Long-term Rates of Knee Arthroplasty in a Cohort of 830,000 Patients with a History of Arthroscopic Partial Meniscectomy

1. S.G.F. Abram[1,2] *BMBCh MA(Oxon) MRCS*
2. A. Judge[1,2,3,4] *M.Sc.(Soton.) PhD*
3. D.J. Beard[1,2] *GDPhys MCSP MA MSc DPhil*
4. A.J. Carr[1,2] *ChM DSc FRCS FMedSci*
5. A.J. Price[1,2] *BA MBBS FRCS(Tr&Orth) DPhil*

Author addresses:
[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, OX3 7LD
[2]NIHR Biomedical Research Centre, Oxford, OX3 9DU
[3]Musculoskeletal Research Unit, University of Bristol, BS8 1QU
[4]NIHR Biomedical Research Centre, Bristol, BS8 1QU

Author titles:
SA: NIHR Doctoral Research Fellow
AJ: Professor of Translational Statistics
DB: Professor of Musculoskeletal Sciences
AC: Nuffield Professor of Orthopaedics
AP: Professor of Orthopaedics

Details of contributors
SA: concept, methodology, analysis, writing and editing paper, guarantor.
AJ: methodology, analysis, editing paper.
DB: concept, editing paper.
AC: editing paper.
AP: concept, methodology, editing paper.

Competing interests
Andrew Judge has received consultancy fees from Freshfields Bruckhaus Deringer (on behalf of Smith & Nephew Orthopaedics Limited), and is a member of the Data Safety and Monitoring Board (which involved receipt of fees) from Anthera Pharmaceuticals, Inc. All other 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.

Funding
This report is independent research supported by the National Institute for Health Research (NIHR Doctoral Research Fellowship, Mr Simon Abram, DRF-2017-10-030), National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), and Bristol Biomedical Research Centre (BRC). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

Corresponding author:
Simon Abram
E: simon.abram@ndorms.ox.ac.uk
T: +44 1865 223425
Botnar Research Centre, University of Oxford
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences
Windmill Road, Oxford OX3 7LD. UK

Keywords
knee; arthroscopy; meniscectomy; meniscal tear; arthroplasty; outcomes; osteoarthritis
Word count:
3028

ABSTRACT

AIM

To determine the long-term risk of undergoing knee arthroplasty in a cohort of patients with meniscal tears who had undergone arthroscopic partial meniscectomy (APM).

METHODS

A retrospective national cohort of patients with a history of isolated APM were identified over a twenty-year period. Patients with prior surgery to the same knee were excluded. The primary outcome was knee arthroplasty. Hazard ratios were adjusted by patient age, sex, year of APM, Charlson comorbidity index, regional deprivation, rurality, ethnicity. Risk of arthroplasty in the index knee was compared to the patient's contralateral knee (with versus without a history of APM).

RESULTS

834,393 patients were included (mean age 50 years; 37% female). Of those with at least 15-years of follow up, 13.49% (16256/120493; 95% CI 13.30-13.69) underwent subsequent arthroplasty within this time. In women, 22.07% (95% confidence interval [CI] 21.64-22.51) underwent arthroplasty within 15 years in comparison to 9.91% men (95% CI 9.71-10.12), corresponding to a risk ratio (RR) of 2.00 (95% CI 1.95-2.06). Relative to the general population, patients with a history of APM were 10.27 times (RR; 95% CI 10.07-10.47) more likely to undergo arthroplasty rising to 39.62 times (RR; 95% CI 27.68-56.70) at a younger age (30-39-years). In patients with a history of APM in only one knee, the risk of arthroplasty in that knee was greatly elevated in comparison to the contralateral knee (no APM) (HR 2.99; 95% CI 2.95-3.02).

CONCLUSIONS

Patients developing a meniscal tear, undergoing APM, are at greater risk of knee arthroplasty than the general population and this risk is three-times greater in the patient's affected knee than the contralateral knee. Women in the cohort were at double the risk of progressing to knee arthroplasty versus men. These important new reference data will inform shared-decision making and enhanced approaches to treatment, prevention, and clinical surveillance.

TAKE HOME MESSAGES

- Thirteen percent of patients underwent knee arthroplasty within 15-years of APM and patients with a history of APM were ten-times more likely to undergo knee arthroplasty annually as individuals without a history of APM.
- Women were twice as likely to undergo subsequent knee arthroplasty as men.
- In patients undergoing APM in only one knee, the rate of subsequent arthroplasty in that knee was three-times that of the other knee (not undergoing APM).

INTRODUCTION

Patients sustaining a meniscal tear in the knee are known to be at risk of osteoarthritis.[1–3] Despite the prevalence of meniscal injury, and a high-rate of surgical intervention, the long-term outcomes in this population are poorly defined.[4,5] Progressive osteoarthritis, especially requirement for subsequent knee arthroplasty, is an important and undesirable outcome, however patient factors, including sex, that may be associated with the risk of progression are poorly defined.[6,7]

Small studies have investigated rates of radiographic progression in patients with meniscal damage, however radiographic findings may not reflect clinical symptoms.[8] In comparison, knee arthroplasty is an objective end-point that has been used as a surrogate marker for end-stage symptomatic osteoarthritis in surgical and pharmacological studies.[6,9–11] Two previous studies of higher risk patients estimated between a three and fifteen times greater risk of knee arthroplasty after arthroscopic partial meniscectomy (APM) surgery or meniscal 'injury' respectively.[12,13] These studies were, however, limited by small study numbers, short follow up, incomplete data capture from insurance company or regional records, failure to identify surgical treatments undertaken, and failure to match by affected knee. An understanding of the risk factors for progressive osteoarthritis is required for individualised consent and to guide optimal care provision.

The purpose of this study was to determine the absolute and relative (versus general population data and the patient's other knee) risk of knee arthroplasty in patients with history of meniscal damage and APM. Differences in outcome associated with sex, age, comorbidity, deprivation, and ethnicity were investigated.

METHODS

Data source

Data from the National Health Service (NHS) Hospital Episode Statistics (HES) database for England, UK, was provided by NHS Digital (application DARS-NIC-68703).[14] HES includes episodes of care delivered in treatment centres (including those in the independent sector) funded by the NHS, episodes of care in England where patients are resident outside of England, and privately funded patients treated within NHS hospitals. Where required, age-sex matched national population estimates were extracted from census publications.[15]

Participants and exposure

All patients undergoing APM or knee arthroplasty between 1 April 1997 and 31 March 2017 were eligible for inclusion. All HES records for these patients were extracted after identification using the recorded Classification of Surgical Operations and Procedures (OPCS-4) procedure codes (Appendix 1).[16] For patients undergoing either APM or knee arthroplasty at any point in the cohort period, all previous and subsequent records were also identified for the same patient and extracted. The index exposure analysed was the first APM recorded, per patient. Only isolated APM cases were eligible for inclusion as index cases, with patients undergoing prior surgery to the same knee, simultaneous ligament reconstruction, or combined meniscal procedures being excluded.

Outcomes

The outcome analysed was knee arthroplasty (first knee arthroplasty; total or partial). Arthroplasty procedures were matched by the side of the procedures (OPCS-4 laterality codes) and the absolute rate of knee arthroplasty was determined over time following the index procedure (APM). Records of repeat APM were identified and the time to repeat APM recorded. Outcomes in the index knee (first knee undergoing an APM) were also compared to the other knee (contralateral knee) considering whether the patient had also undergone APM in the contralateral knee.

Statistical analysis

Stata v15.1 (StataCorp, College Station, Texas, USA) was used to perform all analysis. In accordance with ONS and NHS Digital guidance, small numbers were suppressed where required.[17] The absolute rate of knee arthroplasty was determined at 5 years, 10 years, and 15 years following APM as the proportion of the cohort with each respective minimum period of follow-up. Mortality adjusted Kaplan-Meier survival analysis (survival was defined as not undergoing knee arthroplasty) was performed and stratified by patient age group and sex.

