OPEN ACCESS

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

Tobias Saueressig ,[1] Tobias Braun ,[2,3] Nora Steglich,[2] Frank Diemer,[4] Jochen Zebisch,[1] Maximilian Herbst,[1] Wolfgang Zinser,[5] Patrick J Owen ,[6] Daniel L Belavy [2]

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

[1]Science and Research, Physio Meets Science GmbH, Leimen, Baden-Württemberg, Germany
[2]Department of Applied Health Sciences, Division of Physiotherapy, Hochschule für Gesundheit, Bochum, North Rhine-Westphalia, Germany
[3]HSD Hochschule Döpfer (University of Applied Sciences), Cologne, North Rhine-Westphalia, Germany
[4]DIGOTOR GbR, Brackenheim, Germany
[5]Medical Practice, OrthoExpert, 8735 Fohnsdorf, Austria
[6]Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, VIC, Australia

Correspondence to
Tobias Saueressig, Physio Meets Science GMBH, Leimen, Baden-Württemberg, Germany; t.saueressig@gmx.de

Accepted 4 August 2022

Check for updates

To cite: Saueressig T, Braun T, Steglich N, *et al*. *Br J Sports Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjsports-2021-105359

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 (CrI), 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% CrI): 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.

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 patient-reported 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.

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 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 reviews[26] 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 self-reported 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 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 I^2 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 points[38]: short- (MCID: 16.7 points), medium term (MCID: 17.0 points), long term (MCID: 17.0 points). Back-transformation 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 trial[54] employed evidence-based, progressive rehabilitation, one trial[53] based its rehabilitation on Dutch rehabilitation guidelines and one trial used[52] 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

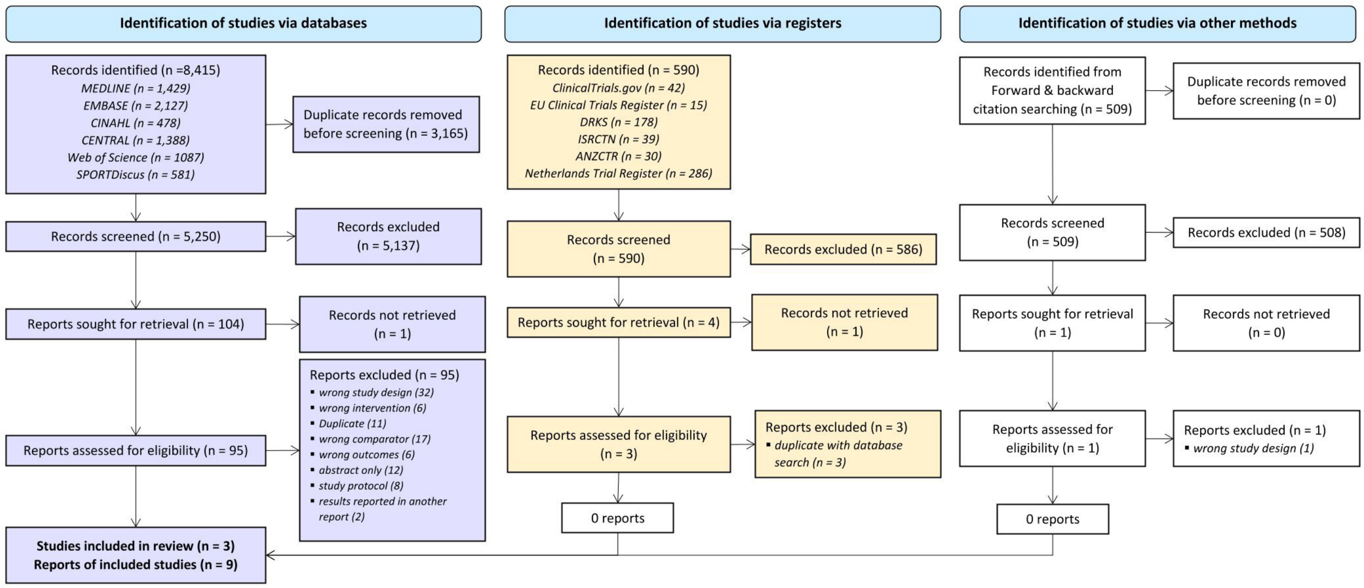

Figure 1 PRISMA flowchart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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 report[56] 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 reports[52–55] were included. Meta-analysis 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 al*[55] 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 report[63] 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

