

The Efficacy of Anterior Cruciate Ligament Reconstruction and Rehabilitation Compared to Conservative Management for Reducing the Incidence of Post-Traumatic Osteoarthritis Following Anterior Cruciate Ligament Injury: A Systematic Review

Catherine McIntosh *Dip Phys, Dip Erg, MHPprac*
APM Workcare Learning and Development Manager, Tauranga, New Zealand

Daniel O'Brien *PhD*
Department of Physiotherapy; Active Living and Rehabilitation: Aotearoa New Zealand, Health and Rehabilitation Research Institute, School of Clinical Sciences, Auckland University of Technology, Auckland, New Zealand

Duncan Reid *DHSc*
Department of Physiotherapy; Active Living and Rehabilitation: Aotearoa New Zealand, Health and Rehabilitation Research Institute, School of Clinical Sciences, Auckland University of Technology, Auckland, New Zealand

Richard Ellis *PhD*
Department of Physiotherapy; Active Living and Rehabilitation: Aotearoa New Zealand, Health and Rehabilitation Research Institute, School of Clinical Sciences, Auckland University of Technology, Auckland, New Zealand

ABSTRACT

Anterior cruciate ligament (ACL) injury is a risk factor for developing post-traumatic osteoarthritis (PTOA). The burden of ACL injuries and PTOA is considerable and predicted to increase if there is no change in their management. The efficacy of different ACL rehabilitation interventions in reducing the incidence of PTOA is unknown. This systematic review aimed to identify, synthesise, and critique research findings that evaluated the effectiveness of anterior cruciate ligament reconstruction (ACLR) plus rehabilitation compared to rehabilitation alone on the incidence of PTOA following ACL injury. A quality critique of the selected studies was undertaken using a modified Downs and Black appraisal tool. Data were extracted and analysed to answer the research question: What is the effect of ACL reconstruction and rehabilitation compared to conservative management on the incidence of PTOA after ACL injury? Six good-quality articles were retained for final review. Five studies compared the effect of surgical and non-surgical management of ACL injuries on developing PTOA. One study investigated the impact of different ACL rehabilitation protocols on the development of PTOA. The incidence of PTOA following ACL injury was comparable regardless of the surgical or non-surgical intervention and rehabilitation compared in each study. Further high-quality studies are needed to inform ACL injury management to reduce the impact of PTOA following ACL injury.

McIntosh, C., O'Brien, D., Reid, D., & Ellis, R. (2024). The efficacy of anterior cruciate ligament reconstruction and rehabilitation compared to conservative management for reducing the incidence of post-traumatic osteoarthritis following anterior cruciate ligament injury: A systematic review. *New Zealand Journal of Physiotherapy*, 52(2), 149–159. <https://doi.org/10.15619/nzjp.v52i2.339>

Key Words: Anterior Cruciate Ligament, Physiotherapy, Post-traumatic Osteoarthritis, Rehabilitation

INTRODUCTION

Anterior cruciate ligament (ACL) injuries frequently occur in active young people involved in pivoting sports such as rugby, netball, and football in Aotearoa New Zealand (New Zealand ACL Registry, 2021). ACL injury permanently escalates the risk of early onset and accelerated progression of knee osteoarthritis (OA) at a comparatively young age (Whittaker, Culvenor et al., 2022). Post-traumatic osteoarthritis (PTOA) results in an extended period of joint disease and reduced quality of life compared to people with non-traumatic OA (Lie et al., 2019). The burden of PTOA following ACL injury is predicted to increase if there is no change in managing these injuries (Chua et al., 2020).

Data suggest that Māori and Pasifika are disproportionately affected by ACL injuries and PTOA in Aotearoa New Zealand (Prymachenko et al., 2023). Māori have higher participation rates than non-Māori in sports identified with an increased risk of acute ACL injuries (KTV Consulting, 2017). For example, Māori are highly represented in all levels of rugby participation (New Zealand Rugby, 2017), recorded as the most common means of ACL injury in Aotearoa New Zealand (New Zealand ACL Registry, 2021).

ACL reconstruction (ACLR) numbers are increasing, with 2,575 people undergoing ACLR in 2021 (New Zealand ACL Registry, 2021). People who require ACLR are five times more likely to experience PTOA (Snoeker et al., 2019), five times more likely to

undergo total knee joint replacement (TKJR), and at a younger age than the comparable non-injured population (McCammon et al., 2021). Pasifika and Māori have the highest rates of TKJR for OA in Aotearoa New Zealand (Lao et al., 2019), tend to be younger at the time of TKJR, and have smaller functional gains post-operatively than non-Māori (Singleton et al., 2013). The social and financial cost of knee OA and TKJR in Aotearoa New Zealand is considerable (Deloitte Access Economics, 2018; Kigozi et al., 2018). The burden of knee OA is predicted to increase for the foreseeable future, as there is no cure and only modest symptom management. By 2038, healthcare costs of knee OA are estimated at \$370 million, with 9,040 TKJR per annum (Wilson & Abbott, 2019). Effective management programmes to reduce the impact of ACL injury and support the growing ACLR population are required (Whittaker, Truong et al., 2022).

Filbay (2019) describes the aim of ACL management as being to restore knee function, address psychological barriers to activity participation, prevent further knee injury (including PTOA), and optimise long-term quality of life supported by the best available evidence at the time regardless of the treatment chosen (surgical or conservative). ACLR is primarily undertaken to improve knee stability and return symptomatic patients to activity. Research suggests that ACLR decreases further injury by increasing knee stability (McCammon et al., 2021). However, the rate of OA remains high in this population (Friel & Chu, 2013). Although ACLR improves knee stability, Abram et al. (2019) suggest it alters the biomechanics, and Watt (2021) the inflammatory pathways within the joint, which may contribute to PTOA and TKJR.

New programmes and interventions, including varying combinations of exercise and advice, with variable delivery methods and variable outcomes, are being developed worldwide in response to the risk and costs of PTOA following ACL injury and reconstruction (Patterson et al., 2021; Whittaker, Truong et al., 2022). These programmes promote self-management and healthy lifestyles with adherence to accompanying exercise, potentially offering additional long-term outcomes and reduction in PTOA after ACL injury (Whittaker, Losciale et al., 2022). While it is recognised that the development of PTOA (following ACL injury) is multifactorial (Wang et al., 2020), a gap in the previous literature was identified considering the impact of rehabilitation following ACL injury on the subsequent incidence of PTOA. This systematic review aimed to critically appraise literature describing rehabilitation interventions following ACL injury and subsequent impact on PTOA to answer the research question: What is the effect of ACL reconstruction and rehabilitation compared to conservative management on the incidence of PTOA after ACL injury?

METHODS

Design, protocol, and registration

This systematic review used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting and reporting systematic reviews (Moher et al., 2009). The review protocol was prospectively registered with PROSPERO (receipt number: 313167).

Search strategy and information sources

A systematic search of CINAHL, SPORTDiscus, MEDLINE (via EBSCO), and Scopus was undertaken in April 2022 to retrieve all relevant articles, using a modification of keywords and MeSH terms to answer the review question (Table 1).

