Long-Term Risk of Knee Arthroplasty After ACL Reconstruction Using the Contralateral Knee as an Internal Control: A National Hospital Episode Statistics Database Study of 135,881 Patients

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Abstract

OBJECTIVE:

Estimate the population-specific relative risk of knee arthroplasty following ACL reconstruction (ACLr) in patients with a history of ACLr in only one knee.

METHODS:

A population-based cohort of patients undergoing their first ACLr, with no previous or subsequent ACLr to their contralateral knee was extracted from National Hospital Episode statistics data, England, UK (1997/1998-2022/2023). Mortality-adjusted Kaplan–Meier survival analysis (survival defined as not undergoing knee replacement) of the index knee undergoing ACLr versus the non-intervened knee. Subgroup analysis was done examining sex, age, index of multiple deprivation, ethnicity, and whether ACLr was performed in isolation or with concurrent meniscal surgery. A comparison of the arthroplasty rate in both knees versus general population data was also performed.

RESULTS:

135,881 ACLr patients were included. At 20-years post ACLr, the rate of ipsilateral knee arthroplasty was 2.44% (95% CI 2.18-2.73) versus the contralateral knee (0.87%, 95% CI 0.72-1.06). The hazard ratio (HR) for knee arthroplasty versus the contralateral knee was 3.00 (95% CI 2.56 to 3.51) in isolated ACLr cases and 3.50 (95% CI 2.55 to 4.81) in cases with simultaneous meniscal surgery. In males, the HR was 3.27 (95% CI 2.72-3.92) versus the contralateral knee, and in females the HR was 2.85 (95% CI 2.28-3.57) versus the contralateral knee. The increased HR of arthroplasty in the ACLr knee remained present across the different strata of index of multiple deprivation, ethnicity, and age. The rate of arthroplasty was slightly higher in the contralateral (non-ACLr) knee when compared to the background population risk of knee arthroplasty.

CONCLUSION:

This is the first study to estimate the population-specific relative risk of knee replacement following an ACL injury and reconstruction by using the contralateral knees of the same patients as the control. The relative risk is approximately three-times that of the contralateral, uninjured knee. Our findings may better inform patients when discussing their long-term prognosis after ACL injury.

Key Messages

What is already known on this topic

- ACL injury is associated with cartilage injury and increased development of subsequent radiographic knee osteoarthritis.
- Patients undergoing ACL reconstruction are more likely than the general population to undergo a knee replacement at a young age.
- Previous studies have not, however, determined how these risks compare to the baseline risk specifically for patients sustaining an ACL injury, as these patients may have a different risk profile due to factors such as their activity level, anatomy, or genetic risk factors.

What this study adds

- This study is the largest cohort of patients with ACL reconstruction that has been reported in the literature and the first to compare the rate of knee replacement in the knee sustaining the injury and undergoing a surgical reconstruction versus the opposite-side knee of the same patient.
- These findings provide novel, population-specific insights on the true relative risk of progression to 'end-stage' osteoarthritis in these patients.
- The relative risk of arthroplasty after ACL reconstruction is approximately three-times the baseline risk in the uninjured knee, and the relative risk is similar by sex, age, and socioeconomic status.

How this study might affect research, practice, or policy

- This study represents reference data for future studies, highlighting the increased risk of knee arthroplasty in patients sustaining ACL ruptures who undergo reconstruction. Future studies may prioritize investigating possible surgical and non-surgical risk modifiers that may lead to an improvement in outcomes, including investigation of the importance of access to early, sustained, high-quality rehabilitation.
- These findings can be shared with patients who frequently ask about prognosis following ACL injury, informing them of the future risk of knee arthroplasty.

Introduction

ACL injury is common and is associated with significant chondral damage and meniscal damage at the time of the injury.[1,2] Injury to the ACL has also been associated with increased risk of early onset osteoarthritis, with studies suggesting up to 35% of patients have symptomatic OA at 10 years post ACL injury.[3] Studies have shown that between 40% and 60% of patients who sustain ACL injuries undergo subsequent reconstructive surgery,[4–6] with the rate of ACL reconstruction in the UK being 24/100,000 as of 2019.[7] ACL injury frequently occurs in younger populations and, as such, longer-term development of early onset osteoarthritis is a concern. Studies report that the symptomatic prevalence of radiographic arthritis 10-years after an ACL injury is approximately 35%.[8]

The main driver of post-traumatic osteoarthritis in the ACL injury population is the primary knee injury, and patients who respond well to non-surgical management and structured rehabilitation suffer a similar rate of subsequently osteoarthritis to those who undergo ACL reconstruction for persistent functional instability.[9] Delayed surgical reconstruction in non-responders with persistent functional instability, however, is associated with repeated chondral and meniscal injuries.[10,11]

Several factors have been reported to affect the outcomes of ACL reconstruction. The presence of meniscal injury at the time of ACL rupture is correlated with worse outcomes.[12,13] Female sex has been associated with worse functional outcomes scores and return to sports rates when compared to males.[14,15] Older patients may have a higher risk of OA and worse functional outcome scores.[16] Social determinants of health such as socioeconomic status and ethnicity may result in poorer outcomes, potentially from the impact of delays in access to care.[17,18]

Knee arthroplasty is a well-established and effective management strategy for end-stage osteoarthritis, with pain and disability that is refractory to conservative managment.[19] In the context of large scale studies, arthroplasty is a powerful surrogate objective indicator of end-stage symptomatic osteoarthritis.[20] The population intervention rates for both ACL reconstruction and knee arthroplasty have increased over the past two decades.[7,21] In a previous study using UK data, it was shown that there is an increased risk of developing osteoarthritis in patients who sustain an ACL injury and undergo reconstruction in comparison to general population data.[22] This previous work was, however, been unable to account for population-specific risk-factors for developing knee osteoarthritis.

The purpose of this study was to investigate the population-specific risk of osteoarthritis after ACL reconstruction by identifying patients with a history of ACL reconstruction in only one knee and comparing the subsequent rate of knee arthroplasty in the reconstructed knees to the contralateral knees in these

individuals. Our primary endpoint was the risk of knee arthroplasty in the ACLr knee when compared to the contralateral, never intervened knee. Secondary outcomes included examining this risk by concomitant meniscal surgery, sex, age at ACLr, socioeconomic status, and ethnicity. Finally, we sought to compare the rates of arthroplasty, in both the ACLr knees and contralateral knees, to the risk in the general population.

