Quantifying effect of age on the risk of revision following hip and knee replacement using life-time risk estimates: an analysis of 117,438 total joint replacements from the UK Clinical Practice Research Datalink

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Abstract

Background

Total Joint replacements for end stage osteoarthritis of the hip (THR) and knee (TKR) have been proven to be both cost-effective and to demonstrate significant clinical improvement. However, robust population based lifetime-risk data for implant revision is not available to aid patient decision-making, a particular problem in young patient groups deciding on best-timing of surgery.

Methods

Implant survival analysis was carried out on all patients within the Clinical Practice Research datalink (CPRD) that had undergone THR or TKR. This data was adjusted for all-cause mortality with data from the Office for National Statistics (ONS) and used to generate lifetime risks of revision surgery based on increasing age at the time of primary surgery.

Findings

63158 THR and 54276 TKR were followed up to a maximum of 20 years. 10 and 20-year implant survival rates for THR were 95.6% (95% CI: 95.3-95.9) & 85.0% (95% CI: 83.2-86.6), and for TKR were 96.1% (95% CI: 95.8-96.4) & 89.7% (95% CI: 87.5-91.5) respectively. The lifetime-risk of requiring revision (LTRR) surgery following THR and TKR is approximately 5% for patients over the age of 70, with no difference between sexes. For patients under 70, however, the lifetime risk of revision increases for younger patients, up to 35% (95% CI: 30.9, 39.1) for men in their early fifties, with large differences seen between male and female patients (15% lower for females in same age group). The median time to revision for patients under the age of 60 is 4.4 years.

Interpretation

The study uses novel methodology to investigate and offer new insight into the importance of young age and risk of revision following total hip or knee replacement. Up to 1 in 3 patients under 60 will require revision, 50% of these revisions occur within five years of primary surgery (median 4.4). In contrast in patients over the age of 70 the likelihood of revision surgery after primary knee

or hip replacement is low; 98% of patients that died during the study period, did so with their primary implant in situ. This evidence challenges the increasing trend for more THR & TKRs to be performed in the younger patient group and this data must be offered to patients as part of the shared decision making process.

Introduction

Hip and knee replacements have been routinely performed for the treatment of end-stage arthritis over the last 40 years [1,2]; 76,000 THRs and 82,000 TKRs were carried out in 2014 in the UK alone[3] with the greatest increase in the number of TKRs over recent years. The outcomes of joint replacement are determined in a number of different ways: mortality[4,5] and morbidity rates following surgery, functional outcome and satisfaction recorded as Patient Reported Outcome Scores (PROMs) [6], and by rates of failure of the implant leading to revision surgery [3,7]. In general THR & TKR have demonstrated improved function[8], reduced pain and improved quality of life[9] for patients and are cost-effective[9]. It is predicted that in the next ten to twenty years primary joint replacement rates will substantially increase not only as a consequence of an increasingly elderly population, but also due to increasing use in younger patients (under the age of 60)[10], who currently represent 15% of the entire population undergoing surgery, but may grow to a greater percentage of the population in the future[11].

This increase in the number of patients under 60 years undergoing surgery is a concern as Joint Registries reveal that 10-year revision rates in this group are higher [3]. For all patients the decision to have surgery is largely based on the balance between potential risk and benefit. The James Lind Alliance Priority Setting Partnership, a public-patient involvement group, has determined that the relationship between timing of joint replacement and best outcome is one of the most significant concerns for patients with osteoarthritis (OA). This is of particular importance in determining optimum timing for surgery in younger patients, where they can be expected to potentially outlive their primary replacement. Therefore the length of time a joint replacement will last (before requiring revision) becomes a major factor in deciding whether to proceed with surgery. The mostly widely used and quoted data regarding the risk of revision come from Joint Registry reports, but are often limited to 10 years of follow-up[3,7,12]. Other studies with longer patient follow-up (over 20 years) are frequently restricted to specific prostheses or small populations, without specific focus on the results from patients under 60 years of age at

implantation[13,14]. Therefore, for the younger patients, information regarding implant revision rates tends to be restricted to 10-years, and although worse than those seen for patients over 60,[3,9,15] may not truly reflect the risk of revision over the longer time frame. In this way the decision making process for younger patients is not fully informed and could potentially lead to inappropriate selection to undergo joint replacement, an issue that has been highlighted by previous authors [15] [16].

