better performance, retention, transfer, and greater movement automaticity for a wide range of movement tasks [17]. A key difference from a motor learning standpoint between internal and external focus of attention cueing is that external focus promotes automaticity of movement [17], meaning the individual is not constrained in their movement profile and are freer to adapt to a changing environment. In recent years, Gokeler et al., (2015) determined the effect of an internal vs. external attentional focus on single leg hop distance and knee kinematics in patients after ACL reconstruction and reported biomechanical outcomes' improvements for the

injured legs after receiving external focus of attention extraining [18]. They concluded that using an external focus puduring rehabilitation of patients after ACL reconstruction received to en in

promotes safer movement patterns compared to an internal focus of attention; thus, external may reduce second ACL injury risk [18].

Therefore, the purpose of our study was to examine the effects of a neuromuscular training program that emphasizes external focus of attention cuing on biomechanics, knee proprioception, and patient-reported function in athletes who had undergone ACL reconstruction and completed conventional post-operative rehabilitation. We expected that athletes who participated in neuromuscular training would exhibit improvements in biomechanics, knee proprioception, and function that exceed those exhibited by athletes who simply continued their typical training routine.

Methods

Twenty-four male athletes participated in this randomized controlled trial (RCT) that was prospectively registered at [IRCT20180412039278N1, date of first registration 21/12/2018].

A sample size estimate indicated that 12 participants per group (24 total athletes) would provide adequate statistical power to detect a group-by-time interaction for a moderate effect size (partial eta squared = 0.06) [19]. This determination was made based on biomechanical and joint position sense data. These data suggest joint position sense can change significantly following neuromuscular training, which yielded a large effect size [20]. Using these data, an alpha of 0.05, a beta of 0.20, the aforementioned moderate effect size of $\eta^2 = 0.06$, and assuming a correlation among repeated measures of 0.85 for our sample size estimate, we arrived at the total Of 24 participants needed. The value used for the correlation among repeated measures was based on the testretest reliability reported for isokinetic testing [16]. G*Power software was used for sample size estimation [21] (Fig. 1).

Athletes were required to have undergone a successful primary, unilateral hamstring tendon autograft ACL reconstruction, performed by the same surgeon, and were cleared to resume sports participation by their medical team. All athletes intended to return to sports, such as soccer, that involve frequent landing and cutting. Clearance for return-to-sport was primarily based on the time since surgery, which is typical [22]. At the time of enrollment in the study, all athletes had undergone ACL reconstruction within the previous 6–12 months. Athletes who sustained a concomitant injury to another knee structure (e.g. medial collateral ligament, meniscus), had a history of previous musculoskeletal surgery to either leg, or experienced a post-operative re-injury were

excluded from participating. The study protocol was approved by the Institutional Review Board at [omitted for review] and all participants provided written informed consent prior to enrollment.

Upon enrollment in the study, the first licensed athletic trainer conducted a preliminary assessment to ensure that it was safe for the athlete to participate in the activities associated with our study. This involved assessing knee pain, effusion, 80% quadriceps strength limb symmetry via handle-held dynamometer, and knee range of joint motion via electro goniometer, as well as observing single leg hopping (i.e., single leg forward hop, triple hop, crossover hop, and 6 m timed hop as previously described) [23]. Athletes were required to exhibit no effusion, report painfree knee active range of motion, and complete all hop tests without pain and at an equivalent distance/rate of at least 80% of the contralateral limb. All athletes who enrolled in the study were deemed safe to participate. Athletes were randomly allocated to an experimental group (n = 12) or a control group (n = 12). Randomization was performed by an independent investigator not familiar with the testing protocol using a random number table. Group allocation was concealed by means of an opaque envelope until after athletes had been enrolled in the study to minimize potential bias. A baseline assessment of hamstrings and quadriceps strength, knee joint position sense, and patient-reported function was completed for each athlete upon enrollment.

Biomechanics testing

Kinematic data were recorded at 250 Hz using a 6camera Motion Analysis system (raptor E with associated Cortex software). Kinetic data were collected at 1500 Hz using an AMTI force plate (AMTI, Watertown, Massachusetts) synchronized with the motion capture system. Retroreflective markers were placed on various anatomic landmarks of the pelvis and lower extremities in accordance with the Plug-in-Gait lower body marker set (right and left anterior superior iliac spines; right and left posterior superior iliac spines; lower lateral surface of the right and left thigh along the line between the hip and knee joint markers; right and left lateral epicondyle of the femur; lower lateral surface of the right and left tibia along the line between knee and ankle joint markers; right and left lateral malleolus; superior proximal end of the second metatarsal of the right and left foot; and posterior aspect of the Achilles tendon of the left and right leg at the same height as the second metatarsal marker). A static calibration trial was conducted with the athletes standing in the anatomical position. Following the static calibration trial, the athletes completed a standardized warm-up which involved various running and jumping tasks in order to become accustomed to the laboratory setting and the presence of the markers [23].

For the single-legged drop-landing task, participants started from a single-legged standing position on a 25 cm high platform placed next to the force plate. The athlete stood on the ACLR limb, jumped onto the force plate, landing on it with the same limb, and then jumped upward as high as possible. Each athlete was allowed to practice the landing task four times. Three trials were collected for each participant. The mean of these three landings was submitted to statistical analysis. No feedback was given during data collection. Kinematic and kinetic data from the single-leg landing trials were filtered using a 4th order, zero-lag, recursive Butterworth filter. A cutoff frequency of 15 Hz was used for the marker data and a cutoff frequency of 50 Hz was used for the force data. Three-dimensional joint angles were calculated for the trunk, hip and knee using an XYZ Cardan sequence, which resulted in joint angles corresponding with flexion/extension, adduction/abduction, and internal/external rotation. Joint angles reflected the orientation of the local coordinate system of the distal segment relative to the local coordinate system of the proximal segment. All kinetic variables were identified during the first 100 ms following initial contact with the force plate. Loading rates were calculated by dividing the peak vGRF by the time to peak force [24]. All kinetic variables were normalized to body mass (e.g., Nm/kg) or bodyweight (BW) as appropriate. All data processing was performed using custom MATLAB scripts (The MathWorks, Inc., Natick, MA, USA) [25] to extract peak angles for trunk, hip, and knee flexion, knee abduction, and knee internal rotation, peak anterior tibial shear force, peak knee extension and abduction moments, loading rate, and peak vGRF during the initial landing phase of the single-legged landing task. For each of these aforementioned dependent variables, the three-trial mean was calculated.

Knee joint position sense

Following biomechanics testing, athletes completed a passive repositioning testing protocol to assess the knee joint position sense of their ACL reconstructed limb. The testing protocol used in this study has been previously described in detail and demonstrates good testretest reliability (ICC = 0.78) [22]. Briefly, athletes were seated upright in the isokinetic dynamometer (Biodex Medical System, Inc., Shirley, NY, USA) with their knee initially flexed to 90° and their eyes closed. Their knee was passively extended to 45° of knee flexion by the isokinetic dynamometer and held for 5 s before returning to the initial position (90° of flexion). We instructed athletes to try to remember the position of their knee during the 5-s hold. The knee was then passively moved

into extension by the isokinetic dynamometer and athletes were asked to press a button when they thought their knee had returned to the target angle of 45° of flexion. The absolute difference between the knee angle at the time of the button press and the target angle ('error') was recorded. Each athlete completed 2 trials and the average error was calculated.

Patient-reported function

Athletes completed the Persian version of the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, which has been validated for use in Persian-speaking individuals after ACL injury [26]. The IKDC Subjective Knee Evaluation Form captures various aspects of knee-related function and is commonly used in athletes following ACL reconstruction [27]. Scores are expressed as a percentage, with 100% indicating full function and no symptoms. The minimal clinically important difference (MCID) for the IKDC has been reported to be 11.5 in athletes post-ACL reconstruction [28]. The MCID reflects the smallest amount of change in a measure that is perceived as meaningful.

We used the Tegner scale to capture the amount and types of physical activity that the athletes were participating in at the time of baseline testing. A higher Tegner score is indicative of a greater amount of activity and/or more demanding activities (ranges from 0 to 10) [27].

Pre and post-test assessments were conducted by the second athletic trainer, at baseline and after intervention. This investigator was blinded to group assignment.

Neuromuscular training program

Following completion of baseline testing, athletes in the experimental group participated in an 8-week progressive neuromuscular training program under the supervision of the third experienced athletic trainer. The program designed to improve lower extremity strength, control, power, balance, and landing technique. The program used in this study has been previously described and shown to improve hip strength and hop distance, and reduce high-risk landing mechanics, in uninjured athletes [29]. Athletes completed 3 sessions per week for weeks 1-6 and 2 sessions per week for weeks 7 and 8 (22 total sessions). Eight exercises were performed as part of the program: double-leg squats, walking lunges, single-leg squats, double-leg drop jumps, single-leg stance on an unstable surface, single-leg countermovement jumps, horizontal bounds, and single-leg standing long jumps. All exercises were performed with bodyweight resistance. Details regarding the exercises performed each week, as well as the sets and repetitions/ time are provided in Table 1. The program components, duration, and frequency are consistent with current

Exercise	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8
Double-leg squats	3×6	3×6	-	-	-	-	-	-
Walking lunges	3×6	3×6	-	-	-	-	-	-
Single-leg squats	3×6	3×6	4×8	4×8	4×12	-	-	-
Double-leg drop jumps	-	-	3×6	4×10	4×12	-	-	-
Single-leg stance, unstable surface	-	-	3 x 30s	3 x 30s	4 x 30s	4 x 30s	3 x 30s	3 x 30s
Single-leg countermovement jumps	-	-	3×6	3×8	4×8	4×10	3×8	3×6
Horizontal bounds	-	-	-	-	-	4×8	5×10	3×8
Single-leg standing long jumps	-	-	-	-	-	4×8	5×8	3×8

Table 1 Neuromuscular training program details

^aSets and repetitions or time for each exercise across the 8-week period

^bWk = week

^cAthletes given 30-60 s of rest between sets

recommendations for primary ACL injury prevention programs [10]. Throughout training, the trainer provided athletes with standard instructions/cues regarding their technique in order to maximize the effectiveness of the program. The specific instructions for each exercise were based on those proposed by Benjaminse et al. (2015) [30]. and were intended to promote an external focus of attention, which has been shown to result in better performance and retention of learned movement patterns for a wide-range of movement tasks (vs. an internal focus) [31]. The specific instructions we provided are included in Table 2. Athletes in the control group continued to complete their routine activities which focused on sport-specific skills training over the same 8-week period but did not receive any formal neuromuscular training.

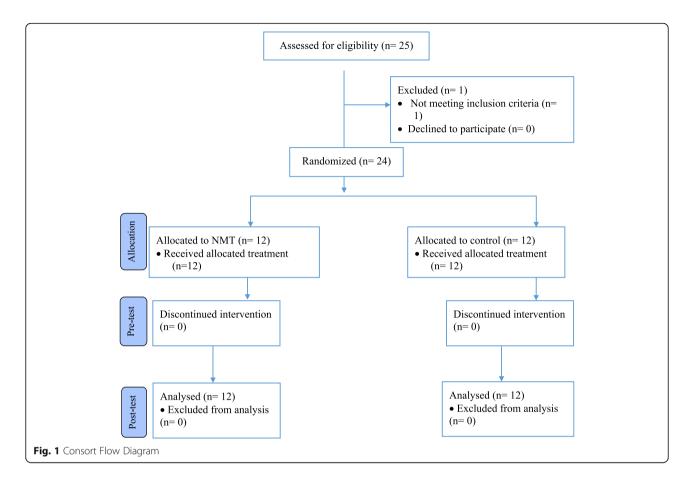
After the 8-week period, follow-up assessments of biomechanics, knee joint position sense, and patient reported function were completed for the athletes in both the experimental and control groups. The testing procedures and materials we used during this follow-up session were consistent with those utilized during baseline testing.

Statistical analysis We used two-tailed independent ttests to compare the age, mass, height, and body mass index (BMI) for the athletes in the experimental and control groups, and a Mann-Whitney U test to compare Tegner Activity Scale scores.