Methods

The national Hospital Episode Statistics (HES) database for England, UK, was interrogated to identify all patients undergoing ACL reconstruction surgery (ACLr) between April 1997 and March2023. The HES admitted patient care (APC) includes all NHS inpatient care episodes, including those which are performed in independent hospitals. Prior to release of the data for analysis, the project was approved by the NHS Digital Independent Group Advising on the Release of Data (IGARD) committee (NHS Digital application DARS-NIC-667559). In accordance with the UK Health Research Authority (HRA) recommendations on analysis of routinely collected observational data, national research ethics committee approval was not required.[23]

Hospital Episode Statistics (HES) data are submitted by individual NHS providers, who are responsible for the accuracy of the data as it underpins reimbursement for activity. NHS England operates a formal data quality assurance process, including submission via a standardised XML schema with mandatory validation rules that records must pass before acceptance into HES. Schema changes are led by NHS England in consultation with data suppliers. In addition, an external auditor, on behalf of the Department of Health and Social Care, audits data submitted to the Secondary Uses Service to ensure providers are correctly paid, providing an additional check on the robustness and completeness of HES data.[24]

Patients and procedures

Patient HES episodes were identified using the classifications of surgical operations and procedures (OPCS-4) code associated with cruciate ligament reconstruction cases. This code is used for both ACL and PCL reconstruction in the UK, but PCL reconstruction is comparatively extremely rare and therefore, for the purposes of this study, whilst the cohort includes all cruciate ligament reconstruction cases, it is strongly representative of the ACL reconstruction population of interest and therefore reported as such.

Records were cleaned to identify patients undergoing their first ACL reconstruction to the index knee, with no previous or subsequent ACL surgery to their contralateral knee. Cases missing essential data (age, sex, procedure date, procedure laterality) were excluded from the study during data cleaning (Figure 1). Cases missing non-essential data (ethnicity) were included except for analyses adjusting for these specific variables. ACLr cases with simultaneous meniscal surgery (meniscectomy or meniscal repair) were identified.

Outcomes

The primary outcome of interest in this study was the absolute and relative rate of ipsilateral knee arthroplasty following ACL reconstruction. Secondary outcomes examined were the risk of arthroplasty in the ACLr knee when compared to the contralateral knee, stratified by concomitant meniscal surgery, age at ACLr, sex,

ethnicity, and socioeconomic status (IMD). Furthermore, we wished to examine the 5-, 10- and 15-year risk of arthroplasty in ACLr knees, the contralateral non-intervened knees, and compare these to the background general population risk of arthroplasty. For the purposes of this study, the rate of arthroplasty in the non/never intervened contralateral knees was used as the internal control. All available patient HES records were extracted for patients who were coded as having an ACLr, and their records were interrogated for any prior ipsilateral or contralateral knee procedures. Patients were only included for analysis if the ACL reconstruction was their first coded knee procedure; that is, they had no previous ipsilateral knee procedures. The data extraction diagram (Figure 1) summarises the patients excluded and the reason for exclusion.

Equality, Diversity, and Inclusion (EDI) Statement

This study of routinely collected data from the England, UK, health service included all patients undergoing an ACL reconstruction under the National Health Service. Specific analysis was planned and undertaken to investigate the association between ethnicity, sex, age, and socioeconomic status on the outcomes reported. The authors acknowledge that a cohort study design such as this can only report on interventions done and note that marginalized communities may struggle to access healthcare.

Statistics

Absolute rates of ipsilateral knee arthroplasty following ACL reconstruction were determined. These were compared with the rates of contralateral knee arthroplasty in the non-intervened knee. Arthroplasty free survival was analysed using Kaplan Meier survival analysis. To calculate relative risks, Kaplan Meier estimates of the cumulative incidence of arthroplasty were obtained at 10, 15 and 20 years. The 95% confidence intervals were derived using a non-parametric cluster bootstrap with resampling (2000 replicates) at the person level, preserving within-person correlation. The distribution of replicate estimates was used to obtain 95% confidence intervals. For survival analysis, origin was set as date of birth, start time (entry time) was date of ACL reconstruction for both reconstructed and non-reconstructed knees. End times were either conversion to arthroplasty (UKA or TKA), death or reaching the maximum study date (March 2023). A Cox proportional hazards model was used to calculate hazard ratios for subsequent arthroplasty over time with the contralateral knee used as reference. Knees were compared overall, by demographic factors, and by whether associated meniscal surgery was undertaken. Demographic factors included sex, age at ACLr, ethnicity and socioeconomic status (index of multiple deprivation). Proportional hazards assumptions were tested using Schoenfeld residuals.

To estimate the probabilities of knee replacement over 5-, 10-, and 15-years in comparison to the general population (without a history of ACL reconstruction), we performed a knee level analysis where time was measured on the attained age scale. Date of birth was set as the origin time, and ACL reconstruction date was set as the analysis start time for ACL reconstructed knees and contralateral knees. Follow up ended at

arthroplasty, death or study completion. Follow up was split into 10-year age bands. Within each band we calculated age-specific incidence rates of knee arthroplasty as the number of events divided by total knee-years. Baseline population rates were derived from national data on all primary knee arthroplasties and age-specific population denominators over the same period, multiplying person-years by two to approximate knee-years. 5-, 10- and 15-year probabilities of knee arthroplasty were estimated from pooled age-specific incidence rates using the exponential relationship $\text{Risk}(t) = 1 - \exp(-\lambda t)$. Probabilities are presented as percentages for ACL-reconstructed knees, contralateral knees, and the baseline population in each age band.

RESULTS

Between April 1997 and March 2023, 179,355 patients underwent ACL surgery, of which 135,881 were eligible for analysis (Figure 1). The median age at ACL reconstruction was 27 (IQR 21 – 34). There was a larger proportion of males (75%), with the most common age group undergoing ACLr being the 20-29 age group (Table 1). Median follow-up was 8.75 years (IQR 4.5–12.5 years.). 97,039 patients were at risk at 5 years, 53,521 at ten years, and 18,280 at 15 years. During follow up 1,005 patients (0.73%) were censored due to death, with the remainder administratively censored (reaching study end date without event or death).