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Therefore, there is a clear for need for more representative long-term data that could be used to inform patients, across the age spectrum, of the risk of revision surgery. One approach that has not previously been used comes from combining data from the Clinical Practice Research Datalink, a database that contains long-term data regarding joint replacement that spans over 20 years, and adopting different methods of analysis that are new to this field. The concept of lifetime risk describes the probability (expressed as a percentage) of an event or disease occurring over the course of a lifetime; it was developed for analysis of survival and recurrence rates in oncology research. It has been used infrequently in musculoskeletal literature[17-19] and has never been used to assess the life-time risk of revision surgery following joint replacement. Lifetime risk data is useful to patients, clinicians and healthcare planners alike as it provides a simple concept to convey to patients and is easier to understand than time-dependent incidence rates (such as ten year risk of revision)[20], which are commonplace both in the explanation of revision risks to patients undergoing primary joint replacement and in the evaluation of prosthesis longevity[3].

The aim of this study was to determine age adjusted estimates of lifetime risk of undergoing a revision procedure following primary Total Hip Replacement or Total Knee Replacement using data from the Clinical Practice Research Datalink and Office for National Statistics.

Methods

Data Sources

Participant data was obtained from the CPRD formerly known as the GPRD (General Practice Research Database). The CPRD comprises the computerised primary care medical records of all patients attending a selection of general practitioners (GPs) in the UK. This population of 6.5 million patients is taken from 433 contributing practices chosen to be representative of the wider UK population[21], thus the CPRD comprises entire general practice populations rather than probability-based samples of patients.

Each patient is registered at one practice, which stores both primary care and hospital episode information. The universal healthcare system in the UK is dependent on primary care for the referrals and funding of hospital episodes, consequently the CPRD is a detailed record of both primary and secondary care. The CPRD dataset for each patient contains all clinical and referral events in both primary and secondary care in addition to comprehensive demographic information, prescription and hospital admissions data. Data is stored using Read and OXMIS codes for diseases that are cross-referenced to the International Classification of Diseases (ICD-9). Read codes are used as the standard clinical terminology system within UK primary care. Only practices that pass quality control are used as part of the CPRD database. Deleting or encoding personal and clinic identifiers ensures confidentiality of information. The CPRD is administered by the Medicines and Healthcare Products Regulatory Agency (MHRA).

Population

All patients in the database with a diagnostic code for primary total hip or knee replacement from 1991 until the end of 2011 were identified. Read/OXMIS codes were used to identify primary THRs and TKRs and subsequent revision surgeries [codes in supplementary information].

Patients were included in the analysis if aged 50 years or over at the time of index primary joint replacement procedure. Participant demographics including age and sex were collated.

Sex-specific all-cause mortality data was obtained from the ONS[22] for the time period 1991-2011.

Analysis

Data from the CPRD was aggregated into single year intervals by age at the time of index procedure (primary joint replacement) and then subdivided into hip & knee replacement and by sex. Age was defined as age at last birthday, starting at age 50; consistent definitions were applied to the death data and timing of any surgery. Person-time incidence rates for revision surgery were calculated by dividing the count of revision THRs and TKRs by the cumulative time with primary implant.

All-cause-mortality rates taken from the ONS data were applied to this population to generate the number of implant-years for each interval i.e. the period of exposure to potential revision surgery (e.g. 100 patients with 1.0% mortality would generate 99 implant-years for the first year interval). All-cause mortality and annual incidence rates were applied as multiple decrements at 1-year intervals. The total number of counts for predicted revisions was summed and divided by the population to produce an estimate of lifetime risk for patients undergoing surgery between the ages of 50 and 100 (in 5 year age bands for ages 50-54 through to 85 & older).