Reference lists from these articles were manually cross-checked to identify any additional literature.

Table 1

Search Strategy for EBSCO Health Database

Search	Keyword(s)
S1	(Acl or "anterior cruciate ligament") n4 (injur*)
S2	(OA or osteoarthritis or PTOA or "post-traumatic osteoarthritis") n4 (knee)
S3	S1 AND S2
S4	Interven* or manage* or treat* or prevent* or rehab*
S5	S3 AND S4
S6	rct or "random* control* trial*" or "clinical trial*"
S7	S5 AND S6

Note. S = search.

Screening and article selection

Titles and abstracts of all the identified articles ($n = 248$) were evaluated based on inclusion and exclusion criteria to screen for eligibility. All articles were imported into EndNote version X9 (Thomson Reuters, Philadelphia, PA USA), where duplicates were excluded ($n = 175$). Full-text articles were obtained and reviewed where the title and abstract met the inclusion criteria ($n = 18$). The primary author (CM) completed all abstract screening, article selection, and data extraction. BD and JS oversaw article selection and data extraction, and each reviewed a selection of articles.

Inclusion and exclusion criteria

The search focused on identifying clinical studies evaluating the efficacy of ACL injury rehabilitation on the development of PTOA in humans. Articles were included if they were randomised controlled trials (RCT) or clinical studies (e.g., prospective/retrospective case studies and cohort trials) considering ACLR and rehabilitation, or conservative management following ACL injury and were available in full text in English. Objective outcome measures of early OA were required for inclusion. Based on previous research, these included imaging using X-ray or magnetic resonance imaging (MRI) (Ajuied et al., 2014) or relevant biomarkers such as bone morphogenetic proteins (BMP) and inflammatory cytokines, such as tumour necrosis factor- α , interleukin-1 (IL-1 β), and IL-6 (Friel & Chu, 2013).

Articles were excluded if OA was implied via clinical measurement of signs and symptoms indicative of impaired knee function (e.g., knee laxity) or via subjective (e.g., Knee Injury and Osteoarthritis Outcomes Score [KOOS]), or objective assessment of knee stability and function. While a clinical diagnosis of OA may be made based on symptoms, these articles were excluded due to the subjectivity and challenges describing the progression of OA disease via symptomology in

the absence of accompanying objective measures. For example, the American College of Rheumatology (Kolasinski et al., 2019) and National Institute for Health and Care Excellence guidelines (2022) better reflect non-traumatic OA. Trials comparing different surgical methods or graft material, and non-surgical interventions such as intra-articular injections were excluded for not meeting the rehabilitation criteria for inclusion. Studies of non-human subjects were also excluded. A minimum follow-up time was not specified due to the low literature volume.

Study quality appraisal

The methodological quality of articles was critically appraised using the Downs and Black checklist (Downs & Black, 1998). The checklist was selected because it is appropriate for various study designs, including RCTs and clinical trials. The checklist includes 27 items designed to assess methodological components of reporting, external and internal (bias and confounding) validity and power. The final item (27) was modified to record Yes = 1 or No = 0 about whether a power calculation was performed rather than allocating a range of study powers with scores up to a maximum of 5 (Zadro et al., 2019). This change made the maximum score possible for the checklist 28 rather than 32. A score of 0 indicated the lowest methodological quality and 28 the highest. Hooper et al. (2008) assigned methodological quality levels to a range of Downs and Black scores to enable categorisation: Excellent (26–28), Good (20–25), Fair (15–19), and Poor (≤ 14).

The primary author (CM), and two additional peer reviewers (BD and JS) (Aotearoa New Zealand registered, practising physiotherapists), independently appraised the quality of each study, with discrepancies in scoring resolved through discussion and consensus. Before the independent evaluation of the included literature, the reviewers met to discuss the checklist and completed a trial evaluation of an article outside the search criteria but consistent with the parameters of being a recent English language RCT to ensure consistency in the application of each question.

Data extraction and synthesis

Data extraction was conducted by CM for all identified articles using the Patient, Intervention, Comparison, Outcome (PICO) framework (Eriksen & Frandsen, 2018). The data extracted included patient demographics, intervention details, comparison interventions, outcome measures for the interventions, and the intervention results. The heterogeneity of the interventions and reported outcomes in the included studies precluded meta-analysis. Hence, a narrative synthesis was used to investigate and report the included studies' similarities, differences, and results.

RESULTS

Study selection

Figure 1 illustrates the process of selecting the studies for quality appraisal and data extraction. The search of electronic databases identified 423 records. After removing duplicates (175), 248 studies were screened by reviewing the title and abstract. After reviewing abstracts, 230 studies were excluded. The three main reasons for exclusion at this stage were not including a radiological measure of OA disease (i.e., X-ray or MRI) or

relevant biomarkers of early OA, animal-based studies, or studies that solely focused on comparing surgical techniques and did not describe rehabilitation. Of the 18 full-text studies retrieved and reviewed in full, two were excluded as they were not RCTs but were study protocols for RCTs, and 10 were excluded as the outcome measures did not include an objective OA measure. Six studies were retained for the final analysis.

All six studies included were RCTs. Five compared surgical to conservative management of ACL injury, with follow-up ranging from 2 to 15 years. One study compared the influence of three different types of ACL injury rehabilitation on OA biomarkers, with follow-up at eight weeks and six months after ACL injury or reconstruction.

Study quality appraisal

Six studies were included in this systematic review, including 488 participants who had sustained a primary ACL injury to a previously un-injured knee. Table 2 shows the individual Downs and Black scores of the included studies. The methodological quality of all studies was categorised as good (Hooper et al., 2008), with studies scoring between 20 and 24 out of 28 on the modified Downs and Black checklist.

Trends were noticed across the appraised studies. All studies scored 0 (No) for item 14 (Was an attempt made to blind study subjects to the intervention they have received?). This is a common finding, as it is difficult to blind participants to the intervention they receive in this type of clinical trial. Conversely, all studies scored 1 (Yes) for item 15 (Was an attempt made to blind those measuring the main outcomes of the intervention?) and scored 1 (Yes) for item 23 (Were study subjects randomised to intervention groups?).

Of note, most studies also scored poorly for item 8 (Have all adverse events that may be a consequence of the intervention been reported?) and item 11, considering external validity (Were the subjects asked to participate in the study representative of the entire population from which they were recruited?).

Three studies (Frobell et al., 2013; Meunier et al., 2007; Nambi et al., 2020) scored highly (10/11) on the first 10 items measuring reporting quality. Three studies (Meunier et al., 2007; Nambi et al., 2020; Wirth et al., 2021) also scored highly (2/3) on items 11 to 13, considering external validity. All studies scored well in items 14 to 20, considering internal validity/bias, with all studies scoring 5 (Frobell, 2011; Nambi et al., 2020) or 6 out of 7. Frobell et al. (2013) and Nambi et al. (2020) scored full marks (6/6) from items 21 to 26, considering internal validity/confounding. The modified power question 27 scored 1 (Yes) in all studies.