Table 1 Study characteristics

Study	Year	Study type	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
Frobell *et al*[54 55]	2010, 2013	RCT	Age: 18–35 years. Recent rotational knee trauma to previously uninjured knee within 4 preceding weeks, ACL insufficiency by clinical exam (positive pivot shift and/or positive Lachmann test), 5–9 points on TAS score before injury, complete ACL tear on MRI in isoloation or combined with meniscus tear, normal radiographic knee joint status or small-avulsed fragment (second fracture) b.JSN grade 1 or osteophytes grade 1	Earlier major knee injury to the index knee, previous knee surgery (other than diagnostic arthroscopy) to index knee, associated PCL injury or MCL injury grade III in index knee, concomitant severe injury to contra- lateral knee at the time of assessment, Injury to the lateral/posterolateral ligament complex with significantly increased Laxity, total collateral ligament rupture, full-thickness cartilage lesion on MRI, unstable longitudinal meniscus tear that requires (a) bi-compartmental extensive meniscus resections, (b) a cartilage injury with full thickness loss down to bone (c) total rupture of MCL/LCL on MRI, pregnancy, claustrophobia, history of DVT, general systemic disease, systemic medication/abuse of steroids	62/59	26.3 (5.1)/25.5 (4.7)	12/20	24.4 (3.2)/23.8 (2.6)	62(100)/ 57(97)	Progressive, supervised rehabilitation with goals for ROM, muscle function, and functional performance (four phases) + early ACL reconstruction (within 10 w after injury) by one of four senior knee surgeons, choice of procedure depended on surgeons preference(patella -tendon autograft, hamstring autograft), meniscal surgery performed as needed.	Progressive, supervised rehabilitation with goals for ROM, muscle function, and functional performance (four phases) + Elective ACL reconstruction by the same surgeons if certain criteria were met (self-reported symptomatic instability caused by ACL insufficiency and positive pivot shift test)	24 m	3 m, 6 m, 12 m, 24 m, 60 m	KOOS (without ADL scale)	SF-36, TAS, knee stability (Lachman test, pivot shift test; KT1000 arthrometry), adverse events, meniscal surgery, and radiographic osteoarthritis, KOOS5 (with ADL scale), Subgroup with KOOS-ADL Score<44
Reijman *et al*[53]	2021	RCT	Age 18–65 years, acute (within 2 m after initial trauma), complete primary ACL rupture (confirmed by MRI and clinical examination), 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, dislocated bucket handle lesion of the meniscus with extension deficit, insufficient command of the Dutch language,	85/82	31.2 (10.3)/ 31.4 (10.7)	36/31	24.3 (3.7)/25 (4.1)	76 (89.4)/ 71 (86.6)	Early ACL reconstruction (within 6 w after randomisation), surgeons chose their preferred technique and graft and decided if more intraarticular surgery was necessary, all surgeons had a minimum of 10 years experience, + physical therapy rehabilitation until good functional control was achieved.	Referral to supervised rehabilitation by physical therapist for a minimum of 3 m, physical therapy was done after Dutch ACL guidelines, after a minimum of 3 m patients had the option for reconstruction of ACL if instability persisted or activity level was not reached.	24 m	3 m, 6 m, 9 m, 12 m	IKDC	KOOS, TAS, Satisfaction (five point likert scale), serious adverse events

Continued

Table 1 Continued

Study	Year	Study type	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
Tsoukas *et al*[52]	2016	RCT	Isolated ACL injuries, BMI<30, no previous major injury or surgery to the knee, patients completed the final follow-up successfully.	Combined ACL injuries, BMI>30, prior knee surgery	17/15	29 (5.1)/ 32.3 (4.7)	17 (0)/15 (0)	NR/NR	NR/NR	ACL reconstruction, median time interval between the initial injury and beginning of treatment 6 w (range 4–8, ACL reconstruction via hamstring autograft performed by one surgeon, +rehabilitation as CON group	Rehabilitation, median time interval between the initial injury and beginning of treatment 6 w (range 4–8), passive knee motions directly after surgery, partial weight bearing for the first 6 w, full knee extension brace, stationary bike, proprioception exercises, short arc quadriceps sets and hamstring curls for 6 w, third postoperative month, jogging, swimming (in straight line), bicycle were allowed, at 6 m pivot sports (eg, ski, tennis, squash) were started, contact sports were permitted after eight m.	Median 120 m (range 120–132 m)	Median 120 m (range 120–132 m)	unclear	IKDC, knee stability (KT1000 arthrometry, 67N, 89N, 134N), knee osteoarthritis, adverse events

ACL, anterior cruciate ligament; BMI, body mass index; CON, rehabilitation (with elective delayed reconstruction); DVT, deep vein thrombosis; IKDC, International knee documentation committee score; INT, (early) surgical reconstruction; JSN, joint space narrowing; KOOS, Knee Injury and Osteoarthritis Outcome Score; m, month; NR, not reported; ROM, Range of Motion; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; TAS, Tegner Activity Scale; w, week; y, year.

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

Outcome **(follow-up time point)**	**Studies included in meta-analysis**	**Total N**	**Intervention**	**Control**	Effect size **(95% CrI)**	95% prediction interval*	Raw mean difference†/risk difference‡ **(95% CrI)**	Certainty rating
Primary outcomes								
Self-reported knee function§ (Short-term)	Frobell *et al*[54], Reijman *et al*[53]	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 *et al*[54], Reijman *et al*[53]	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 *et al*[55], Tsoukas *et al*[52]	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 *et al*[54], Reijman *et al*[53], Tsoukas *et al*[52]	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 *et al*[55], Tsoukas *et al*[52]	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 *et al.*[54], Reijman *et al*([53]	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 *et al*[54], Reijman *et al*[53]	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 *et al*[54], Reijman *et al*[53]	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 *et al*[55], Tsoukas *et al*[52]	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 *et al*[54], Reijman *et al*[53], Tsoukas *et al*[52]	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 *et al*[54], Reijman *et al*[53]	288	Early reconstruction	Rehabilitation+optional reconstruction	OR 2.3, (0.4 to 12.4)	(0.3 to 20)	−26 per 1000 patients, (12, -186)	**Very low¶††**

