BMJ Open

Trajectory of knee health in runners with and without heightened osteoarthritis risk: the TRAIL prospective cohort study protocol

Danilo De Oliveira Silva [1,2] Richard T R Johnston [1,2]
Benjamin F Mentiplay [1,2] Melissa J Haberfield [1,2] Adam G Culvenor [1,2]
Andrea M Bruder,[1,2] Adam I Semciw,[1,2] Michael Girdwood,[1,2] Paula J Pappalardo,[1,2]
Connie Briggs,[1,2] Thomas J West,[1,2] Joshua P Hill,[1,2] Brooke E Patterson [1,2]
Christian J Barton,[1,2,3] Prasanna Sritharan [1,2] James L Alexander,[1,2]
David L Carey [1,2] Anthony G Schache,[1,2] Richard B Souza,[4] Valentina Pedoia,[4]
Edwin H Oei,[5] Stuart J Warden [6] Gustavo F Telles,[1,7] Matthew G King [1,2]
Michael P Hedger,[1,2] Mark Hulett,[8] Kay M Crossley [1,2]

Correspondence to
Dr Danilo De Oliveira Silva;
D.DeOliveiraSilva@latrobe.edu.au

ABSTRACT

Introduction Running is one of the most popular recreational activities worldwide, due to its low cost and accessibility. However, little is known about the impact of running on knee joint health in runners with and without a history of knee surgery. The primary aim of this longitudinal cohort study is to compare knee joint structural features on MRI and knee symptoms at baseline and 4-year follow-up in runners with and without a history of knee surgery. Secondary aims are to explore the relationships between training load exposures (volume and/or intensity) and changes in knee joint structure and symptoms over 4 years; explore the relationship between baseline running biomechanics, and changes in knee joint structure and symptoms over 4 years. In addition, we will explore whether additional variables confound, modify or mediate these associations, including sex, baseline lower-limb functional performance, knee muscle strength, psychological and sociodemographic factors.

Methods and analysis A convenience sample of at least 200 runners (sex/gender balanced) with (n=100) and without (n=100) a history of knee surgery will be recruited. Primary outcomes will be knee joint health (MRI) and knee symptoms (baseline; 4 years). Exposure variables for secondary outcomes include training load exposure, obtained daily throughout the study from wearable devices and three-dimensional running biomechanics (baseline). Additional variables include lower limb functional performance, knee extensor and flexor muscle strength, biomarkers, psychological and sociodemographic factors (baseline). Knowledge and beliefs about osteoarthritis will be obtained through predefined questions and semi-structured interviews with a subset of participants. Multivariable logistic and linear regression models, adjusting for potential confounding factors, will explore changes in knee joint structural features and symptoms, and the influence of potential modifiers and mediators.

Ethics and dissemination Approved by the La Trobe University Ethics Committee (HEC-19524). Findings will be disseminated to stakeholders, peer-review journals and conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ First longitudinal cohort study to explore the changes in knee joint structure and symptoms in runners with and without a history of knee surgery (and heightened osteoarthritis risk) over 4 years.
⇒ Participants will use wearable devices throughout the study, synchronised with a smartphone app, enabling accurate running training load data monitoring over 4 years.
⇒ Retention of participants to the study may be impacted by potential further restrictions due to the COVID-19 pandemic.

BACKGROUND

Running is one of the most popular recreational activities, with participation growing 58% in the past decade.[1] The health benefits of running (eg, 25%–40% reduced risk of premature mortality),[2] combined with its low cost and easy accessibility, contribute to its popularity. Although running has many positive health effects, it is also accompanied by an increased risk of lower-limb overuse injuries and pain.[3]

Repetitive joint loads from running might lead to damaged knee articular cartilage, precipitating knee osteoarthritis (OA) development.[4–7] Preclinical animal studies and observational cohorts identified potential detrimental effects of running on knee cartilage,[8 9] yet systematic reviews and meta-analyses[10–12] have not established a causal

relationship between running and knee OA risk.[13–15] Uninjured joints appear to tolerate the high joint load associated with running,[12] but the impact of running on the knee joints of individuals with, or at heightened risk of, OA remains unknown.[5] One of the most potent risk factors for OA is a traumatic knee injury and subsequent surgical intervention.[16] The impact of running on joint health in those who have undergone knee surgery (eg, anterior cruciate ligament reconstruction (ACLR) and meniscal surgery[16–19]), who have a particularly high risk of cartilage loss and early-onset OA,[17–20] requires exploration. MRI enables the assessment of early knee OA features, and changes over time that may be observed early in the disease trajectory.[21–25] For example, there is evidence of MRI-detected knee OA from one up to 10 years following ACLR in physically active young adults (18–50 years old).[21–25] Furthermore, MRI (particularly qMRI techniques such as T2 mapping) is sensitive to the accelerated progression of early OA features on MRI (eg, cartilage and meniscal defects) that occur in the short to medium term (1–5 years) after knee surgery.[23 26]

The longitudinal trajectory of symptomatic features (eg, pain, function, quality of life) in regular running athletes with a history of knee surgery has not been prospectively explored.[3] In older adults (45–65 years) with early knee OA, those with bilateral lower-limb pain, associated comorbidities or psychological impairments tended to have a worse trajectory of structural and symptomatic features over 5 years.[27–29] While in a younger population (18–55 years) with a history of ACLR, those with patellofemoral cartilage defects and associated injuries (eg, meniscal lesions) tend to have worse quality of life and symptoms at 5 years after surgery.[26 30] But none of these studies investigated the role of regular running loads on the symptomatic or structural OA (knee health) trajectory. Exploring the longitudinal trajectory of symptoms in regular running athletes with a history of surgery and heightened risk of knee OA, could generate insights on specific knee OA prevention and management strategies.

Exposure to running loads (duration, distance, frequency and intensity)[31] may influence knee health trajectory.[32] However, the relationship of device-measured running training load with changes in knee joint structure and symptoms over-time is unknown.[13 33] Running biomechanics are altered following knee injury and not fully restored with surgery.[21 34–37] Understanding whether running biomechanics are associated with knee OA onset and progression could help healthcare professionals to optimise the management of people who wish to run with knee OA and/or following knee surgery.[13 24 34 38] Other prognostic variables that may relate to future knee joint health and symptoms in running athletes with and without a history of knee surgery include sex, baseline lower-limb functional performance, knee muscle strength, psychological and sociodemographic factors.[13 33]

Objectives
Primary objectives
To compare knee joint (ie, patellofemoral and tibiofemoral) structural features on MRI and knee symptoms at baseline and 4-year follow-up in runners with and without a history of knee surgery.