We used two-tailed independent t-tests to compare the groups' baseline performance for each variable. We used two-way ANCOVA with a between factor of group (experimental, control) and a within factor of time (baseline, follow-up) to compare how the groups responded over the 8-week period. In the case of a group-by-time interaction effect, we conducted as post hoc comparisons to examine changes within the groups (follow-up vs. baseline). We used an alpha of 0.05 for all tests of statistical significance. We used SPSS software for statistical analysis (IBM Corp., Armonk, NY, USA). Cohen's d effect size (ES) statistic was calculated by dividing the difference between the means by the standard deviation

Table 2 Instructions/cues provided to athletes in the experimental group during each exercise

Exercise	Instructions/Cues
Double-leg squat	While bending your knees, point your knees toward the cones and pretend you are going to sit on a chair while keeping a ball between your knees Notes: Cones positioned in line with neutral knee positions.
Walking lunge	While pretending you have a plank on your back, point your knee toward an imaginary point in front of you.
Single-leg squat	Stand on one leg and reach slowly toward the cone with your knee while bending your knee. Notes: Cone positioned in line with neutral knee position.
Double-leg drop jump	Jump down from the box, land on the markers on the floor, and point your toes and knees toward the cones Notes: Cones positioned in line with neutral knee positions; 30 cm high box.
Single-leg stance, unstable surface	Keep the bar horizontal. Notes : Athlete held bar in front of them during exercise.
Single-leg countermovement jump	Jump as high as you can and touch the hanging ball. Notes: Ball included as overhead goal; height adjusted for each athlete.
Horizontal bound	Push against the ground as forcefully as possible.
Single-leg standing long jump	Try to jump past the line. Notes: Target line provided; distance adjusted for each athlete.



from the baseline time point. Effect sizes of 0.2, 0.5, and 0.8 were considered 'small', 'moderate', and 'large' [19].

Results

There was no difference between the control and experimental groups in age (P = 0.87), mass (P = 0.91), height (P = 0.44), BMI (P = 0.67), or Tegner scores (P = 0.36) (Table 3). There were also no differences between the groups at baseline for any of the dependent variables of interest ($P \ge 0.100$), which indicates that the groups were comparable with respect to biomechanics and function. Athletes in the experimental group participated in each

Table 3	3	Athlete	demographics.
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	Control ^a	Experimental ^a	P ^c			
Age, years	27.2 ± 3.3	26.9 ± 4.1	.87			
Mass, kg	70.1 ± 6.4	70.3 ± 4.7	.91			
Height, m	1.7 ± 0.1	1.8 ± 0.1	.43			
BMI ^b , kg/m ²	23.2 ± 2.9	22.7 ± 1.7	.67			
Tegner score	4.5 (1–8)	6 (3–8)	.36			
Time since surgery (months)	7.5 ± 1.4	7.8 ± 1.7	0.96			

^aMean \pm SD or median (range) for Tegner score

^bBMI = body mass index

^cp-values (P) based on independent t-tests or Mann-Whitney U test

scheduled training session (100% compliance). All athletes who completed baseline testing also returned for follow-up testing.

The ANCOVA analyses indicated that there were group-by-time interaction effects for the peak trunk flexion (P < 0.001), peak hip flexion (P < 0.001), peak knee flexion (P < 0.001), peak knee abduction (P < 0.001), peak knee internal rotation (P < .001), position sense errors (P < 0.001) peak vGRF (P < 0.001), loading rate (P < 0.001), peak anterior tibial shear force (P < 0.001), peak knee extension moment (P < 0.001), and peak knee abduction moment (P < 0.001). Post hoc comparisons indicated that the experimental group demonstrated increased peak trunk (P = 0.003), hip (P = 0.008) and knee flexion (P = 0.012) during landing following the intervention. Further, the experimental group decreased peak knee abduction (P = 0.018), peak knee internal rotation angles (P = 0.022), loading rate (P = 0.016), peak anterior tibial shear force (P = 0.018), peak knee extension moment (P = 0.022), and peak knee abduction moment (P = 0.014), and position sense errors (P = 0.001) as well as peak vGRF (P = 0.008). There were no changes for the control group (Table 4).

The ANCOVA analyses indicated that there were group-by-time interaction effects for the IKDC scores

	Control Group	dno				Experimental Group	nl Group				
	Baseline ^a	Follow-up ^a	^d ∆ %	۲	Effect size	Baseline ^a	Follow-up ^a	4 ∆ %	Ъ	Effect size	Between group differences (ANCOVA)
Kinematics											
Peak trunk Flexion (°)	27.2 ± 10.8	27.2 ± 10.8 28.3 ± 10.7	<u>†</u> 4.01	0.259	0.050	23.2 ± 10.3	48.3 ± 10.8	108.59¢	<.001	0.76	0.003*
Peak hip Flexion (°)	38.6 ± 10.9 37.9 ±	37.9 ± 12.5	↓ 1.86	0.639	0.205	22.3 ± 6.8	35.3 ± 5.1	158.37	<.001	0.73	0.008*
Peak knee flexion (°)	23.5 ± 9.1	27.3 ± 9.2	†16.34	0.211	0.030	39.7 ± 12.54	56.8 ± 10.3	143.21	.01	09:0	0.012*
Peak knee abduction (°)	7.8 ± 1.1	7.6 ± 0.9	\ 2.68	0.114	0.101	8.1 ± 1.18	5.7 ± 0.8	J 29.64	<.001	0.77	0.018*
Peak knee internal rotation (°)	14.4 ± 1.7	14.5 ± 1.9	10.27	0.870	0.001	15.9 ± 2.15	12.8 ± 1.2	1 19.86	<.001	0.76	0.022*
Kinetics											
Peak reaction force, N/BW	3.9 ± 1.2	3.8 土 1.1	Ļ 1.81	0.075	0.030	3.4 土 1.19	2.2 ± 0.5	J 34.21	<.001	0.54	0.008*
Peak anterior Tibial shear force (BW)	0.8 ± 0.5	0.8 ± 0.7	0	0.085	0.027	0.8 ± 0.6	0.7 ± 0.5	↓ 12.5	0.01	0.66	0.018*
Peak knee extension moment (Nm/kg) 3.8 ± 1.1	3.8 ± 1.1	3.9 ± 0.8	12.6	0.120	0.029	3.5 ± 1.3	2.7 ± 0.7	J 22.85	0.01	0.59	0.022*
Peak Knee Abduction Moment (Nm/kg) 1.5 ± 1.2	1.5 ± 1.2	1.6 ± 1.1	16.66	0.073	0.032	1.6 ± 0.7	1.0 ± 0.8	1 37.5	<.001	0.64	0.014*
Loading rate (BW/S)	45.4 ± 10.7 46.9 ±	46.9 ± 8.1	13.3 1	0.093	0.022	47.6 ± 6.9	34.1 ± 8.5	J 28.36	0.01	0.81	0.016*
Position sense errors $(^{\circ})$	6.7 ± 3.7	6.5 ± 2.9	J 2.96	0.684	0.030	5.8 ± 1.67	2.8 ± 1.1	J 51.90	.01	0.73	0.001*
IKDC scores (%)	67.3 ± 8.1	68.8 ± 11.5	12.2%	.55	0.075	65.6 ± 9.7	84.7 ± 1.8	129.1%	<.001	0.80	0.003*
^a Mean ± standard deviation for each dependent variable of interest during the baseline and follow-up time points ^b % Δ = percent change (follow-up relative to baseline); Iso = isometric, Con = concentric, Ecc = eccentric; IKDC = International Knee Documentation Committee ^c p-values (P) related to post hoc paired t-tests *denoted significant differences (ANCOVA)	nt variable of in aseline); Iso = is imittee	tterest during t sometric, Con =	ne baselir concentr	ic, Ecc =	allow-up time eccentric;	points					

Table 4 Performance during the baseline and follow-up sessions for the control and experimental groups

(P < 0.001). Post hoc comparisons indicated that the experimental group increased IKDC scores (P = 0.003) following training, while there was no change in IKDC scores for the control group (P = 0.550) (Table 4). Importantly, the increase in IKDC scores for the experimental group (19.1%) exceeded the MCID associated with the measure (11.5%) (Table 4).

Discussion

This study aimed to examine the effects of a neuromuscular training program that emphasizes external focus of attention cuing on biomechanics, knee proprioception, and patient-reported function in athletes who had undergone ACL reconstruction and completed conventional post-operative rehabilitation. It is demonstrated that neuromuscular training programs using external focus of attention, such as the one used in our study, could promote improvements in landing biomechanics, proprioception, and patient-reported function in athletes with a history of ACL reconstruction.

The results of our study showed that neuromuscular training with external focus decreased loading rate and peak anterior tibial shear force. Considering that increased anterior tibial shear force is associated with increased ligament loading, this is a beneficial finding [32]. It is also reported that tibial shear force and consequently loading rate are associated with the quadriceps and hamstring muscles' characteristics. Studies have shown that quadriceps force produces anterior tibial shear force and introduces stress and strain to the ACL with the knee near full extension [33, 34]. Conversely, the hamstrings provide posterior tibial shear force, subsequently reducing the force placed on the ACL [35]. Blackburn and colleagues (2013) also stated that peak anterior tibial shear force and loading on ACL are smaller in the individuals with higher hamstrings stiffness [36]. Quadriceps and hamstring muscle forces contribute to the net shear force at the tibiofemoral joint, and therefore have important implications for ACL injury during functional tasks such as jump landing [33]. In the neuromuscular group the patients were provided with strength exercises while receiving external focus instruction. Although muscle activation and strength were not measured in the present study, we postulate that the decrease in tibial shear force and loading rate could be the results of improved dynamic function of the quadriceps and hamstrings after 8-weeks of training.

Neuromuscular training also increased trunk, hip, and knee flexion and decreased knee abduction and internal rotation compared to control participants. Reduced hip and knee flexion and increased knee abduction and internal rotation may collectively increase the risk of ACL injury [29, 37]. That our intervention can reduce these hazardous joint positions is beneficial to the patient. Our findings are consistent with recent evidence suggesting that neuromuscular training with an externally directed focus of attention, may be beneficial for ACLR rehabilitation and prevention of ACLR injury [38].

Athletes who completed our neuromuscular training program demonstrated reductions in landing forces (Table 4). Previous studies that have investigated the effects of similar programs incorporating strength training, plyometric exercise, and movement re-training have also observed significant reductions in landing forces [39]. This is encouraging, as softer landings would likely reduce ACL loading [40]. Importantly, our participants accompanied this reduction in vGRF with reductions in knee extension and abduction moments. Reducing the knee extension moment is important to decreasing ACL injury risk. The internal knee extension moment is reflective of, among other factors, increased quadriceps muscle activity [41, 42]. leading to increase anterior tibial shear force and ACL loading, during landing. Increased knee abduction moments have been suggested to contribute to ACL injury risk [43-45]; therefore, reducing all of these hazardous loads through neuromuscular training can be beneficial.

In this study, neuromuscular training emphasizing an external focus of attention yielded a 51% improvement (from 5.8 at baseline to 2.8 at follow-up stage) in position sense errors. The large improvement in joint position sense suggests that neuromuscular training using an external focus of attention may be a necessary adjunct to standard post-operative rehabilitation. Previous neuromuscular training programs in patients after ACLR have demonstrated improvement (from 5.42 to 4.45 degrees) in joint position sense [46]. We believe the difference between our study and those previously conducted is due to methodological differences in the neuromuscular training approach. The previous studies used neuromuscular training with an internal focus of attention emphasis, whereas the present study relied on external focus of attention during neuromuscular training. So, given that external focus incorporated into neuromuscular training exercises can significantly mitigate defects in proprioception after ACLR, it is recommended to use neuromuscular training with an external focus of attention emphasis for these patients. In order to maximize the effects of a neuromuscular training program it may be critical for patients to perform exercises with proper technique by receiving feedback that promotes an external focus of attention from the clinician.

It is worth noting that there were differences in hip and knee flexion angles between groups at baseline. Specifically, control participants landed with more hip, but less knee flexion compared to the experimental group. This low knee flexion posture may suggest that participants in the control group were quadriceps dominant. Previous research from our lab has demonstrated similar landing positions (e.g., less than 30degrees knee flexion) in females with established quadriceps dominance [43]. Further evidence in support of control participants being quadriceps dominant was the excessive landing contact noise noted by our investigators during testing.

From a physiological point of view, the improved joint position sense observed in this study and the characteristics of peripheral receptors can be connected; however, physiological responses of the proprioception and joint movement have not been investigated. Joint position sense improvement may be due to higher order central nervous system (CNS) adaptations to the peripheral signals from I α muscle spindles and joint receptors at the slow velocities and type II or dynamic muscle spindles at the fast movement velocities [34].

In the present study, patients in the intervention group demonstrated a 17% improvement in IKDC scores at follow-up. Previous authors have reported that the MCID for the IKDC ranges from 6.3 to 16.7 during the first 6 and 12 months, respectively, post-surgery [47]. Therefore, it can be concluded that the exercises present in this study improved patient satisfaction with the injured knee. This may be because the exercises in this study are very close to the athlete's daily movements and the athlete can keep in touch with the movements, thus improving his or her progress and feeling satisfied with their performance.

