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Recruitment and baseline characteristics of young adults at risk of early-onset knee osteoarthritis after ACL reconstruction in the SUPER-Knee trial

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ABSTRACT

Objectives The study aims to (1) report the process of recruiting young adults into a secondary knee osteoarthritis prevention randomised controlled trial (RCT) after anterior cruciate ligament reconstruction (ACLR); (2) determine the number of individuals needed to be screened to include one participant (NNS) and (3) report baseline characteristics of randomised participants.

Methods The SUpervised exercise-therapy and Patient Education Rehabilitation (SUPER)-Knee RCT compares SUPER and minimal intervention for young adults (aged 18–40 years) with ongoing symptoms (ie, mean score of <80/100 from four Knee injury and Osteoarthritis Outcome Score subscales ($KOOS_4$)) 9–36 months post-ACLR. The NNS was calculated as the number of prospective participants screened to enrol one person. At baseline, participants provided medical history, completed questionnaires (demographic, injury/surgery, rehabilitation characteristics) and underwent physical examination.

Results 1044 individuals were screened to identify 567 eligible people, from which 184 participants (63% male) enrolled. The sample of enrolled participants was multicultural (29% born outside Australia; 2% Indigenous Australians). The NNS was 5.7. For randomised participants, mean±SD age was 30±6 years. The mean body mass index was 27.3±5.2 kg/m^2, with overweight (43%) and obesity (21%) common. Participants were, on average, 2.3 years post-ACLR. Over half completed <8 months of postoperative rehabilitation, with 56% having concurrent injury/surgery to meniscus and/or cartilage. The most affected KOOS (0=worst, 100=best) subscale was quality of life (mean 43.7±19.1).

Conclusion Young adults post-ACLR were willing to participate in a secondary osteoarthritis prevention trial. Sample size calculations should be multiplied by at least 5.7 to provide an estimate of the NNS. The SUPER-Knee cohort is ideally positioned to monitor and intervene in the early development and trajectory of osteoarthritis.

Trial registration number ACTRN12620001164987.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Anterior cruciate ligament tears increase the risk of early-onset knee osteoarthritis in young adults.

⇒ Recruiting patients into randomised controlled trials is challenging—having a target population at risk of osteoarthritis onset and progression, who are not necessarily seeking treatment, further complicates recruitment for a secondary prevention trial.

WHAT THIS STUDY ADDS

⇒ Within the first 3 years following anterior cruciate ligament reconstruction, young adults were willing to participate in an exercise therapy-based osteoarthritis secondary prevention trial.

⇒ The SUpervised exercise-therapy and Patient Education Rehabilitation-Knee trial cohort is ideally positioned to monitor and intervene in the early development and trajectory of osteoarthritis.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Sample size calculations for future osteoarthritis secondary prevention trials following anterior cruciate ligament injury should be multiplied by at least 5.7 to estimate the number of individuals needing to be screened to include the desired number of participants.

INTRODUCTION

Knee osteoarthritis (OA) is a leading cause of global disability among older adults.[1] Despite its high prevalence, treatments that modify structural damage in OA have remained elusive.[2] Given knee OA has no current cure, the concept of prevention (delaying or halting OA onset) is an attractive alternative to reduce its tremendous individual and societal burden. However, conducting clinical trials with a structural outcome that takes many years to develop, and identifying a non-diseased target group likely to develop OA,

are significant challenges that have hampered advances towards OA prevention.

Traumatic knee injury is one of the most potent risk factors for OA and provides a promising model for the secondary prevention of OA.[3] Secondary prevention of OA refers to preventing or slowing the onset and/or worsening of symptomatic and/or structural changes in those with early manifestations (or at high risk of) OA, such as following knee injury. Approximately 50% of people with traumatic knee injuries, such as anterior cruciate ligament (ACL) rupture, develop early-onset symptomatic radiographic OA within 5–10 years.[4 5] As many as one-third have MRI defined OA within 1 year.[6] While ACL reconstruction (ACLR) surgery is often thought to reduce the risk of OA,[7] ACLR may result in higher rates of cartilage loss and early OA than rehabilitation alone.[8 9] Knowing that those who undergo ACLR represent an easily identifiable target group of 'at-risk' individuals for the accelerated development and worsening of OA presents an opportunity to design and evaluate treatments to prevent the onset and/or worsening of OA and associated symptoms.[10]

Preventing OA in young adults is an international priority.[11] We devised a pragmatic, parallel-group, assessor-blinded randomised controlled trial (RCT) (SUpervised exercise-therapy and Patient Education Rehabilitation, SUPER-Knee) to evaluate the effectiveness of SUPER compared with minimal intervention control for young adults at risk of knee OA 9–36 months after ACLR. The current paper aims to (1) report the process of recruiting young adults into SUPER-Knee; (2) determine the number of individuals needed to be screened to include one participant; (3) report the baseline characteristics of randomised participants and (4) compare SUPER-Knee baseline characteristics to patients following ACLR from national ligament registries and large observational cohort studies globally.