A Cox proportional-hazards model was used first to calculate the unadjusted hazard ratio of knee arthroplasty over time by age group, sex, index of multiple deprivation (quintile derived from regional factors in England including average income, employment, education, housing, and crime; 1=least deprived area, 5=most deprived), ethnicity, modified Charlson comorbidity index (derived with maximum 5-year diagnosis code lookback period), year of treatment (APM), rurality, and ethnicity respectively.[18–21] The hazard ratios were then adjusted including all these variables in the model.

The relative risk (risk ratio) of knee arthroplasty in the population of patients with a history of APM in comparison to the general population (without a history of APM) was estimated for the year 2016-17. All patients undergoing knee arthroplasty in 2016-17 were identified and the number of these patients with a previously recorded APM (in the prior years of HES data) versus those without a history of APM made up the numerator for each respective population. The APM population denominator was the number of living patients with a history of APM that had not undergone a knee arthroplasty prior to 2016-17. The denominator for the non-APM population was the national mid-year population estimate less the APM population. To aid interpretation, both the absolute and relative risk estimates were stratified according to the age of the patient in 2016-17, irrespective of the year of APM, where applicable.

RESULTS

A total of 938,612 patients (1,088,782 procedures) were identified. After data cleaning and exclusion of patients undergoing concurrent ligament reconstruction, meniscal repair, or with a history of previous arthroscopic interventions, 834,393 patients were included (Figure 1). Extraction of the arthroplasty cohort is summarised in Appendix 2. The mean age of the APM cohort was 49.65 years (standard deviation [SD] 15.04); 36.97% female (Table 1). Overall, 9.78% (53272/544582; 95% confidence interval [CI] 9.70-9.86) underwent knee arthroplasty within 5 years, 12.16% (34215/281291; 95% CI 12.04-12.28) within 10 years, and 13.49% (16256/120493; 95% CI 13.30-13.69) within 15 years (Table 1).

The risk of arthroplasty was greater in women (adjusted hazard ratio [HR] 1.42; 95% CI 1.40-1.43; Table 2, Figure 2A, Figure 2B). At 15 years, females were twice as likely to have undergone knee arthroplasty (risk ratio 2.01; 95% CI 1.95-2.06), with an absolute proportion of 22.07% (95% CI 21.64-22.51) in comparison to 9.91% (95% CI 9.71-10.12) in males. The rate of arthroplasty over time by age-group and sex is shown in Figure 2B.

Older patients (when undergoing APM) were more likely to undergo subsequent arthroplasty (adjusted HR 1.37 per five years; 95% CI 1.37-1.37; Table 2). For patients aged 60-79 years, 34.80% (7449/21408; 95% CI 34.16-35.44) underwent arthroplasty within 15 years (Table 1). Patients with a greater comorbidity index at the time of APM were also at increased risk of subsequently undergoing arthroplasty (adjusted HR 1.04 per five units Charlson index; 95% CI 1.03-1.05). The risk of knee arthroplasty increased over the period of the study (adjusted HR 1.12 per five years; 95% CI 1.11-1.13). Patients in regions of increased deprivation and patients of white ethnicity were at greater risk of subsequent arthroplasty (Table 2).

After undergoing a first APM, overall 6.84% (57,060/834,393; 95% CI 6.78-6.89) patients underwent a further APM at mean 1492 days (SD 1379). Of patients with at least 1-year of follow-up time, 1.40% underwent APM within 1 year (11,024/787,791; 95% CI 1.37-1.43). By age group, the 1-year repeat APM rates were 2.69% (587/21783; 95% CI 2.48-2.92) in the under 20 age group, 1.98% (3477/175,497; 95% CI 1.92-2.05) in the 20-39-year group, 1.42% (5310/374591; 95% CI 1.38-1.46) in the 40-59-year group, 0.78% (1613/206,230; 95% CI 0.74-0.82) in the 60-79-year group, and 0.38% (37/9690; 95% CI 0.27-0.53) in the 80-plus age group.

In 2016-17, the overall rate of knee arthroplasty was 1.81% (95% CI 1.78-1.84) in patients (aged 30 or older) with a recorded history of APM and approximately 0.17% (95% CI 0.17-0.17) in patients without a record of APM. This corresponded to an overall relative risk of knee arthroplasty for the APM cohort patients of 10.27 times (risk ratio [RR]; 95% CI 10.07-10.47) the general population. Although the absolute annual rate of knee arthroplasty was low, the relative risk of undergoing knee arthroplasty in a younger age

group was elevated more than older age groups, as shown in Table 3. Patients aged 30-39 with a history of a previous APM were 39.62 times (RR; 95% CI 27.68-56.70) more likely to undergo knee arthroplasty than the general population, in comparison to 6.44 times (RR; 95% CI 6.22-6.67) more likely for the over 69 age group.

Results comparing the index knee with the contralateral knee are shown in Figure 3. For patients with a history of APM in only one knee (the index knee) the risk of knee arthroplasty in that knee was significantly elevated in comparison to the contralateral knee (without a history of APM) as shown in Figure 3A. This difference corresponds to an adjusted hazard ratio of 2.99 (95% CI 2.95-3.02). Figure 3B shows the outcome in each knee in patients with a history of bilateral APM (either staged or simultaneous). For these patients, the risk of knee arthroplasty was greater in both knees in comparison to the unilateral APM patients. The greater risk of progressive osteoarthritis observed in the index knee in comparison to the contralateral knee (with or without a history of APM) was observed in both males and, to a greater extent, female patients, as shown in Figure 4.

DISCUSSION

Principal findings

This study has defined the long-term risk of undergoing knee arthroplasty in patients with a meniscal tear who had undergone APM. Overall, 13.5% of patients underwent knee arthroplasty within 15-years and women were twice as likely as men to progress to this end-stage outcome. The annual rate of arthroplasty was 1.81% for patients aged 30 years or greater with a history of APM, corresponding to a ten times greater relative risk of knee arthroplasty in comparison to the general population without a recorded history of APM. The risk of subsequent arthroplasty has increased over time and was greater in older patients, patients from deprived regions, and patients of white ethnicity. In patients with a history of APM in only one knee, the risk of knee arthroplasty was greatly elevated in comparison to the other knee without a history of APM.

Comparison with other studies

Previous studies investigating the overall relative risk of knee arthroplasty following meniscal damage are scarce. In one relatively small, high risk, cohort, patients with meniscal tears, undergoing APM, were found to be at three-times increased risk of knee arthroplasty.[12] The relative risk in our study was higher than this in all age groups, but lower than one recent case-control study utilising primary care data, where patients with meniscal 'injury' were found to have an overall fifteen times greater risk of knee arthroplasty.[13] Unlike our study, however, this case-control study may have over-estimated this outcome due to limitations from a failure to control for prior knee surgery, no record of surgical interventions performed, and knee 'laterality' was not known, precluding matching by knee side.[13]

In a recent systematic review of knee arthroplasty rates after knee 'arthroscopy', the absolute annual rate of arthroplasty varied from 1.99% overall to 4.13% in patients with more severe osteoarthritis.[6] The included studies were small and had relatively short periods of follow up, however these reported rates are similar to the findings in our study. The proportion of patients undergoing subsequent arthroplasty in our study was greater in older age groups (23.36% of patients aged 60-79 years) as may be expected from the higher rates of degenerative knee disease in this population.[22,23] Other studies have also reported higher rates of knee arthroplasty in older patients, at 20.1% within two years for patients aged over 65 in an Australian knee arthroscopy and 13.7% within three years for knee arthroscopy patients over the age of 50 years in the United States.[24,25]