We believe that the results of our study provide valuable insight regarding the effects of neuromuscular training with an external focus of attention in athletes who have undergone ACL reconstruction; however, our study has limitations that should be considered. First, our study included a relatively homogenous sample of male athletes who had undergone hamstring autograft ACL reconstruction. As a result, we are unable to determine if our results generalize to female athletes and/or athletes who have undergone other types of ACL reconstruction procedures or had concomitant injuries. Previous studies have often used the uninjured limb as a reference standard for assessing recovery/function of the ACL reconstructed knee by creating limb symmetry indices. However, a limitation of this approach is that the uninvolved limb often becomes deconditioned during recovery, which can lead to an overestimation of the degree of function of the ACL reconstructed limb when the uninvolved limb is used as a reference standard [11]. Additionally, a group performing neuromuscular training with an emphasis on internal focus of attention was not included. Therefore, we are unable to determine if the changes observed in our participants were due to the neuromuscular training or the emphasis on external focus of attention instructions.

Conclusions

Neuromuscular training with external focus of attention cueing improved landing biomechanics in patients after ACL reconstruction. The combination of neuromuscular training with external focus cueing beneficially mitigates second ACL injury risk factors and should be emphasized during and after traditional post-operative rehabilitation.

Abbreviations

ACL: anterior cruciate ligament; IKDC: International Knee Documentation Committee questionnaire; RTS: return to sport; VGRF: vertical ground reaction force; RCT: randomized controlled trial; MCID: minimal clinically important difference; CNS: central nervous system

Acknowledgements

Not applicable.

Authors' contributions

AL, MGH, AT, SK contributed to the original idea, study design and protocol, the conception of the work, conducting the study, data analysis, revising the drafting and editing of the article. AT, and AL contributed to the conception of the work, wrote, and editing of this article. All authors approved the final version of the article.

Funding

None.

Availability of data and materials

The datasets used and/or analysed during the current study are publicly available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Faculty of Physical Education and Sport Science of the Kharazmi University. The patients were informed about the details of the study and provided written informed consent before study enrolment. Informed consent was obtained from all the participants, and procedures were conducted according to the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Received: 1 December 2020 Accepted: 27 April 2021 Published online: 08 May 2021

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CLINICAL PRACTICE GUIDELINES

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Exercise-Based Knee and Anterior Cruciate Ligament Injury Prevention

Clinical Practice Guidelines Linked to the International Classification of Functioning, Disability and Health From the Academy of Orthopaedic Physical Therapy and the American Academy of Sports Physical Therapy

J Orthop Sports Phys Ther. 2023;53(1): CPG1-CPG34. doi:10.2519/jospt.2023.0301

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Summary of Recommendations

SCIENTIFIC LITERATURE FOR EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS

A Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and anterior cruciate ligament (ACL) injuries. Programs for reducing all knee injuries include 11+ and FIFA 11, HarmoKnee, and Knäkontroll, and those used by Emery and Meeuwisse,⁵ Goodall et al,⁷ Junge et al,¹⁵ LaBella et al,¹⁸ Malliou et al,²⁰ Olsen et al,²⁵ Pasanen et al,²⁷ Petersen et al,²⁸ and Wedderkopp et al.³⁷ Programs for reducing ACL injuries include HarmoKnee, Knäkontroll, Prevent Injury and Enhance Performance (PEP), and Sportsmetrics[™], and those used by Caraffa et al,⁴ Heidt et al,¹⁰ LaBella et al,¹⁸ Myklebust et al,²³ Olsen et al,²⁵ and Petersen et al.²⁸

Clinicians may recommend the use of an exercise-based neuromuscular training program in the late phase of ACL reconstruction rehabilitation for the secondary prevention of ACL injuries.

EFFECTIVE EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS FOR SPECIFIC SUBGROUPS OF ATHLETES

Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs prior to practices/training sessions or games in women athletes to reduce the risk of ACL injuries, especially in athletes younger than 18 years of age. Programs that should be implemented include PEP, Sportsmetrics[™], Knäkontroll, HarmoKnee, and those used by Olsen et al²⁵ and Petersen et al.²⁸

A Soccer players, both women and men, should use exercise-based knee injury prevention programs to reduce the risk of severe knee and ACL injuries. Programs beneficial for preventing severe knee injuries include PEP, Knäkontroll, and HarmoKnee. Programs that could be beneficial for specifically preventing ACL injuries include the 11+, Sportsmetrics[™], and the program used by Caraffa et al.⁵

B Men and women team handball players, particularly those 15 to 17 years of age, should implement exercise-based knee injury prevention programs. Programs that could be beneficial for preventing knee injuries include those used by Olsen et al²⁵ and Achenbach et al.¹

COMPONENTS, DOSAGE, AND DELIVERY OF EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS

A Exercise-based knee injury prevention programs used for women should incorporate multiple components, proximal control exercises, and a combination of strength and plyometric exercises.

A Exercise-based knee injury prevention programs should involve training multiple times per week, training sessions that last longer than 20 minutes, and training volumes that are longer than 30 minutes per week.

A Clinicians, coaches, parents, and athletes should start exercise-based knee injury prevention programs in the preseason and continue performing the program through the regular season.

A Clinicians, coaches, parents, and athletes must ensure high compliance with exercise-based knee injury prevention programs, particularly in women athletes.

B Exercise-based knee injury prevention programs may not need to incorporate balance exercises, and balance should not be the sole component of a program.

IMPLEMENTING EXERCISE-BASED KNEE INJURY PREVENTION PROGRAMS

A Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs in all young athletes, not just those athletes identified through screening as being at high risk for ACL injury, to optimally mitigate injuries and reduce cost.

A For the greatest reduction in future medical costs and prevention of ACL injuries, osteoarthritis, and total knee replacements, clinicians, coaches, parents, and athletes should encourage implementation of exercise-based ACL injury prevention programs in athletes 12 to 25 years of age involved in sports with a high risk of ACL injury.

B Clinicians, coaches, parents, and athletes should support implementation of exercise-based knee injury prevention programs led by either coaches or a group of coaches and medical professionals.

11+: an injury prevention program developed originally	the medical committee of FIFA and the predecessor to				
by the FIFA Medical Assessment & Research Center	the 11+				
(F-MARC) (previously known as FIFA 11+)	ICD: International Classification of Diseases				
ACL: anterior cruciate ligament	ICF: International Classification of Functioning, Disability				
AE: athlete exposure	and Health				
AMSTAR: A Measurement Tool to Assess Systematic	JOSPT: Journal of Orthopaedic ଟ Sports Physical Therapy				
Reviews	KLIP: Knee Ligament Injury Prevention program				
APTA: American Physical Therapy Association	NMT: neuromuscular training				
CI: confidence interval	PEDro: Physiotherapy Evidence Database				
CPG: clinical practice guideline	PEP: Prevent Injury and Enhance Performance injury				
EMG: electromyography	prevention program				
FIFA: Fédération Internationale de Football Association	RCT: randomized controlled trial				
(international soccer governing body)	RR: relative risk				
FIFA 11: also known as "the 11," an injury prevention	RTS: return to sport				
program developed originally in association with	SIGN: Scottish Intercollegiate Guidelines Network				

Introduction

AIM OF THE GUIDELINES

The Academy of Orthopaedic Physical Therapy and the American Academy of Sports Physical Therapy have an ongoing effort to create evidence-based clinical practice guidelines (CPGs) for orthopaedic and sports physical therapy management and prevention of musculoskeletal impairments described in the World Health Organization's International Classification of Functioning, Disability and Health (ICF). This particular guideline focuses on the exercise-based prevention of knee injuries. Exercise-based prevention was defined as an intervention requiring the participant(s) to be active and move. This could include physical activity; strengthening; stretching; neuromuscular, proprioceptive, agility, or plyometric exercises; and other training modalities, but excludes passive interventions such as bracing or programs that only involve education. Knee injuries were defined as any knee joint pathology including damage to the joint (patellofemoral and/or tibiofemoral), ligaments, meniscus, or patellar tendon. The recommendations can be followed and implemented by athletes, coaches, athletic trainers, physical therapists, strength and conditioning professionals, sports scientists, physicians, surgeons, and other clinicians or health and fitness professionals.

The objectives of this CPG are as follows:

- Review the evidence in the scientific literature for exercise-based knee injury prevention programs.
- Identify exercise-based knee injury prevention programs that are effective for specific subgroups of athletes.

- Describe the evidence for the components, dosage, and delivery of exercise-based knee injury prevention programs.
- Provide suggestions for the implementation of exercise-based knee injury prevention programs.
- Create a reference publication for athletes, coaches, parents, students, interns, residents, fellows, athletic trainers, orthopaedic and sports physical therapy clinicians, academic instructors, clinical instructors, and physicians and surgeons in orthopaedics and sports regarding the best current practice of exercise-based knee injury prevention programs.

STATEMENT OF INTENT

These guidelines are not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual athlete/patient and are subject to change as scientific knowledge and technology advance and patterns of care evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every athlete or patient, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular injury prevention plan, clinical procedure, or treatment plan must be made based on experience and expertise in light of the presentation of the athlete or patient, the available evidence, available diagnostic and treatment

options, and the athlete or patient's values, expectations, and preferences. However, when providing care for athletes/patients, we suggest that significant departures from accepted guidelines should be documented in the athlete/ patient's medical records at the time the relevant clinical decision is made.

SCOPE

The aims of the revision was to provide a concise summary of the evidence published since the original guideline in 2018. Where appropriate, the revision aimed to update or revise recommendations and evidential support based on the available literature.

Methods

The Academy of Orthopaedic Physical Therapy and the American Academy of Sports Physical Therapy appointed content experts with relevant physical therapy, medical, and surgical expertise as developers and authors of the CPG for exercise-based knee injury prevention. These experts were given the task of conducting a review of the literature and describing the interventions and evidence for exercise-based knee injury prevention. The authors declared relationships and developed a conflict management plan, which included submitting a Conflict-of-Interest form to the Academy of Orthopaedic Physical Therapy, APTA, Inc. Funding was provided by the Academy of Orthopaedic Physical Therapy and American Academy of Sports Physical Therapy, and by the APTA to the CPG development team for travel and expenses for CPG development training. The CPG development team maintained editorial independence.

With the assistance of a research librarian (T.H.), the authors systematically searched PubMed, Scopus, SPORTDiscus, CINAHL, and the Cochrane databases for relevant articles. Literature searches were performed on October 23, 2020, and updated on February 18, 2022. The searches included articles published from 2017 to February 2022 to cover the period since the previous CPG.

Reference lists of included sources were hand searched for additional articles not identified in the searches (see APPEN-DIX A for full search strategies and APPENDIX B for search dates and results, available at www.orthopt.org).

Inclusion and exclusion criteria used to select relevant articles were as follows.

INCLUSION CRITERIA

- · Exercise-based knee injury prevention
- Studies needed to expressly state that knee injuries of any kind were the specific target of the program and outcome measure of the study.

Exercise-based prevention was defined as an intervention requiring the participant to be active and move their body. This could include physical activity; strengthening; stretching; neuromuscular, proprioceptive, agility, or plyometric exercises; and other training modalities, but excluded passive interventions such as bracing or programs that only involved education.

Knee injuries were defined as any knee joint pathology including damage to the joint (patellofemoral and/or tibiofemoral), ligaments, meniscus, or patellar tendon.

- · Articles that focused on preventing knee injuries as a whole were included, but so too were articles focused on only one type of knee injury (eg, anterior cruciate ligament [ACL] injuries or patellofemoral pain). This CPG delineates between evidence related to ACL injuries and all knee injuries.
- · Mechanism of injury included both contact (injuries as a result of collision with another person or object) and noncontact (injuries that do not involve another individual or object).7 This CPG discusses contact and noncontact injuries together, unless specifically noted in the text.
- Meta-analyses
- Systematic reviews
- Randomized controlled trials (RCTs)
- Cost-effectiveness studies
- · High-level cohort studies (critical appraisal score on the Scottish Intercollegiate Guidelines Network [SIGN] checklist of 5 or greater)
- · Published in a peer-reviewed journal
- · Able to access full-text articles
- Published and accessible in English

EXCLUSION CRITERIA

- Injury prevention programs aimed at preventing all lower extremity injuries
- Injury prevention programs aimed at preventing lower extremity injuries other than knee injuries (eg, ankle injury prevention programs)
- Injury prevention programs aimed at modifying risk factors for knee injuries (eg, modifying peak knee abduction moment)
- · Non-exercise-based interventions (eg, prophylactic bracing) Case series

Case-control studies

· Case studies

LITERATURE APPRAISAL

This guideline focuses on exercise-based knee injury prevention programs and excludes broader programs aimed at preventing lower extremity injuries. Lower extremity injury prevention programs target a wide range of pathologies, thus selecting different exercises or focusing athlete feedback on joints other than the knee. Furthermore, mechanisms of prevention may also differ. Programs targeting risk factors for knee injuries (eg, programs focused on modifying knee biomechanics during jump landing) were also excluded from this CPG. There are a number of modifiable and nonmodifiable risk factors for knee injuries. However, the magnitude of each risk factor for an athlete can be dependent on many other variables. For example, hormonal changes as a result of menstruation may affect women, but not men.8 Similarly, asymmetries in jump landing have been associated with knee injuries in women¹² but not, to date, in men. As an international group of experts in prevention, familiar with the prevention literature, as well as that specific to knee injuries, the authors felt that these were appropriate restrictions.