Secondary objectives
In runners with and without a history of knee surgery, to (i) explore the relationships between training load exposures (running volume and/or intensity) and changes in knee joint structure and symptoms over a 4-year period; (ii) explore the relationship between baseline running biomechanics, and changes in knee joint structure and symptoms over a 4-year period.

We will also explore whether additional variables confound, modify or mediate these associations, including sex, baseline lower-limb functional performance, knee muscle strength, biomarkers, psychological and sociodemographic factors.

Tertiary objectives
We propose to (i) explore baseline and longitudinal associations between knee joint structure, patient-reported outcomes, training load exposures and biopsychosocial factors in runners with and without a history of knee surgery; (ii) evaluate the knowledge and beliefs of runners regarding running and the risk of knee OA.

METHODS
Study design
The TRAIL (TRAjectory of knee heaLth in runners) prospective cohort study will recruit a population of runners with and without a history of knee surgery. The project is approved by the La Trobe University Ethics Committee (HEC-19524) and conducted according to the Declaration of Helsinki. The development of this protocol was guided by the PROGnosis RESearch Strategy (PROGRESS 1 and 2) framework.[39 40] Participants who wish to drop out of the study will have their data analysed unless they request their data to be withdrawn.

Setting
Participants will undergo knee MRIs at a private imaging centre. Clinical examination, functional performance tests, three-dimensional (3D) running biomechanics and muscle strength tests will be completed at the University Gait Laboratory. Patient-reported outcome measures will be completed digitally in a customised electronic platform (Smartabase, Fusion Sport Pty Ltd, Australia). Daily session running load exposure data will be obtained through a wearable device (figure 1). Primary and secondary outcomes will be obtained in the following order: (i) patient-reported outcomes, (ii) knee MRI, (iii) biomechanics, performance-based measures and strength tests. Participants will be asked to refrain from taking any analgesic medications and participating in
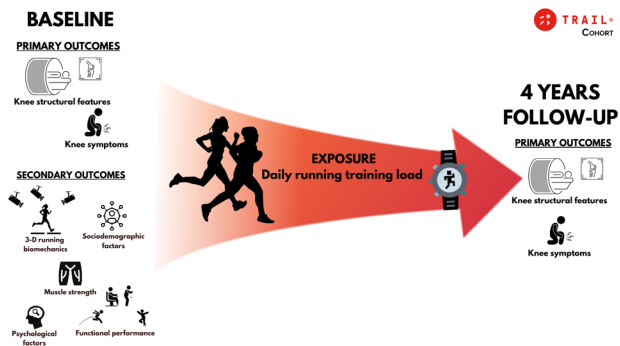
Figure 1 Schematic representation of the design and outcomes of the study. This was created by the authors and are free to use if acknowledgement of the source is provided.

Figure 2 (A) Sagittal proton density fat suppressed; (B) multi-echo-spin-echo (T2 relaxation time); (C) sagittal fast spoiled gradient echo (thickness and bone shape). This image belongs to the authors and are not free to use.

strenuous physical efforts the day prior to data collection or activities they were unaccustomed to.

Recruitment strategy

We will recruit at least 100 (at least 50 women) runners with a history of knee surgery and at least 100 (at least 50 women) control runners (no knee injury/surgery history) from Australia (table 1).[41] To facilitate recruitment we will advertise the study on running clubs, social media and running podcasts. Interested runners will contact the TRAIL research team using a registration recruitment link available at trail.latrobe.edu.au. On registration, an investigator will complete a telephone-based eligibility screening with potential participants. If eligible, participants will complete an electronic consent form to be enrolled in the study.

Outcomes

Primary outcomes will be measured at baseline and 4-year follow-up. Additional variables will be measured at baseline except for training load (daily). A summary of all outcome measures and their respective timepoints are described in figure 1.

Primary outcome: knee joint structural features (baseline and 4-year follow-up)

Knee MRIs will be acquired at baseline and 4-year follow-up using a 3T scanner (Signa Pioneer, General Electric Healthcare, Milwaukee, USA) and an 18-channel knee coil (online supplemental file 1). Sequences acquired will include proton density-weighted fat suppressed fast spin-echo sequences in the sagittal, axial and coronal planes; a sagittal T2 mapping multi-echo spin-echo sequence; and a sagittal fast spoiled gradient echo sequence (figure 2). Changes in cartilage collagen content and orientation in extracellular matrices reflecting degeneration will be defined by quantitative changes in T2 relaxation times[42–44] at baseline and 4-year follow-up. Knee cartilage thickness and bone shape changes over 4 years will also be assessed.[45–47] A custom-written MATLAB-based code (Mathworks, Natick, MA, USA) incorporating deep learning-based automatic segmentation followed by human quality control will be used for bone shape, both T2 relaxation time and cartilage thickness. Knee OA features (eg, cartilage defects, meniscal tears, bone marrow lesions, osteophytes), in patellofemoral and tibiofemoral joints, will be scored with established scoring systems[48 49] at baseline and 4-year follow-up by a trained reader blinded to clinical outcomes. Individual OA feature worsening will be defined as increase in the size or depth of lesions as previously established in cohorts at risk of knee OA.[26 50]

Primary outcome: knee symptoms (baseline and 4-year follow-up)

Knee injury and Osteoarthritis Outcome Score (KOOS$_4$) is the average score for four of the five KOOS subscales, covering pain, symptoms, difficulty in sports and recreational activities, and quality of life, with scores ranging from 0 (worst) to 100 (best).[51] KOOS$_4$ is valid and reliable

Table 1 Participant eligibility criteria

Participants	Inclusion criteria	Exclusion criteria
All participants	Age 18–50 years	Currently pregnant
	Currently running ≥3 times and ≥10 km per week on average in the past 6 months	Contraindications to MRI
		Unable to understand spoken or written English
Runners with a history of knee surgery	History of knee surgery (anterior or posterior cruciate ligament, meniscal, chondroplasty, collateral ligament or arthroscopy)	History of intra-articular knee fracture, arthroplasty, osteotomy, patellar tenotomy or lateral retinacular release. Other lower-limb surgery (eg, hip/ankle)
Asymptomatic control runners		History of lower limb surgery. Any musculoskeletal traumatic or overuse injury in the last 6 months (requiring period of NWB for >24 hours)[104 105]

NWB, non-weight bearing.