METHODS

Study design

The SUPER-Knee trial design and methodology are described in detail elsewhere.[12] The SUPER intervention consists of twice weekly supervised exercise-therapy for 4 months (focused on quadriceps and hamstring strengthening and neuromuscular rehabilitation) at one of 15 collaborating community physiotherapy clinics. The control intervention consists of one education session at baseline provided by a qualified physiotherapist and a booklet containing advice on exercise options (no prescription provided). The primary outcome is the 4-month change in the Knee injury and Osteoarthritis Outcome Score ($KOOS_4$) covering four subscales of pain, symptoms, function in sports and recreational activities and knee-related quality of life (QoL).[13] Secondary outcomes include the onset/progression of structural OA features on MRI over 12 months (eg, cartilage morphology and composition), physical activity and thigh muscle strength.

Participants

We aimed to recruit 184 participants fulfilling eligibility criteria (figure 1) over 3 years to meet a priori sample size requirements to ensure 85% power for the primary self-reported symptomatic outcome and secondary structural outcome (at a two-sided 0.05 significance level, accounting for 20% drop-out). A stopping rule (n=160, 80% power) was established if recruitment took >3 years.

Recruitment procedure

Participants were recruited from three main sources in the state of Victoria, Australia: (1) collaborating orthopaedic surgeons' private practices; (2) collaborating public hospital sites and (3) community advertisements. Individuals who underwent an ACLR during the past 3 years from our network of orthopaedic surgeons and public hospitals (ie, SUPER-Knee Study Group) were mailed study information inviting them to contact a research team member. Volunteers responding to the invitation letter or advertisements were screened for eligibility using a three-step process. First, a research team member asked screening questions via telephone. Potentially suitable volunteers were then sent the KOOS questionnaire electronically (via Research Electronic Data Capture (REDCap)) to confirm their symptomatic status. Finally, baseline MRI scans confirmed the absence of graft rupture and any other major pathology that

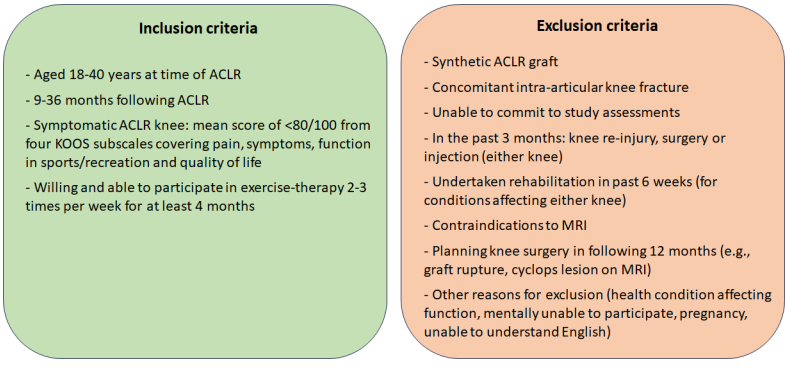

Figure 1 Eligibility criteria. ACLR, anterior cruciate ligament reconstruction; KOOS, Knee injury and Osteoarthritis Outcome Score.

participants were advised to seek a surgical opinion for (eg, bucket handle meniscal tear).[14]

Baseline characteristics

Each participant enrolled in the trial underwent a comprehensive baseline assessment at La Trobe University, which included medical and knee injury/surgery/rehabilitation history (based on self-report and ACLR surgical report where available). A standardised questionnaire was used to obtain self-reported data on country of birth, Indigenous status, smoking status, living/family situation, employment status, educational attainment, family history of OA and current medication (excluding contraceptives). We assessed baseline health literacy with the Rapid Estimate of Adult Literacy in Medicine (REALM)[15] and baseline and preinjury physical activity with the Tegner Activity Scale.[16] Weight was measured on a digital scale while standing height was measured with a wall-mounted stadiometer.

Patient and public involvement

Patients and clinicians were integral throughout each project stage as detailed in the SUPER-Knee protocol.[12] Specific to recruitment and baseline testing, patient and clinician focus groups provided feedback on study recruitment material, participant handbooks and education content.

Statistical analysis

Data are presented descriptively as frequencies, mean (SD) or median (range) as appropriate. We compared (descriptively) the SUPER-Knee participants to typical patients following ACLR from national ligament registries and large observational cohort studies from around the world. The number needed to screen is an established concept that estimates how many patients need to be screened to include one patient in the trial.[17 18] It is calculated by dividing the number of patients screened for eligibility by the number of patients included in the trial.