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

Table 3 Certainty of evidence (GRADE approach) of individual study outcomes

Outcome **(follow-up time point)**	Study	Total N	Intervention	Control	Effect size (95% CI)	Certainty rating
Primary outcomes						
Meniscal injuries (Long-term)	Snoeker *et al*[59]	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 *et al*[55]	120	Early reconstruction	Rehabilitation+optional reconstruction	SMD −0.14, (−0.50 to 0.21)	**Low***
Self-reported return to activity‡ (Short-term)	Reijman *et al*[53]	167	Early reconstruction	Rehabilitation+optional reconstruction	SMD −0.34, (−0.66 to −0.03)	**Moderate§**
Knee stability (Medium-term)	Frobell *et al*[54]	121	Early reconstruction	Rehabilitation+optional reconstruction	MD −1.70, (−2.65 to −0.75)	**Moderate***
knee stability (Long-term)	Tsoukas *et al*[52]	32	Early reconstruction	Rehabilitation+optional reconstruction	MD-3.00, (−3.27 to −2.73)	**Low§**
Patello-femoral cartilage thickness (Medium-term)	Culvenor *et al*[60]	120	Early reconstruction	Rehabilitation+optional reconstruction	MD 76.00, (10.63 to 141.37)	**Moderate***
Patello-femoral cartilage thickness (Long-term)	Culvenor *et al*[60]	120	Early reconstruction	Rehabilitation+optional reconstruction	MD 107.00, (17.33 to 196.67)	**Moderate***
Meniscal surgeries (Long-term)	Snoeker *et al*[59]	121	Early reconstruction	Rehabilitation+optional reconstruction	OR 0.88, (0.47 to 1.62)	**Low***
Cost-effectiveness (Medium-term)	Eggerding *et al*[57]	167	Early reconstruction	Rehabilitation+optional reconstruction	MD 0.04, (p=0.18), not cost-effective	**Moderate§**
Cost-effectiveness (Long-term)	Kiadaliri *et al*[58]	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 *et al*[56]	89	Early reconstruction	Rehabilitation+optional reconstruction	MD 1.10, (−2.98 to 5.18)	**Low***
Single leg-hop limb symmetry index (Long-term)	Flosadottir *et al*[56]	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)*.
NA, not applicable.

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

Results from single studies

One study[55] 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.

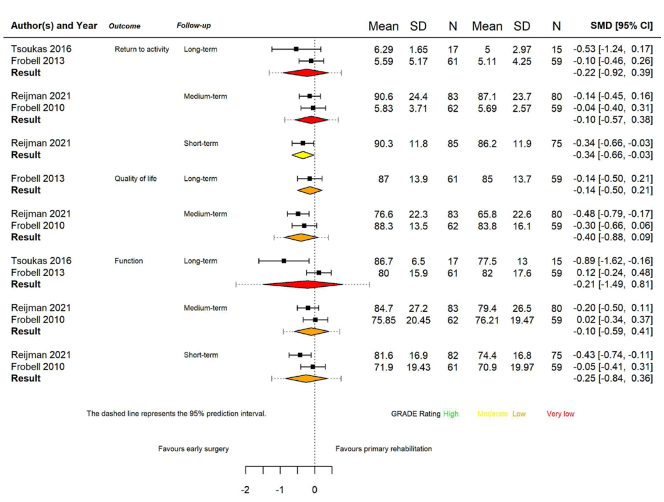

Figure 2 Overview of continuous outcomes for the comparison early surgery versus rehabilitation with optional surgery. The used software sets the limit automatically to the 95% CrIs and not the 95% prediction intervals (dashed lines). As the highest value of a 95% CrI is 0.81 it sets the positive limit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

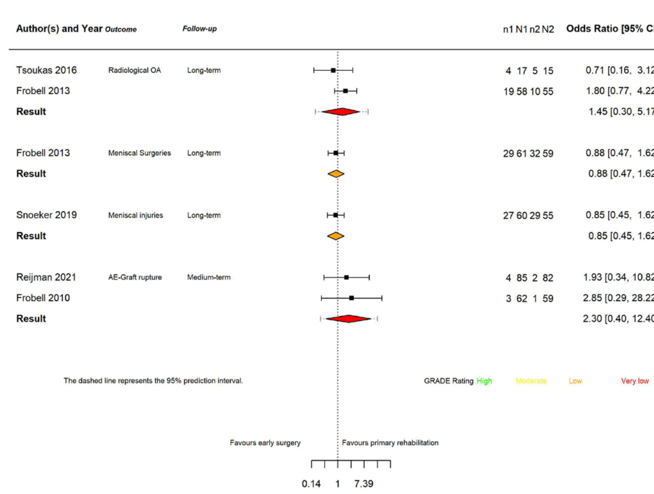

Figure 3 Overview of dichotomous outcomes for the comparison early surgery vs rehabilitation with optional surgery.