Risk of arthroplasty in ACLr knees vs contralateral controls

Overall, the arthroplasty rate in ACLr knees at 10 years was 0.46% (0.42 – 0.51%), compared to 0.14% (95% CI 0.12 to 0.17%) in the non-reconstructed knees. This represents an overall relative risk (RR) of arthroplasty at 3.25 (95% CI 2.67 to 3.97) in the reconstructed knees at 10 years when compared to the non-reconstructed knees. At 15 years, the rate was 1.11% (95% CI 1.02 to 1.22%) in the ACLr group and 0.39% (95% CI 0.33 to 0.45%) in the non-reconstructed group, representing a relative risk of arthroplasty at 15 years of 2.87 (95% CI 2.42 to 3.41). Finally, at 20 years, the arthroplasty rate was 2.44% (95% CI 2.18 to 2.73) in the ACLr knee versus 0.88% (95% CI 0.72 to 1.06) in the contralateral knee. This represents a 20-year RR of arthroplasty of 2.78 (95% CI 2.31 to 3.38) in the ACLr knee compared to the contralateral knee.

Hazard of arthroplasty in ACLr Knees vs Contralateral controls

The arthroplasty-free survival of the native ACLr knees versus the contralateral knees is shown for all patients in Figure 2, and by sex in Figure 3. These findings correspond to an overall hazard for knee arthroplasty of 3.10 (HR; 95% CI 2.69 to 3.57) in the ACLr knee versus the contralateral knee. Having ACL reconstruction alone had a HR of 3.00 (95% CI 2.56 to 3.51); having a simultaneous meniscal surgery resulted in a hazard ratio for arthroplasty of 3.50 (95% CI 2.55 to 4.81). In male patients, the hazard ratio was 3.27 (95% CI 2.72 to 3.92) versus 2.85 (95% CI 2.28 to 3.57) in female patients. The rate of arthroplasty was low within the study period for patients undergoing ACLr under the age of 20 (n=17, 11 ACLr knees and 6 contralateral knees), with a corresponding hazard of 1.83 with wide confidence intervals (95% CI 0.68 to 4.35). In patients aged 20-29-years when they underwent ACLr, the hazard ratio was 3.63 (95% CI 2.41 to 5.48) in the ACLr knee versus contralateral knee, aged 30-39-years the hazard ratio was 3.60 (95% CI 2.78 to 4.67), aged 40-49-years, the hazard was 3.09 (95% CI 2.44 to 3.90), and aged 50-59-years, the hazard ratio was 2.38 (95% CI 1.73 to 3.31).

The hazard of arthroplasty in ACLr knees relative to contralateral knees was elevated across all strata of IMD, with hazard ratios of 2.67 (95% CI 2.07 to 3.42) for the most deprived 0–20%, 2.70 (95% CI 2.02 to 3.60) for the more deprived 20–40%, 4.02 (95% CI 2.90 to 5.58) for the middle 40–60%, 3.74 (95% CI 2.62 to 5.33) for the less deprived 60–80%, and 2.81 (95% CI 1.71 to 4.63) for the least deprived 80–100% group.

When stratified by ethnicity, the hazard ratio was 3.18 (95% CI 2.74 to 3.68) in White patients, 1.90 (95% CI 0.89 to 4.10) in Asian patients, 2.01 (95% CI 0.68 to 5.89) in Black patients, 2.50 (95% CI 0.48 to 12.90) in mixed patients, and 2.00 (95% CI 0.18 to 22.06) in those recorded as other ethnicity. The wide confidence intervals in the non-white ethnicities were a function of the small number of patients in these demographics. These finding are summarised in a forest plot (Figure 4).

Long term probability of arthroplasty

The 5-, 10- and 15-year probabilities of arthroplasty in each age group are shown in figure 5 and table 2. Age group represents the attained age, and characterises the probability of arthroplasty based on whether a knee is ACL reconstructed, the contralateral control knee, or a baseline population knee. In the 10-19 age group and 20-29 age group the probabilities of arthroplasty at 5, 10 and 15 years was negligible across all groups. In the 30-39 ACLr age group the 5-, 10- and 15-year probabilities of arthroplasty were 0.03 (95% CI 0.02–0.05), 0.06 (95% CI 0.04–0.09), and 0.09 (95% CI 0.06–0.14), respectively. With figures for the contralateral knee lower at 0.01 (95% CI 0.00–0.02), 0.02 (95% CI 0.01–0.04), and 0.03 (95% CI 0.01–0.06). Probability remained negligible in the baseline group (≤0.01 (95% CI 0.00–0.02) at 15 years). In the 40-49 ACLr age group probabilities of arthroplasty of 0.18 (0.14–0.22), 0.35 (0.28–0.43), and 0.53 (0.43–0.65) were seen at 5, 10 and 15 years, compared with 0.06 (0.04–0.09), 0.12 (0.08–0.17), and 0.18 (0.12–0.16) in the contralateral knee, and 0.05 (0.05–0.05), 0.10 (0.10–0.10), and 0.15 (0.15–0.16) in the baseline population. In the 50-59 age group, the ACLr knee had 5-, 10- and 15-year probabilities of 1.58 (1.42–1.75), 3.13 (2.82–3.47), and 4.66 (4.29–5.15), respectively. The contralateral knee demonstrated probabilities of 0.41 (0.34–0.51), 0.83 (0.67–1.01), and 1.24 (1.00–1.51), which were higher than those seen in the baseline population at 5-, 10-, and 15-years: 0.34 (0.34–0.34), 0.68(0.67 -0.68), 1.01 (1.01–1.02). Finally in the 60-69 age group the ACLr knee had 5-, 10- and 15-year probabilities of 6.39 (5.70–7.15), 12.38 (11.07–13.78), and 17.98 (16.14–19.95) respectively. The contralateral knee demonstrated probabilities of 2.63 (2.17–3.14), 5.18 (4.30–6.18), and 7.67 (6.38–9.13), which were higher than those seen in the baseline population at 5-, 10-, and 15- years: 1.04 (1.04–1.05), 2.07 (2.07 -2.08), 3.10 (3.09–3.10).

DISCUSSION

Principal findings

This study provides robust data on the relative risk of knee arthroplasty in the population of patients undergoing ACL reconstruction in comparison to their contralateral, unoperated, knees. Overall, the risk of arthroplasty in the ACLr knee was three-times the uninjured knee. It was rare for the 10-19-year age group to undergo arthroplasty within the 26-year duration of this study, but in all other age groups the relative risk of arthroplasty in the ACLr knee versus the contralateral knee was found to be similarly increased, at between 2.4-times and 3.8-times. There was no significant difference in the relative risk for male versus female patients, and no significant difference was observed in patients when ACLr was combined with surgery to the meniscus.