Components of training programs were defined as different exercise approaches involved in the prevention programs. For example, a program that only involved balance exercises was considered to only have 1 component, whereas a program that involved strengthening and plyometric exercises was considered to have multiple components. Common components include flexibility, strengthening, plyometrics, balance, and agility.

One author (D.S.) screened articles for full-text availability and for publication in English and in peer-reviewed journals. Two authors (A.A. and C.D. or R.K.) then independently screened articles for inclusion based on title and abstract. The authors then discussed their findings. Any article that clearly did not meet inclusion criteria based on title and abstract was excluded at this point, and the full text of any article that the authors were unsure of or that seemed to clearly meet inclusion criteria was then reviewed. If a CPG author was the author of a study eligible for potential inclusion, that author did not participate in the inclusion/exclusion decision for that paper. Full-text reviews were performed independently by two authors (A.A. and C.D. or R.K). The authors met to review their findings, and all disagreements on inclusion/exclusion were resolved by discussion and consultation with two other authors (A.G. and D.L.). Consensus was reached on all articles (see APPENDIX C for the flowchart of articles and APPENDIX D for the citations of articles included in this guideline, available at www.orthopt.org).

All authors were involved in the quality-assessment and data-extraction process. Two authors independently assessed

the quality of each article. If a CPG author was the author of an included paper, they did not participate in the quality-assessment or data-extraction process for that paper. The A MeaSurement Tool to Assess systematic Reviews (AM-STAR) tool was used to assess the quality of meta-analyses and systematic reviews.32 The Physiotherapy Evidence Database (PEDro) scale was used to assess the quality of RCTs,34 the SIGN checklist was used to assess the quality of cohort studies.31 Reliability using the quality-appraisal tools was established in the majority of authors during the creating of the 2018 guidelines. Two new authors, who did not participate in the 2018 guideline, established reliability with the lead author through independently assessing and then discussing scoring of three papers. Discrepancies in quality ratings were resolved through discussion between the 2 authors, and when needed, the lead author (A.A.) made a final decision. Studies that were authored by a reviewer were assigned to an alternate reviewer. Studies with a quality score less than 5 on any scale were considered low quality and were not used in the development of these guidelines²⁰ (see APPENDIX E for quality-assessment scores, available at www.orthopt.org). Recommendations were written based on the included articles and were agreed on by all authors. APPENDICES A to G are available on the CPG web page at www.orthopt.org.

This guideline was issued in 2023 based on the published literature up to January 2022. The guideline committee will review this CPG in 2027, or sooner if significant new evidence becomes available. Any updates to the guideline in the interim will be posted on the Academy of Orthopaedic Physical Therapy website (www.orthopt.org).

LEVELS OF EVIDENCE

Articles were graded according to criteria adapted from the Centre for Evidence-based Medicine, Oxford, United Kingdom, for diagnostic, prospective, and therapeutic studies.³¹ One team of four authors (A.A., C.D., R.K., D.L.) came to consensus and assigned a level of evidence based on the quality assessment of each article, the entire author group then approved the decisions (see **APPENDICES F** and **G** for the evidence table and details on procedures used for assigning levels of evidence, available at www.orthopt.org). An abbreviated version of the grading system is provided below.

- I Evidence obtained from systematic reviews, high-quality diagnostic studies, prospective studies, or randomized controlled trials
- II Evidence obtained from systematic reviews, lesser-quality diagnostic studies, prospective studies, or randomized controlled trials (eg, weaker diagnostic criteria and reference standards, improper randomization, no blinding, less than 80% follow-up)
- III Case-control studies or retrospective studies
- IV Case series
- V Expert opinion

GRADES OF EVIDENCE

The authors developed recommendations based on the strength of evidence, including how directly the studies addressed exercise-based knee injury prevention programs. The strength of the evidence supporting each recommendation was graded according to the previously established methods and is provided on the next page. In developing their recommendations, the authors considered the strengths and limitations of the body of evidence and the health benefits and risks of interventions.

GRA	DES OF RECOMMENDATION	STRENGTH OF EVIDENCE
A	Strong evidence	A preponderance of level I and/or level II studies support the recommendation. This must include at least one level I study
В	Moderate evidence	A single high-quality randomized controlled trial or a preponderance of level II studies support the recommendation
С	Weak evidence	A single level II study or a preponderance of level III and IV studies, including state- ments of consensus by content experts, support the recommendation
D	Conflicting evidence	Higher-quality studies conducted on this topic disagree with respect to their conclusions. The recommendation is based on these conflicting studies
E	Theoretical/foundational evidence	A preponderance of evidence from animal or cadaver studies, from conceptual models/ principles, or from basic science/bench research supports the recommendation
F	Expert opinion	Best practice based on the clinical experience of the guidelines development team

DESCRIPTION OF GUIDELINE REVIEW PROCESS AND VALIDATION

Identified reviewers who are experts in knee injury prevention or CPG methodology reviewed the CPG draft for integrity, accuracy, and ensuring that it fully represented the current evidence for the condition. The guideline draft was also posted for public comment and review on www.orthopt.org, and a notification of this posting was sent to the members of the Academy of Orthopaedic Physical Therapy, APTA, Inc. In addition, a panel of consumer/patient representatives and external stakeholders, such as coaches, athletes, parents, team organizers academic educators, clinical educators, physician specialists, and researchers, also reviewed the guideline. All comments, suggestions, and feedback from the expert reviewers, public, and consumer/patient representatives were provided to the authors and editors for consideration and revisions. Guideline development methods, policies, and implementation processes are reviewed at least yearly by the Academy of Orthopaedic Physical Therapy, APTA's ICF-Based Clinical Practice Guideline Advisory Panel, including consumer/patient representatives, external stakeholders, and experts in physical therapy practice guideline methodology.

DISSEMINATION AND IMPLEMENTATION TOOLS

In addition to publishing this guideline in the *Journal of Orthopaedic & Sports Physical Therapy (JOSPT)*, it will be highlighted and posted on the CPG web page of the *JOSPT* and the Academy of Orthopaedic Physical Therapy, APTA, and APTA websites. These web pages have unrestricted public access. Implementation tools and associated implementation strategies that will be made available for athletes, coaches, patients, physicians, surgeons, clinicians, educators, payers, policy makers, and researchers are listed in **TABLE 1**.

ANI TABLE 1 AN	LANNED STRATEGIES D TOOLS TO SUPPORT HE DISSEMINATION TO IMPLEMENTATION OF THIS CLINICAL RACTICE GUIDELINE		
Tool	Strategy		
"Perspectives for Patients" and videos for clinicians, coaches, and athletes	Patient-oriented guideline summary available on www.jospt.org and www.orthopt.org (FIGURE 1, TABLE 2)		
Mobile applications of guideline-based exercises for patients/clients, athletes, coaches, and health care practitioners	Marketing and distribution of app using www.orthopt.org		
Clinician's quick-reference guide	Summary of guideline recommenda- tions available on www.orthopt.org		
Read for Credit SM continuing education content ^a	Continuing education content available from JOSPT		
Webinar-based educational offerings for health care practitioners	Guideline-based instruction available for practitioners on www.orthopt.org		
Videos of knee injury prevention warm- up exercise sequences for field and court sport athletes	Free-access links to videos of exercise sequences available via this CPG and on www.orthopt.org and www. jospt.org		
Mobile and web-based applications for health care practitioner training	Marketing and distribution of app using www.orthopt.org		
Non-English versions of the guidelines and guideline implementation tools	Development and distribution of trans- lated guidelines and tools to JOSPT's international partners and global audience via www.jospt.org		
Interactive digital learning modules and skill-building seminars for practi- tioners to improve their knowledge of and skills for implementation of the CPGs for prevention and manage- ment of common musculoskeletal conditions	Digital resources available through www. orthopt.org and AOPT's vendor part- ners, and standardized skill-building seminar available from AOPT's CPG seminar cosponsors, worldwide		
clinical practice guideline.	^C Orthopaedic Physical Therapy; CPG, examination scores have the oppor- ory of CPG knowledge competency,		

which will be widely accessible to clients, practitioners, employers, and

payors.

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CLASSIFICATION

The primary International Classification of Diseases, Tenth Revision (ICD-10), codes and conditions associated with exercise-based knee injury prevention are as follows: "S83.2 Tear of the (medial) (lateral) meniscus of the knee," "S83.4 Sprain and strain involving (fibular) (tibial) collateral ligament of knee," "S83.5 Sprain and strain involving (anterior) (posterior) cruciate ligament of knee," "S83.7 Injury to multiple structures of knee," "S83.6 Sprain and strain of other unspecified parts of the knee," and "M22.2 Patellofemoral disorders."

The primary ICF activities and participation codes associated with exercise-based knee injury prevention are as follows: "d410 Changing basic body positions," "d450 Walking," "d4552 Running," "d4553 Jumping," "d4559 Moving around," "specified as direction changes while walking or running," "d9200 Play," "d9201 Sports," and "d9202 Arts and culture."

ORGANIZATION OF THE GUIDELINE

This CPG is arranged in relation to the following CPG objectives:

- Review the evidence in the scientific literature for exercise-based knee injury prevention programs. Evidence includes systematic reviews and meta-analyses that look at prevention programs across populations.
- Identify exercise-based knee injury prevention programs that are effective for specific subgroups of athletes. Evidence includes systematic reviews, meta-analyses, and cohort studies that specifically delineate populations.
- Describe the evidence for components, dosage, and delivery of exercise-based knee injury prevention programs.
- Provide suggestions for implementation of exercise-based knee injury prevention program

For each objective, the recommendations from the 2018 guideline are presented followed by a summary of the evidence, including the levels of evidence, a synthesis of the new evidence, a discussion of gaps in the literature, and then the new 2022 guidelines. Based on this new evidence and evidence synthesis, the updated 2022 recommendations including grades are presented at the end of each objective.

Clinical Practice Guideline

A summary of the studies included in this 2022 update are found in **TABLE 2**.

OBJECTIVES

Review the evidence in the scientific literature for exercise-based knee injury prevention programs. Evidence includes systematic reviews and meta-analyses that look at prevention programs across populations (**TABLE 2**).

2018 Recommendation

Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and ACL injuries. Programs for reducing all knee injuries include 11+ and FIFA 11, HarmoKnee, and Knäkontroll, and those used by Emery and Meeuwisse,⁵ Goodall et al,⁷ Junge et al,¹⁵ LaBella et al,¹⁸ Malliou et al,²⁰ Olsen et al,²⁵ Pasanen et al,²⁷ Petersen et al,²⁸ and Wedderkopp et al.³⁷ Programs for reducing ACL injuries include HarmoKnee, Knäkontroll, Prevent Injury and Enhance Performance (PEP), and Sportsmetrics[™], and those used by Caraffa et al,⁴ Heidt et al,¹⁰ LaBella et al,¹⁸ Myklebust et al,²³ Olsen et al,²⁵ and Petersen et al.²⁸

Evidence Update

A meta-analysis of 8 meta-analyses examined the efficacy of ACL injury prevention.³⁶ All meta-analyses indicated injury prevention programs significantly reduced the risk of ACL injury. There was a 67% reduction in risk for noncontact ACL injuries among women athletes. The findings of this meta-analysis were also supported in a systematic review by Olivares-Jabalera et al.²⁴

A systematic review with meta-analysis was performed to determine how protective ACL injury prevention programs are and what the important components of a prevention program are when accounting for study quality (randomized and cluster-randomized controls and studies that included incidence rate).¹³ Eight studies with a total of 13 562 participants were included and demonstrated a significant, 53% reduction in ACL injury rates in those participating in an injury prevention program. The specific components for injury prevention programs were not identified; however, all but 2 studies provided feedback on exercises and included at least 3 types of exercise.