RESULTS

Recruitment and number needed to screen

Individuals were recruited from 9 public hospital sites and 12 private orthopaedic surgeons, who sent out 1492 and 868 invitation letters to their patients with ACLR, respectively (figure 2). A further 112 individuals responded to advertisements in the community.

A total of 1044 individuals were screened to identify 567 eligible people, from which the a priori target sample size of 184 participants was enrolled. The main reasons for eligible people to decline participation were inconveniences related to being too busy to commit to trial assessments/interventions (n=263) or being located too far away (n=97). The resultant number needed to screen to include one participant in the trial was 5.7 individuals. The number needed to screen was similar across recruitment pathways (public patients 5.4, private patients 5.8; advert responders 6.7). For recruitment through the healthcare system (hospitals, surgeons), half to two-thirds of patients did not respond to the invitation letter.

The main reasons for not meeting eligibility criteria were no/minimal knee symptoms and not being in the eligibility window for age or time postsurgery (figure 2). Four individuals were excluded due to an unexpected ACL graft rupture on MRI screening.

A period of 26 months was required to recruit and randomise the 184 participants. The first SUPER-Knee participant was randomised on 26 February 2021, and the final participant was randomised on 20 April 2023. Randomisation occurred during the COVID-19 pandemic—four government-mandated lockdowns in Melbourne, Australia, spanning 103 days during this time resulted in the forced temporary shutdown of university campuses (no baseline assessments or randomisation could be completed) and many elective surgeries (less potentially eligible patients with ACLR), which extended the time required to recruit and randomise all participants by approximately 3–4 months. Nevertheless, the a priori planned stopping rule (if recruitment took >3 years) was not required.

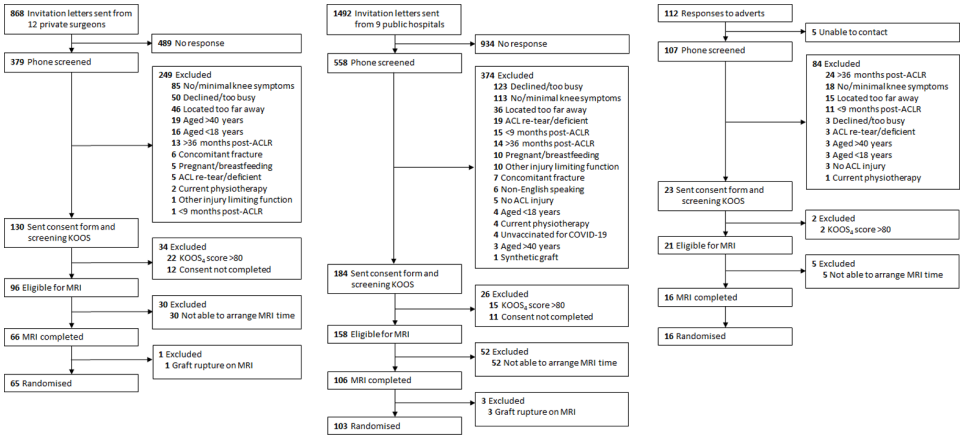

Figure 2 Flow chart of the recruitment process in the SUPER-Knee trial. ACL, anterior cruciate ligament; ACLR, ACL reconstruction; KOOS, Knee injury and Osteoarthritis Outcome Score.

Table 1 Participant baseline demographic characteristics*

Baseline variable	N=184
Female sex, n (%)	68 (37)
Age, years	30±6
Height, m	1.74±0.08
Weight, kg	82.4±16.5
Body mass index, kg/m^2	27.3±5.2
Body mass index categories	
Normal weight (body mass index <25 kg/m^2), n (%)	66 (36)
Overweight (body mass index ≥25 kg/m^2), n (%)	80 (43)
Obese (body mass index ≥30 kg/m^2), n (%)	38 (21)
Born outside Australia, n (%)†	53 (29)
Indigenous Australian, n (%)	3 (2)
Dominant leg left, n (%)	16 (9)
Current smoker, n (%)	21 (11)
Living status (with whom), n (%)	
Partner/own family	98 (53)
Parents	42 (23)
Friends	23 (13)
Alone	21 (11)
Children living in household, n (%)	
0	151 (82)
1	13 (7)
2	13 (7)
3	7 (4)
Employment status, n (%)	
Full time	127 (69)
Part time	17 (9)
Casual	19 (10)
Unemployed/student	21 (11)
Employment classification,‡ n (%)	
Manager/administrator	13 (8)
Professional	62 (38)
Associate professional	26 (16)
Tradesperson or related worker	15 (9)
Advanced clerical or service worker	10 (6)
Clerical, sales or service worker	13 (8)
Production or transport worker	2 (1)
Elementary clerical, sales or service worker	12 (7)
Labourers or related worker	9 (6)
Educational attainment, n (%)	
Postgraduate degree	35 (19)
Bachelor degree	69 (38)
Vocational/technical/trade school	26 (14)
High school or equivalent	51 (28)
Less than high school	3 (2)
Low health literacy§, n (%)	13 (7)
Family history of osteoarthritis, n (%)	29 (16)
Tegner Activity Scale preinjury¶, median (IQR)	8 (7–9)
Tegner Activity Scale current¶, median (IQR)	5 (3–6)
Socioeconomic status, median (IQR) percentile**	67 (35–84)