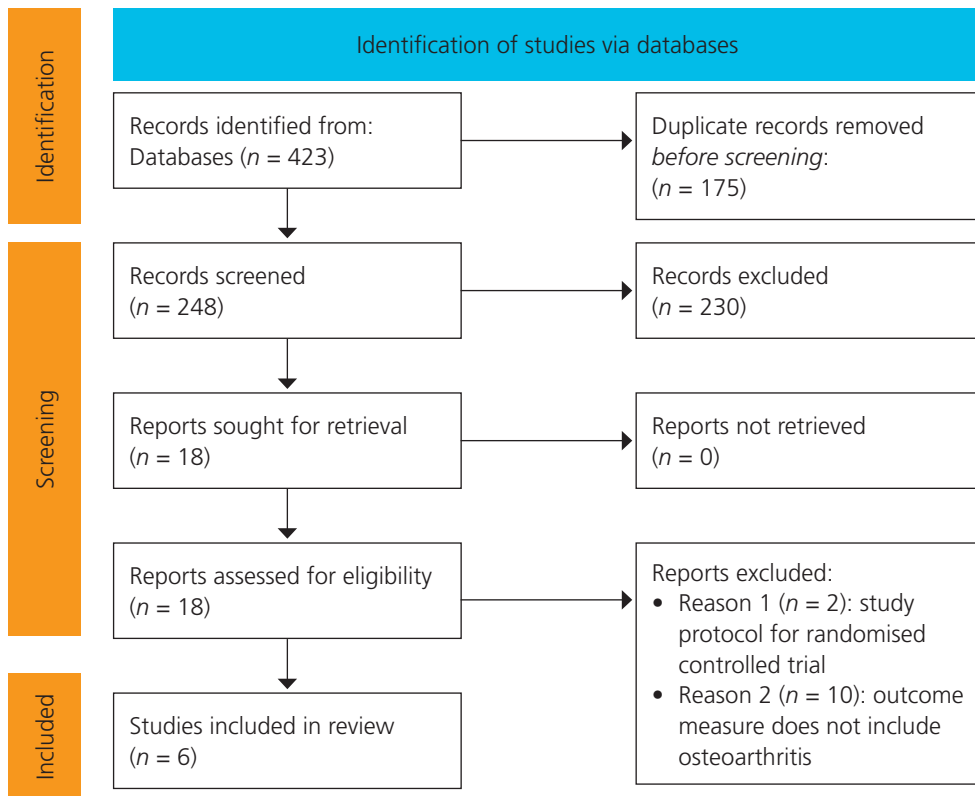
Table 3 demonstrates the key characteristics extracted from the retained studies using the PICO format and the corresponding Downs and Black scores.

Participants and population

The participants in all six studies were described as previously physically active, aged between 18 and 35 years and had sustained a primary acute ACL knee injury. Four of the six studies included participants with meniscal tears but excluded other associated injuries known to be risk factors for PTOA, such

Figure 1

PRISMA Diagram Demonstrating Study Selection



as total collateral ligament rupture and chondral injuries. Nambi et al. (2020) and Tsoukas et al. (2016) excluded participants with other soft tissue injuries.

The mean duration since ACL injury ranged from 2 to 15 years after injury, except for Nambi et al. (2020), who failed to report this. Four studies included male and female participants, and two (Nambi et al., 2020; Tsoukas et al., 2016) included males only. Five studies recorded body mass index (BMI), with all participants' mean scores between 22 and 24 (kgs/m²), indicating they were within healthy ranges. Meunier et al. (2007) did not report BMI scores. Most studies reported no or very few losses to follow-up, except for Wirth et al. (2021) who did not report on this. Participants were recruited from hospital attendance for ACL injuries in Sweden (Frobell, 2011; Frobell et al., 2013; Meunier et al., 2007; Wirth et al., 2021) and Saudi Arabia (Nambi et al., 2020). Mean Tegner scores > 5 and < 10 indicated participants were from moderately active to competitive sporting populations while excluding professional athletes (Lysholm & Tegner, 2007). Most ACL injuries occurred while participating in competitive sports (Frobell, 2011; Frobell et al., 2013; Nambi et al., 2020; Wirth et al., 2021), with mean Tegner scores > 7.

Intervention

The impact of a variety of interventions was investigated across the included studies. Surgical ACLR via hamstring or bone-patellar tendon-bone autografts were described in the more recent surgical comparisons (Frobell, 2011; Frobell et al., 2013; Wirth et al., 2021). However, Meunier et al. (2007) considered

augmented and un-augmented ACLR occurring between 1980 and 1983. Delayed ACLR was an option for participants experiencing ongoing instability in four studies (Frobell, 2011; Frobell et al., 2013; Meunier et al., 2007; Wirth et al., 2021). Details of physiotherapy-supervised, structured rehabilitation was described in four studies (Frobell, 2011; Frobell et al., 2013; Nambi et al., 2020; Wirth et al., 2021). In the follow-up to the KANON trial (Frobell, 2011; Frobell et al., 2013; Wirth et al., 2021), rehabilitation was based on a best-practice consensus-informed programme, commencing with early weight bearing, followed by goal-based progressions combining closed- and open-kinetic chain quadriceps strengthening and neuromuscular training (Frobell et al., 2010). Nambi et al. (2020) describe participants receiving isokinetic, sensory-motor training or a standard home exercise programme. Intervention durations were described in four studies and varied from 4 weeks (Nambi et al., 2020) to 8 months (Tsoukas et al., 2016). Participant compliance with study interventions was high in four of six studies but could not be determined in the remaining two (Frobell, 2011; Nambi et al., 2020).

Control or comparison

Table 3 shows that five studies compared the impact of initial surgical ACLR with conservative management on the development of PTOA after ACL injuries. Three of these (Frobell, 2011; Frobell et al., 2013; Wirth et al., 2021) provided sufficient detail about the conservative management to compare surgical ACLR with a structured, supervised rehabilitation programme. The other two (Meunier et al., 2007; Tsoukas et al., 2016

Table 2
Downs and Black Checklist

Author (date)	Total	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Frobell et al. (2013)	24	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Nambi et al. (2020)	24	1	1	1	1	2	1	1	0	1	1	0	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1
Meunier et al. (2007)	23	1	1	1	1	2	1	1	0	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	0	0	1	1
Wirth et al. (2021)	21	1	1	1	1	1	1	1	0	0	1	0	1	1	0	1	1	1	1	1	1	1	1	1	0	1	0	1
Tsoukas et al. (2016)	20	1	1	1	1	0	1	1	1	1	1	0	0	0	0	1	1	1	1	1	1	1	0	1	1	1	0	1
Frobell (2011)	20	1	1	1	1	1	1	1	0	1	1	1	0	1	0	1	1	1	1	0	1	0	0	1	0	1	1	1