Comparison to previous studies

Recent large cohort and registry studies have indicated that in addition to cartilage or meniscal injuries sustained at the time of an ACL injury, delays to surgical reconstruction increase the risk of further injuries in this population.[10,11] Previous case-control studies of ACL injury and ACL reconstruction have reported an approximately seven-times greater risk of knee arthroplasty in comparison to the general population, but these studies were limited by the study design and control group matching.[25,26] For example, one ACL injury study was unable to identify patients that had undergone surgical interventions, and neither previous study could identify and match the side of the injury or intervention, which would have led to an over-reporting of the corresponding arthroplasty rate.[25,26] A previous UK study, using similar data, reported up to a twenty-times higher rate of knee arthroplasty at a young age (30-39-years) than would be expected in the general population.[22] The major limitation and potential criticism of this paper was that it was unable to control for differences in the ACL-injury population as a whole. That is, these patients may generally be at greater risk of osteoarthritis, with or without an ACL reconstruction, perhaps due to their activity level, associated unrelated injuries, genetic, biological, or biomechanical reasons. The present study was designed to overcome this potential confounding by using an internal population control, i.e. the contralateral knee of patients with history of ACL reconstruction on only one side.

The present study is the first to compare the arthroplasty rate in the injured and reconstructed knee to the contralateral knee of the same patients to deliver a population-specific estimate for the relative risk of arthroplasty following an ACL injury and reconstruction. In a previous study, using similar methodology, in patients with a history of arthroscopic partial meniscectomy in only one knee, the risk of arthroplasty in that knee was found to be greatly elevated in comparison with the contralateral knee (no history of APM; HR 2.99; 95% CI 2.95 to 3.02).[27] The findings in the ACL injury and reconstruction group from this study are

similar both for isolated ACLr (HR 3.00; 95% CI 2.56 to 3.51) and for cases where ACLr was combined with a meniscal procedure (HR 3.50; 95% CI 2.55 to 4.81).

Further analysis in the present study was done in comparison to general population data. Because this study includes all ACL reconstruction patients over the 25-year cohort period, an age-matched comparator population could be constructed to determine the related rates of knee arthroplasty at 5-year, 10-years, and 15-years respectively. These data demonstrate that the baseline risk of arthroplasty in these time periods for the ACL reconstruction population (in the non-operated knee) is similar to the general population at attained age groups from 10 to 49. When control knees of the ACLr patients reach 50-59, they have a slight increase in 15-year probability of knee arthroplasty when compared to the baseline population. This increases sharply when these knees reach 60-69, with the non-intervened knee having significantly higher 5-, 10-, and 15-year probability of arthroplasty compared to the baseline population. This is the first time such data has been reported in the literature.

Clinical trials have been done that inform us about patient choice and decision making following ACL injury.[5,28,29] At least half of ACL injury patients choose to have an ACL reconstruction due to the disabling nature of their knee instability and risk of future injuries.[28,29] Whilst some patients may be able to rehabilitate and tolerate an ACL deficient knee, especially with lifestyle modification, for those with functional instability, choosing to undergo an ACL reconstruction offers benefits.[29] This discretionary approach to clinical management, with patients choosing ACL reconstruction according to their symptoms and functional demands, is standard practice in the UK NHS, the source of the data reported in the present study. This is important as these previous trials, whilst informative in terms of the proportion of patients needing to undergo an ACL reconstruction, were unable to draw meaningful conclusions about the relative risk of knee osteoarthritis. The present study therefore adds important contextually relevant data about this outcome, that can be considered by patients and clinicians alongside the clinical trial evidence.

Strengths and weaknesses

This study is the largest cohort of ACL reconstruction cases that has been reported. Cases were carefully extracted to identify patients with a history of cruciate ligament reconstruction in only one knee, so that outcomes could be compared to the natural history of their other knee, without a history of this procedure. In this way, we have been able to precisely report the relative risk of arthroplasty for these patients over the study period of a maximum of 26 years. The methodology has enabled us to report for the first time a 'population-specific' relative risk of knee arthroplasty for patients undergoing ACL reconstruction. Despite these strengths, an observational study of this nature is still unable to determine the extent to which the ACL reconstruction was protective of the knee. Damage occurs at the time of the injury and from any subsequent pivoting injuries, but the nature of these injuries is unknown. Whilst historic comparative data is

informative, the natural history of the ACL injured knees had ACL reconstruction not been done cannot be proven in data of this nature, as patients with disabling instability will usually elect to undergo reconstruction to regain their knee function.[30–33] Whilst great care was taken in cleaning the data for data quality and in extracting the study population of interest, it is inevitable that some coding errors will occur in a national dataset such as this. For HES data, although the specific coding accuracy of ACL reconstruction and arthroplasty procedures has not been determined, previous studies have been supportive of the level of accuracy of these data.[34,35] It should be noted that intra-articular ligament reconstruction codes were used to identify the ACL reconstruction cases, and therefore, as described in the methods, these codes will also have captured and included some PCL reconstruction cases.[36,37] PCL reconstruction is, however, comparatively very rare, and these data should be considered representative of ACL reconstruction. For an inpatient care database such as this, it should also be noted that some patients could have sustained an ACL injury to their contralateral knee (or subsequent re-injury of the ipsilateral knee) and not undergone ACL reconstruction. This should be acknowledged, but we believe our findings are still representative of the 'real-world' natural history of the knee of patients who undergo an ACL reconstruction.

Clinical implications

This is largest cohort of ACL reconstruction patients that has been reported in the literature and the first to report the objective relative risk of knee arthroplasty in the ACL injured knee undergoing an ACL reconstruction in comparison to the contralateral knee. These patients can now be informed of the three-times relative risk of knee arthroplasty in comparison to their own contralateral, non-reconstructed knee, as well as the average baseline risk in the general population.

Unanswered questions and future research

The extent to which the ACL reconstruction may have been protective in terms of reducing repeat cartilage injuries in this population is unknown. Previous RCTs have also been unable to answer this question, in part because the trials are small and knee replacement is a long-term and uncommon outcome, and because ACL reconstruction is done for symptomatically unstable knees, meaning that patients will self-select or cross-over to choose ACL reconstruction when these instability symptoms are disabling. Future clinical or radiographic research may shed some more light on this question, but the present study is strongly representative of anticipated patient outcomes following the current clinical treatment pathway for ACL injury.