Revision incidence rates were also applied to the censored (i.e. implant in situ at the end of the study period) and lost-to-follow-up populations to generate an adjusted revision-incidence (Lost & Censored Population (LCP)) which was also then adjusted for ONS mortality rates in the same fashion.

Lifetime risk of revision surgery was calculated by grouping the one-year intervals into 5-year age-bands[23]. An actuarial life-table method was applied, as previously described, to a hypothetical population of the same magnitude as the sub-group under investigation.

Count data for incidence of revision surgery was assumed to be a count-random variable and as such a Poisson distribution was used to calculate Confidence Intervals set at the 95% level[17].

Smoothed Hazard plots showing instantaneous risk of revision (risk of revision following a given period of implant survival) were generated for both sexes.

All statistical analyses were performed in Stata (Statacorp. 2014; Stata Statistical Software: Release Version IC 13.1. College Station, Texas, USA) & Microsoft Excel 2011 (Microsoft Corporation, Redmond, WA).

Role of the funding source

Results

117,438 patients were identified from the database as having undergone a THR (N=63,158) or TKR (N=54,276) during the study period (flowchart 1). The mean age of patients undergoing joint replacement was 69.4 (SD 11.1) for THR and 70.1 (SD 9.6) for TKR; 15% of patients were aged 50-60 in both THR and TKR and similarly 15% were older than 79 in both. The number of women undergoing surgery was greater for both THR and TKR (Table 1). Mean THR follow-up was 5.8 years (range 0, 23.1; median 4.9), and for TKR was 5.2 years (range; 0, 22.5; median 4.5).

Ten and twenty-year implant survival rates were 95.6% (95% CI: 95.3-95.9) & 85% (95% CI: 83.2-86.6) for THR (Table 2) and 96.1% (95% CI: 95.8-96.4) & 89.7% (95% CI: 87.5-91.5) for TKR (Table 3) respectively. In both THR and TKR, implant survival over time was higher for female patients and older patients (Graphs 1 & 2, survival curves included in supplementary information), with the lowest survival rates seen in patients in their 50s at the time of index surgery.

The estimated lifetime risk of revision (LTRR) increased with deceasing age at the time of primary surgery for both hip and knee replacements (Graphs 1&2). For patients at 70 years of age (mean age of implantation) the LTRR was between 4.4% and 7.7% (higher in males and THR patients). Above this age the LTRR reduced with time for both THR and TKR, consistent between sexes. For patients between 60 and 70 years at the time of primary surgery the LTRR increases with decreasing age reaching approximately 15% for both THR and TKR at 60 years, with greater risk in male compared to female patients. For female patients between the ages of 50 and 60 at primary surgery the LTRR does not change a great deal for THR and increases by a few percentage points for TKR. However, a significant increase in LTRR is seen in younger male patients, with values of 29.6% (95% CI 26.6-32.6) for THR and 35% (95% CI 30.9-39.1) for TKR seen for the youngest patient group (50-54 years).

14% of the study population died during the study period, with a mean age of 75.3 (SD 7.9) at time of surgery and a mean age of 80.8 (SD 8.11) at death. Of these patients 98% died with their primary implant still in situ.

The timing of revision surgery shows a peak incidence within 5 years of primary implantation in all age ranges, with a mean time to revision surgery of 6.56 years (95% CI 6.05-7.08) in THR and 4.55 (95% CI 4.07-5.02) in TKR for patients in their sixth decade and 4.08 (95% CI 3.73, 4.39) for THR and 3.57 (95% CI 3.26, 3.88) for TKR in their eighth decade. The smoothed Hazard plots in Graphs 3 & 4 show consistently higher revision risks for male and younger patients at all time points. Importantly these graphs also show that the trends of timing to revision surgery are similar across all age bands, with the exception of the most elderly patient groups where follow-up is limited by life expectancy.