Table 3
PICO Framework of Study Criteria

Author (date)	D&B	Objective	Participant characteristics	Intervention	Control	Outcome measure(s)	Results
Meunier et al. (2007) RCT	23 Good	To compare the prevalence of radiological OA changes at 15 years between those treated with surgical repair or non-surgical treatment following an acute ACL rupture	n = 100 (68 male, 32 female) Age < 30 years ACL rupture	Structured rehabilitation plus ACLR at 15 years' FU: n = 44 (33 male, 11 female); mean age = 22 years	Conservative management at 15 years FU: n = 56 (35 male, 21 female); mean age = 21 years Delayed ACLR: n = 16 (30%)	KOOS, Lysholm Knee Score, radiographic OA	No significant differences in radiographic OA between groups. 16 initially managed conservatively progressed to ACLR due to instability. ACLR neither reduced risk of OA nor increased subjective outcome scores.
Frobell (2011) Follow up to RCT	20 Good	To compare the 2-year development of cartilage thickness between patients who received (a) rehabilitation and early ACLR; (b) rehabilitation and optional delayed ACLR; and (c) rehabilitation only following acute ACL injury	n = 58 (42 male, 16 female) Mean age = 26.7 years ACL injury (a cohort of the first patients of the KANON study who completed all scheduled study MRI)	Early ACLR: n = 34 Delayed optional ACLR: n = 11 (40%)	Rehabilitation only: n = 16	Cartilage thickness (mm), joint fluid volumes (mm ³) and bone marrow lesions measured via MRI Tegner scale of activity	No significant difference between groups for cartilage thickness. All patients showed significant cartilage thinning in the femoral trochlea (mean (SD) change = 0.11mm (0.12), p < 0.001), plus posteromedial and posterolateral cartilage.

Author (date) Study design	D&B	Objective	Participant characteristics	Intervention	Control	Outcome measure(s)	Results
Frobell et al. (2013) RCT	24 Good	To compare the 5-year radiographic outcomes between those treated with (a) rehabilitation plus early ACLR and (b) rehabilitation and optional delayed ACLR	n = 121 ^a Mean age = 26 years Mean BMI = 24 No previous knee injury	Structured rehabilitation plus early ACLR at 5-year FU: n = 59 (47 male, 12 female); mean age = 27 years; mean BMI = 24.4	Structured rehabilitation with optional delayed ACLR at 5-year FU: n = 59 (39 male, 20 female); mean age = 25.7 years; mean BMI = 23.8 Delayed ACLR: n = 30 (51%)	KOOS, SF-36, Tegner activity scale, meniscal surgery, radiographic OA	No statistically significant differences in radiographic OA between the two groups.
Tsoukas et al. (2016) RCT	20 Good	To compare the incidence of radiological OA after ACL rupture between patients treated (a) conservatively and (b) with ACLR via hamstring tendon graft	n = 37 (all male) Mean age = 32 years BMI < 30 ACL rupture to previously uninjured knee	ACLR with hamstring autograft at 10 years: n = 17; mean age = 31 years	Conservative management at 10 years: n = 15; mean age = 33 years	Tegner & Lysholm activity scales, IKDC scores, KT-1000 arthrometer laxity measurement, radiological OA	Each showed early signs of radiologic post-traumatic OA with no significant difference between groups. Laxity improved with ACLR for anterior-posterior tibial translation: mean (SD) 1.5 (0.2) mm (SD 0.2) versus 4.5 (0.5) mm ($p = 0.03$)
Nambi et al. (2020) RCT	24 Good	To determine the effects of isokinetic training of knee muscles on bone morphogenetic proteins and inflammatory biomarkers in post-traumatic OA after ACL injury	n = 60 (all male) Age = 18–25 years Mean BMI = 22.6 With PTOA > 3 months' post ACL injury VAS = 4–8/10	Isokinetic training: n = 20; mean age = 22.3 years; mean BMI = 22.5 Sensory-motor training: n = 20; mean age = 22.4 years; mean BMI = 22.8	Conventional home exercise programme: n = 20; mean age = 22.9 years; mean BMI = 22.6	Pain VAS, Functional disability WOMAC scale, bone morphogenic proteins, inflammatory biomarker serum levels	At 6 months: VAS mean improvement isokinetic 89%, sensory motor 62%, control 59%. Bone morphogenic proteins have no significant difference across all groups. Inflammatory biomarkers significant improvement (decreased CRP, TNF- α , IL-2 and IL-4) isokinetic compared with sensory-motor and no significant difference with home exercise programme control.
Wirth et al. (2021) RCT	21 Good	To compare the 5-year change in FTJ cartilage thickness between those treated with structured rehabilitation and (a) early ACLR or (b) optional delayed ACLR following acute ACL tear	n = 117 (85 male, 32 female) Mean age = 26 years Mean BMI = 24 ACL injury to previously uninjured knee	Structured rehabilitation plus early ACLR at 5-year FU: n = 59 (47 male, 12 female); mean age = 27 years; mean BMI = 24.4	Structured rehabilitation plus optional delayed ACLR at 5-year FU: n = 58 (38 male, 20 female); mean age = 25.7 years; mean BMI = 23.8 Delayed ACLR: n = 30 (51%)	Overall FTJ cartilage thickness, measured on MRI	Increase in FTJ cartilage thickness in all groups with no significant difference in mean change in FTJ cartilage thickness between groups

Note. ACL = anterior cruciate ligament; ACLR = anterior cruciate ligament reconstruction; BMI = body mass index; D&B = Downs & Black score; CRP = C-Reactive Protein; FU = follow up, FTJ = femorotibial joint; IKDC = International Knee Documentation Committee; IL-2 = interleukin-2; IL-4 = interleukin-4; KOOS = Knee Injury and Osteoarthritis Outcome Score; MRI = magnetic resonance imaging; OA = osteoarthritis; RCT = randomised control trial; TNF- α = Tumour Necrosis Factor alpha; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Arthritis Index.

^a Of the 121 participants enrolled in the trial, one participant was lost to the 5-year follow up and two participants who were assigned to an early ACLR did not have a reconstruction.

provided insufficient information about the conservative intervention for the same comparative analysis; instead, their comparison was limited to that of surgical ACLR with conservative management. Nambi et al. (2020) compared the impact of training regimes on existing PTOA after ACL injury and failed to record if participants had or had not undergone ACLR. Several studies (Frobell, 2011; Frobell et al., 2013; Meunier et al., 2007; Wirth et al., 2021) allowed delayed ACLR for participants randomised to the conservative management group. In these studies, between 30% and 50% of participants progressed from conservative management to having ACLR.

Outcomes

The outcome column of Table 3 includes the objective outcome measures of OA, with suitable sensitivity and specificity identified as inclusion criteria for this review. While the outcome measures varied across studies introducing clinical diversity and preventing direct comparisons, the studies included known valid and reliable measures. Follow-up durations ranged from 2 to 15 years' duration from the index injury.

Study results

All six studies reported no significant differences between the intervention and the comparison/control groups for evidence of radiographic OA, MRI visualisation of cartilage thickness, or bone morphologic proteins. Nambi et al. (2020) reported a reduction in inflammatory biomarkers at 6 weeks and 8 months after a 4-week isokinetic training programme compared to a sensory-motor or standard home exercise programme.

PTOA was recorded within 2 to 15 years of ACL injury in five of the six included studies. Nambi et al. (2020) reported PTOA measures at 8 weeks and 6 months following rehabilitation intervention, with an unclear duration since the original ACL injury. Study participants were between 18 and 35 years old at the time of ACL injury, meaning PTOA following ACL injury occurred in a disproportionately younger population than other forms of OA would be anticipated.