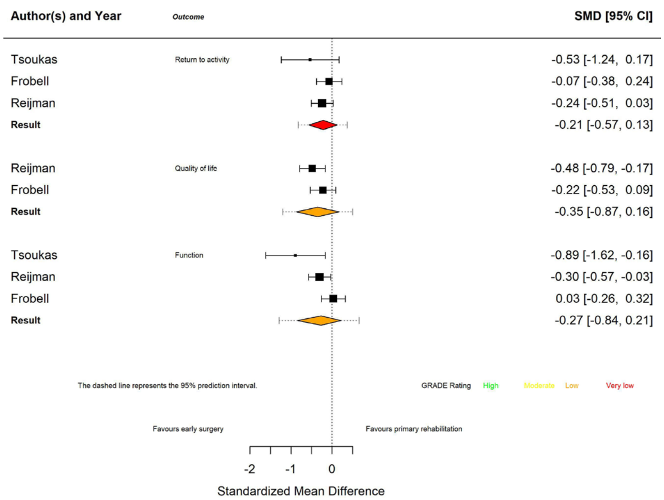

Figure 4 Overview of continuous outcomes for the comparison early surgery versus rehabilitation with optional surgery for all time points combined. SMD, standardised mean difference.

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 al*[55] 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 study[53] 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 report[55] 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 study[53] was funded by a professional organisation. Another study[54] had mixed funding of private or professional and governmental organisations. One study[52] did not report their funding source. The authors declared no conflict of interest in two studies,[52 53] whereas one study[54] 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 osteoarthritis[71] 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 recommendation[92] 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 decision-making 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, patient-centred form of care that discusses the potential treatment options with the patient.

Twitter Tobias Saueressig @PhysioMeScience, Patrick J Owen @PatrickOwenPhD and Daniel L Belavy @belavyprof

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.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs
Tobias Saueressig http://orcid.org/0000-0002-3332-3856
Tobias Braun http://orcid.org/0000-0002-8851-2574
Patrick J Owen http://orcid.org/0000-0003-3924-9375
Daniel L Belavy http://orcid.org/0000-0002-9307-832X

REFERENCES

1 Moses B, Orchard J, Orchard J. Systematic review: annual incidence of ACL injury and surgery in various populations. *Res Sports Med* 2012;20:157–79.
2 Montalvo AM, Schneider DK, Webster KE, *et al*. Anterior cruciate ligament injury risk in sport: a systematic review and meta-analysis of injury incidence by sex and sport classification. *J Athl Train* 2019;54:472–82.
3 Bram JT, Magee LC, Mehta NN, *et al*. Anterior cruciate ligament injury incidence in adolescent athletes: a systematic review and meta-analysis. *Am J Sports Med* 2021;49:1962–72.
4 Filbay SR, Ackerman IN, Russell TG, *et al*. Health-Related quality of life after anterior cruciate ligament reconstruction: a systematic review. *Am J Sports Med* 2014;42:1247–55.
5 Filbay SR, Culvenor AG, Ackerman IN, *et al*. Quality of life in anterior cruciate ligament-deficient individuals: a systematic review and meta-analysis. *Br J Sports Med* 2015;49:1033–41.
6 Filbay SR, Crossley KM, Ackerman IN. Activity preferences, lifestyle modifications and re-injury fears influence longer-term quality of life in people with knee symptoms following anterior cruciate ligament reconstruction: a qualitative study. *J Physiother* 2016;62:103–10.
7 Cameron KL, Thompson BS, Peck KY, *et al*. Normative values for the KOOS and WOMAC in a young athletic population: history of knee ligament injury is associated with lower scores. *Am J Sports Med* 2013;41:582–9.
8 Lai CCH, Ardern CL, Feller JA, *et al*. Eighty-three per cent of elite athletes return to preinjury sport after anterior cruciate ligament reconstruction: a systematic review with meta-analysis of return to sport rates, graft rupture rates and performance outcomes. *Br J Sports Med* 2018;52:128–38.