(Intraclass Correlation Coefficient (ICC)>0.96)[52] to assess self-reported knee-related issues from acute knee injury through to the development and progression of OA.[53] In addition to the primary timepoints (baseline and 4-year follow-up), we will collect $KOOS_4$ data six-monthly.[54] Individual KOOS subscales will also be obtained and explored as secondary outcomes, including the activities of daily living subscale and the patellofemoral subscale, which are both valid and demonstrate good reliability (ICC>0.86).[52 55–58]

Exposure outcome: running training load (daily until 4-year follow-up)
External running loads (running volume and intensity): all participants
Over the 4-year study period, all participants will use an electronic wearable device to provide daily session running training load data. The wearable device will allow for data extraction via an app (Smartabase, Fusion Sport Pty Ltd, Australia) to provide daily session running: distance (km); duration (min); pace (average min/km) and cadence (average steps/min).[32 33] The Smartabase was set up to send monthly correspondence to the participants.

Internal running loads (heart rate): subset of participants
Average and maximum heart rates[59] will be extracted from a subset of participants, whose electronic wearable device (Garmin or Apple Watch) captures heart rate data from each recorded running session. Heart rate monitoring will provide data on the participants' physiological stress responses during each running session.[60]

Exposure outcome: running biomechanics (baseline)
Set up
3-D kinematic data will be captured using a 10-camera motion capture system (VICON Motion Systems Ltd, Oxford, UK), sampling at a frequency of 200 Hz. Ground reaction force data will be recorded from two force plates (AMTI, Massachusetts, USA) embedded in the laboratory floor and blinded to participants, sampling at 1000 Hz. Participants will wear their own shoes, shorts and crop top. Forty-eight spherical reflective markers (14 mm) will be attached to various locations on the trunk, upper-limbs and lower-limbs to track trunk and lower extremity motion during the tasks (online supplemental file 2).[61]

Procedures
Prior to performing the dynamic trials, a static trial will be captured with the participant assuming a neutral upright stance pose with all markers in situ.[38 62 63] Participants will then run through a 25 m space at an 'easy pace' running speed (3–3.5 m/s) and then at a faster running pace (5–6 m/s).[64 65] Laser timing gates (Fusion Sport Smart Speed Pty Ltd, Australia) will be set up 5 m apart, on either side of the calibrated measurement field to record running speed.[65] Before commencing the running trials, all participants will complete a warm-up consisting of two repeated easy pace running trials to familiarise themselves with the experimental conditions.[38 65] Participants will complete at least eight successful trials at each running speed (starting with 3.5 m/s). A successful trial is defined as meeting the required running speed and clear foot contact on the force plates. One two-dimensional (2D) Vicon Bonita motion camera will also be used to record the foot strike pattern of each running trial.

Additional variables
For all functional performance and strength tests, both legs will be tested, with the left leg always tested first.

Sociodemographic factors and participant characteristics (baseline)
Sociodemographic factors include address, highest education level, current employment status, current occupation, if participants are from Aboriginal or Torres Strait Islander (Indigenous) background. At baseline, we will also obtain participant's age, sex, height, body mass, knee injury and surgery history, and use of pain medication. Knee injury and surgery type(s) and date(s) will be recorded and classified with the Orchard Sports Injury Classification System.[66] Running behaviour will include previous training experience and running training characteristics (duration, distance, frequency, performance, type of training, shoe preferences and use of other running accessories). We will also obtain data regarding participation in other weight-bearing sports and frequency.

Lower-limb functional performance (baseline)
Hop for distance
Participants will stand on a starting line, weight bearing on a single lower limb with both hands held behind their back, then instructed to hop as far forward as possible landing on the same foot. The distance hopped (cm) will be measured from the toe at take-off to the heel at landing, and the furthest of three trials will be recorded.[67–70] The trial will be considered unsuccessful if the participant loses their balance or needs to support their body mass on the non-tested limb. In the case of an unsuccessful trial, an additional trial will be performed. The single-leg hop for distance demonstrates excellent test–retest reliability (ICC=0.94).[71]

Side hop
Participants will hop side to side between two parallel strips of tape, placed 40 cm apart with their hands on their waist.[72] Participants will be instructed to hop as many times as possible for 30 s. A successful side hop is defined as a hop performed over the two strips of tape without touching the tape. An assessor will record the number of successful and unsuccessful hops. This test demonstrates good test–retest reliability in people following surgery (ICC=0.87).[72]

One leg rise
Participants will be positioned sitting on the edge of an adjustable plinth with the heel of the test leg positioned on a line marked on the floor 10 cm in front of the edge

of the plinth. The plinth height will be adjusted so that the angle of the testing knee is 90° for all participants. Participants will keep their arms folded across their chest during the whole test. Participants will be instructed to rise from the sitting position to an upright standing position, until they achieve full knee extension, and to return to sitting in a controlled manner. Cadence of one leg rises will be paced with electronic auditory metronome at 45 bpm and the maximum number of successful repetitions recorded. The repetition will be considered unsuccessful if the participant does not achieve full knee extension or if they do not seat down in a controlled manner. One-leg rise test demonstrates good intra-rater reliability in a post-surgical population (ICC=0.84).[73]

Vertical hop (leg stiffness)
Participants will place both hands on their waist, stand on one leg, then hop vertically for 30 s on a force plate.[74] A metronome will be used (120 bpm) to standardise hop pace. The test will be performed on both legs, 1 min rest will be allowed between each leg.[74] Participants will complete five practice hops on each leg before starting the test. The trials will be recorded by the 2D Vicon Bonita motion camera and participants will wear the reflective markers described in online supplemental file 2. Leg stiffness will be calculated as described by Dalleau *et al.*[74]

Knee extensors and flexors muscle strength (baseline)
Bilateral peak isometric torque and rate of torque development (RTD) will be assessed using an isokinetic dynamometer at 60° of knee flexion (Biodex System 4 Pro, New York, NY, USA) with a sampling frequency of 100 Hz.[75 76] This test is reliable in people following knee surgery (ICC=0.92).[76]

Participants will be instructed to perform a contraction as powerful, and quickly as possible.[75] Standardised verbal encouragement will encourage participants to achieve maximum power and strength. Participants will perform one submaximal familiarisation contraction for knee extensors and flexors (6 s) prior to performing three maximal isometric contractions for both each muscle group (6 s duration with 30 s rest between each contraction).[75] Torque data will be normalised to participant body mass ($N \cdot m \cdot kg^{-1}$). RTD will be derived from the slope of the torque/time curve, obtained by dividing the normalised torque variation ($N \cdot m \cdot kg^{-1}$, represented as %) by the time variation (ms) from the onset of the contraction.[77 78]

Clinical knee examination (baseline)
Participants will undergo a standardised clinical knee examination by an experienced physiotherapist (>10 years of experience managing running athletes). On both knees, we will assess: (i) passive knee flexion range of motion in supine with a goniometer[79]; (ii) knee extension difference between legs in prone with both knees over the edge of a plinth (record the heel-height difference in cm[80]); (iii) medial and lateral knee joint line tenderness in supine (graded present or absent); (iv) assessor-based knee joint crepitus (graded positive or negative). An assessor will place the palm of their hands on the knee joint and ask participants to perform two consecutive bilateral squats to 90° of knee flexion.[54 81 82] The test will be considered positive for knee crepitus when a grinding, crackling or crunching sensation during knee extension or flexion is detected (one or two clicks or pops will not be considered crepitus).