Although the absolute risk of undergoing a knee arthroplasty at a young age was low, the relative risk was markedly elevated for patients with a history of APM in comparison to the general population. This finding confirms that meniscal injury may accelerate osteoarthritic progression, causing individuals to reach an endpoint of advanced, painful, osteoarthritis at a younger age than otherwise susceptible individuals in the general population. Indeed, it has previously been reported that isolated meniscal pathology is associated with an increased odds of radiographic osteoarthritis even within 2 years.[26] Our study utilised knee

arthroplasty as the primary outcome rather than a radiographic outcome which is subjective and may not be correlated with symptomatology.[8,9] One previous study utilising a radiographic outcome, however, reported that half of patients have evidence of osteoarthritis radiographically 10-20 years after meniscectomy.[27] This corresponded to a ten times greater odds in comparison to an age-sex matched group without a history of knee injury and was therefore very similar to the relative risk of knee arthroplasty we observed in our cohort.[27] Another interesting study of primary care data estimated an approximately six times increased consultation rate for 'knee osteoarthritis' in patients with a history of APM, in comparison to the general population.[28]

Previous studies have suggested a higher prevalence of osteoarthritis, including knee osteoarthritis, in women in comparison to men.[23,29] Despite this, there is evidence that, at a population level, women may be less likely to undergo arthroplasty.[29,30] Our findings are different and women in our cohort of patients were twice as likely as men to undergo arthroplasty within fifteen-years of APM for a meniscal tear. One possible reason for the higher rate of progressive osteoarthritis in women could have been pre-existent osteoarthritis at the time of APM, however our exclusion of patients undergoing previous knee surgery reduces this possibility and, furthermore, the sex difference in outcome was detected even after age-group matching and multi-variable adjustments. Our study does not determine the causative pathobiology that may underlie this observation, but hormonal influences are one proposed mechanism underlying observed differences in musculoskeletal pain and osteoarthritis in women and this should be a focus for further research.[31,32]

Other patient factors associated with an increased risk of knee arthroplasty in our study were regional deprivation, white ethnicity. Patients with a higher comorbidity score were also slightly more likely to undergo subsequent arthroplasty, as has previously been shown following ACL reconstruction.[33] The reasons for these observations are likely to be multi-factorial, related to differences in care seeking behaviour or differences in access to treatment.[34,35] Communication challenges and cultural differences may also play a role in access to healthcare.[36] It must be noted, however, that all patients in our cohort had already 'sought care', undergoing APM surgery at the point of inclusion, and therefore we caution that the observed differences in subsequent arthroplasty rates should not be solely attributed to differences in care seeking behaviour or access to healthcare.

Recently, the rate of adverse outcomes occurring within 90-days of APM has been reported in the same population as this study.[37] For patients with persistently symptomatic meniscal tears, considering undergoing APM, the findings from the present study complement these data and this information will be important to informed consent discussion and shared decision making between patients and clinicians. It was concerning to find the rate of arthroplasty following APM has risen slightly over time. With refined treatment guidelines, fewer patients may undergo APM in future and a greater proportion may be treated with meniscal preservation strategies.[38,39] Our study will enable comparison of outcomes from newly

implemented treatment strategies, including the use of meniscal repair and non-operative treatments, especially those aimed at improving outcomes in women and other high-risk patients.

Strengths and limitations

Despite the exclusions of all patients with a history of a prior knee surgery or simultaneous arthroscopic procedures including ligament reconstruction, this is the largest cohort of meniscal injury or APM patients that has been reported. This large sample size of prospectively recorded longitudinal data enhances the precision of our findings and ability to investigate the influence of patient-specific factors.

We were able to calculate the relative risk of knee arthroplasty in comparison to individuals in the general population without a history of APM. There are, however, some potential sources of unmeasured confounding such as body mass index, severity of pre-existing osteoarthritis, and any coexistent inflammatory arthropathy such as rheumatoid arthritis. We aimed to minimise the impact of these factors by the inclusion of Charlson comorbidity index and age-group in our analysis, and by using an objective criterion for inclusion (undergoing APM). The population prevalence of rheumatoid arthritis is estimated to be 0.5-1.0% and therefore the inclusion of patients with a diagnosis of rheumatoid arthritis in the cohort is unlikely to have materially altered the findings reported in this study.[40] Hospitals rely on procedure coding in HES for financial reimbursement, providing a strong incentive for coding accuracy.[14] The coding of arthroscopic and arthroplasty procedures has not been specifically validated but other validation studies are supportive.[41,42]

Our cohort of patients first sustained a meniscal tear and then underwent APM surgery, and the potential impact from both these events must be considered.[43–48] Comparing outcomes to the other knee in patients that had undergone unilateral APM versus bilateral APM we found that patients with history of APM in only one knee were three times more likely to undergo knee arthroplasty in that knee in comparison to the contralateral knee without a history of APM. This comparison attempted to control for an individual's innate risk of progressive osteoarthritis and the difference between the index knee and the contralateral knee was observed in both males and females. Patients with a history of bilateral APM were at greater risk of undergoing subsequent knee arthroplasty in both knees in comparison to unilateral APM patients. This interesting finding could be due to this population having a greater anatomical or biological predisposition to progressive osteoarthritis or meniscal injury in both knees.

Conclusion

Our findings confirm that patients with meniscal tears, undergoing APM, are a cohort at high-risk of progression to end-stage osteoarthritis and justify a need for careful surveillance of this population. Our study is the first to precisely inform patients and clinicians of the long-term outcomes following APM, but further study into the outcomes of non-operative treatment is still required. Women were found to be at

greater risk of progressive osteoarthritis than men, but the biological, hormonal, genetic, or healthcare provision factors that might underlie this observation are unknown. Comparison of the outcomes from emerging treatments aimed at reducing the risk of osteoarthritis must await further data but, informed by this study, these treatment strategies should be targeted especially to women and other high-risk groups.

REFERENCES

1 Bhattacharyya T, Gale D, Dewire P, *et al.* The Clinical Importance of Meniscal Tears Demonstrated by Magnetic Resonance Imaging in Osteoarthritis of the Knee. *J Bone Jt Surgery, Am Vol* 2003; **85**: 4–9.

2 Zanetti M, Pfirrmann CW a, Schmid MR, Romero J, Seifert B, Hodler J. Patients with Suspected Meniscal Tears : Prevalence of Abnormalities Seen. *Am J Radiol* 2003; **181**: 635–41.

3 Englund M, Guermazi A, Gale D, *et al.* Incidental meniscal findings on knee MRI in middle-aged and elderly persons. *N Engl J Med* 2008; **359**: 1108–15.

4 Englund M, Roemer FW, Hayashi D, Crema MD, Guermazi A. Meniscus pathology, osteoarthritis and the treatment controversy. *Nat Rev Rheumatol* 2012; **8**: 412–9.

5 Beaufils P, Becker R, Kopf S, Matthieu O, Pujol N. The knee meniscus: management of traumatic tears and degenerative lesions. *EFORT Open Rev* 2017; **2**: 195–203.

6 Winter AR, Collins JE, Katz JN. The likelihood of total knee arthroplasty following arthroscopic surgery for osteoarthritis: a systematic review. *BMC Musculoskelet Disord* 2017; **18**: 408.

7 Papalia R, Del Buono A, Osti L, Denaro V, Maffulli N. Meniscectomy as a risk factor for knee osteoarthritis: A systematic review. *Br Med Bull* 2011; **99**: 89–106.

8 Petty CA, Lubowitz JH. Does arthroscopic partial meniscectomy result in knee osteoarthritis? A systematic review with a minimum of 8 years' follow-up. *Arthrosc - J Arthrosc Relat Surg* 2011; **27**: 419–24.