*Values are mean±SD unless indicated otherwise.
†See online supplemental appendix 1 for details.
‡Australian Standard Classifications of Occupations.
§Defined as Rapid Estimate of Adult Literacy in Medicine score <61 out of 66.
¶Tegner Activity Scale score ranges from 0 (sick leave because of knee problems) to 10 (elite level football).
**To quantify socioeconomic status, the Index of Relative Social Advantage and Disadvantage (median=50th percentile) was determined for each participant (based on their residential address) from Australian Bureau of Statistics census data for the state of Victoria.

Baseline demographic characteristics

For the 184 randomised participants, table 1 shows the overall distribution of baseline demographic characteristics. The mean age was 30±6 years, with a male predominance (63%). The sample was multicultural (29% born outside Australia; 2% Indigenous Australians) (online supplemental appendix 1) and socioeconomically diverse, ranging from the lowest to the highest percentile of socioeconomic disadvantage (table 1). Mean body mass index (BMI) was 27.3±5.2, with overweight (43% with BMI≥25 kg/m^2) and obesity (21% with BMI≥30 kg/m^2) common. Participants tended to have lower (knee demanding) physical activity levels at baseline (Tegner median 5, equivalent to competitive cycling or recreational jogging) compared with preinjury (Tegner median 8, equivalent to competitive racquet sports or alpine skiing). Most participants were employed in a full-time capacity (69%) and were health literate (93% scored ≥61/66 on REALM).

Knee injury and surgery characteristics

Participants were, on average, 2.3±0.7 years post-ACLR, with the majority (82%) having a hamstring-tendon autograft (table 2). Surgery was a revision ACLR for 12% and a second revision ACLR for 2% of participants. Surgical records were obtained from 183 (99%) participants, which showed 103 participants (59%) had a concomitant meniscal/cartilage lesion. Most (91%) injured their ACL while participating in sports (online supplemental appendix 2). Before enrolment, 16 (9%) participants had an ACLR on the contralateral knee, with 2 (1%) having a contralateral revision. Postoperative rehabilitation varied. Over half (58%) completed less than 8 months of supervised rehabilitation, including 17% who completed fewer than four physiotherapy sessions (table 2).

Table 2 Participant knee injury and surgery characteristics*

Variable	N=184
ACLR index knee	
Primary	158 (86)
Revision	22 (12)
Second revision	3 (2)
Third revision	1 (1)
Graft type of most recent index ACLR†	
Hamstring tendon	150 (82)
Quadriceps tendon	17 (9)
Bone-patellar tendon bone	12 (7)
Donor (allograft)	4 (2)
Tibialis anterior	1 (1)
Index knee type of injury‡	
Isolated ACL injury	75 (41)
Combined ACL injury with injury/surgery to meniscus or cartilage	108 (59)
Contralateral knee ACLR prior to enrolment	
Primary	14 (8)
Revision	2 (1)
Index ACLR limb left side, n (%)	81 (44)
Index ACLR limb dominant side,§ n (%)	107 (58)
Months between ACL injury and ACLR, median (IQR)	4.6 (2.1–9.8)
Years between ACLR and baseline, mean±SD‡	2.3±0.7
Non-contact mechanism of injury	119 (65)
Injured ACL during sports participation	167 (91)
Private healthcare for ACLR	81 (44)
Number of physiotherapy sessions during index ACLR rehabilitation	
0	9 (5)
1–3	22 (12)
4–10	71 (39)
>10	82 (45)
Duration of physiotherapy rehabilitation for index ACLR	
None completed	9 (5)
<1 month	7 (4)
1–3 months	26 (14)
3–6 months	32 (17)
6–8 months	32 (17)
8–10 months	22 (12)
10–12 months	20 (11)
>12 months	36 (20)

*Values are self-reported numbers (%) unless indicated otherwise.
†Data obtained from surgical records or self-report when surgical records unavailable.
‡Data obtained from surgical record of n=183. Combined injury refers to the presence of a concomitant meniscal tear (either untreated or treated surgically) and/or a cartilage defect treated surgically (eg, debridement).
§Leg used to kick a ball.
ACL, anterior cruciate ligament; ACLR, ACL reconstruction.