Biomarkers: subset of participants
Blood samples will be collected from a subset of participants with and without knee surgery. Venous blood (~6 mL) will be collected from the antecubital vein, processed (centrifuge for 10 min at ~1500 rcf) and plasma frozen (−80°C).[83] Flow cytometry-based cytometric bead array assays (BD Biosciences) will be used to analyse plasma samples for cytokine levels (interleukin (IL) 1b, IL-6, IL-8, IL-10, tumor necrosis factor-a). The assays will be performed and analysed on a FACS Canto II (BD Biosciences) using FCAP Array V.3.0.1 software per the manufacturer's instructions.

Health well-being (baseline)
Sleep
The Athlete Sleep Screening Questionnaire (ASSQ) is a 16-item questionnaire validated in athletic populations, to measure both sleep and circadian factors related to sleep (ie, quantity, quality, disturbance).[84 85] Five items are used to generate a 'sleep difficulty score' which classifies athletes into a category of a clinical sleep problem: no problem (score 0–4); mild (score 5–7); moderate (score 8–10) or severe (score 11–17). The ASSQ demonstrates good diagnostic sensitivity (81%), specificity (93%) and positive predictive value (Cohen's kappa=0.84).[85]

Health satisfaction
The Patient Acceptable Symptom State (PASS)[86] asks about participants perception about their own health. The participants will complete yes or no to the following question 'Considering your knee function, do you feel that your current state is satisfactory? With knee function, you should take into account all activities during your daily life, sport and recreational activities, your level of pain and other symptoms, and also your knee-related quality of life'. PASS responses are associated with disease severity in people with OA.[87]

Psychological factors (baseline)
Fear of movement
The Tampa Scale for Kinesiophobia (TSK) was designed to identify fear of movement or activity avoidance in chronic and acute musculoskeletal pain.[88] The TSK consists of 17 items and is scored on a 4-point Likert scale.[88–90] A high score indicates a strong fear of pain-related movement. The TSK has good construct validity and reliability (Cronbach alpha, 0.74–0.87; ICC=0.80).[91 92]

Knee self-efficacy

The Knee-Self Efficacy Scale (K-SES) is designed to assess self-efficacy beliefs related to behaviours after knee surgery.[93] The K-SES consists of 22 items measuring daily activities, sports and leisure activities, physical activity and knee function in the future. The K-SES is valid and demonstrates good reliability (ICC=0.95).[94]

Running and OA beliefs and experiences (subset of participants throughout study period)
Qualitative data

Semi-structured interviews, guided by a prestructured topic guide will explore beliefs and experiences related to running and OA, including perceived benefits and risks of running. Purposive sampling will be used to recruit and interview participants of different sexes and age. Approximately 40 interviews (20 runners with a history of knee surgery; 20 control runners), will be conducted. Interviews will be audio recorded, transcribed, and analysed using Framework Analysis,[95] supported by Nvivo software.

Quantitative data

Participant's beliefs regarding running and knee OA will be collected using a questionnaire developed for people with and without medical background and knowledge.[96 97]

Data analysis plan
Sample size calculation

A sample size of 144 will enable the proportion of participants with structural change over 4 years to be estimated at the hypothesised value of 16%[98] with a precision of 6% (alpha=0.05).[62] Allowing for 28% dropouts and missing data,[99] 200 participants will be recruited.

Statistical analysis of baseline characteristics, and 4-year trajectory of knee joint structural features on MRI and knee symptoms will be performed descriptively and comparatively using parametric or non-parametric statistics depending on the nature of the data, with adjustment for potential confounders by multivariable regression analysis. To explore the relationships between (i) training load (exposure) and (ii) running biomechanics with change in knee OA structural features and symptoms (outcomes) in the knee surgery and control groups, multivariable logistic regression models and linear regression models, respectively, will be constructed adjusting for potential confounding variables (eg, age, time since surgery). The influence of moderating or mediating variables will be explored. Data will be transformed as necessary. Further models will be developed to explore relationships between changes in knee OA structural and symptomatic features and clinical symptoms, biomechanical, functional performance, muscle strength, biomarkers, psychological, social and factors.

Participant retention strategies

We developed engagement activities to maximise response rate and participant retention. These activities include (i) monthly correspondence; (ii) recruitment of two ambassadors to promote the importance of ongoing participation in the study (eg, female Australian Olympic marathon runner and a male runner with a history of knee surgery); (iii) publication of podcasts on a variety of running-related projects targeted to participants on our customised study website and (iv) sharing annual newsletters updating participants with interim outcomes.

Patient and public involvement

Interviews with 27 ACLR participants from a previous trial[100] informed the design and development of the research questions of our prospective cohort study. Their knowledge and beliefs about running and OA risk after knee surgery ('I want to be able to go for a run – but my surgeon told me running was bad for my knees'; 17/27 agree/strongly agree that repetitive joint loading increased the risk of OA) highlighted the need to better understand the relationship between running exposure with knee joint health and symptoms. Running was a common goal after ACLR (12/27 had returned to running and only 5/27 returned to their preinjury sport), and many (44%) re-valued their goals to aim for return to running instead of sport ('overall very happy with improvements in pain everyday activities, would like to be able to increase running tolerance'). The views of and data from participants following ACLR highlighted the need for this longitudinal prospective study in runners with a history of knee surgery.

We will disseminate the findings in peer-reviewed journals and social media.[101] We expect to publish several articles based on data collected at the baseline and follow-up. All results (negative, positive and inconclusive findings) will be disseminated and published. Participants will be notified of all published studies and receive an infographic with a summary of the findings.