DISCUSSION

This systematic review identified six good-quality RCTs that explored the impact of ACL injury management approaches on the development of PTOA. Five of the six studies compared surgical approaches with conservative management, and the synthesis of these studies suggests the likelihood of developing PTOA may not be affected by receiving surgical or conservative management after ACL injury. In contrast, only one study (Nambi et al., 2020) compared post-operative rehabilitation approaches.

Synthesis of the reviewed studies shows that the rates of PTOA following ACL injury appear comparable regardless of whether someone undergoes surgical or conservative management. This summation is supported by Filbay (2019) and Friel and Chu (2013), who propose early ACLR is not superior to evidence-based rehabilitation in reducing subsequent PTOA after ACL injury. Some researchers argue that the onset of PTOA is caused by ACL injury (Frobell et al., 2013) and is not influenced by post-injury management interventions. Cuzzolin et al. (2021) proposes that the mechanism of ACL injury has a traumatic impact on all knee structures, predisposing the knee to PTOA,

and is not just a ligament injury. Potter et al. (2012) found that all ACL injuries are associated with chondral damage at the time of injury and proposed that this will deteriorate over time. Moreover, Frobell et al. (2013) hypothesises that events at the time of ACL injury may cause a cascade of biologic sequelae contributing to early PTOA, with the later progression of PTOA linked to altered biomechanics following ACL injury and reconstruction. To establish controlled research cohorts, isolated ACL rupture, excluding other soft tissue injuries, was studied by Nambi et al. (2020) and Tsoukas et al. (2016). This limits the generalisability of their studies to ACL injury epidemiology more broadly due to the prevalence of other associated injuries in the general population at the time of ACL rupture.

Although the modified Downs and Black tool scores suggested that the quality of the included studies was "good", some fundamental limitations remain. Three such limitations include the relatively short length of follow-up (between 6 months and 5 years) and small sample sizes in many studies, plus the different measures of PTOA across studies employed different sensitivity. These study limitations potentially limit the precision of their reported findings and the accurate reporting of PTOA. Additionally, four studies (Frobell, 2011; Frobell et al., 2013; Meunier et al., 2007; Wirth et al., 2021), allowed optional delayed ACLR. Cross-over from conservative management to surgical treatment occurred with 30% to 50% of participants in these studies, further limiting the ability to appreciate between-group differences.

Therefore, our synthesis of the available studies indicates limited evidence of a difference between ACLR and rehabilitation compared to conservative management on the incidence of PTOA after ACL injury. Research indicates surgery may provide benefits by improving joint stability and reducing the risk of a secondary injury such as meniscal tears (Chu, 2019). There is also conflicting evidence that surgery may exacerbate and prolong the intraarticular inflammatory response, subsequently increasing the risk of PTOA (Thomas et al., 2017). Shen et al. (2022) report that early ACLR, compared to optional delayed ACLR, does not show improved functional outcomes. Synopsis of the current literature suggests considering delayed ACLR in some circumstances may optimise the benefits of surgical stability and offset the risks of the inflammatory response. For example, early ACLR when ACL injury is associated with other joint injuries, and delayed ACLR for ongoing or recurrent instability.

Limited recommendations can be made following this systematic review about differing rehabilitation protocols following ACL injury because only one included study compares different ACL injury rehabilitation protocols (Nambi et al., 2020). This study shows that including isokinetic muscular training within structured rehabilitation after ACL injury (plus or minus ACLR) might reduce inflammatory biomarkers compared to sensory-motor and standard home exercise programme rehabilitation protocols. The impact of this on PTOA is unclear, particularly since the follow-up period was so small in this study. This finding is supported by Wang et al. (2020), who report that the involvement of ACL injury in the development of PTOA is complex and multifactorial, proposing structural, mechanical, and neuromuscular factors in addition to biological

(inflammatory) factors; however, they conclude that the precise mechanism remains unclear. Whittaker and Roos (2019) highlight the gap in knowledge about evidence-based rehabilitation to prevent or delay the onset of PTOA after an ACL injury and are trialling an approach combining exercise and education based on the current evidence-based understanding of causal factors of OA (Whittaker, Culvenor et al., 2022).

The findings of this review have identified a significant gap in the current literature, highlighting limited evidence comparing different rehabilitation options following ACL injury or ACLR to reduce the likelihood of developing PTOA. Increased understanding of the causes of PTOA will also improve the management of the onset and progression after ACL injury and lead to future studies comparing specific intervention protocols targeting the causal mechanisms. In the meantime, future studies should consider comparing modes of ACL injury rehabilitation delivery to optimise adherence to a healthy lifestyle, including education and exercise boosted with periodic face-to-face supervision (Cinthuja et al., 2022), group rehabilitation (da Silva et al., 2015), or app-based rehabilitation (Clark et al., 2019; Clausen et al., 2020) to enhance engagement, monitored over an extended duration. Moreover, a recent consensus statement by Whittaker, Culvenor et al. (2022) to guide clinical practice without empirical research supports these recommendations.

Strengths and limitations

Strengths of this systematic review include prospective registration with PROSPERO (receipt number: 313167) and using the Downs and Black checklist by multiple reviewers following a structured search of available literature leading to a robust, reproducible, structured synthesis of current research. Several limitations, in addition to the previously noted limitations within the studies themselves, should be considered when interpreting the findings of this review. A potential limitation is completing abstract screening, article selection, and data extraction using one reviewer. Rigorous application of the search strategy excluded non-English publications and studies lacking an objective measure of OA. These excluded studies focused on subjective measures, including clinical indicators of OA such as pain and laxity. This limited data extraction to only six studies that assessed the efficacy of ACL injury management on objective outcome measures of OA included in this systematic review. Heterogeneity is noted in these studies, and quantitative analysis by pooling outcome data (meta-analysis) was impossible. While quantitative synthesis of the findings was not possible due to the heterogeneity of the interventions and outcome measures used, the findings were broadly consistent. In the existing literature, only one study investigated the impact of particular rehabilitation protocols on OA outcomes following ACL injury.

Future research

This review supports findings that ACL injury may increase the likelihood of PTOA regardless of injury management. Considering this, long-term engagement in healthy lifestyle behaviours (i.e., weight management and physical activity) may be needed to reduce the potential sequelae of the injury (Frobell et al., 2010). However, more clinical trials comparing the impact of different rehabilitation approaches over time on the incidence, progression, and burden of PTOA, and the inclusion

of a wider variety of outcome measures to assess efficacy and impact, are required before clinical recommendations are made for one rehabilitation strategy over another in relation to ACL injury management. Furthermore, using a consensus definition of symptomatic PTOA (Lie et al., 2019) and standardised clinical criteria for radiographic OA (Øiestad et al., 2009) will enable meta-analysis of future study findings. Recent pre-clinical (Aman et al., 2022) and initial human studies (Lattermann et al., 2017; Wang et al., 2017) have looked at whether early modification of the inflammatory response to injury and surgery may have a protective effect on the development of PTOA. Future research considering how this may integrate with rehabilitation-based approaches may support improved clinical outcomes after ACL injury. Māori and Pasifika are overrepresented in rates of ACL injury and TKJR for OA. Further research to consider culturally acceptable programmes for ACL injury prevention and management, and secondary prevention of PTOA is indicated to ensure equitable application in Aotearoa New Zealand.