Comorbidities and medication use

Comorbidities were uncommon in this young adult population, with asthma being most frequently reported (12%) (online supplemental appendix 3). Current (past month) medication use was minimal; 8 (4%) participants were taking analgesic medication (paracetamol), and 15 (8%) were taking a non-steroidal anti-inflammatory (not necessarily for their knee) (online supplemental appendix 4).

The SUPER-Knee population compared with ACL registries and large cohort studies

The SUPER-Knee population was of similar age and had a similar proportion of females compared with existing national ACLR registries from Scandinavia and the UK, and observational cohorts from the USA (table 3). Other similarities include the proportion of ACL injuries defined as isolated injuries (ie, no other concomitant injuries) and the proportion of people with a contralateral ACL injury history. BMI and the ACLR revision rate tended to be higher in SUPER-Knee (table 3). Reflecting the symptomatic eligibility of the SUPER-Knee trial, at a similar time post-ACLR (~2 years postoperatively), SUPER-Knee participants had, on average, worse KOOS scores on all five subscales compared with all other national registries and cohorts (figure 3). The KOOS QoL subscale was the most affected in SUPER-Knee participants—mean±SD KOOS subscale scores: pain 78.9±11.6, other symptoms 71.9±12.6, activities of daily living 89.1±10.6; function in sport and recreation 62.3±19.5; knee-related QoL 43.7±19.1.

DISCUSSION

The recruitment of patients into RCTs is a well-recognised challenge—having a target population at risk of disease onset and progression, who are not necessarily seeking treatment, further complicates recruitment into a secondary prevention trial. SUPER-Knee is the first fully powered RCT of a comprehensive guideline-based exercise and education rehabilitation programme to prevent post-traumatic OA in young adults following ACLR. Through a targeted recruitment strategy, we were able to enrol the a priori sample size of 184 young adults with ongoing knee symptoms. Participants were, on average, 2.3 years post-ACLR and broadly representative of the culturally diverse Australian population. Similar characteristics to large ACLR registries and other cohorts (apart from being more symptomatic by design) support the generalisability of SUPER-Knee when completed.

Recruitment challenges

The number needed to screen for the SUPER-Knee trial (5.7) is consistent with other RCTs following ACL injury. The Swedish KANON trial that compared rehabilitation plus early ACLR versus rehabilitation plus optional later ACLR for an acute ACL injury reported a number needed to screen of 5.5.[18] Our recruitment strategy was deliberately broad (ie, an invitation letter sent to all patients 9–36

Table 3 Comparison of SUPER-Knee participants with national registry and observational cohorts

Variable	SUPER-Knee trial	National registries and observational cohorts			
		Norwegian Registry[28]	Swedish Registry[28]	MOON (USA) Cohort[39]	UK Registry[29]
Participants, n	184	5329	7331	393	4593
Time post-ACLR, years	2±1	2	2	2	2
Age, years	30±6	29	27	27	32
Female sex, %	37	43	42	44	31
Body mass index, kg/m^2	27±5	25	25	25	–
Isolated ACL injury, n	41	~55	~35	~60	56
Revision ACLR, %	14	5	6	8	2
Hamstring-tendon autograft, %	82	61	86	26	91
Contralateral knee ACL injury	9	8	8	–	–

Data are presented as mean (±SD) unless indicated otherwise.
ACL, anterior cruciate ligament; ACLR, ACR reconstruction; KOOS, Knee injury and Osteoarthritis Outcome Score; MOON, Multicenter Orthopaedic Outcome Network; SUPER, SUpervised exercise-therapy and Patient Education Rehabilitation.

months post-ACLR, irrespective of knee symptom status). Narrowing this strategy (eg, inviting only those seeking treatment) may reduce the number needed to screen but may be too restrictive (ie, unnecessarily limiting the population of potential participants). Based on our prior work,[19 20] we anticipated that many receiving the invitation letter would not meet our symptomatic eligibility criteria of $KOOS_4$<80/100. Indeed, the lack of ongoing knee symptoms was the overwhelming reason most prospective participants were excluded. Given recruitment occurred during parts of the COVID-19 pandemic, it is possible that the consequences of COVID-19 and the government-imposed restrictions may have increased or decreased non-response to the initial invitation letter and impacted the number needed to screen.