DISCUSSION

Repetitive joint loads associated with running have been hypothesised to be detrimental to knee joint health.[4 8 10] The TRAIL study will be the first prospective cohort study to challenge the belief that 'running is bad for your knees'[96] by evaluating knee joint structural features and knee symptoms at baseline and 4-year follow-up in runners, and comparing the changes in those with and without a history of knee surgery. A strength of our study is the use of MRI techniques, such as T2 mapping, which can detect early signs of knee OA features after knee surgery.[26] Interestingly, a systematic review reported that T2 values would decrease immediately after running, and then return to baseline in the next 24 hours.[102] However, a prospective study with longer-term follow-up is necessary to understand the impact of regular running on knee joint structural features.

We will also quantify the association of device-measured running load exposure and running biomechanics with changes in knee joint structural features and symptoms over time. Previous reports suggest that MRI-based superficial and medial areas of knee cartilage and meniscus

seem to be more susceptible to mechanical loading.[102] But no prior study has investigated the role of regular running loads or the knee joint load (eg, knee extension and abduction net external joint torques, tibiofemoral and patellofemoral reaction forces) during running itself on MRI knee joint structural features. Clinically, our study may offer clinicians the ability to identify modifiable factors that could be suitable targets for prevention and intervention strategies such as running retraining and load management.[32 103]

We will redress the gender/sex bias in this research field by including a balanced number of women and men runners. For example, the recent systematic review exploring the association of running with hip and knee OA included 125 810 participants, where approximately 71% were male runners.[10] TRAIL will tackle the underrepresentation of female runners, producing results that can be applied to all people who run.

Limitations

Our study has some limitations that should be acknowledged. Conducting a 4-year longitudinal cohort study has an inherent risk of follow-up loss; we developed participant retention strategies to mitigate this risk. Capturing 'real-world' running load data through wearables over 4 years will provide valuable insight into the association between load, overuse injury and knee health. However, there is a risk of participants stopping or making inconsistent use of their wearables despite our risk mitigation strategies (ie, monthly correspondence with participants). Participants may change their running behaviour (for a number of reasons, including injury), and drop below the eligibility criteria for inclusion. Different wearable brands (Garmin or Apple Watch) may result in slightly different measures of internal running loads (eg, heart rate).

Author affiliations

[1]La Trobe Sport and Exercise Medicine Research Centre (LASEM), School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Victoria, Australia
[2]Australian International Olympic Committee (IOC) Research Centre, Melbourne, Victoria, Australia
[3]Department of Physiotherapy, Podiatry and Prosthetics and Orthotics, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Victoria, Australia
[4]Department of Radiology and Biomedical Imagining, University of California San Francisco, San Francisco, California, USA
[5]Department of Radiology & Nuclear Medicine, Erasmus Universiteit Rotterdam, Rotterdam, The Netherlands
[6]Department of Physical Therapy, Indiana University, Indianapolis, Indiana, USA
[7]Rehabilitation Science Postgraduation Program, Augusto Motta University Centre, Rio de Janeiro, Brazil
[8]Department of Biochemistry and Chemistry, La Trobe Institute for Molecular Science, La Trobe University, Melbourne, Victoria, Australia

ORCID iDs
Danilo De Oliveira Silva http://orcid.org/0000-0003-0753-2432
Richard T R Johnston http://orcid.org/0000-0002-0090-6991
Benjamin F Mentiplay http://orcid.org/0000-0002-4360-8310
Melissa J Haberfield http://orcid.org/0000-0002-6366-0896
Adam G Culvenor http://orcid.org/0000-0001-9491-0264
Brooke E Patterson http://orcid.org/0000-0002-6570-5429
Prasanna Sritharan http://orcid.org/0000-0001-9543-4108
David L Carey http://orcid.org/0000-0001-6388-8957
Stuart J Warden http://orcid.org/0000-0002-6415-4936
Matthew G King http://orcid.org/0000-0003-0470-5924
Kay M Crossley http://orcid.org/0000-0001-5892-129X

REFERENCES

1 Andersen J. The state of running. 2019. Available: https://runrepeat.com/state-of-running
2 Lee D-C, Brellenthin AG, Thompson PD, *et al*. Running as a key lifestyle medicine for longevity. *Prog Cardiovasc Dis* 2017;60:45–55.
3 Messier SP, Martin DF, Mihalko SL, *et al*. A 2-year prospective cohort study of overuse running injuries: the runners and injury longitudinal study (trails). *Am J Sports Med* 2018;46:2211–21.
4 Qiu L, Perez J, Emerson C, *et al*. Biochemical changes in knee articular cartilage of novice half-marathon runners. *J Int Med Res* 2019;47:5671–9.
5 Esculier J-F, Jarrett M, Krowchuk NM, *et al*. Cartilage recovery in runners with and without knee osteoarthritis: a pilot study. *Knee* 2019;26:1049–57.
6 Coburn SL, Crossley KM, Kemp JL, *et al*. Is running good or bad for your knees? A systematic review and meta-analysis of cartilage morphology and composition changes in the tibiofemoral and patellofemoral joints. *Osteoarthritis and Cartilage* 2023;31:144–57.
7 Hart HF, Patterson BE, Crossley KM, *et al*. May the force be with you: understanding how patellofemoral joint reaction force compares across different activities and physical interventions—a

systematic review and meta-analysis. *Br J Sports Med* 2022;56:521–30.

8 Lapveteläinen T, Nevalainen T, Parkkinen JJ, *et al*. Lifelong moderate running training increases the incidence and severity of osteoarthritis in the knee joint of C57BL mice. *Anat Rec* 1995;242:159–65.

9 Walker JM. Exercise and its influence on aging in rat knee joints. *J Orthop Sports Phys Ther* 1986;8:310–9.

10 Alentorn-Geli E, Samuelsson K, Musahl V, *et al*. The association of recreational and competitive running with hip and knee osteoarthritis: A systematic review and meta-analysis. *J Orthop Sports Phys Ther* 2017;47:373–90.

11 Timmins KA, Leech RD, Batt ME, *et al*. Running and knee osteoarthritis: a systematic review and meta-analysis. *Am J Sports Med* 2017;45:1447–57.

12 Khan MCM, O'Donovan J, Charlton JM, *et al*. The influence of running on lower limb cartilage: a systematic review and meta-analysis. *Sports Med* 2022;52:55–74.