Conclusion

Patients undergoing ACLr have over three-fold higher risk of undergoing arthroplasty in their reconstructed knee when compared to their contralateral knee. This finding is consistent whether there was concomitant meniscal surgery, and across sex, age, ethnicity and socioeconomic status. In comparison to the general

population, patients with a history of ACLr in one of their knees have an increased risk of arthroplasty in both their ipsilateral and their contralateral knee. These findings will allow us to better inform patients of the potential long-term outcomes of their ACL injured knee following reconstructive surgery.

Details of contributors

CH: analysis, writing and editing paper.

JM: methodology, editing paper.

AP: concept, methodology, editing paper.

SA: concept, methodology, writing and editing paper. Guarantor.

Transparency declaration and Guarantor.

The senior author (SA) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and registered) have been explained.

Competing interests

The authors declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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Patient Involvement

This study directly addresses a Top-10 research priority from the NIHR James Lind Alliance Priority Setting Partnership regarding soft tissue knee injury: "What are the implications of soft tissue knee injuries on future knee disease?" - https://www.jla.nihr.ac.uk/priority-setting-partnerships/first-time-soft-tissue-knee-injuries.
The application to use patient data for this study was independently reviewed by the NHS England Advisory Group for Data (AGD) which includes patient and public member representation. Patients or the public were not, however, directly involved in the design, conduct, reporting, or dissemination plans of our research.

Ethical approval

Not required.

Data sharing

No additional data available.

FIGURES

Figure 1. Flow chart illustrating extraction of patient level cohort.

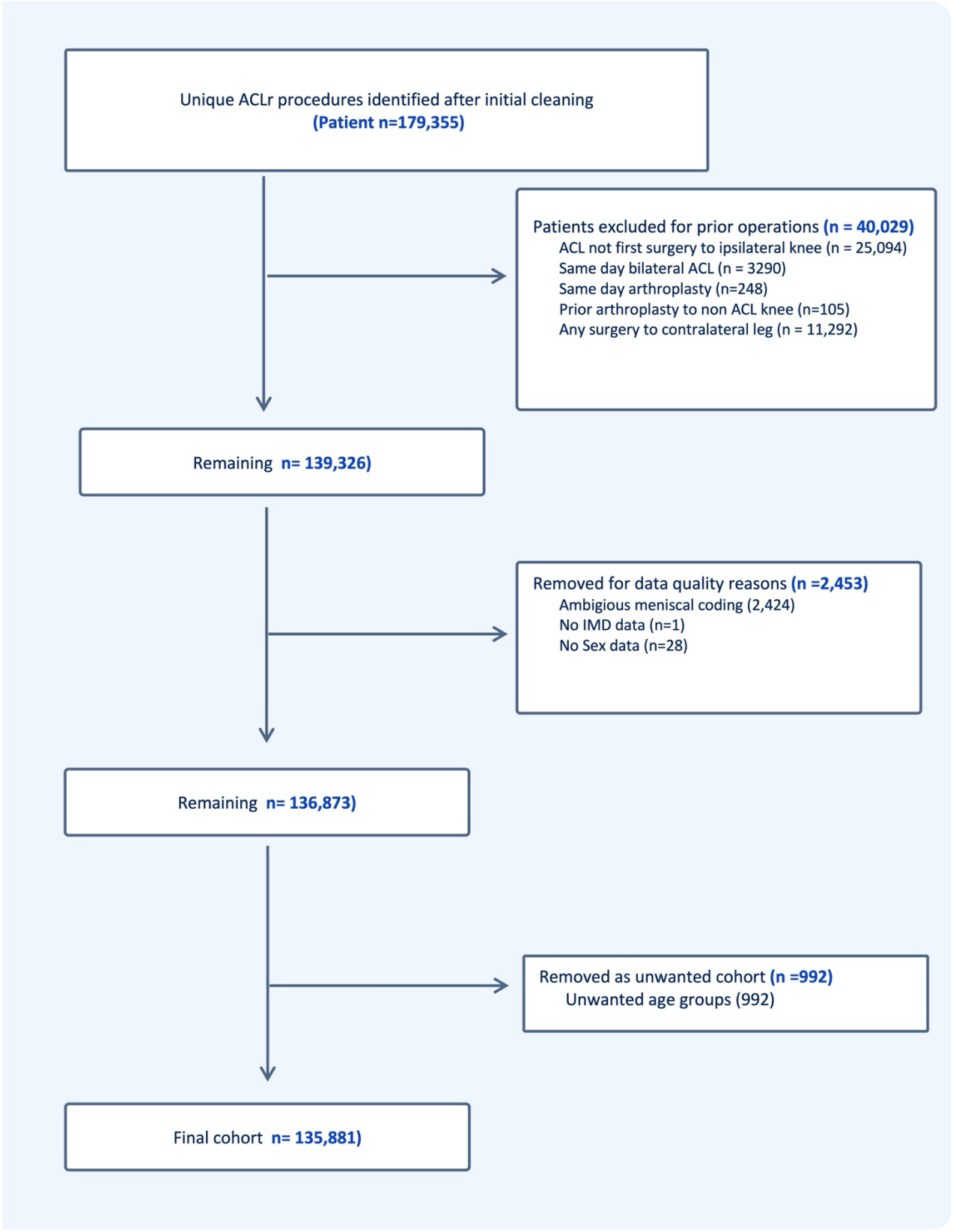


Figure 2. Arthroplasty free survival in ACL reconstructed knee (blue) vs contralateral non-reconstructed knee (red). Shaded area represents 95% confidence interval.