9 Parry E, Ogollah R, Peat G. Significant pain variability in persons with, or at high risk of, knee osteoarthritis: preliminary investigation based on secondary analysis of cohort data. *BMC Musculoskelet Disord* 2017; **18**: 1–11.

10 Raynauld J-P, Martel-Pelletier J, Haraoui B, *et al.* Risk factors predictive of joint replacement in a 2-year multicentre clinical trial in knee osteoarthritis using MRI: results from over 6 years of observation. *Ann Rheum Dis* 2011; **70**: 1382–8.

11 Bruyere O, Pavelka K, Rovati LC, *et al.* Total joint replacement after glucosamine sulphate treatment in knee osteoarthritis: results of a mean 8-year observation of patients from two previous 3-year, randomised, placebo-controlled trials. *Osteoarthr Cartil* 2008; **16**: 254–60.

12 Rongen JJ, Rovers MM, van Tienen TG, *et al.* Increased risk for knee replacement surgery after arthroscopic surgery for degenerative meniscal tears: a multi-center longitudinal observational study using data from the osteoarthritis initiative. *Osteoarthr Cartil* 2017; **25**: 23–9.

13 Khan T, Alvand A, Prieto-Alhambra D, *et al.* ACL and meniscal injuries increase the risk of primary total knee replacement for osteoarthritis: a matched case-control study using the Clinical Practice Research Datalink (CPRD). *Br J Sports Med* 2018; : bjsports-2017-097762.

14 NHS Digital. Hospital Episode Statistics. http://content.digital.nhs.uk/hes (accessed Dec 4, 2017).

15 Population estimates - Office for National Statistics.

https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates (accessed June 26, 2018).

16 NHS Digital. National clinical coding standards: OPCS-4 (2017). Stationery Office, 2017.

17 NHS Digital. Hospital Episode Statistics (HES) Analysis Guide. 2015. http://content.digital.nhs.uk/media/1592/HES-analysis-guide/pdf/HES_Analysis_Guide_March_2015.pdf (accessed Dec 4, 2017).

18 HSCIC. Summary Hospital-level Mortality Indicator (SHMI). Indicator Specification. Version 1.25. 2017 https://www.digital.nhs.uk/SHMI.

19 Charlson ME, Pompei P, Ales KL, MacKenzie R. A new method of classifying prognostic in longitudinal studies: development and validation. J. Chronic Dis. 1987; **40**: 373–83.

20 Zhang JX, Iwashyna TJ, Christakis NA. The performance of different lookback periods and sources of information for Charlson comorbidity adjustment in Medicare claims. *Med Care* 1999; **37**: 1128–39.

21 Noble M, Wright} G, Smith G, Dibben} C. Measuring multiple deprivation at the small-area level. *Environ Plan A* 2006; **38**: 169–85.

22 Loeser RF. Age-Related Changes in the Musculoskeletal System and the Development of Osteoarthritis. *Clin Geriatr Med* 2010; **26**: 371–86.

23 Arden N, Nevitt MC. Osteoarthritis: Epidemiology. *Best Pract Res Clin Rheumatol* 2006; **20**: 3–25.

24 Harris IA, Madan NS, Naylor JM, Chong S, Mittal R, Jalaludin BB. Trends in knee arthroscopy and subsequent arthroplasty in an Australian population: a retrospective cohort study. *BMC Musculoskelet Disord* 2013; **14**: 1–6.

25 Boyd JA, Gradisar IM. Total Knee Arthroplasty After Knee Arthroscopy in Patients Older Than 50 Years. *Orthopedics* 2016; **39**: 1–4.

26 Roemer FW, Kent Kwoh C, Hannon MJ, *et al.* What comes first? multitissue involvement leading to radiographic osteoarthritis: Magnetic resonance imaging-based trajectory analysis over four years in the osteoarthritis initiative. *Arthritis Rheumatol* 2015; **67**: 2085–96.

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

28 Persson F, Turkiewicz A, Bergkvist D, Neuman P, Englund M. The risk of symptomatic knee osteoarthritis after arthroscopic meniscus repair vs partial meniscectomy vs the general population. *Osteoarthr Cartil* 2018; **26**: 195–201.

29 Hawker GA, Wright JG, Coyte PC, *et al.* Differences between Men and Women in the Rate of Use of Hip and Knee Arthroplasty. *N Engl J Med* 2000; **342**: 1016–22.

30 Borkhoff CM, Hawker GA, Kreder HJ, Glazier RH, Mahomed NN, Wright JG. The effect of patients' sex on physicians' recommendations for total knee arthroplasty. *Cmaj* 2008; **178**: 681–7.

31 Dugan SA, Powell LH, Kravitz HM, Everson Rose SA, Karavolos K, Luborsky J. Musculoskeletal Pain and Menopausal Status. *Clin J Pain* 2006; **22**: 325–31.

32 Watt FE. Musculoskeletal pain and menopause. *Post Reprod Heal* 2018; **24**: 34–43.

33 Leroux T, Ogilvie-Harris D, Dwyer T, *et al.* The risk of knee arthroplasty following cruciate ligament reconstruction : A population-based matched cohort study. *J Bone Jt Surg - Ser A* 2014; **96**: 2–10.

34 Adamson J, Ben-Shlomo Y, Chaturvedi N, Donovan J. Ethnicity, socio-economic position and gender - Do they affect reported health-care seeking behaviour? *Soc Sci Med* 2003; **57**: 895–904.

35 Chaturvedi N, Rai H, Ben-Shlomo Y. Lay diagnosis and health-care-seeking behaviour for chest pain in south Asians and Europeans. *Lancet* 1997; **350**: 1578–83.

36 FitzGerald C, Hurst S. Implicit bias in healthcare professionals: a systematic review. *BMC Med Ethics* 2017; **18**: 19.

37 Abram SGF, Judge A, Beard DJ, Price AJ. Adverse outcomes after arthroscopic partial meniscectomy: a study of 700 000 procedures in the national Hospital Episode Statistics database for England. *Lancet* 2018; **392**: 2194–202.

38 Lubowitz JH, Poehling GG. Save the meniscus. *Arthrosc - J Arthrosc Relat Surg* 2011; **27**: 301–2.

39 Beaufils P, Pujol N. Management of traumatic meniscal tear and degenerative meniscal lesions. Save the meniscus. *Orthop Traumatol Surg Res* 2017; **103**: S237–44.

40 Silman AJ, Pearson JE. Epidemiology and genetics of rheumatoid arthritis. *Arthritis Res* 2002; **4 Suppl 3**: S265-72.

41 Crooks CJ, West J, Card TR. A comparison of the recording of comorbidity in primary and secondary care by using the Charlson Index to predict short-term and long-term survival in a routine linked data cohort. *BMJ Open* 2015; **5**: 1–9.

42 Wright FL, Green J, Canoy D, Cairns BJ, Balkwill A, Beral V. Vascular disease in women: comparison of diagnoses in hospital episode statistics and general practice records in England. *BMC Med Res Methodol* 2012; **12**: 161.

43 Buchbinder R. Meniscectomy in Patients with Knee Osteoarthritis and a Meniscal Tear? *N Engl J Med* 2013; **368**: 1741–3.

44 Katz JN, Losina E. Arthroscopic partial meniscectomy for degenerative tears: Where do we stand? *Osteoarthr Cartil* 2014; **22**: 1749–51.

45 Thorlund JB, Juhl CB, Roos EM, Lohmander LS. Arthroscopic surgery for degenerative knee: systematic review and meta-analysis of benefits and harms. *Bmj* 2015; **350**: h2747–h2747.

46 Beaufils P, Becker R, Kopf S, *et al.* Surgical management of degenerative meniscus lesions: the 2016 ESSKA meniscus consensus. *Knee Surgery, Sport Traumatol Arthrosc* 2017; **25**: 335–46.