Clinical implications

This review provides evidence from a small collection of studies that show we do not yet know if undergoing ACLR or not changes the likelihood of developing PTOA after ACL injury. In parallel with the multifactorial contributors to PTOA following ACL injury, there appear to be multifactorial considerations for injury management. Delaying ACLR in conjunction with rehabilitation, regular, ongoing review, and shared decision-making may help align client expectations with outcomes for ACLR and improve satisfaction with outcomes in many instances. An ACL injury can have a life-long impact, so multiple rehabilitation interactions, over an extended duration are likely beneficial for optimal long-term clinical outcomes (Whittaker, Culvenor et al., 2022). Isokinetic training may reduce inflammatory biomarkers more than other rehabilitation programmes (Nambi et al., 2020); however, this finding should be treated cautiously as the mechanism and association with PTOA remain unclear. In addition, ACL injury prevention is an essential consideration for physiotherapists working with young athletes participating in pivoting sports. Primary ACL injury prevention mirrors re-injury prevention and further injury (PTOA) management (Thorborg et al., 2017), providing a double layer of protection against initial ACL injury and the sequelae of PTOA.

CONCLUSION

The results of this review highlight that surgical and conservative management appear to have comparable outcomes for most people following ACL injury, but neither approach necessarily reduces the chances of developing PTOA in the long term. However, limitations within the studies mean further research is needed to conclude definitively that there is no difference in the likelihood of developing PTOA with ACLR or not. Few clinical trials assess the impact of different rehabilitation programmes on the onset and progression of PTOA after ACL injury. Given the known burden of PTOA following ACL, more high-quality studies are needed to inform best practice. However, it is crucial that clinicians apply the current evidence for ACL injury prevention and management and encourage people at risk of PTOA to seek and receive ongoing rehabilitation beyond acute injury or surgical reconstruction.

KEY POINTS

1. There are increased rates of PTOA in the ACL-injured population regardless of intervention.
2. There is no evidence of a difference in rates of PTOA with surgical or conservative management of ACL injury.
3. There is limited research considering the efficacy of rehabilitation on the development of PTOA following ACL injury, and further research is required.
4. Physiotherapists should provide ACL injury prevention and management advice throughout the lifespan for people at risk of PTOA after ACL injury.

DISCLOSURES

There are no conflicts of interest that may be perceived to interfere with or bias this study.

PERMISSIONS

None.

ACKNOWLEDGEMENTS

The authors would like to acknowledge and thank the anonymous peer reviewers from the New Zealand Journal of Physiotherapy for their valuable comments and physiotherapy colleagues, Brian Doherty and Jo Smith, for their quality appraisal of studies within the systematic review.

CONTRIBUTIONS OF AUTHORS

Design conceptualisation and methodology, DO, DR and CM; validation, DO, DR and CM; formal analysis, DO, DR and CM; data curation, DO, DR and CM; supervision, DO and DR; writing—original draft preparation, DO, DR, CM and RE; writing—review and editing, DO, DR, CM and RE.

ADDRESS FOR CORRESPONDENCE

Catherine McIntosh, 1/251 Fraser Street, Greerton, Tauranga 3112, New Zealand.

Email: catherine.mcintosh@apmworkcare.co.nz

REFERENCES

- Abram, S. G. F., Judge, A., Khan, T., Beard, D. J., & Price, A. J. (2019). Rates of knee arthroplasty in anterior cruciate ligament reconstructed patients: A longitudinal cohort study of 111,212 procedures over 20 years. *Acta Orthopaedica*, *90*(6), 568–574. <https://doi.org/10.1080/17453674.2019.1639360>
- Ajuied, A., Wong, F., Smith, C., Norris, M., Earnshaw, P., Back, D., & Davies, A. (2014). Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: A systematic review and meta-analysis. *American Journal of Sports Medicine*, *42*(9), 2242–2252. <https://doi.org/10.1177/0363546513508376>
- Aman, Z. S., DePhillipo, N. N., Familiari, F., Dickens, J. F., LaPrade, R. F., & Dekker, T. J. (2022). Acute intervention with selective interleukin-1 inhibitor therapy may reduce the progression of posttraumatic osteoarthritis of the knee: A systematic review of current evidence. *Arthroscopy*, *38*(8), 2543–2556. <https://doi.org/10.1016/j.arthro.2022.02.009>
- Chu, C. R. (2019). Concepts important to secondary prevention of posttraumatic osteoarthritis. *Journal of Athletic Training*, *54*(9), 987–988. <https://doi.org/10.4085/1062-6050-54.082>