13 Miller RH. Joint loading in runners does not initiate knee osteoarthritis. *Exerc Sport Sci Rev* 2017;45:87–95.

14 Konradsen L, Hansen EMB, Søndergaard L. Long distance running and osteoarthrosis. *Am J Sports Med* 1990;18:379–81.

15 Leech RD, Edwards KL, Batt ME. Does running protect against knee osteoarthritis? or promote it? assessing the current evidence. *Br J Sports Med* 2015;49:1355–6.

16 Whittaker JL, Losciale JM, Juhl CB, *et al*. 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. *Br J Sports Med* 2022;56:1406–21.

17 Lohmander LS, Englund PM, Dahl LL, *et al*. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med* 2007;35:1756–69.

18 Culvenor AG, Cook JL, Collins NJ, *et al*. Is patellofemoral joint osteoarthritis an under-recognised outcome of anterior cruciate ligament reconstruction? A narrative literature review. *Br J Sports Med* 2013;47:66–70.

19 Filbay S, Gauffin H, Andersson C, *et al*. Prognostic factors for tibiofemoral and patellofemoral osteoarthritis 32-37 years after anterior cruciate ligament injury managed with early surgical repair or rehabilitation alone. *Osteoarthritis Cartilage* 2021;29:1682–90.

20 Patterson BE, Culvenor AG, Barton CJ, *et al*. Patient-reported outcomes one to five years after anterior cruciate ligament reconstruction: the effect of combined injury and associations with osteoarthritis features defined on magnetic resonance imaging. *Arthritis Care Res (Hoboken)* 2020;72:412–22.

21 Williams JR, Neal K, Alfayyadh A, *et al*. Knee cartilage T2 relaxation times 3 months after ACL reconstruction are associated with knee gait variables linked to knee osteoarthritis. *J Orthop Res* 2022;40:252–9.

22 Whittaker JL, Toomey CM, Woodhouse LJ, *et al*. Association between MRI-defined osteoarthritis, pain, function and strength 3-10 years following knee joint injury in youth sport. *Br J Sports Med* 2018;52:934–9.

23 van Meer BL, Oei EHG, Meuffels DE, *et al*. Degenerative changes in the knee 2 years after anterior cruciate ligament rupture and related risk factors: a prospective observational follow-up study. *Am J Sports Med* 2016;44:1524–33.

24 Van Ginckel A, Verdonk P, Victor J, *et al*. Cartilage status in relation to return to sports after anterior cruciate ligament reconstruction. *Am J Sports Med* 2013;41:550–9.

25 Culvenor AG, Collins NJ, Guermazi A, *et al*. Early knee osteoarthritis is evident one year following anterior cruciate ligament reconstruction: a magnetic resonance imaging evaluation. *Arthritis Rheumatol* 2015;67:946–55.

26 Patterson BE, Culvenor AG, Barton CJ, *et al*. Worsening knee osteoarthritis features on magnetic resonance imaging 1 to 5 years after anterior cruciate ligament reconstruction. *Am J Sports Med* 2018;46:2873–83.

27 Holla JFM, van der Leeden M, Heymans MW, *et al*. Three trajectories of activity limitations in early symptomatic knee osteoarthritis: a 5-year follow-up study. *Ann Rheum Dis* 2014;73:1369–75.

28 Wesseling J, Bastick AN, ten Wolde S, *et al*. Identifying trajectories of pain severity in early symptomatic knee osteoarthritis: a 5-year followup of the cohort hip and cohort knee (check) study. *J Rheumatol* 2015;42:1470–7.

29 Paradowski PT, Englund M, Lohmander LS, *et al*. The effect of patient characteristics on variability in pain and function over two years in early knee osteoarthritis. *Health Qual Life Outcomes* 2005;3:59.

30 Patterson B, Culvenor AG, Barton CJ, *et al*. Poor functional performance 1 year after ACL reconstruction increases the risk of early osteoarthritis progression. *Br J Sports Med* 2020;54:546–53.

31 von Rosen P, Frohm A, Kottorp A, *et al*. Multiple factors explain injury risk in adolescent elite athletes: applying a biopsychosocial perspective. *Scand J Med Sci Sports* 2017;27:2059–69.

32 Paquette MR, Napier C, Willy RW, *et al*. Moving beyond weekly " distance": optimizing quantification of training load in runners. *J Orthop Sports Phys Ther* 2020;50:564–9.

33 Johnston R, Cahalan R, Bonnett L, *et al*. Training load and baseline characteristics associated with new injury/pain within an endurance sporting population: a prospective study. *Int J Sports Physiol Perform* 2019;14:590–7.

34 Sritharan P, Schache AG, Culvenor AG, *et al*. Between-limb differences in patellofemoral joint forces during running at 12 to 24 months after unilateral anterior cruciate ligament reconstruction. *Am J Sports Med* 2020;48:1711–9.

35 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.

36 Sritharan P, Schache AG, Culvenor AG, *et al*. Patellofemoral and tibiofemoral joint loading during a single-leg forward hop following ACL reconstruction. *J Orthop Res* 2022;40:159–69.

37 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.

38 Schache AG, Blanch PD, Dorn TW, *et al*. Effect of running speed on lower limb joint kinetics. *Med Sci Sports Exerc* 2011;43:1260–71.

39 Hemingway H, Croft P, Perel P, *et al*. Prognosis research strategy (progress) 1: a framework for researching clinical outcomes. *BMJ* 2013;346:e5595.

40 Riley RD, Hayden JA, Steyerberg EW, *et al*. Prognosis research strategy (progress) 2: prognostic factor research. *PLoS Med* 2013;10:e1001380.

41 Ramskov D, Nielsen RO, Sørensen H, *et al*. The design of the run clever randomized trial: running volume, -intensity and running-related injuries. *BMC Musculoskelet Disord* 2016;17:177.

42 Pedoia V, Lee J, Norman B, *et al*. Diagnosing osteoarthritis from T2 maps using deep learning: an analysis of the entire osteoarthritis initiative baseline cohort. *Osteoarthritis Cartilage* 2019;27:1002–10.

43 Razmjoo A, Caliva F, Lee J, *et al*. T 2 analysis of the entire osteoarthritis initiative dataset. *J Orthop Res* 2021;39:74–85.

44 Xia Y, Moody JB, Alhadlaq H. Orientational dependence of T2 relaxation in articular cartilage: a microscopic MRI (micromri) study. *Magn Reson Med* 2002;48:460–9.

45 Iriondo C, Liu F, Calivà F, *et al*. Towards understanding mechanistic subgroups of osteoarthritis: 8-year cartilage thickness trajectory analysis. *J Orthop Res* 2021;39:1305–17.