The mean annual rate of patients lost to follow-up (excluding censored patients) is 2.2% for THR (95% CI: 2.0-2.4) and 1.8% for TKR (95% CI 1.7-2.0). Adjusting for these lost and censored patients increased the estimate of LTRR similarly in each age group.

The lost and censored sub-populations were analysed at a number of time points and found to consistently be of the same demographics as the remaining population for that time-period.

Discussion

Our results demonstrate that for the 15% of patients who are below the age of 60 at primary surgery, their lifetime risk of revision increases significantly reaching levels of up to 1 in 3 in those patients aged between 50 and 55. These figures are in contrast to older patients where our data shows that for patients undergoing hip or knee arthroplasty at or over the age of 70, the lifetime risk of requiring revision surgery lies between 1-6%; this estimate applies to approximately half the patients undergoing this type of surgery. In addition the time to revision surgery reaches a peak incidence at approximately 5-years following implantation, with over half the total number of revisions occurring within the first six years after primary surgery for all age groups. This is the first time this methodology has been applied to the revision joint replacement literature and it emphasises the dramatic effect age has on risk of revision following surgery.

Our data is supported by previously published data in this area where a higher revision rate in younger patients has been identified[3,24,25]. However, most population studies that specifically address this issue are based on 10-year follow-up data from registries. In fact, no previous studies have quantified the risk of revision over the patient's life and examined when revision is likely to occur. In contrast our study not only highlights a lifetime revision risk for young patients of up to 35% with risk of revision higher than in other age-groups at all time points, but also that the time to revision in many cases is within 5 years which itself carriers a higher re-revision risk[3]. As a result, young patients are likely to spend many more years than previously expected with a revision implant, which carries with it poorer outcomes[26].

We found that sex has a significant influence on the estimated lifetime revision rate for both THR and TKR. Below the age of 70 men have a consistently higher estimated LTRR. The effects are seen most dramatically in the youngest age group (50-55) where LTRR for men is 24% after TKR, approximately 1.7 times greater than for women undergoing the same procedure, with similar trend after THR. These same trends are also demonstrated by the smoothed hazard plots (graphs 3 &4) with the instantaneous risk of revision in these groups being higher at all time points.

Whilst no information exists to date on lifetime risk data for revision joint replacement, the technique has been previously used to study primary joint replacement for hip and knee osteoarthritis; lifetime risk for the development of osteoarthritis is estimated at 25% for the hip and 45% for the knee [18] and lifetime risk of undergoing THR is 11.6% & 7.1% and for TKR 10.8% and 8.1% for women and men respectively[17].

As well as presenting the novel use of lifetime revision estimates, we also performed survival analysis on the CPRD dataset. This allows us to compare and validate our data against published work from the Joint Registries that use the same methodology. The UK National Joint Registry (UK NJR) published figures for 10 year revision risks of THR and TKR are 5.75% and 4.47% respectively, which compares favourably with the survival analysis results in this study: 5.0% for THR and 4.7% for TKR[3], with similar trends for reducing survival in younger patients over a ten year horizon. However, we believe our data suggests that 10-year survival does underestimate the scale of the problem for the younger patient. For instance, in an older patient with a 10-year life expectancy, an estimate of the potential 10-year survival of the implant provides good insight into the likely chance of undergoing revision. However, for a patient under 60, who may live for 30-40 years, a 10-year survival incidence may underestimate exposure to the real risk of revision. A much more representative figure is the estimate of life-time risk (in this case based on a dataset with up to 20 year follow-up).

The study has a number of potential limitations that must be addressed. This study focuses on implant survival as an indicator of successful outcome following joint replacement; we acknowledge that a patient's outcome after surgery is more complex than this simple measure. Patient reported outcomes, morbidity and mortality data are equally as important to patients. Ideally data regarding these factors and LTRR would all be available to patients who are deciding whether or not to undergo surgery.