47 Abram SGF, Judge A, Beard DJ, Wilson HA, Price AJ. Temporal trends and regional variation in the rate of arthroscopic knee surgery in England: analysis of over 1.7 million procedures between 1997 and 2017. Has practice changed in response to new evidence? *Br J Sports Med* 2018; : bjsports-2018-099414.

48 Bennell KL, Katz JN. Potential harms of isolated arthroscopic partial meniscectomy. *Lancet* 2018; **6736**: 9–10.

TABLES

TABLE 1:

Demographics and proportion of patients with at least 5, 10, and 15 years follow-up undergoing subsequent TKA in the period

	All index procedures		5-year outcome			10-year outcome			15-year outcome		
	n	**%**	**n**	**n TKA**	**% (95% CI)**	**n**	**n TKA**	**% (95% CI)**	**n**	**n TKA**	**% (95% CI)**
Total	834393	100.00	544,582	53272	9.78% (9.70, 9.86)	281,291	34215	12.16% (12.04, 12.28)	120,493	16256	13.49% (13.30, 13.69)
Sex											
Male	525877	63.03	349,854	23568	6.74% (6.65, 6.82)	189,731	16226	8.55% (8.43, 8.68)	85,048	8432	9.91% (9.71, 10.12)
Female	308516	36.97	194,728	29704	15.25% (15.09, 15.41)	91,560	17989	19.65% (19.39, 19.91)	35,445	7824	22.07% (21.64, 22.51)
Age group (years)											
< 20	22879	2.74	-	-	-	-	-	-	-	-	-
20 - 39	183585	22.00	137,852	361	0.26% (0.24, 0.29)	87,414	588	0.67% (0.62, 0.73)	44,719	666	1.49% (1.38, 1.61)
40 - 59	398883	47.81	259,726	18349	7.06% (6.97, 7.16)	130,109	14152	10.88% (10.71, 11.05)	53,323	7860	14.74% (14.44, 15.04)
60 - 79	218878	26.23	140,008	32702	23.36% (23.14, 23.58)	60,536	18567	30.67% (30.30, 31.04)	21,408	7449	34.80% (34.16, 35.44)
80 +	10168	1.22	6,996	1860	26.59% (25.55, 27.64)	3,232	908	28.09% (26.55, 29.68)	1,043	281	26.94% (24.27, 29.74)
Charlson comorbidity index											
0	692111	82.95	468,095	39989	8.54% (8.46, 8.62)	254,369	28371	11.15% (11.03, 11.28)	112,851	14522	12.87% (12.67, 13.07)
1 - 15	136544	16.36	73,652	12614	17.13% (16.86, 17.40)	26,042	5626	21.60% (21.11, 22.11)	7,449	1688	22.66% (21.71, 23.63)
16 - 30	5354	0.64	2,677	635	23.72% (22.12, 25.38)	834	207	24.82% (21.92, 27.90)	193	46	23.83% (18.01, 30.48)
31 - 50	384	0.05	158	34	21.52% (15.39, 28.75)	46	11	23.91% (12.59, 38.77)	-	-	-
Index of multiple deprivation (quintiles)											
1 = least deprived	186631	22.37	123,658	12118	9.80% (9.63, 9.97)	64,509	8001	12.40% (12.15, 12.66)	27,054	3805	14.06% (13.65, 14.48)
2	182705	21.90	120,060	12205	10.17% (10.00, 10.34)	62,701	8141	12.98% (12.72, 13.25)	26,509	3797	14.32% (13.90, 14.75)
3	174721	20.94	115,137	11641	10.11% (9.94, 10.29)	59,596	7491	12.57% (12.30, 12.84)	25,420	3565	14.02% (13.60, 14.46)
4	152008	18.22	98,454	9400	9.55% (9.36, 9.73)	50,609	5960	11.78% (11.50, 12.06)	22,227	2882	12.97% (12.53, 13.41)
5 = most deprived	129817	15.56	82,092	7459	9.09% (8.89, 9.28)	41,618	4437	10.66% (10.37, 10.96)	18,420	2156	11.70% (11.24, 12.18)
Missing	8511	1.02									
Rurality											
Urban	637911	76.45	414,851	39885	9.61% (9.52, 9.70)	215,014	25567	11.89% (11.75, 12.03)	92,915	12118	13.04% (12.83, 13.26)
Rural	192136	23.03	127,627	13271	10.40% (10.23, 10.57)	65,297	8611	13.19% (12.93, 13.45)	27,046	4117	15.22% (14.80, 15.66)
Missing	4346	0.52									
Ethnicity											
White	735248	88.12	482,429	51048	10.58% (10.49, 10.67)	246,714	32876	13.33% (13.19, 13.46)	103,915	15692	15.10% (14.88, 15.32)
Asian	22557	2.70	12,633	1076	8.52% (8.04, 9.02)	5,165	598	11.58% (10.72, 12.48)	1,722	231	13.41% (11.84, 15.12)
Black	12136	1.45	6,861	300	4.37% (3.90, 4.88)	2,805	193	6.88% (5.97, 7.88)	1,083	88	8.13% (6.57, 9.92)
Mixed	4752	0.57	2,598	144	5.54% (4.69, 6.49)	1,017	93	9.14% (7.44, 11.09)	291	33	11.34% (7.94, 15.56)
Other	5404	0.65	3,136	84	2.68% (2.14, 3.31)	1,495	39	2.61% (1.86, 3.55)	755	19	2.52% (1.52, 3.90)
Missing	54296	6.51									

- = suppressed due to small numbers; CI = confidence interval; TKA = total or partial knee arthroplasty; APM = arthroscopic partial meniscectomy

TABLE 2:

Hazard ratios (subsequent TKA within maximum of 20 years) of APM

	Unadjusted Risk Subsequent TKA		Adjusted Risk Subsequent TKA	
	HR	**95% CI**	**HR**	**95% CI**
Sex				
Male	1.00	1.00	1.00	1.00
Female	2.21	2.18, 2.24	1.42	1.40, 1.43
Age (years; per five years) ‡				
Age	1.41	1.41, 1.41	1.37	1.37, 1.37
Year of treatment (APM; per five years)				
Year	1.28	1.27, 1.29	1.12	1.11, 1.13
Charlson comorbidity index (per five units)				
Charlson index	1.41	1.40, 1.42	1.04	1.03, 1.05
Index of multiple deprivation (quintile)				
1 = least	1.00	1.00	1.00	1.00
2	1.04	1.02, 1.06	1.07	1.05, 1.09
3	1.02	1.00, 1.04	1.11	1.09, 1.13
4	0.96	0.94, 0.98	1.15	1.13, 1.18
5 = most	0.91	0.89, 0.93	1.20	1.18, 1.23
Rurality				
Urban	1.00	1.00	1.00	1.00
Rural	1.11	1.09, 1.13	1.01	1.00, 1.03
Ethnicity				
White	1.00	1.00	1.00	1.00
Asian	0.78	0.75, 0.81	0.94	0.90, 0.99
Black	0.41	0.38, 0.45	0.54	0.50, 0.58
Mixed	0.55	0.49, 0.62	0.77	0.69, 0.86
Other	0.23	0.20, 0.27	0.37	0.32, 0.43

HR = hazard ratio; CI = confidence interval; TKA = total or partial knee arthroplasty; - suppressed due to small numbers

**adjusted by all variables in the table; ‡ age <20 years suppressed due to small numbers*

TABLE 3:

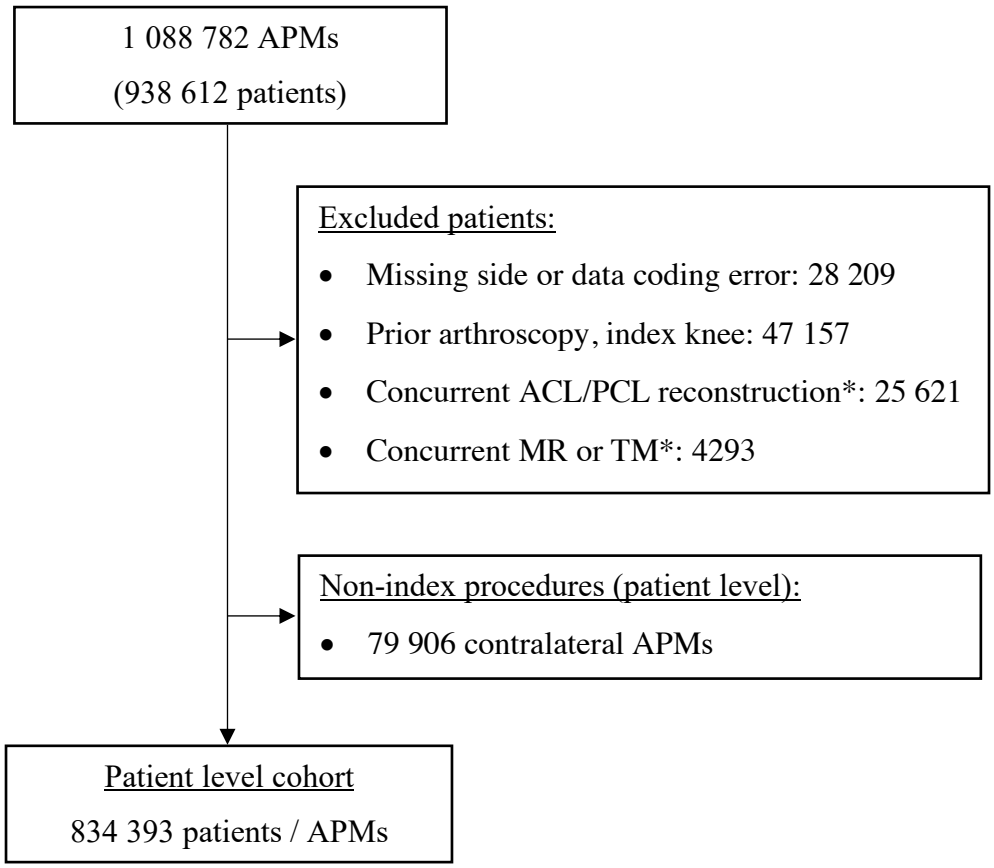
Rates and relative risk of undergoing TKA with previous APM (within prior 20 years) by age at TKA in 2016-17

	Prior APM		**Without Prior APM**		**Relative Risk**	
Age at TKA (years)	**Annual Rate TKA /100k**	**95% CI**	**Annual Rate TKA /100k**	**95% CI**	**RR**	**95% CI**
30 - 39	59.69 (0.06%)	42.84, 80.96 (0.04%, 0.08%)	1.51 (0.00%)	1.24, 1.81 (0.00%, 0.00%)	39.62	27.68, 56.70
40 - 49	490.48 (0.49%)	454.28, 528.79 (0.45%, 0.53%)	16.24 (0.02%)	15.33, 17.18 (0.02%, 0.02%)	30.07	27.37, 33.03
50 - 59	1725.09 (1.73%)	1667.14, 1784.51 (1.67%, 1.78%)	105.70 (0.11%)	103.34, 108.11 (0.10%, 0.11%)	16.06	15.42, 16.73
60 - 69	2859.27 (2.86%)	2778.80, 2941.42 (2.78%, 2.94%)	333.79 (0.33%)	329.11, 338.52 (0.33%, 0.34%)	8.36	8.10, 8.62
70 +	3190.51 (3.19%)	3085.56, 3298.02 (3.09%, 3.30%)	482.41 (0.48%)	477.05, 487.82 (0.48%, 0.49%)	6.44	6.22, 6.67
Overall (30 +)	1808.22 (1.81%)	1776.35, 1840.50 (1.78%, 1.84%)	173.21 (0.17%)	171.81, 174.61 (0.17%, 0.17%)	10.27	10.07, 10.47

TKA = total or partial knee arthroplasty; APM = arthroscopic partial meniscectomy; CI = confidence interval; RR = risk ratio.