9 Ardern CL, Webster KE, Taylor NF, *et al*. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med* 2011;45:596–606.
10 Webster KE, Hewett TE. Anterior cruciate ligament injury and knee osteoarthritis: an umbrella systematic review and meta-analysis. *Clin J Sport Med* 2022;32:145–52.
11 Poulsen E, Goncalves GH, Bricca A, *et al*. Knee osteoarthritis risk is increased 4-6 fold after knee injury - a systematic review and meta-analysis. *Br J Sports Med* 2019;53:1454–63.
12 Ekås GR, Ardern CL, Grindem H, *et al*. Evidence too weak to guide surgical treatment decisions for anterior cruciate ligament injury: a systematic review of the risk of new meniscal tears after anterior cruciate ligament injury. *Br J Sports Med* 2020;54:520–7.
13 Davies L, Cook J, Leal J, *et al*. Comparison of the clinical and cost effectiveness of two management strategies (rehabilitation versus surgical reconstruction) for non-acute anterior cruciate ligament (ACL) injury: study protocol for the ACL SNNAP randomised controlled trial. *Trials* 2020;21:405.
14 Herzog MM, Marshall SW, Lund JL, *et al*. Cost of outpatient arthroscopic anterior cruciate ligament reconstruction among commercially insured patients in the United States, 2005-2013. *Orthop J Sports Med* 2017;5:2325967116684776.
15 Zbrojkiewicz D, Vertullo C, Grayson JE. Increasing rates of anterior cruciate ligament reconstruction in young Australians, 2000-2015. *Med J Aust* 2018;208:354–8.
16 Mather RC, Hettrich CM, Dunn WR, *et al*. Cost-Effectiveness analysis of early reconstruction versus rehabilitation and delayed reconstruction for anterior cruciate ligament tears. *Am J Sports Med* 2014;42:1583–91.
17 Filbay SR, Grindem H. Evidence-Based recommendations for the management of anterior cruciate ligament (ACL) rupture. *Best Pract Res Clin Rheumatol* 2019;33:33–47.
18 Zadro JR, Pappas E. Time for a different approach to anterior cruciate ligament injuries: educate and create realistic expectations. *Sports Med* 2019;49:357–63.
19 Diermeier TA, Rothrauff BB, Engebretsen L, *et al*. Treatment after ACL injury: panther symposium ACL treatment consensus group. *Br J Sports Med* 2021;55:14–22.
20 Paschos NK, Howell SM. Anterior cruciate ligament reconstruction: principles of treatment. *EFORT Open Rev* 2016;1:398–408.
21 Monk AP, Davies LJ, Hopewell S, *et al*. Surgical versus conservative interventions for treating anterior cruciate ligament injuries. *Cochrane Database Syst Rev* 2016;4:CD011166.
22 Krause M, Freudenthaler F, Frosch K-H, *et al*. Operative versus conservative treatment of anterior cruciate ligament rupture. *Dtsch Arztebl Int* 2018;115:855–62.
23 Lien-Iversen T, Morgan DB, Jensen C, *et al*. Does surgery reduce knee osteoarthritis, meniscal injury and subsequent complications compared with non-surgery after ACL rupture with at least 10 years follow-up? A systematic review and meta-analysis. *Br J Sports Med* 2020;54:592–8.
24 Chalmers PN, Mall NA, Moric M, *et al*. Does ACL reconstruction alter natural history?: a systematic literature review of long-term outcomes. *J Bone Joint Surg Am* 2014;96:292–300.