Two papers reported on men and women in the same RCT examining secondary ACL injury prevention. Johnson et al¹⁴ found no significant difference in rate or side of second ACL injury (P = .77 and P = .25, respectively) between the control and intervention groups in women athletes. Additionally, no statistically significant difference was found in rate of second ACL injuries based on age categories (22.8% for <25 years old, 28.1% for <20 years old, and 30.8% for <18 years old). Although there was no difference based on type of intervention, the overall second injury rate, particularly the contralateral second injury rate was lower than the published literature.

Arundale et al² found 95% of men athletes who participated in ACL-SPORTS trial and passed RTS criteria after 1 year, with 78% of athletes returning to preinjury level of play. After 2 years, 100% passed RTS criteria and 95% returned to preinjury level. Overall second ACL injury rate was 0.025 injuries per athlete, also lower than the published literature.

Note: Studies regarding secondary ACL injury prevention were screened for both the 2018 CPG and 2022 update; however in 2018 none met inclusion/exclusion criteria. This was due to programs not being specifically targeted at second knee/ACL injuries, or the outcome measure of the study not being knee/ACL injuries.

Evidence Synthesis

2022: The evidence published since 2018 provides further support of the previous recommendation on the use of exercise-based knee and ACL injury prevention. In systematic reviews, meta-analyses, and meta-analyses of meta-analyses, there seems to be strong evidence for the benefits of exercise-based knee injury prevention programs, including reduction in risk for all knee injuries and for ACL injuries specifically, with little risk of adverse events and minimal cost.

Two studies from the same RCT provided new evidence potentially suggesting exercise-based knee injury prevention could be beneficial in secondary ACL injury prevention.

Gaps in Knowledge

Gaps in the literature still exist. Most of the exercise-based knee and ACL injury prevention programs included in this CPG are designed to be performed as dynamic warm-ups prior to training sessions/practices or games. Recently, programs not specifically focused on knee and ACL prevention have explored alternative implementation models, such as executing strengthening portions at the end of training sessions/practices.³⁸ Given the success of these programs with alternative structures, both in efficacy and implementation,

further research on alternative implementation models within knee and ACL prevention could be valuable.

Early research indicates potential value in "augmented NMT."9 Biofeedback and virtual reality present developing opportunities for athlete self-evaluation; however, research into whether an athlete's focus is internal or external and the impact of cues given during prevention programs is also needed. Thus far, many prevention programs have been focused on the physical aspects of preventing injury; however, future prevention programs may also target the brain.

Further research regarding secondary prevention using exercise-based programs is needed. Additionally, greater diversity in the athlete populations studied is crucial. The majority of exercise-based knee and ACL injury prevention studies currently come from the United States, Northern Europe, and Australia, and report minimal data sample characteristics beyond age and sex. The research and clinical communities should support communities currently underrepresented in the literature, as well as those underserved or overlooked by current health care systems.

2022 Recommendations

Clinicians should recommend use of exercise-based knee injury prevention programs in athletes for the prevention of knee and ACL injuries. Programs for reducing all knee injuries include 11+ and FIFA 11, HarmoKnee, and Knäkontroll, and those used by Emery and Meeuwisse,5 Goodall et al,7 Junge et al,15 LaBella et al,18 Malliou et al,20 Olsen et al,²⁵ Pasanen et al,²⁷ Petersen et al,²⁸ and Wedderkopp et al.³⁷ Programs for reducing ACL injuries include HarmoKnee, Knäkontroll, PEP, and Sportsmetrics[™], and those used by Caraffa et al,⁴ Heidt et al,¹⁰ LaBella et al,¹⁸ Myklebust et al,²³ Olsen et al,25 and Petersen et al.28

Clinicians may recommend the use of an exer-()cise-based neuromuscular training (NMT) program in the late phase of ACL reconstruction rehabilitation for the secondary prevention of ACL injuries.

OBJECTIVES

Identify exercise-based knee injury prevention programs that are effective for specific subgroups of athletes. Evidence includes systematic reviews, meta-analyses, and cohort studies that specifically delineate populations (TABLE 2).

2018 Recommendations

Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention А programs prior to athletic training sessions/practices or games in women athletes to reduce the risk of ACL injuries, especially in athletes younger than 18 years of age. Programs that should be implemented include PEP, Sportsmetrics[™], Knäkontroll, HarmoKnee, and those used by Olsen et al²⁵ and Petersen et al.²⁸

Soccer players, especially women, should use exercise-based knee injury prevention programs to re-A duce the risk of severe knee and ACL injuries. Programs that could be beneficial for preventing severe knee injuries include PEP, Knäkontroll, and HarmoKnee. Programs that could be beneficial for specifically preventing ACL injuries include the 11+, Sportsmetrics[™], and the program used by Caraffa et al.⁴

Men and women team handball players, particu-B larly those 15 to 17 years of age, should implement exercise-based knee injury prevention programs. Programs that could be beneficial for preventing knee injuries include those used by Olsen et al25 and Achenbach et al.¹

Evidence Update

Men

No new information.

Women



In a meta-analysis of studies looking at interventions aiming to reduce incidence of ACL injuries in women athletes, Petushek et al²⁹ found injury prevention programs that included NMT reduced ACL injury risk from 1 in 54 to 1 in 111 (odds ratio (OR), 0.51: 95% CI, 0.37, 0.69). Reduction in injury risk was greater for middle school- and high school-aged athletes (OR = 0.38; 95% CI, 0.24, 0.60) than for college and professional athletes (OR = 0.65; 95% CI, 0.48, 0.89).

Soccer

Silvers-Granelli et al33 found an overall decrease in the rate of ACL injuries in men Division I and II soccer players who participated in FIFA 11+ versus the control group (relative risk [RR] = 0.24; 95% CI: 0.07, 0.81). Examining the rate of ACL injuries in games vs practices, amongst playing positions, between field types, or only within Division I players, there were no differences in ACL injuries between the intervention and control groups. However, there was a reduction in ACL injury rate between intervention group and control groups when looking only at Division II players (RR = 0.12; 95% CI, 0.02, 0.93).

Krutsch et al¹⁷ aimed to quantify the incidence of severe knee injuries in elite football (soccer) over 1 season by comparing the injury incidence between the implementation of training modules and standard training

programs for the prevention of knee injuries. In a large scale cohort study of 26 teams (n = 529) in the intervention group and 36 teams (n = 601) in the control group, they reported a significant reduction in severe knee injury in the intervention group (0.38 per 1000 hours of football exposures; prevalence 9.8%) as compared to the control group (0.68 per 1000 hours of football exposures; prevalence 18.0% (*P* < .05).

Team Handball

No new information.

Basketball

No new information.

Vollevball

No new information.

Evidence Synthesis

The new Level 1 evidence published since 2018 around the use of exercise-based prevention programs in soccer players continues to demonstrate efficacy in reducing the risk of knee and ACL injuries. This new evidence bolsters support for the 2018 recommendations, with little risk of adverse events and minimal cost.

Gaps in Knowledge

Research in sports outside soccer is needed. There was no new research in basketball or volleyball, and high-risk team sports such as Netball, Australian Rules Football, and individual sports like skiing should be both targets of funding organizations and researchers.

2022 Recommendations



Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs prior to practices/training sessions or

games in women athletes to reduce the risk of ACL injuries, especially in athletes younger than 18 years of age. Programs that should be implemented include PEP, Sportsmetrics[™], Knäkontroll, HarmoKnee, and those used by Olsen et al²⁵ and Petersen et al.28



Soccer players, both women and men, should use exercise-based knee injury prevention programs to reduce the risk of severe knee and ACL injuries.

Programs beneficial for preventing severe knee injuries include PEP, Knäkontroll, and HarmoKnee. Programs that could be beneficial for specifically preventing ACL injuries include the 11+, Sportsmetrics[™], and the program used by Caraffa et al.4



Men and women team handball players, particularly those 15 to 17 years of age, should implement exercise-based knee injury prevention programs.

Programs that could be beneficial for preventing knee injuries include those used by Olsen et al²⁵ and Achenbach et al.1

OBJECTIVES

Describe the evidence for components, dosage, and delivery of exercise-based knee injury prevention programs.

2018 Recommendations



Exercise-based knee injury prevention programs used for women should incorporate multiple components, proximal control exercises, and a combination of strength and plyometric exercises.



Exercise-based knee injury prevention programs should involve training multiple times per week, training sessions that last longer than 20 minutes, and training volumes that are longer than 30 minutes per week.



Clinicians, coaches, parents, and athletes should start exercise-based knee injury prevention programs in the preseason and continue performing the program throughout the regular season.

Clinicians, coaches, parents, and athletes must en-А sure high compliance with exercise-based knee injury prevention programs, particularly in women athletes.



Exercise-based knee injury prevention programs may not need to incorporate balance exercises, and balance should not be the sole component of a program.

Evidence Update

Components

A prospective interventional study demonstrated that participation in hip-focused NMT reduced noncontact ACL injuries in collegiate women's basketball.27 Participants received 3 educational sessions on ACL injury-related biomechanics and then completed the intervention program 3 times a week (average of 20-minute sessions) and exercises were progressed 3 times throughout the season. Exercises included hip strengthening exercises, balance exercises, and basketball-specific jump-landing exercises. The RR for noncontact ACL injury in the intervention period versus the observation period was 0.37 and the number needed to treat for noncontact ACL injury was 41.3. Compliance rate throughout the intervention period was 89%. The authors concluded that the reduction in ACL injuries was secondary to a program with multiple components, a focus on the hip, and compliance with the intervention.

Dosage and Delivery

No new information.

Compliance

No new information.

Evidence Synthesis

There was very little new research in the area of components, dosage and delivery, as well as compliance that met the inclusion criteria of this CPG published since 2018. Only one level II study, supporting the use of proximal control/hip strengthening components within exercise-based knee and ACL injury prevention programs was added. Therefore, the evidence continues to support the previous recommendations showing benefits of exercise-based knee injury prevention programs, including reduction of risk for knee and/or ACL injuries, with little risk of adverse events and minimal cost.

Gaps in Knowledge

More research is still needed on the dose-response relationship of exercise-based knee and ACL injury prevention programs, as well as around improving compliance and adherence.

2022 Recommendations



Exercise-based knee injury prevention programs used for women should incorporate multiple components, proximal control exercises, and a combination of strength and plyometric exercises.



Exercise-based knee injury prevention programs should involve training multiple times per week, training sessions that last longer than 20 min-

utes, and training volumes that are longer than 30 minutes per week.



Clinicians, coaches, parents, and athletes should start exercise-based knee injury prevention programs in the preseason and continue performing the program throughout the regular season.



Clinicians, coaches, parents, and athletes must ensure high compliance with exercise-based knee injury prevention programs, particularly in female athletes.



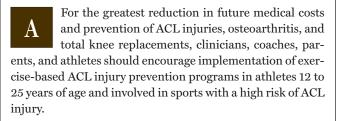
Exercise-based knee injury prevention programs may not need to incorporate balance exercises, and balance should not be the sole component of a program.

OBJECTIVES

Provide suggestions for implementation of exercise-based knee injury prevention programs.

2018 Recommendations

Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs in all young athletes, not just those athletes identified through screening as being at high risk for ACL injury, to optimize the numbers needed to treat while reducing costs.





Clinicians, coaches, parents, and athletes should support implementation of exercise-based knee injury prevention programs led by either coaches or a group of coaches and medical professionals.

Evidence Update



A retrospective survey-based study examined availability of NMT programs in high schools,²² and whether availability of these programs impacted ACL injury rates. Over 2/3 of respondents reported their high school athletes participated in NMT. Men's soccer teams participating in NMT had a significantly lower ACL injury rate (P < .005) compared to the literature when an athletic trainer was available for the team. The authors concluded that athletic trainers may help facilitate execution of training programs.

Evidence Synthesis

There was very little new evidence, meeting the inclusion criteria of this CPG, published since 2018 on implementation. The new level III evidence continues to support the previous Level I and II studies and 2018 recommendations that there is no increase in risk of adverse events when all athletes perform prevention programs compared to only athletes screened as high risk, and there is no harm in performing prevention programs. Although cost may minimally increase (depending on the program) as more athletes participate, the small increase in program costs is likely outweighed by long-term health care costs and by the reduction in ACL injuries.

Gaps in Knowledge

Research around how to engage key stakeholders in exercise-based knee and ACL injury prevention implementation is ongoing and implementation remains a crucial step to reducing the burden of knee and ACL injuries.³ Examples of key stakeholders include national governing bodies, leagues, clubs, referees and referee associations, teams, coaches, parents, athletes, health, fitness and med-

ical professionals, media professionals and networks, and many more. More research, particularly larger-scale implementation studies (observational and RCTs) are needed to bolster the evidence.