Lifetime risk estimates in this large population study may be affected by the smaller numbers in the stratified age and sex sub-groups in the final follow-up periods. As such, where appropriate, our estimates were based on 15-year follow-up data to maintain population sub-group size.

This study does not include data relating to the indication for surgery or implant type (including metal-on-metal or ceramic bearing surfaces); whereas evidence exists that these factors can contribute to variations in implant survival[3,7]. To limit these effects, patients under the age of 50 were excluded to avoid including the more complex pathology seen in younger patients requiring surgery. An analysis of annual revision rates across the 20-year follow-up period was consistent, suggesting the effect of changing trends in implant use was minimal. Laterality data for each patient was not available, nor was coding for previous contralateral procedure. Whilst this should not have a significant effect on the lifetime risk estimations, it was not possible to adjust for bilateral disease as a potential risk factor for revision. The first chronological codes for primary surgery and revision were consistently taken for each patient so this may have had the effect of underestimating how quickly these patients underwent revision.

The lifetime risk calculation is a standard method permitting multiple decrements to account for competing risks (all-cause mortality), but it does not afford the flexibility of model-based methods in dealing with predictor variables. In this study the lifetime risk calculation is based on follow-up data of up to twenty years and so could under-estimate the revision rates seen, particularly in younger patients, where predicted life-expectancy exceeds 20 years. The use of all-cause mortality data from the ONS does not account for the lower mortality rates seen in patients presenting for joint replacement compared to the general population[27] and as such may over-estimate mortality rates and subsequently over-estimate LTRR estimates.

The study also showed a number of patients were lost to follow-up; these patients were subsequently accounted for, re-introduced into the population after having the same revision incidence applied to them found at the time they left the study, and the same principle was applied to censored patients. Previous studies have advocated treating patients in these loss-to-follow-up

groups with higher failure rates than those seen in the surveyed population; this is often the consequence of analysis of single-centre series. The nature of the CRPD is such that patients are lost to follow-up if they move geographical location and subsequently out of the catchment of their primary care practice; census data suggests people are more likely to move when medically well.

Given the nature of the CPRD population, care should be taken when extrapolating these results to other populations where healthcare behaviours and practices differ from those in the UK.

However, the strength of this study is its population-level data and subsequently large sample. In addition the CPRD represents a large population dataset selected to be representative of the UK as a whole[21]; as a consequence results derived from this dataset will be less at risk of confounding factors often found in smaller data sets and those collected from smaller regions where local factors (including demographic, socio-economic and referral thresholds) may vary.

What is the relevance of this work?

This work sheds new light on to the risk of revision surgery for patients under the age of 60. Although it has been previously established in the literature that this group of patients have a higher 10-year revision rate than patients over the age of 60, we believe that the true risk to patients is much higher than previously thought. On average for younger patients, under 60, who make up approximately 15% of all patients, the lifetime risk of revision increases up to 1 in 3, with the highest levels of revision seen in males between the ages of 50-55. These higher lifetime risks are paired with higher risks of revision at all time points and short mean times to revision meaning a patient in their fifties with a potential life expectancy of greater than 30 years could spend many years living with a revision joint replacement with limited functional ability. On a broader level with the numbers of joint replacements increasing year on year this issue will create a significant health economic burden for any health-care system[28]. In contrast for older patients (above 60) the risk of revision decrease and by the age of 70 the likelihood of revision surgery is below 1 in 20. In effect in this age group 95% of patients will outlive their prosthesis and demonstrates that long term revision rates are not as high as they may be perceived to be[3,29].

At a personal level this new data has significant implications for patients under the age of 60, who must consider the possibility of living with a revision procedure for many years if they undergo THR or TKR and subsequently require early revision. Patients who are considering undergoing joint replacement must balance the potential benefits of an improvement in their quality of life against the potential risks of the intervention: death, medical complications, infection, poor functional outcome and the need for revision surgery. Patients have indicated that they require better information regarding these outcomes, particularly in relationship to deciding on the correct time to have surgery. A patient's age and sex affect these outcomes and hence their decision. Patients are most often informed about risk of revision in terms of the likely 10-year survival of their implant, which can be an abstract and potentially confusing concept[20]. It is important to be able to answer these concerns in as accurate and clear a form as possible to provide useful information to aid patient decision-making. We believe that an estimate of the lifetime risk of revision is likely to be a valuable addition to the decision making process. This is particularly relevant given the findings of this study, where differences in outcome highlight the requirement for a more personalised approach to estimating potential risks and benefits for patients who are considering this procedure.