25 Smith TO, Postle K, Penny F, *et al*. Is reconstruction the best management strategy for anterior cruciate ligament rupture? A systematic review and meta-analysis comparing anterior cruciate ligament reconstruction versus non-operative treatment. *Knee* 2014;21:462–70.
26 Winters M, de Vos R-J, van Middelkoop M, *et al*. Stay alive! what are living systematic reviews and what are their advantages and challenges? *Br J Sports Med* 2021;55:519–20.
27 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
28 Ardern CL, Büttner F, Andrade R, *et al*. Implementing the 27 PRISMA 2020 statement items for systematic reviews in the sport and exercise medicine, musculoskeletal rehabilitation and sports science fields: the persist (implementing Prisma in exercise, rehabilitation, sport medicine and sports science) guidance. *Br J Sports Med* 2022;56:175–95.
29 Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. *Clin Orthop Relat Res* 2016;474:1886–93.
30 Herbert R, Jamtvedt G, Hagen KB. *Practical evidence-based Physiotherapy-E-Book*. Elsevier Health Sciences, 2011.
31 Sterne JAC, Savović J, Page MJ, *et al*. Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
32 Higgins JPT, Thomas J, Chandler J. *Cochrane Handbook for systematic reviews of interventions*. John Wiley & Sons, 2019.
33 Nikolakopoulou A, Higgins JPT, Papakonstantinou T, *et al*. Cinema: an approach for assessing confidence in the results of a network meta-analysis. *PLoS Med* 2020;17:e1003082.
34 Borenstein M, Higgins JPT, Hedges LV, *et al*. Basics of meta-analysis: I^2 is not an absolute measure of heterogeneity. *Res Synth Methods* 2017;8:5–18.
35 Guyatt GH, Oxman AD, Montori V, *et al*. GRADE guidelines: 5. Rating the quality of evidence--publication bias. *J Clin Epidemiol* 2011;64:1277–82.
36 Hespanhol L, Vallio CS, Costa LM, *et al*. Understanding and interpreting confidence and credible intervals around effect estimates. *Braz J Phys Ther* 2019;23:290–301.
37 Cohen J. *Statistical power analysis for the behavioral sciences*. *2nd edn*. Hillsdale, NJ, USA: Á/L. Erbaum Press, 1988.
38 Çelik D, Çoban Özge, Kılıçoğlu Önder. Minimal clinically important difference of commonly used hip-, knee-, foot-, and ankle-specific questionnaires: a systematic review. *J Clin Epidemiol* 2019;113:44–57.
39 Borenstein M, Hedges LV, Higgins JP. *Introduction to meta-analysis*, 2009.
40 Friede T, Röver C, Wandel S, *et al*. Meta-Analysis of two studies in the presence of heterogeneity with applications in rare diseases. *Biom J* 2017;59:658–71.
41 Friede T, Röver C, Wandel S, *et al*. Meta-Analysis of few small studies in orphan diseases. *Res Synth Methods* 2017;8:79–91.
42 Bender R, Friede T, Koch A, *et al*. Methods for evidence synthesis in the case of very few studies. *Res Synth Methods* 2018;9:382–92.
43 Saueressig T, Pedder H, Bowe SJ. *Six meta-analyses on treatments for femoroacetabular impingement syndrome in a year and readers are none the Wiser: methods advice for researchers planning meta-analysis of data from fewer than 5 trials*. JOSPT, 1033 North Fairfax Street, Suite 304, Alexandria, VA …: JOSPT, Inc, 2021.
44 Mavridis D, Salanti G. How to assess publication bias: funnel plot, trim-and-fill method and selection models. *Evid Based Ment Health* 2014;17:30.
45 McGrath S, Sohn H, Steele R, *et al*. Meta-Analysis of the difference of medians. *Biom J* 2020;62:69–98.
46 R Core Team. *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing, 2017. https://www.R-project.org/
47 Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health* 2019;22:153–60.
48 Röver C. Bayesian Random-Effects Meta-Analysis Using the **bayesmeta** *R* Package. *J Stat Softw* 2020;93.
49 Viechtbauer W. Conducting Meta-Analyses in *R* with the **metafo***r* Package. *J Stat Softw* 2010;36:1–48.
50 Rücker G, Krahn U, König J. netmeta: network meta-analysis using Frequentist methods, 2021. Available: https://CRAN.R-project.org/package=netmeta
51 van Valkenhoef G, Lu G, de Brock B, *et al*. Automating network meta-analysis. *Res Synth Methods* 2012;3:285–99.
52 Tsoukas D, Fotopoulos V, Basdekis G, *et al*. No difference in osteoarthritis after surgical and non-surgical treatment of ACL-injured knees after 10 years. *Knee Surg Sports Traumatol Arthrosc* 2016;24:2953–9.
53 Reijman M, Eggerding V, van Es E, *et al*. Early surgical reconstruction versus rehabilitation with elective delayed reconstruction for patients with anterior cruciate ligament rupture: compare randomised controlled trial. *BMJ* 2021;372:n375.
54 Frobell RB, Roos EM, Roos HP, *et al*. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med* 2010;363:331–42.
55 Frobell RB, Roos HP, Roos EM, *et al*. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *BMJ* 2013;346:f232.
56 Flosadottir V, Frobell R, Roos EM, *et al*. Impact of treatment strategy and physical performance on future knee-related self-efficacy in individuals with ACL injury. *BMC Musculoskelet Disord* 2018;19:50.
57 Eggerding V, Reijman M, Meuffels DE, *et al*. Acl reconstruction for all is not cost-effective after acute ACL rupture. *Br J Sports Med* 2022;56:24–8.