2022 Recommendations



and reduce cost.

Clinicians, coaches, parents, and athletes should implement exercise-based knee injury prevention programs in all young athletes, not just those athletes identified through screening as being at high risk for ACL injury, to optimally mitigate injuries

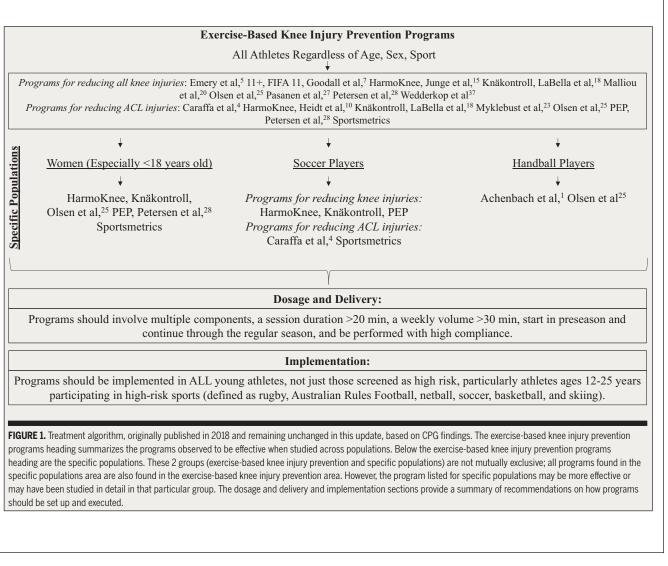


For the greatest reduction in future medical costs and prevention of ACL injuries, osteoarthritis, and total knee replacements, clinicians, coaches, parents, and athletes should encourage implementation of exercise-based ACL injury prevention programs in athletes 12 to 25 years of age who are involved in sports with a high risk of ACL injury.



Clinicians, coaches, parents, and athletes should support implementation of exercise-based knee injury prevention programs led by either coaches or a group of coaches and medical professionals.

The recommendations made in this guideline are summarized in FIGURE 1. Supplementary videos, originally published in 2018 and located at https://www.jospt.org/doi/ suppl/10.2519/jospt.2018.0303, also remain a clinical reference for clinicians based on the findings of both the 2018 and 2022 CPGs.



Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Arundale et al ²	Randomized control study	1	 Three to nine months after unilateral ACL re- construction Eighty percent quadriceps strength limb sym- metry (quadriceps index) Minimal effusion, no pain, full range of motion, and successful completion of a running progres- sion 	Athletes were exclud- ed if they (1) had a concomitant >1 cm ² full-thick- ness chondral defect (assessed via arthroscopy or MRI) or grade 3 ligamentous injury (eg, MCL or LCL), (2) had previous ACL reconstruction or a history of major lower extremity injury or surgery to either limb, or (3) had already returned to sport.	$\begin{split} N &= 40 \\ n &= 20 \text{ (intervention)} \\ n &= 20 \text{ (control)} \\ \text{Level I/II men athletes} \\ \text{Age: 15-54 years} \\ \text{Mean height: } 1.79 \pm \\ 0.07 \text{ m} \\ \text{Mean weight:} \\ 85.39 \pm 9.32 \text{ (kg)} \\ \text{Mechanism of injury:} \\ 18 \text{ contact and } 22 \\ \text{noncontact} \\ \text{Graft type: allograft =} \\ 13, \text{ hamstring} \\ \text{ autograft = 19, and} \\ \text{bone-patellar tendon-bone ligament} \\ \text{ autograft = 8} \end{split}$	Primary: Number of athletes who returned to sport Secondary: Number of athletes who re- turned to preinjury level of sport and number of second ACL injuries	Primary: 1 year after ACL-R, 95% returned to sport; 2 years after ACL-R, 100% returned to sport Secondary: 1 year after ACL-R, 78% returned to preinjury level; 2 years after ACL-R, 95% returned to preinjury level. 1 year after ACL-R, 0 athletes had a second ACL injury; 2 years after ACL-R, athlete had a second ACL injury
lohnson et al ¹⁴	Randomized control study	1	 Age: 13-55 years Planned to return to cutting/pivot- ing/jumping sport for more than 50 hours per year No previous ACL injury No history of ma- jor lower extremity injury/surgery 	 Not a level 1 or 2 athlete Previous ACL/ lower extremity injury Greater than 9 months from ACL-R Continued impair- ments Concomitant injuries 	N = 39 n = 19 (intervention) n = 20 (control) Level I/II women athletes Height: 1.65 ± 0.08 m Graft type: patella tendon = 16, ham- string autograft = 18, allograft = 5	Primary: Rate of second ACL injury in women athletes after ACL-R Secondary: Rate of ipsilateral second ACL injury	Primary: 23% reinjuny rate Secondary: 10% ipsilateral second injuny rate
				injunes			Table continues on next pag

Article	Tupo of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Poculto
luang et al ¹³	Type of Study Meta-analysis	1	 (1) The intervention aimed to prevent ACL injury. (2) The study recorded the incidence rate (IR) or other outcome data such as injury counts and AEs (ie, time at risk) that made it pos- sible to calculate ACL IR for both the intervention and control groups reported. (3) The study used a prospective randomized con- trolled trial (RCT) or cluster-RCT design. 	 Exclusion Criteria (1) Review articles (2) Editorials (3) Non-full text articles such as lectures, commentaries, abstracts, case studies, or surgical techniques (4) Articles that were not peer reviewed or not written in English 	8 studies n = 13 562 Men and women with age ranges from 12 to 25.9 years playing soccer, handball, basket- ball, or volleyball		Important Results Primary: IR = 0.47; 95% CI, 0.30- 0.73; P = .001. The rate of ACL injury was 53% less in athletes who received IPPs compared with the athletes who did not receive IPPs. Secondary: All but 2 studies met the minimum best practice recommendations of having at least 3 exercise components and provided feedback on proper exercise technique. Specific exercises and method: of delivery and training were highly variable. Subgroup analysis was not conducted given the absence of significan heterogeneity in effects across studies.
Jiivares- Jabalera et al ²⁴	Systematic review	1	 Adult (16-40 years old) soccer players, both men and women, of any level who have not suffered a severe injury in previous 2 years Exercise or training-based interventions lasted at least 4 weeks, performed twice a week Either contact or noncontact ACL injury incidence or rate of injury Test measure- ments evaluating any modifiable risk factor previously reported to have an influence in ACL injury RCTs, nonrandom- ized studies, and single-arm studies 	 Included different cohorts of athletes apart from football players Included interven- tions performed with exogenous modalities or exercise-based interventions lasting less than 4 weeks Did not explicitly report overall injury incidence of ACL-type injuries Had test-mea- sured evaluating nonmodifiable risk factors Were system- atic reviews, meta-analysis, conference papers, book chapters, or studies published in languages other than English 	N = 29 n = 6 (studies investigating exercise-based interventions on ACL injury rates) n = 23 (studies investigating exercise-based interventions on modifiable risk factors for ACL injury) Level I/II athletes Age: 16-40 years Study types: parallel RCTs = 11, cluster RCTs = 4, non-RCTs:= 8, and single-arm = 6	 Primary: Effect of exercise-based interventions on ACL injury rate for adult football players Secondary: Effect of exercise-based interventions on modifiable risk factors for ACL injury for adult football players 	 Primary: PEP and 11+ could effectively reduce ACL injury incidence. Secondary: The secondary outcomes of this study are not reported in this CPG as they are not within the scope of this CPG
							Table continues on next page

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Vebster and Hewett ³⁶	Meta-analysis	1	 (1) A meta-analysis of RCTs or prospec- tive cohort studies that evaluated the effectiveness of an ACL injury prevention training program (2) Reported data on the incidence of ACL injuries (3) Written in English 	 (1) Systematic reviews that did not pool data or perform a meta-analysis (2) Narrative reviews or those without a search algorithm or failed to de- scribe how studies were selected for the review (3) Reviews that evaluated a general or sports injury prevention program that was not specific to ACL injury prevention (4) Reviews that in- cluded nontraining interventions such as education or an external device, that is, bracing (5) Reviews that did not report ACL injury data. Meta-analyses that only focused on components of training programs (ie, specific exer- cises or dosage), compliance, or only one sport were excluded. 		Primary: Odds ratios with 95% Cls ACL injury Secondary: Odds ratios for ACL injuries in women and noncontact ACL injuries in women	Primary: ACL injuries demonstrat- ed a 50% reduction (OR = 0.5 [0.41-0.59]; I2 = 15%) in the risk of all ACL injuries in all athletes Secondary: The summary meta-analysis for noncontact ACL injuries demonstrated a 67% reduction (OR = 0.33 [0.27-0.41]; I2 = 15%) in the risk of noncontact ACL injuries in women.
							Table continues on next pag

rticle	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
vidence fo rutsch et al ¹⁷	r Specific Subgroup Cohort study	2	 (1) Elite men football player on a partici- pating team (2) Played in at least one official match during the season 	 Incomplete questionnaire No playing time during the investi- gated season Injuries prior to the start of the season. 	8 studies 26 teams; n = 529 (intervention) 36 teams; n = 601 (control) Men, mean age: 22.2 ± 4.3 years (inter- vention), 21.9 ± 4.1 (control); mean height: 1.8 ± 4.4 m; mean weight 76.3 \pm 7.5 kg	Primary: Severe knee injury incidence Secondary: ACL or PCL, MCL or LCL, cartilage or meniscus, fracture, patella dislocation, thigh injuries, ankle injuries	 Primary: Significant reduction in severe knee injury (0.38 vs 0.68/1000 h) in the interventior group Secondary: No significant differ- ence in overall injury incidence (intervention, 3.27/1000 h; control, 3.23/1000 h) No significant difference in thigh injuries, ankle injuries, or knee injuries overall MCL/LCL was significantly higher in the control group (0.3/1000 h) was injuries were the most common severe injuries in the intervention group, but not significantly different from the control group. No difference in incidence of ACL/ PCL, cartilage, fracture, or patella dislocation between the intervention and control groups
etushek et al ²⁹	Meta-analysis	1	 A prospective controlled trial study design An NMT inter- vention aimed to reduce incidence of ACL injury Included a com- parison group Recorded ACL injury incidence Women 	(1) No abstracts, posters, review papers, and irrele- vant studies	18 studies N = 27 231 Young women athletes	Primary: ACL injury odds ratio Secondary: Heterogeneity and publication bias	Primary: As a whole, NMT reduced the risk for ACL injury from 1 in 54 to 1 in 111 (OR = 0.51; 95% Cl, 0.37-0.69). Secondary: Because substantial heterogeneity was found in programming characteristics between studies (training exercises, target population, etc) and moderate statistical heterogeneity was noted, subgroup and meta-regression analyses were conducted. No significant publication bias or funnel plot asymmetry was foun- when standard error (Z = 0.92, P = .36), sample size (Z = 1.86, P = .06), and sample variance (Z = 1.07, $P = .28$) were used as predictors. Grouped ORs were similar between randomized trials (k = 11; OR = 0.54; 95% Cl, 0.35-0.83) and nonrandomized trials (k = 9; OR = 0.46; 95% Cl, 0.28-0.76).