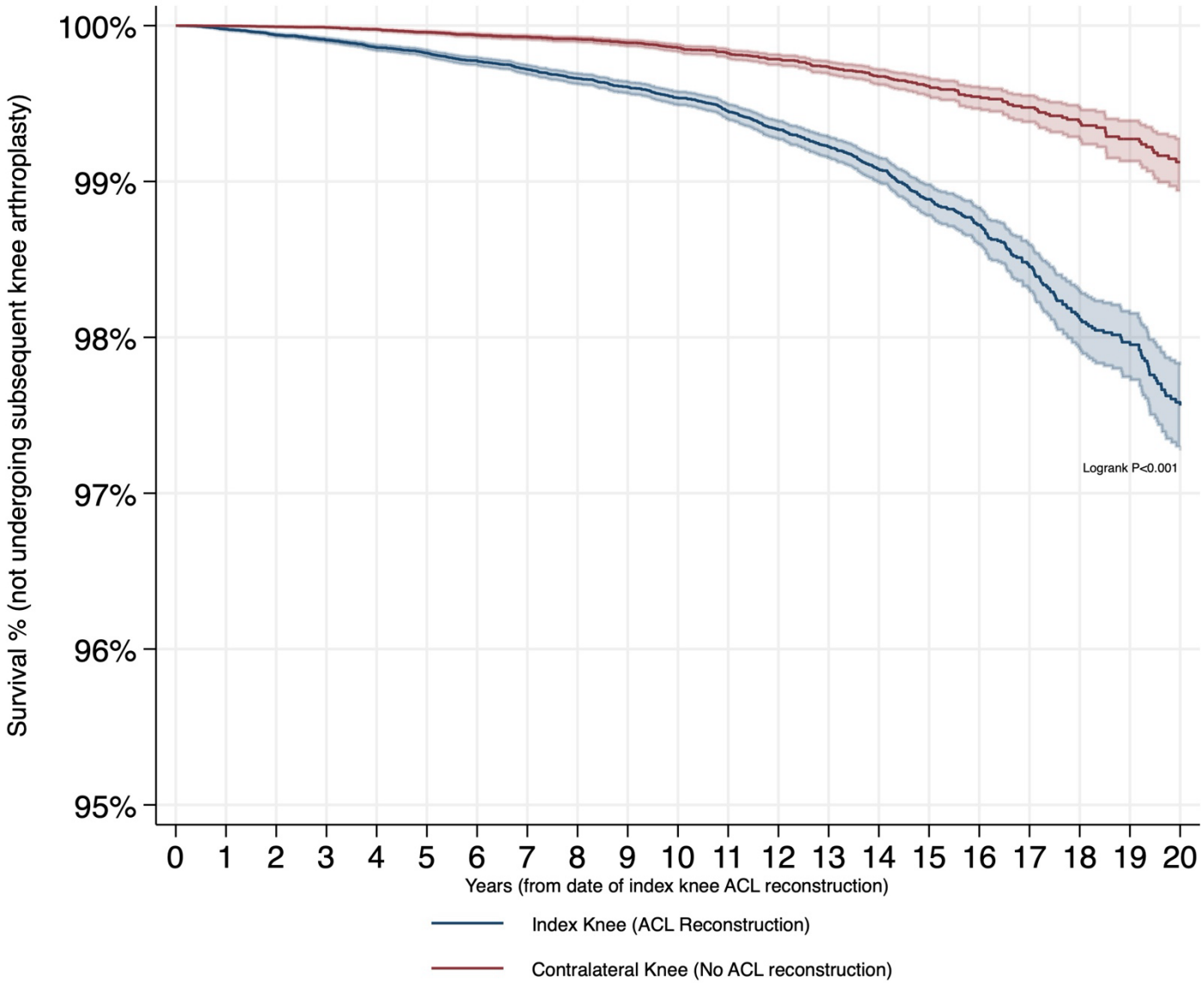
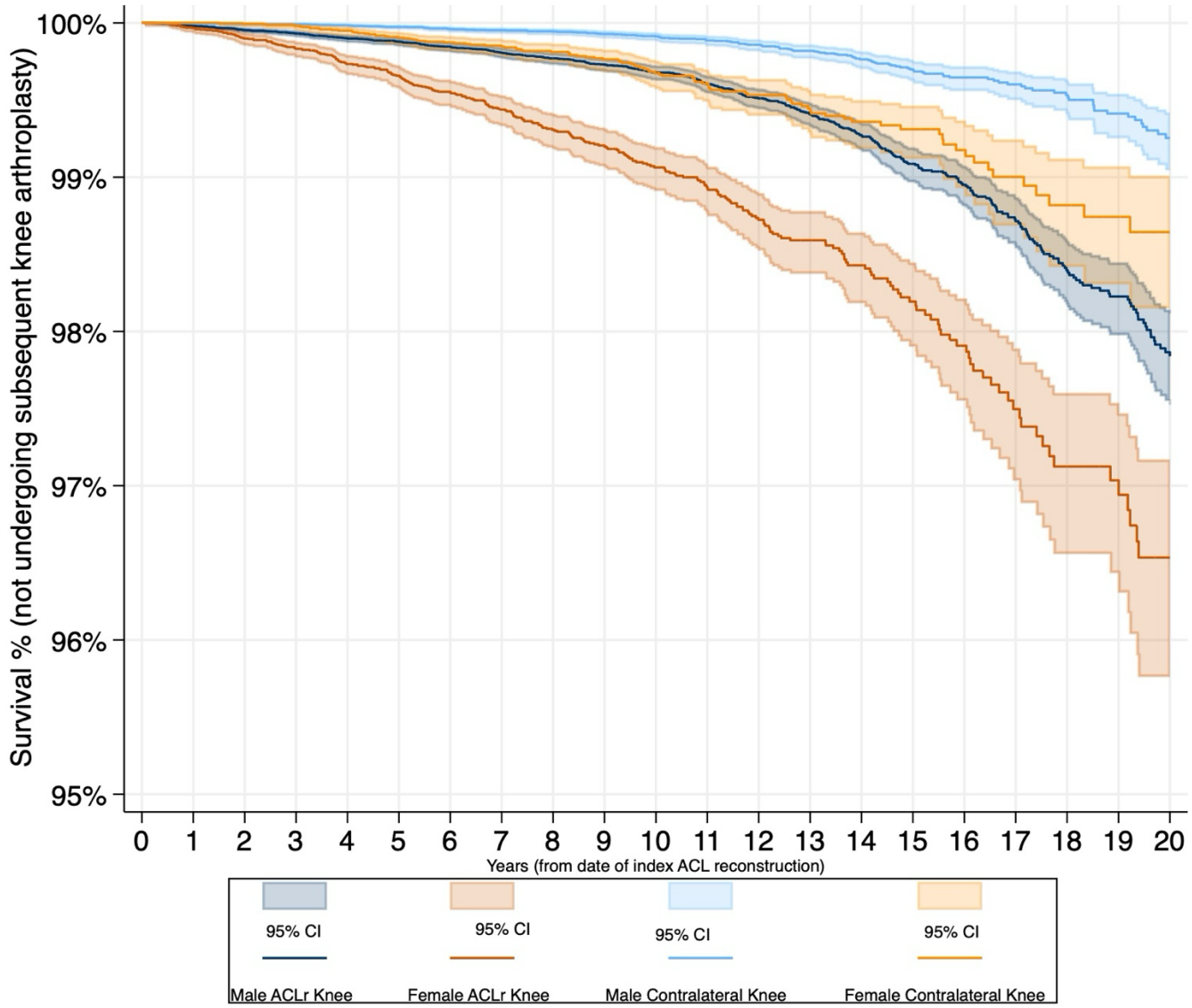