- Chua, J., Briggs, A. M., Hansen, P., Chapple, C., & Abbott, J. H. (2020). Choosing interventions for hip or knee osteoarthritis – What matters to stakeholders? A mixed-methods study. *Osteoarthritis and Cartilage Open*, *2*(3), Article 100062. <https://doi.org/10.1016/j.ocarto.2020.100062>
- Cinhuja, P., Krishnamoorthy, N., & Shivapatham, G. (2022). Effective interventions to improve long-term physiotherapy exercise adherence among patients with lower limb osteoarthritis. A systematic review. *BMC Musculoskeletal Disorders*, *23*, Article 147. <https://doi.org/10.1186/s12891-022-05050-0>
- Clark, H., Bassett, S., & Siegert, R. (2019). The effectiveness of web-based patient education and action and coping plans as an adjunct to patient treatment in physiotherapy: A randomized controlled trial. *Physiotherapy Theory and Practice*, *35*(10), 930–939. <https://doi.org/10.1080/09593985.2018.1467521>
- Clausen, J.-D., Nahen, N., Horstmann, H., Lasch, F., Krutsch, W., Krettek, C., & Weber-Spickschen, T. S. (2020). Improving maximal strength in the initial postoperative phase after anterior cruciate ligament reconstruction surgery: Randomized controlled trial of an app-based serious gaming approach. *JMIR Serious Games*, *8*(1), Article e14282. <https://doi.org/10.2196/14282>
- Cuzzolin, M., Previtali, D., Zaffagnini, S., Deabate, L., Candrian, C., & Filardo, G. (2021). Anterior cruciate ligament reconstruction versus nonoperative treatment: Better function and less secondary meniscectomies but no difference in knee osteoarthritis-A meta-analysis. *Cartilage*, *13*(Suppl 1), 1658S–1670S. <https://doi.org/10.1177/19476035211046041>
- da Silva, F. S., de Melo, F. E. S., do Amaral, M. M. G., Caldas, V. V. A., Pinheiro, Í. L. D., Abreu, B. J., & Vieira, W. H. B. (2015). Efficacy of simple integrated group rehabilitation program for patients with knee osteoarthritis: Single-blind randomized controlled trial. *Journal of Rehabilitation Research & Development*, *52*(3), 309–322. <https://doi.org/10.1682/JRRD.2014.08.0199>
- Deloitte Access Economics. (2018). *The economic cost of arthritis in New Zealand in 2018*. Arthritis New Zealand. <https://www.arthritis.org.nz/wp-content/uploads/2018/09/Economic-cost-of-Arthritis-in-New-Zealand-2018.pdf>
- Downs, S. H., & Black, N. (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology and Community Health*, *52*(6), 377–384. <https://doi.org/10.1136/jech.52.6.377>
- Eriksen, M. B., & Frandsen, T. F. (2018). The impact of patient, intervention, comparison, outcome (PICO) as a search strategy tool on literature search quality: A systematic review. *Journal of the Medical Library Association*, *106*(4), 420–431. <https://doi.org/10.5195/jmla.2018.345>
- Filbay, S. R. (2019). Early ACL reconstruction is required to prevent additional knee injury: A misconception not supported by high-quality evidence. *British Journal of Sports Medicine*, *53*(8), 459–461. <https://doi.org/10.1136/bjsports-2018-099842>
- Friel, N. A., & Chu, C. R. (2013). The role of ACL injury in the development of posttraumatic knee osteoarthritis. *Clinics in Sports Medicine*, *32*(1), 1–12. <https://doi.org/10.1016/j.csm.2012.08.017>
- Frobell, R. B. (2011). Change in cartilage thickness, posttraumatic bone marrow lesions, and joint fluid volumes after acute ACL disruption: A two-year prospective MRI study of sixty-one subjects. *The Journal of Bone & Joint Surgery*, *93*(12), 1096–1103. <https://doi.org/10.2106/jbjs.j.00929>
- Frobell, R. B., Roos, E. M., Roos, H. P., Ranstam, J., & Lohmander, L. S. (2010). A randomized trial of treatment for acute anterior cruciate ligament tears. *The New England Journal of Medicine*, *363*(4), 331–342. <https://doi.org/10.1056/nejmoa0907797>
- Frobell, R. B., Roos, H. P., Roos, E. M., Roemer, F. W., Ranstam, J., & Lohmander, L. S. (2013). Treatment for acute anterior cruciate ligament tear: Five year outcome of randomised trial. *BMJ*, *346*, Article f232. <https://doi.org/10.1136/bmj.f232>
- Hooper, P., Jutai, J. W., Strong, G., & Russell-Minda, E. (2008). Age-related macular degeneration and low-vision rehabilitation: A systematic review. *Canadian Journal of Ophthalmology*, *43*(2), 180–187. <https://doi.org/10.3129/i08-001>