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Silvers- Granelli et al ³³	Randomized control study	1	 Men's college soccer player that is between the ages of 18 and 25 years in good academic standing and was medically cleared to participate in the 2012 season Teams confirmed that they had not participated in an injury prevention program in the past 4 academic years. 	 Not meeting inclusion criteria Refused to participate 	27 teams N = 675 (intervention group) 34 teams; N = 850 (control group) Men college soccer player between the ages of 18 and 25 years	Primary: Reduction in overall number of ACL injuries Secondary: Reduc- tion in rate of ACL injuries based on (1) game vs practice setting, (2) player position, (3) level of play, (4) field type	Primary: Risk of ACL injuries reduced in intervention group (RR = 0.24; 95% Cl, 0.07-0.81, P = .021 Secondary: (1) No difference between groups in injury risk during games vs practices (RR = 0.31; 95% Cl, 0.09-1.11, P = .073); (2) no difference between groups in injury rate based on player position; (3) no difference between groups in Division I (RR = 0.3; 95% Cl, 0.06-1.45; $P = .136$); however, fewer ACL injuries in Division II intervention group (RR = 0.12; 95% Cl, 0.02-0.93; $P = .042$); (4) no difference between groups in ACL occurring on grass vs artificial turf (RR = 0.36; 95% Cl, 0.08-1.73; $P = .201$
Evidence for Murray	Components, Dosa Retrospective	age, and Del 3	ivery of Exercise-based Athletic directors	Knee Injury Prevention None reported	Programs 611 teams	Primary: Number of	Primary: 167 (0.6%)
et al ²²	cohort study		in Minnesota high schools that participated in high school boys' football and soccer, and girls' volleyball and soccer		N = 12 799 football (men) n = 7672 volleyball (women) n = 3111 soccer (women) and 3753 soccer (men) All athletes in high school competing for their school team	ACL injuries during sports season Secondary: Number of programs that performed IPP with a licensed athletic trainer	Secondary: 13 955 (51%) NMT was associated with fewer ACL injuries for men but not women athletes.
							Table continues on next pag

Article	Type of Study	Evidence Rating	Inclusion Criteria	Exclusion Criteria	Sample Characteristics	Outcome Measures	Important Results
Article Omi et al ²⁶	Type of Study Cohort study	2	Inclusion Criteria Must play for a women's Japanese collegiate basket- ball team	Exclusion Criteria None stated	Characteristics N = 757 n = 309 during observation period n = 448 during intervention period Women collegiate basketball players Age: 19.6 ± 1.1 years	Outcome Measures Primary: IR of all ACL injuries and noncontact ACL injuries in observa- tion vs intervention periods I and II Secondary: IR of all ACL injuries and noncontact ACL injuries in observa- tion vs intervention periods I and II RR, absolute risk re- duction, numbers needed to treat	Important Results Primary: Incidence All ACL injuries Observation 0.25/1000 AEs Intervention Periods I + II 0.10/1000 AEs RR = 0.38 (95% Cl, 0.17-0.87; $P = .017$) Incidence Noncontact ACL injuries Observation 0.21/1000 AEs Rer = 0.37 (95% Cl, 0.15-0.92; P = .026) Secondary: All ACL injuries: ARR for periods I and II = .032 (95% Cl, 0.027-0.037) while the NNT was 31.6 (95% Cl, 27.1-377) All noncontact ACL injuries: ARR for periods I and II = .0024 (95% Cl, 0.020-0.029) and NNT = 41.3 (95% Cl, 34.6-51.3) Period I Incidence All ACL = 0.11/1000 AEs RR = 0.43 (95% Cl, 0.17-1.10; $P = .07$) ARR of 0.029 (95% Cl, 0.024-0.035) and NNT of 34.0 (95% Cl, 28.9- 41.4) relative to observation Incidence Noncontact ACL = 0.09/1000 AEs. RR = .44 (95% Cl, 0.16-1.24; $P = .11$) ARR = 0.023 (95% Cl, 0.019-0.028) and NNT = 42.7 (95% Cl, 35.5- 53.6) relative to observation Period II Incidence All ACL = 0.08/1000 AEs RR = 0.32 (95% Cl, 0.09-1.09; $P = .053$) ARR = 0.035 (95% Cl, 0.030-0.040) and NNT = 28.5 (95% Cl, 24.9- 33.2) Incidence noncontact ACL = 0.08/1000 AEs RR = 0.39 (95% Cl, 0.11-1.37; P = .127) ARR = 0.025 (95% Cl, 0.021-0.031) and NNT = 39.4 (95% Cl, 3.3-48.2) Rates of compliance with the HIP training protocol during intervention periods I and II were 88% and 91%, respec- tively (TABLE 3). The mean compliance rate during the combination of intervention periods I and II was 89%.

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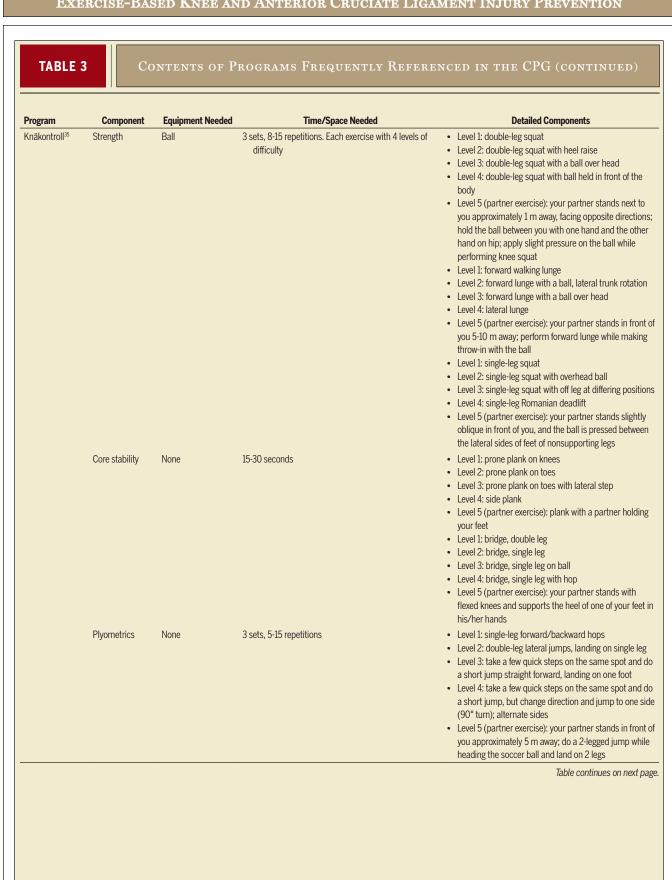
Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
Harmoknee ¹⁶	Flexibility	None	Muscle activation: approximately 2 minutes of total time, holding position and contracting the muscle for approximately 4 seconds, focusing on "finding" your muscles. Stretching is only recommended in cases of limited range of motion	 Standing calf stretch Standing quadriceps stretch Half-kneeling hamstring stretch Half-kneeling hip flexor stretch Butterfly adductor stretch Modified figure-of-four stretch
	Running	None	As part of warm-up, 10 minutes total, separate times for each	 Jogging (4-6 minutes) Backward jogging on toes (1 minute) High-knee skipping (30 seconds) Defensive pressure technique: sliding slowly, zigzag backward (30 seconds) Alternating forward zigzag running and pressure technique: zigzag backward (2 minutes)
	Strength	None	1 minute each	 Lunges in place (alternating anterior lunges) Nordic hamstring eccentric strengthening Single-leg squat with toe raise
	Core stability	None	1 minute each	Sit-upsPlank on elbowsBridging
	Plyometrics	Ball optional	30 seconds each	 Forward and backward double-leg jumps Lateral single-leg jumps Forward and backward single-leg jumps Double-leg jump with or without a ball
PEP ²¹	Flexibility	None	50 yd each, 30 × 2 repetitions each	 Calf stretch Quadriceps stretch Figure-of-four hamstring stretch Inner thigh stretch Hip flexor stretch
	Running	None	50 yd each, 2 repetitions each	 Jog from line to line of soccer field (cone to cone) Shuttle run (side to side) Backward running Shuttle run with forward/backward running (40 yd) Diagonal runs (40 yd) Bounding run (45-50 yd)
	Strength	None	Varies by exercise	 Walking lunges, 20 yd × 2 sets Russian hamstring, 3 sets × 10 repetitions or 30 seconds Single toe raises, 30 repetitions each side
	Plyometrics	Cones (5-15 cm tall)	20 repetitions or 30 seconds each	Lateral hops over coneForward/backward hops over cone

journal of orthopaedic & sports physical therapy \mid volume 53 \mid number 1 \mid january 2023 \mid CPG19



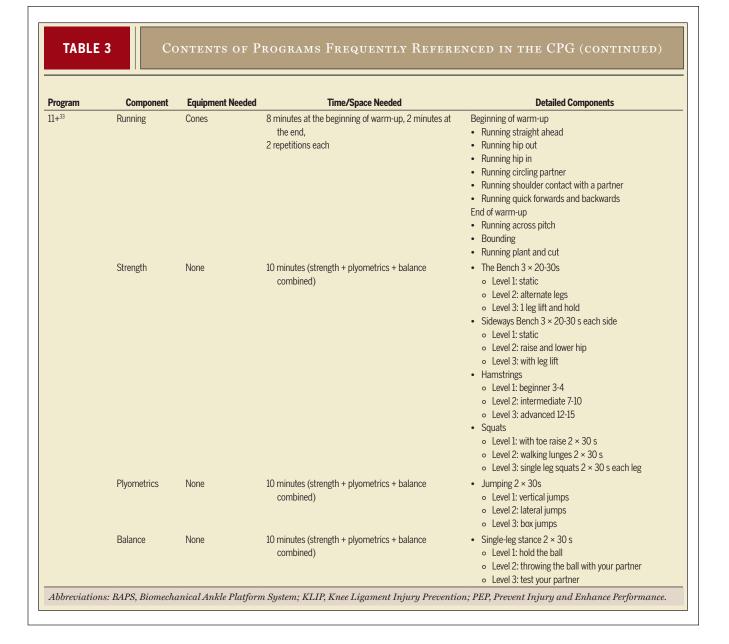
TABLE 3				CRENCED IN THE CPG (CONTINUED)
Program	Component	Equipment Needed	Time/Space Needed	Detailed Components
Olsen et al ²⁵	Running	None	30 seconds and 1 repetition each	 Jogging Backward running with sidesteps Forward running with knee lifts and heel kicks Sideways running with crossovers ("carioca") Sideways running with arms lifted ("parade") Forward running with trunk rotations Forward running with intermittent stops Speed run Bounding strides Planting and cutting
	Balance	Balance mat or wobble board	4 minutes and 2 × 90 seconds each	 Passing the ball (2-leg stance) Squats (1- or 2-leg stance) Passing the ball (1-leg stance) Bouncing the ball with eyes closed Pushing each other off balance
	Strength	None	2 minutes and 3 \times 10 repetitions each	Squats to 80° of knee flexionNordic harnstring eccentric strengthening
	Plyometrics	None	4 minutes and 5 × 30 seconds each	Jump-shot landingsForward jumps
Achenbach et al ¹	Balance	Ball optional	Not specified	Standing on 1 leg with eyes closed, try to destabilize the partner by pressing against their body
	Plyometrics	None	Not specified	Multidirectional single-leg jumps"Ice-skater" jumpsJump run
	Strength	None	Not specified	Nordic hamstring eccentric strengthening
	Core stability	None	Not specified	PlankSide plank
Caraffa et al ⁴	Balance	Rectangular wobble board, round balance board, combined round/ rectangular board, BAPS board	2.5 minutes, 4 times a day for each exercise	 Phase 1: single-leg stance, with no board Phase 2: single-leg stance on a rectangular board (on 45°) Phase 3: single-leg stance on a round board Phase 4: single-leg stance on a combined round and a rectangular board Phase 5: single-leg stance on a BAPS board
	Strength	Step	Not specified (prior to balance training)	Anterior step-upPosterior step-up
Myklebust et al ²³	Balance	Balance mat, wobble board	Not specified	 Single-leg stance on mat with throwing Standing on a mat with a partner, try to push your partner off Jump onto mat while catching the ball, then turn 180° Double-leg balance on wobble board with throwing Double-leg squat on wobble board Single-leg squat on wobble board Single-leg stance on wobble board with bounding ball Two players on wobble boards: try to push the other off
	Plyometrics	None	Not specified	 Run and plant Double-leg jump forward/backward; the partner pushes the player (perturbation) Jump shot (handball) from the 30- to 40-cm box with soft landing Step off the 30- to 40-cm box with single-leg landing

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Journal of orthopaedic \mathfrak{S} sports physical therapy \mid volume 53 \mid number 1 \mid January 2023 \mid CPG23

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ACKNOWLEDGMENTS: The authors acknowledge the contributions of George Washington University Himmelfarb Health Sciences librarian Tom Harrod for his guidance and assistance in the design and implementation of the literature search, and Doctor of Physical Therapy students Meghan Henderson and Rachel Vazque, at George Washington University for screening articles.