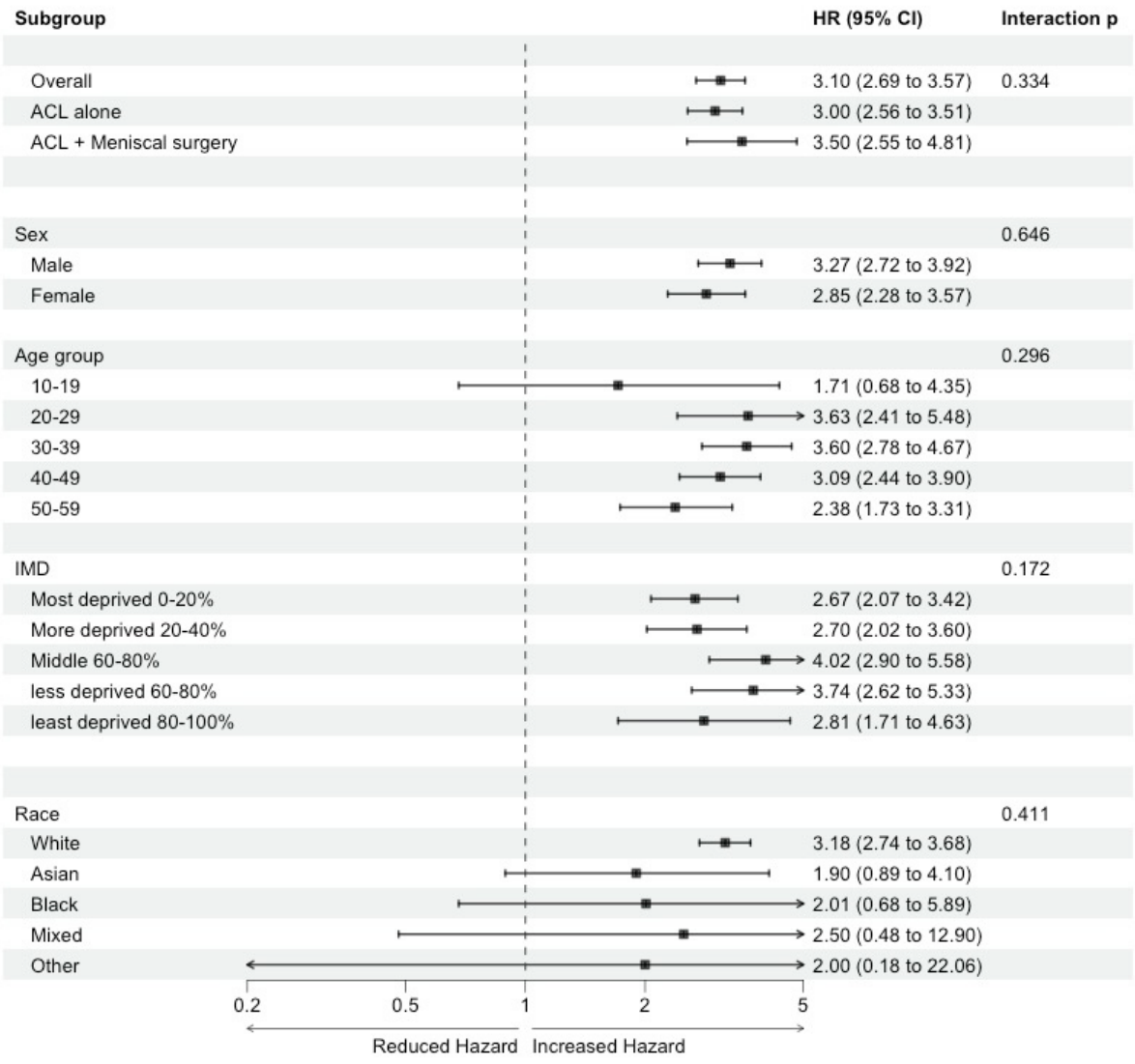