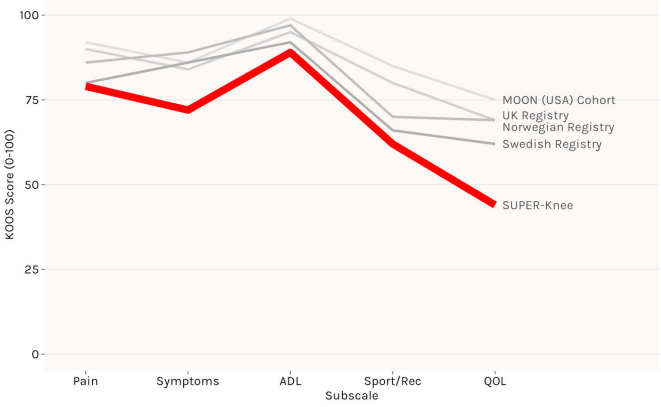

Figure 3 Comparison of SUPER-Knee participants with 2-year post-ACLR data from national registry and observational cohorts. ACLR, anterior cruciate ligament reconstruction; ADL, activities of daily living; KOOS, Knee injury and Osteoarthritis Outcome Score; MOON, Multicenter Orthopaedic Outcome Network; QOL, quality of life; Sport/Rec, function in sport and recreational activities; SUPER, SUpervised exercise-therapy and Patient Education Rehabilitation.

The number needed to screen is affected by recruitment and screening strategy, clinical inclusion criteria and planned interventions, and hence will vary considerably for different trial designs. Within the SUPER-Knee RCT itself, the different recruitment strategies resulted in a varied number needed to screen—community advertisements resulted in a slightly higher number needed to screen (6.7) compared with private (5.8) and public hospital (5.4) invitation letters. Given that the main reason for excluding those responding to community advertisements was being >36 months post-ACLR, reinforcing this key selection criteria in future advertising strategies may be helpful. Furthermore, the large geographical recruitment area (the entire state of Victoria, Australia) and potential to be randomised to attend twice weekly supervised sessions at 1 of our 15 (mostly metropolitan Melbourne) physiotherapy clinics meant that many eligible individuals declined participation due to an inability to commit to travel if randomised to the SUPER intervention. Including more geographically diverse physiotherapy clinics as intervention sites may reduce the number needed to screen in future exercise-based trials. However, it must also be balanced with increased intervention training and support resources to ensure treatment fidelity.

Baseline demographic characteristics representative of the Australian population

The SUPER-Knee recruitment strategy, targeting both public and private healthcare settings, was developed to maximise the chances of enrolling a representative sample of participants from Australia's sociodemographically and culturally diverse population of young adults. 29% of SUPER-Knee participants were born outside Australia,

the same proportion in the Australian population.[21] SUPER-Knee participants were also socioeconomically diverse. Although the overall ranking of socioeconomic status (67th percentile) was above the state median (50th percentile) for Victoria[22] (likely indicating a cohort from mostly metropolitan Melbourne), socioeconomic status ranged from the lowest to the highest level of advantage and disadvantage. Similarities also existed between SUPER-Knee participants and Australian population data from the Australian Institute of Health and Welfare[23] for the proportion of (1) indigenous Australians (SUPER-Knee 2%, Australia-wide 4%); (2) smokers (SUPER-Knee and Australia-wide both 11%); (3) level of education at least a bachelor's degree (SUPER-Knee 57%, Australia-wide 51%); (4) private health insurance holders (SUPER-Knee 44%, Australia-wide 57%) and (5) overweight and obesity prevalence in young adulthood (SUPER-Knee 64%, Australia-wide ~56%). As expected, comorbidities in this young adult population were rare. Such a high proportion of overweight (43%) and obese (21%) participants was somewhat unexpected given most ACL injuries occur in active individuals during sports. As overweight and obesity are the most potent risk factors for the development of knee OA, second only to knee trauma,[24] the high BMI levels in SUPER-Knee, together with the ACL injury history of participants, means the SUPER-Knee cohort is at a particularly high risk of early OA onset and accelerated progression. This provides an ideal platform to assess the effectiveness of OA prevention strategies over a relatively short time horizon.