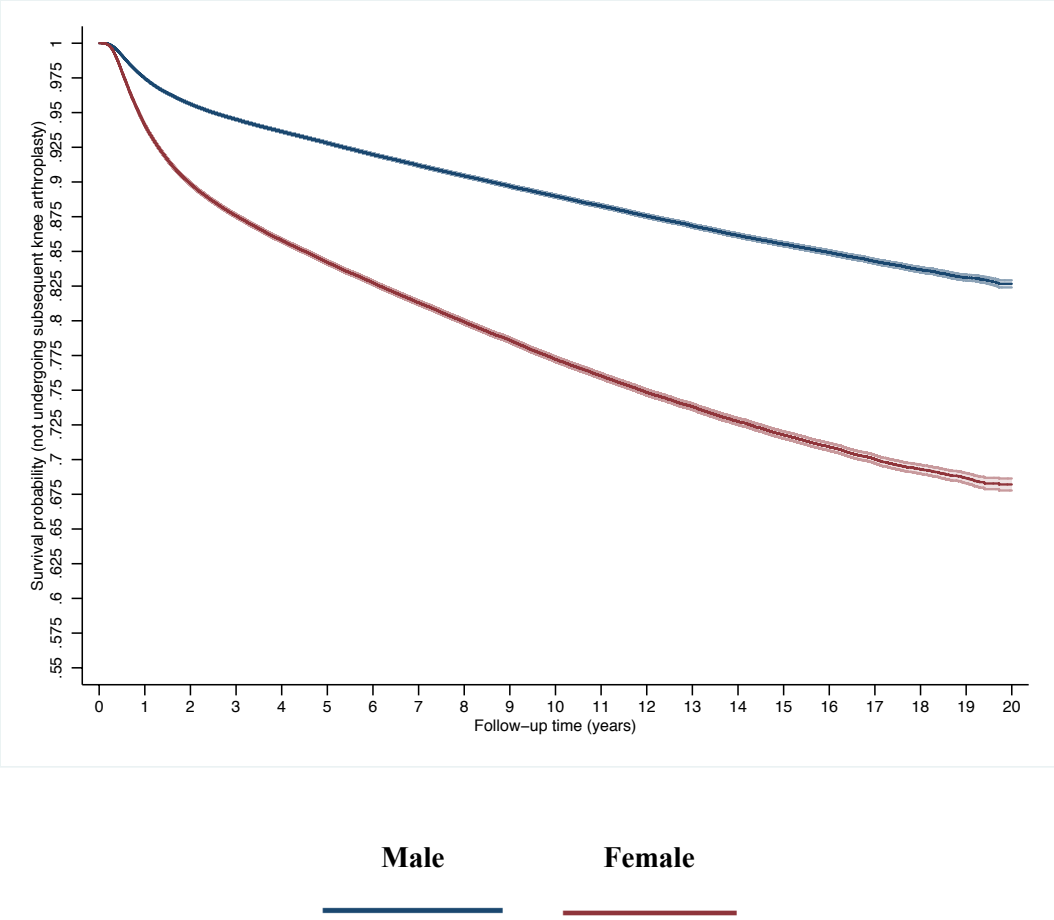
FIGURES

FIGURE 1: Flow chart illustrating extraction of patient level cohort



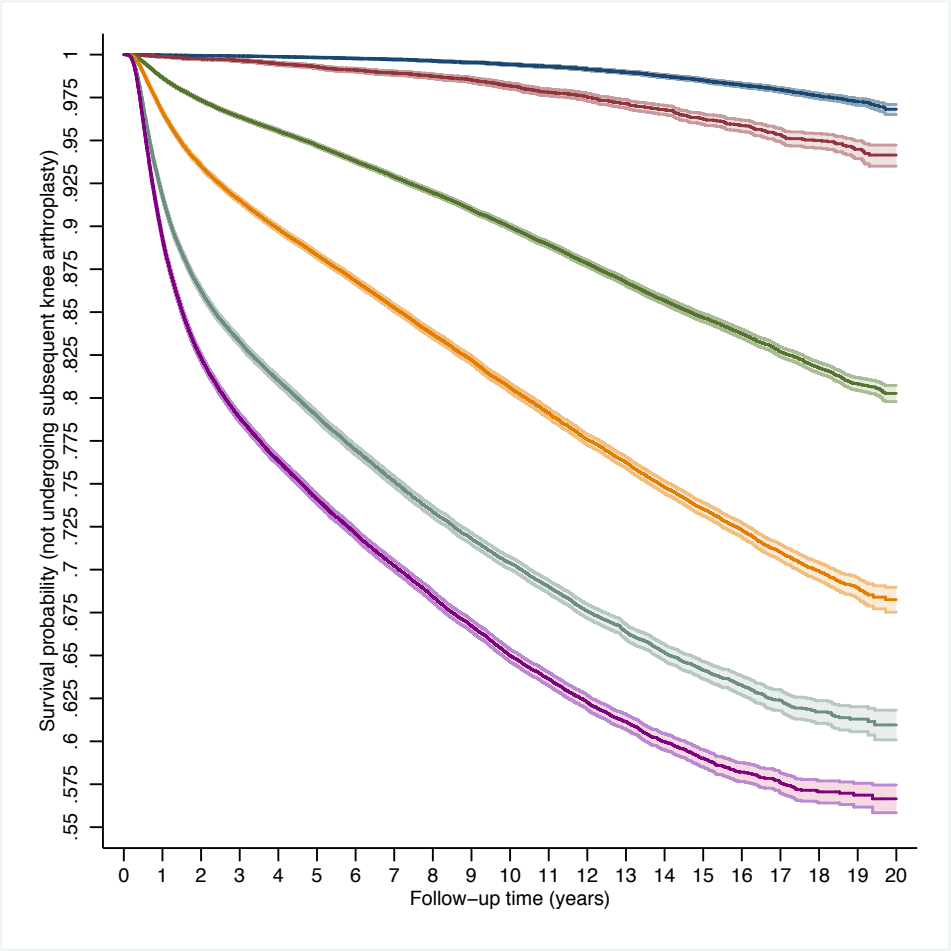
** not mutually exclusive; ACL = anterior cruciate ligament; PCL = posterior cruciate ligament; MR = meniscal repair; TM = total meniscectomy.*

FIGURE 2A: Survival curve (knee not undergoing subsequent knee arthroplasty after APM) by sex *



** Age group < 20 years suppressed due to small numbers*

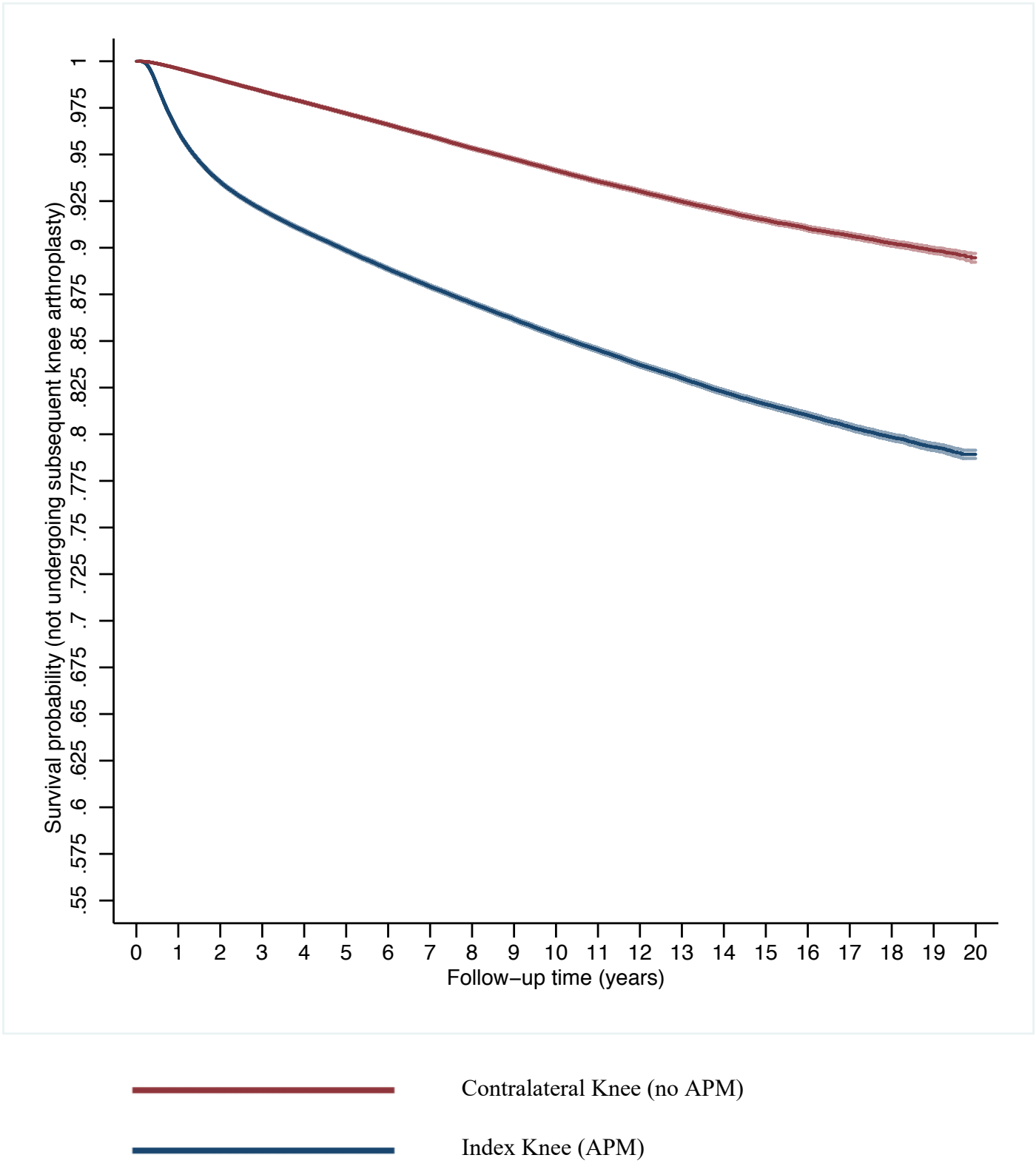
FIGURE 2B: Survival curve (knee not undergoing subsequent knee arthroplasty after APM) by age and sex *