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APPENDIX A

SEARCH STRATEGY FOR ALL DATABASES SEARCHED

PubMed Search Strategy Search Limits (Sports [MeSH] OR Athletes [MeSH] OR Exercise [MeSH] OR Athletic Injuries [MeSH]) English only, then Clinical Trial, Clinical Trial Phase I, Clinical Trial Phase II, Clinical Trial AND ((Knee Injuries [MeSH]) OR ((Wounds and Injuries [MeSH] OR injur* [TW]) Phase III, Clinical Trial Phase IV, Comparative Study, Controlled Clinical Trial, Evaluation AND (ACL [TW] OR Anterior Cruciate Ligament* [TW] OR Anterior Cruciate Ligament Studies, Guideline, Introductory Journal Article, Journal Article, Meta-Analysis, [MeSH]))) AND (Risk Reduction Behavior [MeSH] OR Prevent* [TW] OR Predict* Multicenter Study, Observational Study, Practice Guideline, Pragmatic Clinical Trial, [TW]) Randomized Control Trial, Systematic Reviews, Twin Study Scopus Search Strategy Search Limits (TITLE-ABS-KEY (Sport*) OR TITLE-ABS-KEY (Athlet*) OR TITLE-ABS-KEY (Exercise) OR TITLE-ABS-KEY (Athletic Injur*)) AND ((TITLE-ABS-KEY (Athletic Injur*)) AND ((TITLE-ABS-KEY (Athletic Injur*)) AND ((TITLE-ABS-KEY (Athletic Injur*))) AND ((TITLE-ABS-KEY (Athletic Injur*)))) AND ((TITLE-ABS-KEY (Athletic Injur*))) AND ((TITLE-ABS-KEY (Athletic Injur*)))) AND ((TITLE-ABS-KEY (Athletic Injur*)))) AND ((TITLE-ABS-KEY (Athletic Injur*)))) AND ((TITLE-ABS-KEY (Athletic Injur*)))) AND ((TITLE-ABS-KEY (Athletic Injur*))))) English only, limit to Article, Review, KEY (Knee Injur*)) OR ((TITLE-ABS-KEY(Wound*) OR TITLE-ABS-KEY (Injur*)) AND (TITLE-ABS-KEY (Anterior Cruciate Ligament) OR and Article in Press TITLE-ABS-KEY (ACL)))) AND (TITLE-ABS-KEY (Risk Reduction) OR TITLE-ABS-KEY (Prevent*) OR TITLE-ABS-KEY (Predict*)) **SPORTDiscus** Search Strategy Search Limits ((TI (Sport*) OR AB (Sport*) OR (DE "Sports")) OR (TI (Athlet*) OR AB (Athlet*) OR (DE "ATHLETICS")) OR (TI (Exercise) OR AB (Ex-English, English Abstract only, Peer-Reercise) OR (DE "EXERCISE")) OR (TI (Athletic Injur*) OR AB (Athletic Injur*))) AND ((TI (Knee Injur*) OR AB (Knee Injur*)) OR ((((TI viewed. Academic Journal (Wound*) OR AB (Wound*)) OR (TI (Injur*) OR AB (Injur*))) OR (DE "WOUNDS & injuries")) AND ((TI (Anterior Cruciate Ligament) OR AB (Anterior Cruciate Ligament) OR (DE "ANTERIOR cruciate ligament")) OR (TI (ACL) OR AB (ACL))))) AND ((TI (Risk Reduction) OR AB (Risk Reduction)) OR (TI (Prevent*) OR AB (Prevent*) OR (DE "PREVENTION")) OR (TI (Predict*) OR AB (Predict*))) **CINAHL** Search Strategy Search Limits ((TI (Sport*) OR AB (Sport*) OR (MH "Sports+")) OR (TI (Athlet*) OR AB (Athlet*)) OR (TI (Exercise) OR English Language checkbox, Adolescent, Adult, Middle-Aged, Aged 65+. AB (Exercise) OR (MH "Exercise+")) OR (TI (Athletic Injur*) OR AB (Athletic Injur*) OR (MH "Athletic In-Aged 80+, Clinical Trial, Corrected Article, Journal Article, Practice juries+"))) AND ((TI (Knee Injur*) OR AB (Knee Injur*) OR (MH "Knee Injuries+")) OR ((TI (Wound*) OR Guidelines, Research, Systematic Review AB (Wound*) OR TI (Injur*) OR AB (Injur*) OR (MH "Wounds and Injuries+")) AND (TI (Anterior Cruciate Ligament) OR AB (Anterior Cruciate Ligament) OR TI (ACL) OR AB (ACL) OR (MH "Anterior Cruciate Ligament+")))) AND ((TI (Risk Reduction) OR AB (Risk Reduction)) OR (TI (Prevent*) OR AB (Prevent*)) OR (TI (Predict*) OR AB (Predict*))) Cochrane Search Strategy Search Limits ((Sport*) OR (Athlet*) OR (Exercise) OR (Athletic Injur*)) AND (((Knee Injur*)) OR (((Wound*) OR (Injur*)) Cochrane Reviews - ALL, Other Reviews, Trials, Technology Assess-AND ((Anterior Cruciate Ligament) OR (ACL)))) AND ((Risk Reduction) OR (Prevent*) OR (Predict*)) ments, Economic Evaluations

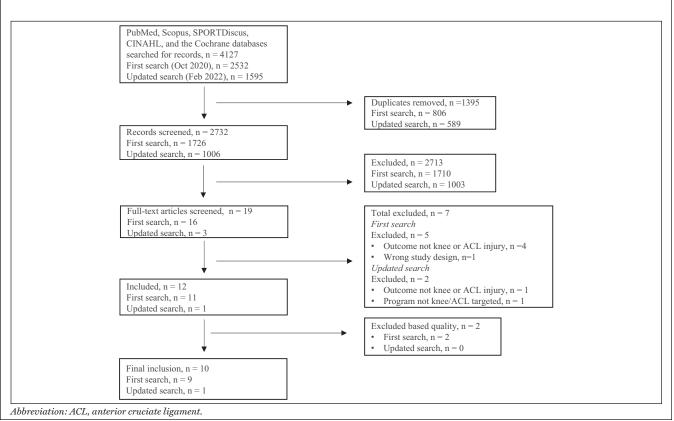
APPENDIX B

SEARCH DATES AND RESULTS

Database	Search 10/23/2020	Search 2/18/2022
PubMed	342	208
Scopus	1297	904
SportsDiscus	238	141
CINAHL	227	129
Cochrane Library	328	213
Cochrane reviews	68	36
Cochrane protocols	13	9
Trials	246	167
Clinical answers	1	1
Total	2532	1595
Total with duplicates removed	1742	1221

APPENDIX C

FLOWCHART OF LITERATURE REVIEW PROCESS



APPENDIX D

INCLUDED ARTICLES

2022

- Arundale AJH, Capin JJ, Zarzycki R, Snyder-Mackler L, Smith AH. Two year ACL reinjury rate of 2.5%: outcomes report of the men in a secondary ACL injury prevention program (ACL-Sports). *Int J Sports Phys Ther*. 2018;13:422-431. https://doi.org/10.26603/ ijspt20180422
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APPENDIX D (CONTINUED)

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APPENDIX E

QUALITY-ASSESSMENT SCORES

Systematic Reviews and Meta-analyses: AMSTAR Checklist^{a,b}

Study	1	2	3	4	5	6	7	8	9	10	11	Quality ^b
Huang et al ¹³	Х	Х	Х			Х	Х	Х	Х	Х	Х	9
Olivares-Jabalera et al ²⁴	Х		Х			Х	Х				Х	5
Petushek et al ²⁹	Х	Х	Х			Х	Х	Х	Х	Х	Х	9
Webster and Hewett ³⁶		Х		Х	Х	Х		Х				5

Abbreviation: AMSTAR, A MeaSurement Tool to Assess systematic Reviews.

*Yes/no. Items: 1, Was an a priori design provided? 2, Was there duplicate study selection and data extraction? 3, Was a comprehensive literature search performed? 4, Was the status of publication (ie, gray literature) used as an inclusion criterion? 5, Was a list of studies (included and excluded) provided? 6, Were the characteristics of the included studies provided? 7, Was the scientific quality of the included studies assessed and documented? 8, Was the scientific quality of the included studies used appropriately in formulating conclusions? 9, Were the methods used to combine the findings of studies appropriate? 10, Was the likelihood of publication bias assessed? 11, Was the conflict of interest included?

^bWhat is your overall assessment of the methodological quality of this review? Quality rating: 8 or higher, high; 5, 6, or 7, acceptable; 4 or less, reject.

Randomized Controlled Trials: Physiotherapy Evidence Database Scale (PEDro)^a

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Study	1	2	3	4	5	6	7	8	9	10	11	Quality ^b
Arundale et al ²	Х	Х	Х	Х			Х	Х	Х	Х	Х	9
Johnson et al ¹⁴	Х	Х	Х	Х			Х	Х	Х	Х	Х	9
Silvers-Granelli et al ³³	Х	Х		Х				Х	Х	Х	Х	7

"Items: 1, Eligibility criteria were specified; 2, Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received); 3, Allocation was concealed; 4, The groups were similar at baseline regarding the most important prognostic indicators; 5, There was blinding of all subjects; 6, There was blinding of all therapists who administered the therapy; 7, There was blinding of all assessors who measured at least 1 key outcome; 8, Measures of at least 1 key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9, All subjects for whom outcome measures were available received the treatment or control condition as allocated, or where this was not the case, data for at least 1 key outcome were analyzed by "intention to treat"; 10, The results of between-group statistical comparisons were reported for at least 1 key outcome; 11, The study provides both point measures and measures of variability for at least 1 key outcome.

^bQuality rating: 8 or higher, high; 5, 6, or 7, acceptable; 4 or less, reject.

Cohort Studies: Scottish Intercollegiate Guidelines Network Checklist (SIGN)^a

				<u> </u>						· · ·					
Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Quality ^b
Krutsch et al ¹⁷	Х	Х	Х		Х		Х								5
Murray et al ²²	Х	Х			N/A	N/A	Х	N/A	Х				Х	Х	6

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

^bHow well was the study done to minimize the risk of bias or confounding? Quality rating: 8 or higher, high; 5, 6, or 7, acceptable; 4 or less, reject.

APPENDIX F

LEVELS OF EVIDENCE TABLE^A

Level	Intervention/Prevention	Pathoanatomic/Risk/Clinical Course/ Prognosis/Differential Diagnosis	Diagnosis/Diagnostic Accuracy	Prevalence of Condition/ Disorder	Exam/Outcomes
I	Systematic review of high-quality RCTs High-quality RCT⁵	Systematic review of prospective cohort studies High-quality prospective cohort study ^c	Systematic review of high-qual- ity diagnostic studies High-quality diagnostic study ^d with validation	Systematic review, high-quality cross-sec- tional studies High-quality cross-sec- tional study ^e	Systematic review of prospective cohort studies High-quality prospec- tive cohort study
Ι	Systematic review of high-quality cohort studies High-quality cohort study ^c Outcomes study or ecological study Lower-quality RCT ^r	Systematic review of retrospective cohort study Lower-quality prospective cohort study High-quality retrospective cohort study Consecutive cohort Outcomes study or ecological study	Systematic review of explor- atory diagnostic studies or consecutive cohort studies High-quality exploratory diagnostic studies Consecutive retrospective cohort	Systematic review of stud- ies that allows relevant estimate Lower-quality cross-sec- tional study	Systematic review of low- er-quality prospective cohort studies Lower-quality prospective cohort study
III	Systematic reviews of case-con- trol studies High-quality case-control study Lower-quality cohort study	Lower-quality retrospective cohort study High-quality cross-sectional study Case-control study	Lower-quality exploratory diagnostic studies Nonconsecutive retrospec- tive cohort	Local nonrandom study	High-quality cross-sec- tional study
IV	Case series	Case series	Case-control study		Lower-quality cross-sec- tional study
V	Expert opinion	Expert opinion	Expert opinion	Expert opinion	Expert opinion

High-quality cohort study includes greater than 80% follow-up.

^dHigh-quality diagnostic study includes consistently applied reference standard and blinding.

*High-quality prevalence study is a cross-sectional study that uses a local and current random sample or censuses.

Weaker diagnostic criteria and reference standards, improper randomization, no blinding, and less than 80% follow-up may add bias and threats to validity.

APPENDIX G

PROCEDURES USED FOR ASSIGNING LEVELS OF EVIDENCE

Level of evidence is assigned based on the study design using the Levels of Evidence table (**APPENDIX F**), assuming high quality (eg, for intervention, randomized clinical trial starts at level I).

Study quality is assessed using the critical appraisal tool, and the study is assigned 1 of 4 overall quality ratings based on the critical appraisal results.

Level-of-evidence assignment is adjusted based on the overall quality rating:

- High quality (high confidence in the estimate/results): the study remains at the assigned level of evidence (eg, if the randomized clinical trial is rated high quality, its final assignment is level I). High quality should include the following:
 - a randomized clinical trial with greater than 80% follow-up, blinding, and appropriate randomization procedures
- a cohort study with greater than 80% follow-up
- a diagnostic study with consistently applied reference standard and blinding
- a prevalence study, which is a cross-sectional study that uses a local and current random sample or censuses
- Acceptable quality (the study does not meet requirements for high quality, and the weaknesses limit the confidence in the accuracy
 of the estimate): downgrade 1 level (based on critical appraisal results).
- Low quality: the study has significant limitations that substantially limit confidence in the estimate: downgrade 2 levels (based on critical appraisal results).
- Unacceptable quality: serious limitations-exclude from consideration in the guideline (based on critical appraisal results).