Baseline ACL injury and surgery characteristics

91% of SUPER-Knee participants tore their ACL while playing sports, reflecting the most common cause of ACL ruptures more broadly. Results of our baseline evaluation also revealed similarities to large epidemiological studies and national registries in relation to other ACL injury and ACLR characteristics. This further supports the generalisability of the results of our intervention when completed. For example, the mean age of participants enrolled in SUPER-Knee was 30 years at baseline, with a male predominance typical of the broader population with ACLR.[25] In a meta-analysis of 45 studies, the proportion of ACL injuries due to a non-contact mechanism was estimated to be 55% (95% CI 48% to 62%).[26] The corresponding rate in the SUPER-Knee cohort was 65%. Over half (56%) of SUPER-Knee participants had a combined ACL injury (ie, concurrent injury/surgery to meniscus and/or cartilage), very similar to Scandinavian national registry data (54%).[27] Most (82%) SUPER-Knee participants had a hamstring-tendon autograft ACLR, consistent with current trends in graft preference in Sweden,[28] the UK[29] and elsewhere.[30] Graft rupture is expected to occur in approximately 12% of patients in the first 5 years post-ACLR.[31] The revision ACLR rate (following a graft rupture) in SUPER-Knee was 14% at a mean of 2 years post-ACLR, which is higher than typical registry rates (~8% at 2 years). This could reflect the symptomatic status of SUPER-Knee participants, as revision surgery is associated with poorer symptomatic outcome.[32] Finally, the initial postoperative rehabilitation that SUPER-Knee participants completed was, in many cases, not aligned with clinical guidelines that recommend at least 9 months of supervised rehabilitation.[10 33] Approximately 17% of SUPER-Knee participants completed fewer than four physiotherapy sessions, and 58% completed less than 8 months of supervised rehabilitation. The standard rehabilitation programmes of many SUPER-Knee participants were interrupted by physiotherapy clinic closures during the COVID-19 pandemic, which may have contributed to the large number of participants who completed inadequate rehabilitation. Limited access to post-ACLR rehabilitation is common in Australia, with a 2016 survey of patients indicating that 20% participated in less than 3 months of supervised rehabilitation post-ACLR.[34]

Comparison of SUPER-Knee symptoms with national registries and large cohort studies

SUPER-Knee participants were selected based on the presence of ongoing symptoms; consequently, they reported worse scores, on average, across all five KOOS subscales compared with typical patients at the same timepoint post-ACLR. Function in Sport and Recreation and knee-related QoL were the KOOS subscales that were most impaired, indicating that pain was not generally the primary complaint for participants. The mean SUPER-Knee participant scores on all KOOS subscales fell below the established 'patient acceptable symptom state' thresholds,[35] confirming a broad dissatisfaction with current knee function. The KOOS-QoL subscale was so impaired that the mean score (43/100) approached the patient-reported 'treatment failure' threshold of 42/100,[35] indicating that many participants may have perceived their ACLR had failed them.

Limitations

The SUPER-Knee RCT builds on a foundation of prior work in post-traumatic OA,[36 37] including our pilot trial,[38] but is not without limitations. First, SUPER-Knee was run from a single site only (Victoria, Australia). However, we could still enrol a representative sample of the Australian young-adult population with ACL injury/surgery characteristics that were similar to other ACLR registries and cohorts internationally. Second, we could not compare demographic/injury/surgery characteristics between those individuals accepting and declining participation in the RCT as we did not routinely collect this information from those who declined to participate. We also did not statistically compare reasons for exclusion between the three recruitment pathways as individuals often met more than one exclusion criterion. Third, information regarding ACL injury information (eg, date, mechanism) and rehabilitation characteristics (eg, number of supervised sessions completed) may be at risk of recall bias as we relied on retrospective recall at the time of RCT enrolment (up to 3 years post-injury). Finally, our open-ended

questioning regarding comorbidities and medication use may have resulted in the under-reporting of concurrent health conditions and medication use. Nevertheless, the nature of the condition (ACL injury in mostly physically active healthy young adults) meant that a low number of comorbidities and regular medications were expected.

CONCLUSION

Young adults with ongoing symptoms post-ACLR were willing to participate in an OA secondary prevention trial. The SUPER-Knee study successfully enrolled a large number of participants who are at particularly high risk of early-onset knee OA. Apart from being more symptomatic (by design), baseline demographics of SUPER-Knee participants were generally similar to contemporary epidemiological and observational registry studies of ACLR. A priori sample size calculation for similar future trials should be multiplied by at least 5.7 to estimate the number needed to screen and include the desired number of participants. The SUPER-Knee cohort is ideally positioned to monitor and intervene in the early onset and trajectory of OA.

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Contributors AGC, KC, CJB, EMR, EHGO and SMM conceived the study and obtained funding. AGC, KC and CJB designed the study protocol with input from EMR, EHGO and SMM. SMM provided statistical expertise and will conduct primary statistical analysis. TJW, BP, MAG and JLC conducted eligibility screening and baseline assessments. AGC, AB and MJS coordinated participant randomisation and clinical management. Members of the SUPER-Knee Study Group either performed the surgery and assisted with recruitment in the private health sites (HM, NW, ME, AGC, JW, DvB, MA, ST, RK, LS and RH), were site investigators assisting with recruitment at the public hospital sites (LK, SL, EC, CC, AH, PC, LR, LS, PT, PS, KB, RP and LL) or assisted with baseline assessments (MH, SE and LT). AGC drafted the manuscript with input from TJW, KC, CJB, EMR, EHGO, SMM, RS, JL, AB, BP, MAG, JLC and MJS. AGC is the guarantor. All authors approved the final manuscript.