Age group	Male	Female
20-39 years		
40-59 years		
60-79 years		

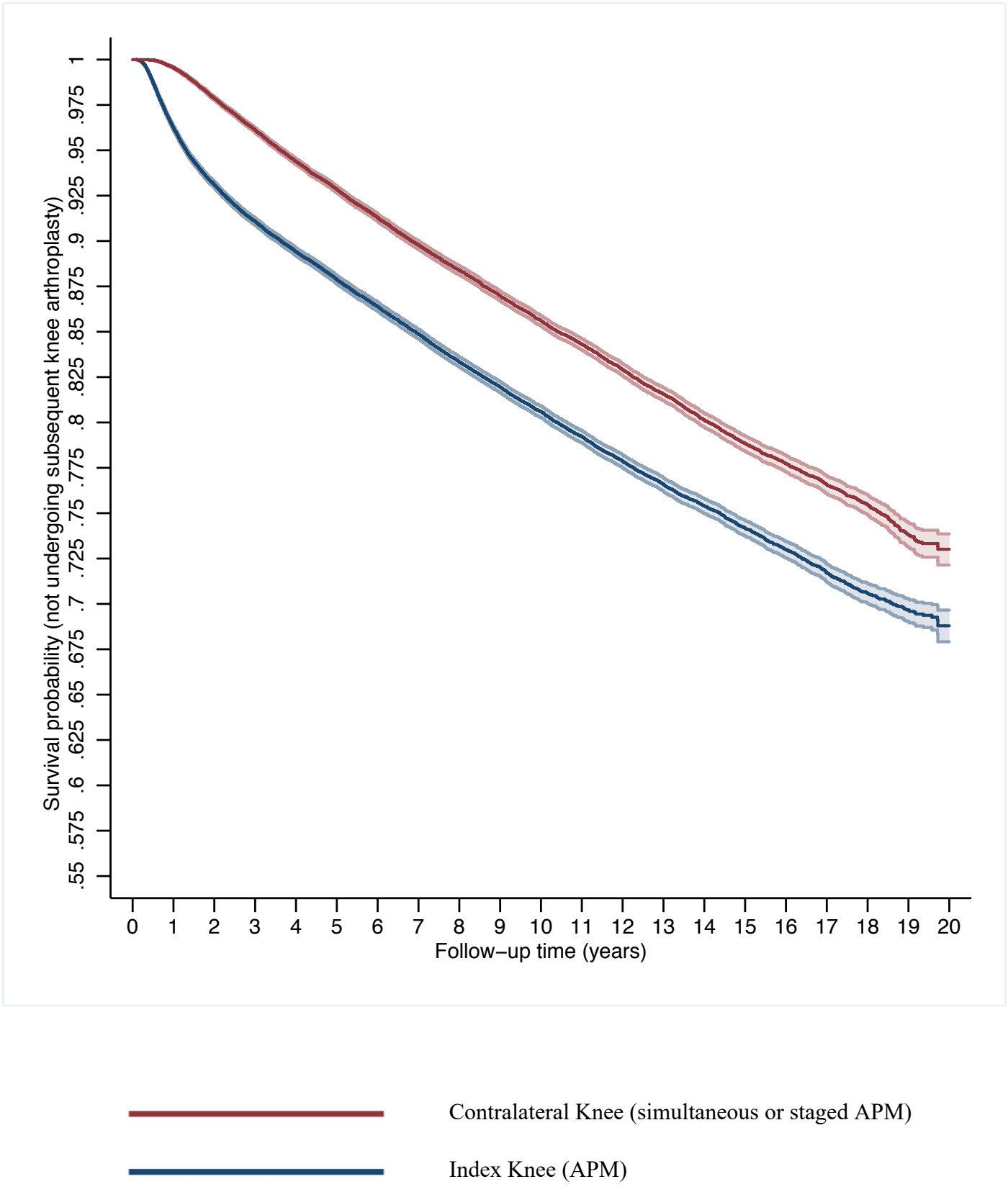
** Age group < 20 years and 80+ suppressed due to small numbers*

FIGURE 3A: Rate of subsequent arthroplasty in patients undergoing unilateral APM: Index knee versus contralateral knee (no APM) *



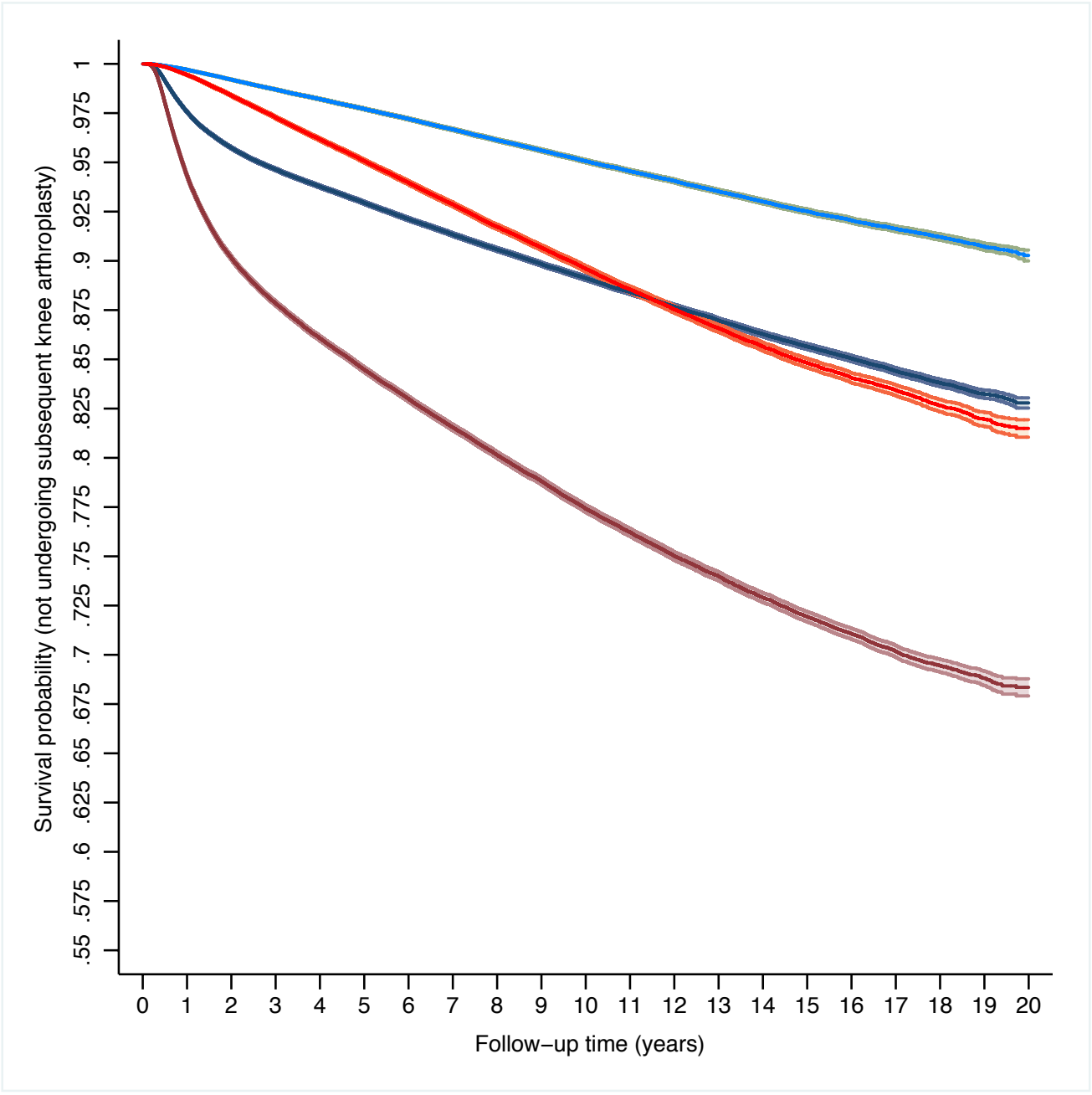
** Age group < 20 years and 80+ suppressed due to small numbers*

FIGURE 3B: Rate of subsequent arthroplasty in patients undergoing bilateral APM: Index knee versus contralateral knee (simultaneous or staged APM) *



** Age group < 20 years and 80+ suppressed due to small numbers*

FIGURE 4: Rate of subsequent arthroplasty for index knee (APM) versus contralateral knee (with or without APM) for male versus female patients *



** Age group < 20 years due to small numbers.*