- Kigozi, J., Jowett, S., Nicholls, E., Tooth, S., Hay, E. M., Foster, N. E., & BEEP trial team. (2018). Cost-utility analysis of interventions to improve effectiveness of exercise therapy for adults with knee osteoarthritis: The BEEP trial. *Rheumatology Advances in Practice*, 2(2), Article rky018. <https://doi.org/10.1093/rap/rky018>
- Kolasinski, S. L., Neogi, T., Hochberg, M. C., Oatis, C., Guyatt, G., Block, J., Callahan, L., Copenhaver, C., Dodge, C., Felson, D., Gellar, K., Harvey, W. F., Hawker, G., Herzig, E., Kwoh, C. K., Nelson, A. E., Samuels, J., Scanzello, C., White, D., Wise, B., ... Reston, J. (2020). 2019 American College of Rheumatology/Arthritis Foundation Guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Care & Research*, 72(2), 149–162. <https://doi.org/10.1002/acr.24131>
- KTV Consulting (2017, January). *Māori participation in community sport review* [Board Paper]. Sport New Zealand. <https://sportnz.org.nz/media/1436/maori-participation-review-report.pdf>
- Lao, C., Lees, D., Patel, S., White, D., & Lawrenson, R. (2019). Geographical and ethnic differences of osteoarthritis-associated hip and knee replacement surgeries in New Zealand: A population-based cross-sectional study. *BMJ Open*, 9, Article e032993. <https://doi.org/10.1136/bmjopen-2019-032993>
- Lattermann, C., Jacobs, C. A., Proffitt Bunnell, M., Huston, L. J., Gammon, L. G., Johnson, D. L., Reinke, E. K., Huebner, J. L., Kraus, V. B., & Spindler, K. P. (2017). A multicenter study of early anti-inflammatory treatment in patients with acute anterior cruciate ligament tear. *American Journal of Sports Medicine*, 45(2), 325–333. <https://doi.org/10.1177/0363546516666818>
- Lie, M. M., Risberg, M. A., Storheim, K., Engebretsen, L., & Øiestad, B. E. (2019). What's the rate of knee osteoarthritis 10 years after anterior cruciate ligament injury? An updated systematic review. *British Journal of Sports Medicine*, 53(18), 1162–1167. <https://doi.org/10.1136/bjsports-2018-099751>
- Lysholm, J., & Tegner, Y. (2007). Knee injury rating scales. *Acta Orthopaedica*, 78(4), 445–453. <https://doi.org/10.1080/17453670710014068>
- McCammon, J., Zhang, Y., Prior, H. J., Leiter, J., & MacDonald, P. B. (2021). Incidence of total knee replacement in patients with previous anterior cruciate ligament reconstruction. *Clinical Journal of Sport Medicine*, 31(6), e442–e446. <https://doi.org/10.1097/jsm.0000000000000852>
- Meunier, A., Odensten, M., & Good, L. (2007). Long-term results after primary repair or non-surgical treatment of anterior cruciate ligament rupture: A randomized study with a 15-year follow-up. *Scandinavian Journal of Medicine & Science in Sports*, 17(3), 230–237. <https://doi.org/10.1111/j.1600-0838.2006.00547.x>
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *British Medical Journal*, 339(7716), 332–336. <https://doi.org/10.1371/journal.pmed.1000097>
- Nambi, G., Kamal Abdelbasset, W., Alrawaili, S. M., Elnegamy, T. E., Abodonya, A. M., Saleh, A. K., & Verma, A. (2020). Effects of isokinetic knee muscle training on bone morphogenic proteins and inflammatory biomarkers in post-traumatic osteoarthritis after anterior cruciate ligament injury: A randomized trial. *Journal of Rehabilitation Medicine*, 52(9), Article jrm0098. <https://doi.org/10.2340/16501977-2732>
- New Zealand ACL Registry. (2021). *New Zealand ACL registry: Annual report 2021*. <https://www.aclregistry.nz/reports/>
- New Zealand Rugby. (2017). *Annual report 2017*. <https://www.nzrugby.co.nz/about-nzr/governance/annual-reports/>
- National Institute for Health and Care Excellence. (2022). *Osteoarthritis in over 16s: Diagnosis and management* (NICE guideline NG226). <https://www.nice.org.uk/guidance/ng226>
- Øiestad, B. E., Engebretsen, L., Storheim, K., & Risberg, M. A. (2009). Knee osteoarthritis after anterior cruciate ligament injury: A systematic review. *The American Journal of Sports Medicine*, 37(7), 1434–1443. <https://doi.org/10.1177/0363546509338827>
- Patterson, B. E., Barton, C. J., Culvenor, A. G., Cooper, R. L., & Crossley, K. M. (2021). Exercise-therapy and education for individuals one year after anterior cruciate ligament reconstruction: A pilot randomised controlled trial. *BMC Musculoskeletal Disorders*, 22, Article 64. <https://doi.org/10.1186/s12891-020-03919-6>
- Potter, H. G., Jain, S. K., Black, B. R., Fung, S., Ma, Y., & Lyman, S. (2012). Cartilage injury after acute, isolated anterior cruciate ligament tear: Immediate and longitudinal effect with clinical/MRI follow-up. *American Journal of Sports Medicine*, 40(2), 276–285. <https://doi.org/10.1177/0363546511423380>
- Pryymachenko, Y., Wilson, R., & Abbott, J. H. (2023) Epidemiology of cruciate ligament injuries in New Zealand: Exploring differences by ethnicity and socioeconomic status. *Injury Prevention*, 29, 213–218. <https://doi.org/10.1136/ip-2022-044761>
- Shen, X., Liu, T., Xu, S., Chen, B., Tang, X., Xiao, J., & Qin, Y. (2022) Optimal timing of anterior cruciate ligament reconstruction in patients with anterior cruciate ligament tear: A systematic review and meta-analysis. *JAMA Network Open*, 5(11), Article e2242742. <https://doi.org/10.1001/jamanetworkopen.2022.42742>
- Singleton, N., Buddicom, E., Vane, A., & Poutawera, V. (2013). Are there differences between Māori and non-Māori patients undergoing primary total hip and knee arthroplasty surgery in New Zealand? A registry-based cohort study. *New Zealand Medical Journal*, 126(1379), 23–30.
- Snoeker, B., Turkiewicz, A., Magnusson, K., Frobell, R., Yu, D., Peat, G., & Englund, M. (2019). Risk of knee osteoarthritis after different types of knee injuries in young adults: A population-based cohort study. *British Journal of Sports Medicine*, 54(12), 725–730. <https://doi.org/10.1136/bjsports-2019-100959>
- Thomas, A. C., Hubbard-Turner, T., Wikstrom, E. A., & Palmieri-Smith, R. M. (2017). Epidemiology of posttraumatic osteoarthritis. *Journal of Athletic Training*, 52(6), 491–496. <https://doi.org/10.4085/1062-6050-51.5.08>
- Thorborg, K., Krommes, K. K., Esteve, E., Clausen, M. B., Bartels, E. M., & Rathleff, M. S. (2017). Effect of specific exercise-based football injury prevention programmes on the overall injury rate in football: A systematic review and meta-analysis of the FIFA 11 and 11+ programmes. *British Journal of Sports Medicine*, 51(7), 562–571. <https://doi.org/10.1136/bjsports-2016-097066>
- Tsoukas, D., Fotopoulos, V., Basdekis, G., & Makridis, K. G. (2016). No difference in osteoarthritis after surgical and non-surgical treatment of ACL-injured knees after 10 years. *Knee Surgery, Sports Traumatology, Arthroscopy*, 24(9), 2953–2959. <https://doi.org/10.1007/s00167-015-3593-9>
- Wang, L.-J., Zeng, N., Yan, Z.-P., Li, J.-T., & Ni, G.-X. (2020). Post-traumatic osteoarthritis following ACL injury. *Arthritis Research & Therapy*, 22, Article 57. <https://doi.org/10.1186/s13075-020-02156-5>
- Wang, Y., Shimmin, A., Ghosh, P., Marks, P., Linklater, J., Connell, D., Hall, S., Skerrett, D., Itescu, S., & Cicuttini, F. M. (2017). Safety, tolerability, clinical, and joint structural outcomes of a single intra-articular injection of allogeneic mesenchymal precursor cells in patients following anterior cruciate ligament reconstruction: A controlled double-blind randomised trial. *Arthritis Research & Therapy*, 19(1), Article 180. <https://doi.org/10.1186/s13075-017-1391-0>
- Watt F. E. (2021). Posttraumatic osteoarthritis: What have we learned to advance osteoarthritis? *Current Opinion in Rheumatology*, 33(1), 74–83. <https://doi.org/10.1097/BOR.0000000000000760>
- Whittaker, J. L., Culvenor, A. G., Juhl, C. B., Berg, B., Bricca, A., Filbay, S. R., Holm, P., Macri, E., Urhausen, A. P., Ardern, C. L., Bruder, A. M., Bullock, G. S., Ezzat, A. M., Girdwood, M., Haberfield, M., Hughes, M., Ingelsrud, L. H., Khan, K. M., Le, C. Y., ... & Crossley, K. M. (2022). OPTIKNEE 2022: Consensus recommendations to optimise knee health after traumatic knee injury to prevent osteoarthritis. *British Journal of Sports Medicine*, 56(24), 1393–1405. <https://doi.org/10.1136/bjsports-2022-106299>

- Whittaker, J. L., Losciale, J. M., Juhl, C. B., Thorlund, J. B., Lundberg, M., Truong, L. K., Miciak, M., van Meer, B., Culvenor, A. G., Crossley, K. M., Roos, E. M., Lohmander, S., & van Middelkoop, M. (2022). Risk factors for knee osteoarthritis after traumatic knee injury: A systematic review and meta-analysis of randomised controlled trials and cohort studies for the OPTIKNEE Consensus. *British Journal of Sports Medicine*, *56*(24), 1406–1421. <https://doi.org/10.1136/bjsports-2022-105496>
- Whittaker, J. L., & Roos, E. M. (2019). A pragmatic approach to prevent post-traumatic osteoarthritis after sport or exercise-related joint injury. *Best Practice & Research in Clinical Rheumatology*, *33*(1), 158–171. <https://doi.org/10.1016/j.berh.2019.02.008>
- Whittaker, J. L., Truong, L. K., Losciale, J. M., Silvester-Lee, T., Miciak, M., Pajkic, A., Le, C. Y., Hoens, A. M., Mosewich, A., Hunt, M. A., Li, L. C., & Roos, E. M. (2022). Efficacy of the SOAR knee health program: Protocol for a two-arm stepped-wedge randomized delayed-controlled trial. *BMC Musculoskeletal Disorders*, *23*, Article 85. <https://doi.org/10.1186/s12891-022-05019-z>
- Wilson, R., & Abbott, J. H. (2019). The projected burden of knee osteoarthritis in New Zealand: Healthcare expenditure and total joint replacement provision. *New Zealand Medical Journal*, *132*(1503), 53–65.
- Wirth, W., Eckstein, F., Culvenor, A. G., Hudelmaier, M. I., Stefan Lohmander, L., & Frobell, R. B. (2021). Early anterior cruciate ligament reconstruction does not affect 5 year change in knee cartilage thickness: Secondary analysis of a randomized clinical trial. *Osteoarthritis and Cartilage*, *29*(4), 518–526. <https://doi.org/10.1016/j.joca.2021.01.004>
- Zadro, J., O’Keeffe, M., & Maher, C. (2019). Do physical therapists follow evidence-based guidelines when managing musculoskeletal conditions? Systematic review. *BMJ Open*, *9*, Article e032329. <https://doi.org/10.1136/bmjopen-2019-032329>