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Competing interests CJB is the owner of a business providing physiotherapy treatment and exercise classes for some participants enrolled in this study. CJB will have no role in the decision of which clinic participants attend for study treatment. EMR is the copyright holder for KOOS.

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Culvenor et al., SUPER-Knee trial baseline characteristics

Supplementary Information

Appendix 1. Country of birth

Appendix 2. Sport/activity participating in when injured ACL

Appendix 3. Medical history

Appendix 4. Baseline medication use

Appendix 1. Country of birth

Country	Number (%)
Australia	131 (71)
India	10 (5)
United Kingdom	7 (4)
New Zealand	6 (3)
Iran	5 (3)
China	2 (1)
Colombia	2 (1)
Jordan	2 (1)
Pakistan	2 (1)
Philippines	2 (1)
Saudi Arabia	2 (1)
Thailand	2 (1)
Vietnam	2 (1)
Afghanistan	1 (1)
Brazil	1 (1)
Cuba	1 (1)
Fiji	1 (1)
Italy	1 (1)
Singapore	1 (1)
South Africa	1 (1)
Syria	1 (1)
United States of America	1 (1)

Appendix 2. Sport/activity participating in when injured ACL

Sport/activity	Number (%)
Sport-related	**167 (91)**
Soccer	40 (22)
Basketball	26 (14)
Australian football	25 (14)
Netball	22 (12)
Futsal	15 (8)
Skiing	8 (4)
Martial arts	6 (3)
Ultimate frisbee	3 (2)
Trampoline	2 (1)
Cricket	2 (1)
Cheerleading	2 (1)
Rugby	2 (1)
Running	2 (1)
Snowboarding	2 (1)
Cycling	1 (1)
Gymnastics	1 (1)
Volleyball	1 (1)
Powerlifting	1 (1)
Roller Derby	1 (1)
Baseball	1 (1)
American football	1 (1)
Kickboxing	1 (1)
Squash	1 (1)
Tennis	1 (1)
Non-sport related	**17 (9)**
Walking/stairs	5 (3)
Dancing	4 (2)
Work-related	3 (2)
Motorbike	2 (1)
Jumping/hopping (not sport related)	2 (1)
Horse riding	1 (1)

Appendix 3. Medical history

Condition	Number (%)
Asthma	22 (12)
Gastro-oesophageal reflux	6 (3)
Depression/anxiety	5 (3)
Attention-deficit/hyperactivity disorder	4 (2)
Iron deficiency	3 (2)
Ulcerative colitis	3 (2)
Eczema	2 (1)
Hypothyroidism	2 (1)
Migraines	2 (1)
Polycystic ovary syndrome	2 (1)
Pulmonary embolism	2 (1)
Inguinal hernia	2 (1)
Alopecia	1 (1)
Celiac disease	1 (1)
Deep vein thrombosis	1 (1)
Epilepsy	1 (1)
Hypercholesterolemia	1 (1)
Lupus	1 (1)
Medullary sponge kidney	1 (1)
Oesophagitis	1 (1)
Pericarditis	1 (1)
Ventricular septal defect	1 (1)
Wheeze	1 (1)

Appendix 4. Baseline medication use (in the past month)

Medication	Number (%)
Analgesic	
Paracetamol	8 (4)
Non-steroidal anti-inflammatory	
Ibuprofen	8 (4)
Dicofenac	6 (3)
Mefenamic acid	1 (1)
Respiratory	
Budesonide-formoterol	4 (2)
Salbutamol	4 (2)
Budesonide	2 (1)
Fluticasone	2 (1)
Seretide	2 (1)
Salmeterol	2 (1)
Gastrointestinal	
Esomeprazole	4 (2)
Mesalamine	1 (1)
Nizatidine	1 (1)
Sulfasalazine	1 (1)
Tofacitinib	1 (1)
Immunosuppressant	
Azathioprine	3 (2)
Betamethasone dipropionate	1 (1)
Antidepressant	
Escitalopram	3 (2)
Fluoxetine	1 (1)
Diazepam	1 (1)
Other	1 (1)
Other	
Hydroxychloroquine	2 (1)
Thyroxin	2 (1)
Dexamphetamine sulfate	2 (1)
Ritalin	1 (1)
Aspirin	1 (1)
Atorvastatin	1 (1)
Minoxidil	1 (1)
Spironolactone	1 (1)
Prednisone	1 (1)
Lamotrigine	1 (1)
Cetirizine	1 (1)
Azelastine-fluticasone	1 (1)

* excludes contraceptive medication