58 Kiadaliri AA, Englund M, Lohmander LS, *et al*. No economic benefit of early knee reconstruction over optional delayed reconstruction for ACL tears: registry enriched randomised controlled trial data. *Br J Sports Med* 2016;50:558–63.
59 Snoeker BAM, Bowes MA, Roemer FW, *et al*. Is meniscal status in the anterior cruciate ligament injured knee associated with change in bone surface area? an exploratory analysis of the KANON trial. *Osteoarthritis Cartilage* 2021;29:841–8.
60 Culvenor AG, Eckstein F, Wirth W, *et al*. Loss of patellofemoral cartilage thickness over 5 years following ACL injury depends on the initial treatment strategy: results from the KANON trial. *Br J Sports Med* 2019;53:1168–73.
61 Ekås GR. Improving the Treatment of Anterior Cruciate Ligament Tears in Norway With Register-RCTs - Who Should Have Surgery. clinicaltrials.gov, 2021. Available: https://clinicaltrials.gov/ct2/show/NCT04770233 [Accessed 22 Sep 2021].
62 Smeets A, Ghafelzadeh Ahwaz F, Bogaerts S, *et al*. Pilot study to investigate the feasibility of conducting a randomised controlled trial that compares immediate versus optional delayed surgical repair for treatment of acute anterior cruciate ligament injury: IODA pilot trial. *BMJ Open* 2022;12:e055349.
63 Snoeker BA, Roemer FW, Turkiewicz A, *et al*. Does early anterior cruciate ligament reconstruction prevent development of meniscal damage? results from a secondary analysis of a randomised controlled trial. *Br J Sports Med* 2020;54:612–7.
64 Escobar A, Quintana JM, Bilbao A, *et al*. Responsiveness and clinically important differences for the WOMAC and SF-36 after total knee replacement. *Osteoarthritis Cartilage* 2007;15:273–80.
65 Harris JD, Brand JC, Cote MP, *et al*. Research pearls: the significance of statistics and perils of pooling. Part 1: clinical versus statistical significance. *Arthroscopy* 2017;33:1102–12.
66 Roos EM, Boyle E, Frobell RB, *et al*. It is good to feel better, but better to feel good: whether a patient finds treatment 'successful' or not depends on the questions researchers ask. *Br J Sports Med* 2019;53:1474–8.
67 Muller B, Yabroudi MA, Lynch A, *et al*. Defining thresholds for the patient acceptable symptom state for the IKDC subjective knee form and KOOS for patients who underwent ACL reconstruction. *Am J Sports Med* 2016;44:2820.
68 Nordenvall R, Bahmanyar S, Adami J, *et al*. Cruciate ligament reconstruction and risk of knee osteoarthritis: the association between cruciate ligament injury and post-traumatic osteoarthritis. A population based nationwide study in Sweden, 1987-2009. *PLoS One* 2014;9:e104681.
69 Harris KP, Driban JB, Sitler MR, *et al*. Tibiofemoral osteoarthritis after surgical or nonsurgical treatment of anterior cruciate ligament rupture: a systematic review. *J Athl Train* 2017;52:507–17.
70 Diemer F, Zebisch J, Saueressig T. [Consequences of anterior cruciate ligament rupture: a systematic umbrella review]. *Sportverletz Sportschaden* 2022;36:18–37.
71 Ajuied A, Wong F, Smith C, *et al*. Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: a systematic review and meta-analysis. *Am J Sports Med* 2014;42:2242–52.
72 Luc B, Gribble PA, Pietrosimone BG. Osteoarthritis prevalence following anterior cruciate ligament reconstruction: a systematic review and numbers-needed-to-treat analysis. *J Athl Train* 2014;49:806–19.
73 Achtnich A, Akoto R, Petersen W. Indikation zum Ersatz des vorderen Kreuzbandes. *Knie J* 2019;1:83–4.
74 Petersen W, Scheffler S, Mehl J. Der präventive Effekt Der Kreuzband-Plastik Im Hinblick auf sekundäre Meniskus- und Knorpelschäden. *Sports Orthopaedics and Traumatology* 2018;34:93–104.
75 Mehl J, Scheffler S, Petersen W. Protektiver Effekt Der Vorderen-Kreuzband-Plastik. *Knie J* 2019;1:85–90.
76 Hunt ER, Jacobs CA, Conley CE-W, *et al*. Anterior cruciate ligament reconstruction reinitiates an inflammatory and chondrodegenerative process in the knee joint. *J Orthop Res* 2021;39:1281–8.
77 Larsson S, Struglics A, Lohmander LS, *et al*. Surgical reconstruction of ruptured anterior cruciate ligament prolongs trauma-induced increase of inflammatory cytokines in synovial fluid: an exploratory analysis in the KANON trial. *Osteoarthritis Cartilage* 2017;25:1443–51.
78 Whittaker JL, Roos EM. A pragmatic approach to prevent post-traumatic osteoarthritis after sport or exercise-related joint injury. *Best Pract Res Clin Rheumatol* 2019;33:158–71.
79 Tashman S, Zandiyeh P, Irrgang JJ, *et al*. Anatomic single- and double-bundle ACL reconstruction both restore dynamic knee function: a randomized clinical trial-part II: knee kinematics. *Knee Surg Sports Traumatol Arthrosc* 2021;29:2676–83.
80 Irrgang JJ, Tashman S, Patterson CG, *et al*. Anatomic single vs. double-bundle ACL reconstruction: a randomized clinical trial-Part 1: clinical outcomes. *Knee Surg Sports Traumatol Arthrosc* 2021;29:2665–75.
81 Nagai K, Gale T, Irrgang JJ, *et al*. Anterior cruciate ligament reconstruction affects Tibiofemoral joint Congruency during dynamic functional movement. *Am J Sports Med* 2018;46:1566–74.
82 Eckstein F, Wirth W. Quantitative cartilage imaging in knee osteoarthritis. *Arthritis* 2011;2011:1–19.