Figure 3. Sex differences in arthroplasty free survival in ACL reconstructed knee vs contralateral non reconstructed knee. Shaded area represents 95% confidence interval.



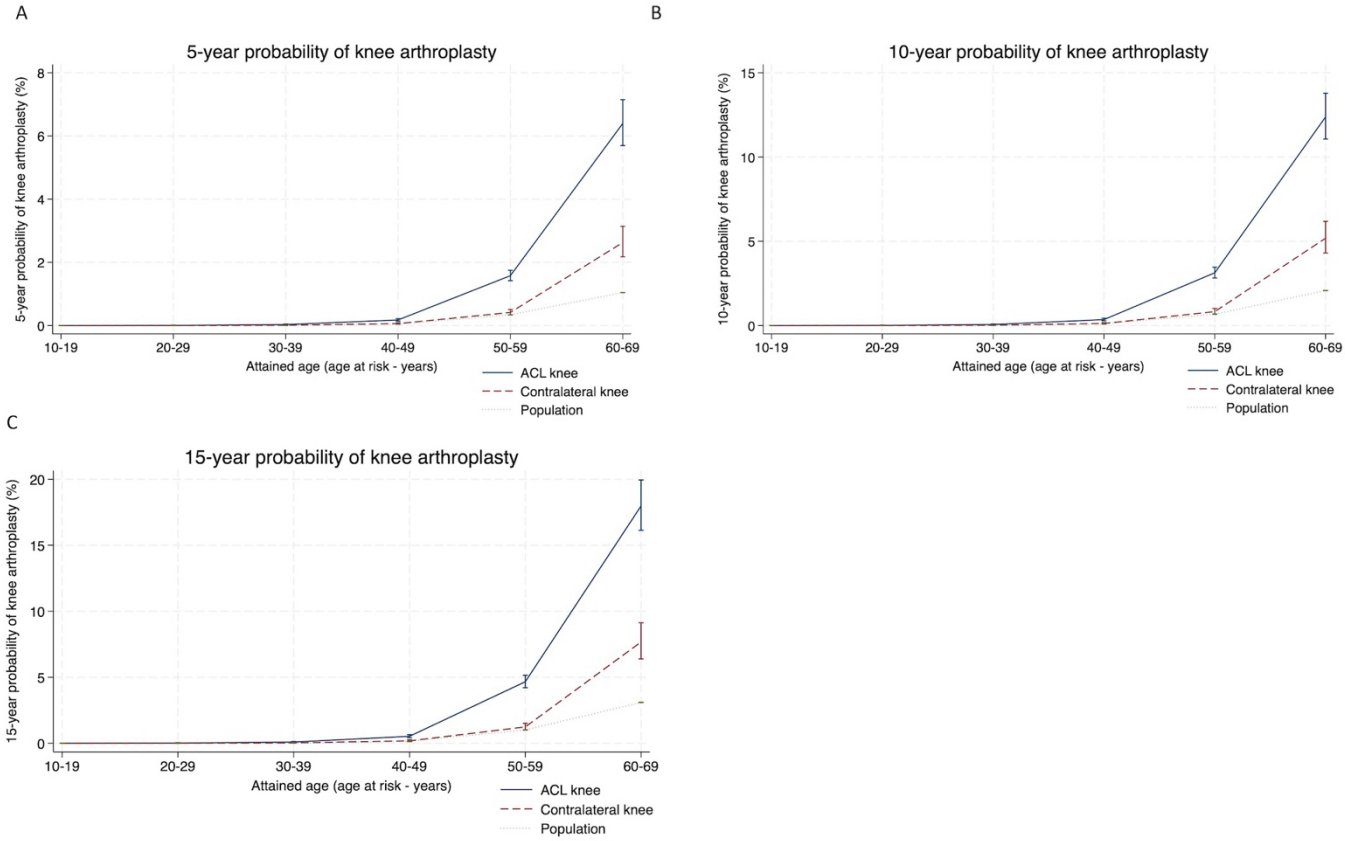
Logrank test: Male ACLr vs. Male Contralateral P<0.001; Male ACLr vs. Female ACLr P<0.001; Male ACLr vs. Female Contralateral P<0.05; Female ACLr vs. Female Contralateral P<0.001

Figure 4: Hazard for Subsequent Knee Arthroplasty for ACLr Knee versus Contralateral Knee



HR = Hazard ratio

Figure 5: 5-, 10-, and 15-year probabilities of knee arthroplasty based on knee status and attained age.



A. *5-year probability of knee arthroplasty based on attained age.*
B. *B 10-year probability of knee arthroplasty based on attained age.*
C. *C. 15-year probability of knee arthroplasty based on attained age.*

Error bars represent 95% CIs for probability estimates. Population refers to the baseline population probability of arthroplasty within 5, 10 and 15 years given the current age.

TABLES

Table 1. Demographics

	n	%
Overall	135,881	100
ACL alone	86,299	63.51
ACL + Meniscal surgery	49,582	36.48
Sex		
Male	102,275	75.27
Female	33,606	24.73
Age at ACLr(years)		
10 - 19	23,885	17.58
20 - 29	59,973	44.14
30 - 39	33,320	24.52
40 - 49	14,950	11.00
50-59	3,753	2.76
Ethnicity		
White	102,012	75.07
Black	3,183	2.34
Asian	7,092	5.22
Mixed	1,892	1.39
Other	2,710	1.99
Unknown	18,992	13.98
IMD		
Most deprived 0-20%	31,264	23.01
More deprived 20-40%	28,571	21.03
Middle 40-60%	27,663	20.36
Less deprived 60-80%	25,651	18.88
Least deprived 80-100%	22,732	16.73

Table 2. 5-, 10-, and 15-year probabilities of undergoing knee arthroplasty by attained 'knee-age', in ACL reconstructed knees, non-intervened knees, and in the general population respectively.

	Age group	*ACLr Knee*	*Contralateral knee*	*Baseline population*
5 year	10 - 19	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)
10 year	10 - 19	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)
15 year	10 - 19	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)
5 year	20-29	0.01 (0.00 - 0.01)	0.00 (0.00 - 0.01)	0.00 (0.00 - 0.00)
10 year	20-29	0.01 (0.01 - 0.03)	0.00 (0.00 - 0.02)	0.00 (0.00 - 0.00)
15 year	20-29	0.02 (0.01 - 0.04)	0.00 (0.00 - 0.02)	0.00 (0.00 - 0.00)
5 year	30-39	0.03 (0.02 - 0.05)	0.01 (0.00 - 0.02)	0.00 (0.00 - 0.01)
10 year	30-39	0.06 (0.04 - 0.09)	0.02 (0.01 - 0.04)	0.01 (0.01 - 0.01)
15 year	30-39	0.09 (0.06 - 0.14)	0.03 (0.01 - 0.06)	0.01 (0.01 - 0.02)
5 year	40-49	0.18 (0.14 - 0.22)	0.06 (0.04 - 0.09)	0.05 (0.05 - 0.05)
10 year	40-49	0.35 (0.28 - 0.43)	0.12 (0.08 - 0.17)	0.10 (0.10 - 0.10)
15 year	40-49	0.53 (0.43 - 0.65)	0.18 (0.12 - 0.16)	0.15 (0.15 - 0.16)
5 year	50-59	1.58 (1.42 - 1.75)	0.41 (0.34 - 0.51)	0.34 (0.34 - 0.34)
10 year	50-59	3.13 (2.82 - 3.47)	0.83 (0.67 - 1.01)	0.68 (0.67 - 0.68)
15 year	50-59	4.66 (4.29 - 5.15)	1.24 (1.00 - 1.51)	1.01 (1.01 - 1.02)
5 year	60-69	6.39 (5.70 – 7.15)	2.63 (2.17 – 3.14)	1.04 (1.04 – 1.05)
10 year	60-69	12.38 (11.07 – 13.78)	5.18 (4.30 – 6.18)	2.07 (2.07 – 2.08)
15 year	60-69	17.98 (16.14 – 19.95)	7.67 (6.38 – 9.13)	3.10 (3.09 – 3.10)

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