46 Pedoia V, Su F, Amano K, *et al*. Analysis of the articular cartilage T1ρ and T2 relaxation times changes after ACL reconstruction in injured and contralateral knees and relationships with bone shape. *J Orthop Res* 2017;35:707–17.

47 Liao TC, Jergas H, Tibrewala R, *et al*. Longitudinal analysis of the contribution of 3D patella and trochlear bone shape on patellofemoral joint osteoarthritic features. *J Orthop Res* 2021;39:506–15.

48 Roemer FW, Frobell R, Lohmander LS, *et al*. Anterior cruciate ligament osteoarthritis score (ACLOAS): longitudinal MRI-based whole joint assessment of anterior cruciate ligament injury. *Osteoarthritis Cartilage* 2014;22:668–82.

49 Hunter DJ, Guermazi A, Lo GH, *et al*. Evolution of semi-quantitative whole joint assessment of knee oa: MOAKS (MRI osteoarthritis knee score). *Osteoarthritis Cartilage* 2011;19:990–1002.

50 Runhaar J, Schiphof D, van Meer B, *et al*. How to define subregional osteoarthritis progression using semi-quantitative MRI osteoarthritis knee score (MOAKS). *Osteoarthritis Cartilage* 2014;22:1533–6.

51 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.

52 Collins NJ, Misra D, Felson DT, *et al*. Measures of knee function: international knee documentation committee (IKDC) subjective knee evaluation form, knee injury and osteoarthritis outcome score (KOOS), knee injury and osteoarthritis outcome score physical function short form (KOOS-PS), knee ou. *Arthritis Care Res* 2011;63:S208–28.

53 Roos EM, Roos HP, Lohmander LS, *et al*. Knee injury and osteoarthritis outcome score (KOOS) -- development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28:88–96.

54 de Oliveira Silva D, Barton C, Crossley K, *et al*. Implications of knee crepitus to the overall clinical presentation of women with and without patellofemoral pain. *Phys Ther Sport* 2018;33:89–95.

55 Salavati M, Akhbari B, Mohammadi F, *et al*. Knee injury and osteoarthritis outcome score (KOOS): reliability and validity in competitive athletes after anterior cruciate ligament reconstruction. *Osteoarthritis Cartilage* 2011;19:406–10.

56 Roos EM, Lohmander LS. The knee injury and osteoarthritis outcome score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64.

57 Gudbergsen H, Bartels EM, Krusager P, *et al*. Test-retest of computerized health status questionnaires frequently used in the monitoring of knee osteoarthritis: a randomized crossover trial. *BMC Musculoskelet Disord* 2011;12:190.

58 Crossley KM, Macri EM, Cowan SM, *et al*. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation using the COSMIN checklist. *Br J Sports Med* 2018;52:1130–6.

59 Seiler S, Tønnessen E. Intervals, thresholds, and long slow distance: the role of intensity and duration in endurance training. *Training* 2009;13:32–53.

60 Schneider C, Hanakam F, Wiewelhove T, *et al*. Heart rate monitoring in team sports-A conceptual framework for contextualizing heart rate measures for training and recovery prescription. *Front Physiol* 2018;9:639.

61 Kemp JL, Johnston RTR, Coburn SL, *et al*. Physiotherapist-led treatment for femoroacetabular impingement syndrome (the physiofirst study): a protocol for a participant and assessor-blinded randomised controlled trial. *BMJ Open* 2021;11:e041742.

62 Crossley KM, Pandy MG, Majumdar S, *et al*. Femoroacetabular impingement and hip osteoarthritis cohort (force): protocol for a prospective study. *J Physiother* 2018;64:55.

63 De Oliveira Silva D, Willy RW, Barton CJ, *et al*. Pain and disability in women with patellofemoral pain relate to kinesiophobia, but not to patellofemoral joint loading variables. *Scand J Med Sci Sports* 2020;30:2215–21.

64 Alizadeh S, Mattes K. How anterior pelvic tilt affects the lower extremity kinematics during the late swing phase in soccer players while running: a time series analysis. *Hum Mov Sci* 2019;66:459–66.

65 Mentiplay BF, Kemp JL, Crossley KM, *et al*. Relationship between hip muscle strength and hip biomechanics during running in people with femoroacetabular impingement syndrome. *Clin Biomech (Bristol, Avon)* 2022;92:105587.

66 Til L, Orchard J, Rae K. The orchard sports injury classification system (OSICS) version 10. *Apunt Med l'Esport* 2008;43:109–12.

67 Bolgla LA, Keskula DR. Reliability of lower extremity functional performance tests. *J Orthop Sports Phys Ther* 1997;26:138–42.

68 Munro AG, Herrington LC. Between-session reliability of four hop tests and the agility t-test. *J Strength Cond Res* 2011;25:1470–7.

69 Priore LB, Azevedo FM, Pazzinatto MF, *et al*. Influence of kinesiophobia and pain catastrophism on objective function in women with patellofemoral pain. *Phys Ther Sport* 2019;35:116–21.

70 Nunes GS, de Oliveira Silva D, Pizzari T, *et al*. Clinically measured hip muscle capacity deficits in people with patellofemoral pain. *Phys Ther Sport* 2019;35:69–74.

71 Dingenen B, Truijen J, Bellemans J, *et al*. Test-retest reliability and discriminative ability of forward, medial and rotational single-leg hop tests. *Knee* 2019;26:978–87.

72 Gustavsson A, Neeter C, Thomeé P, *et al*. A test battery for evaluating hop performance in patients with an ACL injury and patients who have undergone ACL reconstruction. *Knee Surg Sports Traumatol Arthr* 2006;14:778–88.

73 Bremander AB, Dahl LL, Roos EM. Validity and reliability of functional performance tests in meniscectomized patients with or without knee osteoarthritis. *Scand J Med Sci Sports* 2007;0:061120070736056.

74 Dalleau G, Belli A, Viale F, *et al*. A simple method for field measurements of leg stiffness in hopping. *Int J Sports Med* 2004;25:170–6.

75 Ferreira AS, de Oliveira Silva D, Barton CJ, *et al*. Impaired isometric, concentric, and eccentric rate of torque development at the hip and knee in patellofemoral pain. *J Strength Cond Res* 2021;35:2492–7.

76 Mentiplay BF, Perraton LG, Bower KJ, *et al*. Assessment of lower limb muscle strength and power using hand-held and fixed dynamometry: a reliability and validity study. *PLoS One* 2015;10:e0140822.