83 Pairot-de-Fontenay B, Willy RW, Elias ARC, *et al*. Running biomechanics in individuals with anterior cruciate ligament reconstruction: a systematic review. *Sports Med* 2019;49:1411–24.
84 Hart HF, Culvenor AG, Collins NJ, *et al*. Knee kinematics and joint moments during gait following anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Br J Sports Med* 2016;50:597–612.
85 Hajizadeh M, Hashemi Oskouei A, Ghalichi F, *et al*. Knee kinematics and joint moments during Stair negotiation in participants with anterior cruciate ligament deficiency and reconstruction: a systematic review and Meta-Analysis. *Pm R* 2016;8:563.
86 Nawasreh Z, Logerstedt D, Cummer K, *et al*. Functional performance 6 months after ACL reconstruction can predict return to participation in the same preinjury activity level 12 and 24 months after surgery. *Br J Sports Med* 2018;52:375.
87 Pietrosimone B, Lepley AS, Harkey MS, *et al*. Quadriceps strength predicts self-reported function post-acl reconstruction. *Med Sci Sports Exerc* 2016;48:1671–7.
88 Pietrosimone B, Pfeiffer SJ, Harkey MS, *et al*. Quadriceps weakness associates with greater T1ρ relaxation time in the medial femoral articular cartilage 6 months following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2019;27:2632–42.
89 Culvenor AG, Patterson BE, Guermazi A, *et al*. Accelerated return to sport after anterior cruciate ligament reconstruction and early knee osteoarthritis features at 1 year: an exploratory study. *Pm R* 2018b;10:349–56.
90 Haberfield MJ, Patterson BE, Crossley KM, *et al*. Should return to pivoting sport be avoided for the secondary prevention of osteoarthritis after anterior cruciate ligament reconstruction? A prospective cohort study with MRI, radiographic and symptomatic outcomes. *Osteoarthritis Cartilage* 2021;29:1673–81.
91 Øiestad BE, Holm I, Risberg MA. Return to pivoting sport after ACL reconstruction: association with osteoarthritis and knee function at the 15-year follow-up. *Br J Sports Med* 2018;52:1199–204.
92 Diermeier T, Rothrauff BB, Engebretsen L, *et al*. Treatment after anterior cruciate ligament injury: panther symposium ACL treatment consensus group. *Knee Surg Sports Traumatol Arthrosc* 2020;28:2390–402.
93 Grindem H, Eitzen I, Engebretsen L, *et al*. Nonsurgical or surgical treatment of ACL injuries: knee function, sports participation, and knee Reinjury: the Delaware-Oslo ACL cohort study. *J Bone Joint Surg Am* 2014;96:1233–41.
94 Waldén M, Hägglund M, Magnusson H, *et al*. Anterior cruciate ligament injury in elite football: a prospective three-cohort study. *Knee Surg Sports Traumatol Arthrosc* 2011;19:11–19.
95 Keays SL, Newcombe P, Keays AC. Nearly 90% participation in sports activity 12 years after non-surgical management for anterior cruciate ligament injury relates to physical outcome measures. *Knee Surg Sports Traumatol Arthrosc* 2019;27:2511–9.
96 Grindem H, Eitzen I, Moksnes H, *et al*. A pair-matched comparison of return to pivoting sports at 1 year in anterior cruciate ligament-injured patients after a nonoperative versus an operative treatment course. *Am J Sports Med* 2012;40:2509–16.
97 Buerba RA, Zaffagnini S, Kuroda R, *et al*. Acl reconstruction in the professional or elite athlete: state of the art. *J Isakos* 2021;6:226–36.
98 Thoma LM, Grindem H, Logerstedt D, *et al*. Coper classification early after anterior cruciate ligament rupture changes with progressive neuromuscular and strength training and is associated with 2-year success: the Delaware-Oslo ACL cohort study. *Am J Sports Med* 2019;47:807.
99 Jaecker V, Drouven S, Naendrup J-H, *et al*. Increased medial and lateral tibial posterior slopes are independent risk factors for graft failure following ACL reconstruction. *Arch Orthop Trauma Surg* 2018;138:1423–31.
100 Webb JM, Salmon LJ, Leclerc E, *et al*. Posterior tibial slope and further anterior cruciate ligament injuries in the anterior cruciate ligament-reconstructed patient. *Am J Sports Med* 2013;41:2800–4.
101 Barry MJ, Edgman-Levitan S. Shared decision making--pinnacle of patient-centered care. *N Engl J Med* 2012;366:780–1.
102 Grevnerts HT, Sonesson S, Gauffin H, *et al*. Decision making for treatment after ACL injury from an orthopaedic surgeon and patient perspective: results from the NACOX study. *Orthop J Sports Med* 2021;9:232596712110050.
103 Moatshe G, Kweon CY, Gee AO, *et al*. Anterior cruciate ligament reconstruction is not for all-a need for improved patient selection. *Br J Sports Med* 2021;55:1245–6.
104 Grindem H, Wellsandt E, Failla M, *et al*. Anterior cruciate ligament Injury-Who succeeds without reconstructive surgery? The Delaware-Oslo ACL cohort study. *Orthop J Sports Med* 2018;6:232596711877425.
105 Pedersen M, Grindem H, Johnson JL, *et al*. Clinical, functional, and physical activity outcomes 5 years following the treatment algorithm of the Delaware-Oslo ACL cohort study. *J Bone Joint Surg Am* 2021;103:1473–81.
106 Culvenor AG, Barton CJ. Acl injuries: the secret probably lies in optimising rehabilitation. *Br J Sports Med* 2018;52:1416–8.
107 Grindem H, Risberg MA, Eitzen I. Two factors that may underpin outstanding outcomes after ACL rehabilitation. *Br J Sports Med* 2015;49:1425.
108 Fu FH, van Eck CF, Tashman S, *et al*. Anatomic anterior cruciate ligament reconstruction: a changing paradigm. *Knee Surg Sports Traumatol Arthrosc* 2015;23:640–8.
109 Cantin O, Magnussen RA, Corbi F, *et al*. The role of high tibial osteotomy in the treatment of knee laxity: a comprehensive review. *Knee Surg Sports Traumatol Arthrosc* 2015;23:3026–37.
110 Spang RC, Getgood A, Strickland SM, *et al*. Optimizing anterior cruciate ligament (ACL) outcomes: what else needs fixing besides the ACL? *Instr Course Lect* 2020;69:653–60.
111 Cinque ME, Kunze KN, Williams BT, *et al*. Higher incidence of radiographic posttraumatic osteoarthritis with transtibial femoral tunnel positioning compared with anteromedial femoral tunnel positioning during anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Am J Sports Med* 2022;50:255–63.
112 Rothrauff BB, Jorge A, de Sa D, *et al*. Anatomic ACL reconstruction reduces risk of post-traumatic osteoarthritis: a systematic review with minimum 10-year follow-up. *Knee Surg Sports Traumatol Arthrosc* 2020;28:1072–84.
113 Culvenor AG, Barton CJ. Acl injuries: the secret probably lies in optimising rehabilitation. *Br J Sports Med* 2018a;52:1416–8.