77 Suetta C, Aagaard P, Magnusson SP, *et al*. Muscle size, neuromuscular activation, and rapid force characteristics in elderly men and women: effects of unilateral long-term disuse due to hip-osteoarthritis. *J Appl Physiol (1985)* 2007;102:942–8.

78 Ferreira AS, Mentiplay BF, Taborda B, *et al*. Overweight and obesity in young adults with patellofemoral pain: impact on functional capacity and strength. *Journal of Sport and Health Science* 2020.

79 Hancock GE, Hepworth T, Wembridge K. Accuracy and reliability of knee goniometry methods. *J Exp Orthop* 2018;5:46.

80 Schlegel TF, Boublik M, Hawkins RJ, *et al*. Reliability of heel-height measurement for documenting knee extension deficits. *Am J Sports Med* 2002;30:479–82.

81 de Oliveira Silva D, Pazzinatto MF, Priore LBD, *et al*. Knee crepitus is prevalent in women with patellofemoral pain, but is not related with function, physical activity and pain. *Phys Ther Sport* 2018;33:7–11.

82 Pazzinatto MF, de Oliveira Silva D, Faria NC, *et al*. What are the clinical implications of knee crepitus to individuals with knee osteoarthritis? an observational study with data from the osteoarthritis initiative. *Braz J Phys Ther* 2019;23:491–6.

83 Izaguirre A, González-Gutiérrez G, Galindo-López SE, *et al*. Evaluation of biomarkers of joint damage in patients subjected to arthroscopy. *Int Orthop* 2021;45:1413–20.

84 Samuels C, James L, Lawson D, *et al*. The athlete sleep screening questionnaire: a new tool for assessing and managing sleep in elite athletes. *Br J Sports Med* 2016;50:418–22.

85 Bender AM, Lawson D, Werthner P, *et al*. The clinical validation of the athlete sleep screening questionnaire: an instrument to identify athletes that need further sleep assessment. *Sports Med Open* 2018;4:23.

86 Tubach F, Ravaud P, Baron G, *et al*. Evaluation of clinically relevant states in patient reported outcomes in knee and hip osteoarthritis: the patient acceptable symptom state. *Ann Rheum Dis* 2005;64:34–7.

87 Conti F, Ceccarelli F, Massaro L, *et al*. Evaluation of the patient acceptable symptom state (PASS) in italian patients affected by systemic lupus erythematosus: association with disease activity indices. *PLoS One* 2013;8:e73517.

88 Shelby RA, Somers TJ, Keefe FJ, *et al*. Brief fear of movement scale for osteoarthritis. *Arthritis Care Res (Hoboken)* 2012;64:862–71.

89 Larsson C, Ekvall Hansson E, Sundquist K, *et al*. Kinesiophobia and its relation to pain characteristics and cognitive affective variables in older adults with chronic pain. *BMC Geriatr* 2016;16:128.

90 de Oliveira Silva D, Barton CJ, Briani RV, *et al*. Kinesiophobia, but not strength is associated with altered movement in women with patellofemoral pain. *Gait Posture* 2019;68:1–5.

91 Larsson C, Hansson EE, Sundquist K, *et al*. Psychometric properties of the tampa scale of kinesiophobia (TSK-11) among older people with chronic pain. *Physiother Theory Pract* 2014;30:421–8.

92 French DJ, France CR, Vigneau F, *et al*. Fear of movement/ (re) injury in chronic pain: a psychometric assessment of the original english version of the tampa scale for kinesiophobia (TSK). *Pain* 2007;127:42–51.

93 Thomeé P, Währborg P, Börjesson M, *et al*. A new instrument for measuring self-efficacy in patients with an anterior cruciate ligament injury. *Scand J Med Sci Sports* 2006;16:181–7.

94 Ezzat AM, Whittaker JL, Brusson M, *et al*. The english knee self-efficacy scale is a valid and reliable measure for knee-specific self-efficacy in individuals with a sport-related knee injury in the past 5 years. *Knee Surg Sports Traumatol Arthrosc* 2021;29:616–26.

95 Collins CS, Stockton CM. The central role of theory in qualitative research. *International Journal of Qualitative Methods* 2018;17:160940691879747.

96 Esculier JF, Krowchuk NM, Li LC, *et al*. What are the perceptions about running and knee joint health among the public and healthcare practitioners in canada? *PLoS One* 2018;13:e0204872.

97 Esculier J-F, Besomi M, Silva D de O, *et al*. Do the general public and health care professionals think that running is bad for the knees? A cross-sectional international multilanguage online survey. *Orthopaedic Journal of Sports Medicine* 2022;10:232596712211241.

98 Cibere J, Sayre EC, Guermazi A, *et al*. Natural history of cartilage damage and osteoarthritis progression on magnetic resonance imaging in a population-based cohort with knee pain. *Osteoarthritis and Cartilage* 2011;19:683–8.

99 Teague S, Youssef GJ, *et al*, the SEED Lifecourse Sciences Theme. Retention strategies in longitudinal cohort studies: a systematic review and meta-analysis. *BMC Med Res Methodol* 2018;18:1–22.

100 Patterson BE, Barton CJ, Culvenor AG, *et al*. Exercise-therapy and education for individuals one year after anterior cruciate ligament reconstruction: a pilot randomised controlled trial. *BMC Musculoskelet Disord* 2021;22.

101 De Oliveira Silva D, Taborda B, Pazzinatto MF, *et al*. The altmetric score has a stronger relationship with article citations than journal

impact factor and open access status: a cross-sectional analysis of 4022 sport sciences articles. *J Orthop Sports Phys Ther* 2021;51:536–41.

102 Shu D, Chen F, Guo W, *et al*. Acute changes in knee cartilage and meniscus following long-distance running in habituate runners: a systematic review on studies using quantitative magnetic resonance imaging. *Skeletal Radiol* 2022;51:1333–45.

103 Davis IS, Futrell E. Gait retraining. *Arch Phys Med Rehabil Clinics of North America* 2016;27:339–55.

104 Berry PA, Wluka AE, Davies-Tuck ML, *et al*. Sex differences in the relationship between bone mineral density and tibial cartilage volume. *Rheumatology (Oxford)* 2011;50:563–8.

105 Brennan SL, Cicuttini FM, Pasco JA, *et al*. Does an increase in body mass index over 10 years affect knee structure in a population-based cohort study of adult women? *Arthritis Res Ther* 2010;12:R139.