In conclusion, using a large population-based dataset we have estimated lifetime risk of revision to show that for patients under the age of 60, particularly males, the revision rate is much higher than previous estimates using 10-year survival data, with over half the number of revisions occurring within the first 5 years of implantation. This important information must be shared by professionals with patients in the decision making process and may mitigate against the trend for more THR & TKRs to be performed in the younger patient group.

Acknowledgements

Author statements

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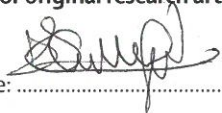
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agree with: the plan to submit to The Lancet; the contents of the manuscript; to being listed as an author; and to the conflicts
of interest statement as summarised. I have had access to all the data in the study (for original research articles) and accept
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statements included in this paper are correct and have been approved by all co-authors.

Table 1: Demographic data

		Total Hip Replacement				Total Knee Replacement		
		Female	Male	Total		Female	Male	Total
N=		39289	23869	63158		31682	22594	54276
Mean age		70.4	67.7	69.4		70.7	69.4	70.1
(SD)		(11.1)	(11.0)	(11.1)		(9.6)	(9.4)	(9.6)
Sex (%)		62	38			58.5	41.5	

Flowchart 1: population selection

CPRD population
6.5 million
(approx.)

primary THR and
TKR codes
117456

complete datasets
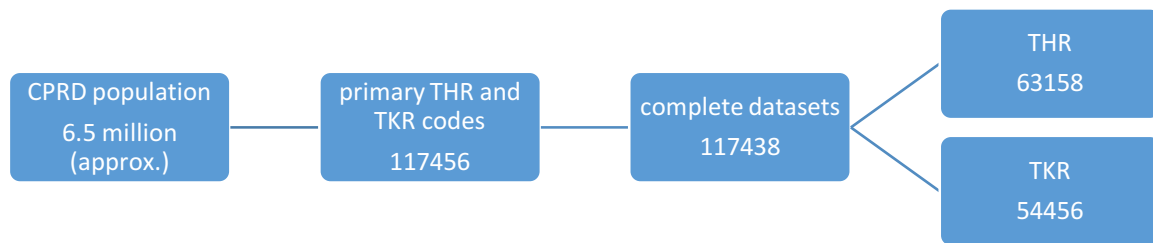117438

THR
63158

TKR
54456

Table 2: 20-year Implant survival actuarial table for THR

| Year	Total	Revision	Deaths	Lost	Survival	95% Confidence Interval	LCP adjusted survival
5	37066	144	991	4845	0.979	(0.9779, 0.9804)	0.977
10	13203	62	514	2330	0.956	(0.9534, 0.9585)	0.950
15	3312	33	158	691	0.910	(0.9029, 0.9157)	0.893
20	444	3	19	199	0.850	(0.8323, 0.8663)	0.812

Table 3: 20-year Implant survival actuarial table for TKR

| Year	Total	Revision	Deaths	Lost	Survival	95% Confidence Interval		LCP adjusted survival
5	30056	89	1427	5648	0.9798	0.9784	0.9812	0.977
10	8261	25	495	2128	0.9612	0.9583	0.9639	0.953
15	1717	12	155	523	0.9294	0.9217	0.9364	0.912
20	152	0	12	72	0.8969	0.8745	0.9154	0.862

Graph 1: Lifetime risk of revision following THR:

Plot showing estimates of lifetime risk of THR revision against age at the time of THR primary surgery (in 5-year age bands) and stratified by sex (results adjusted for LCP)
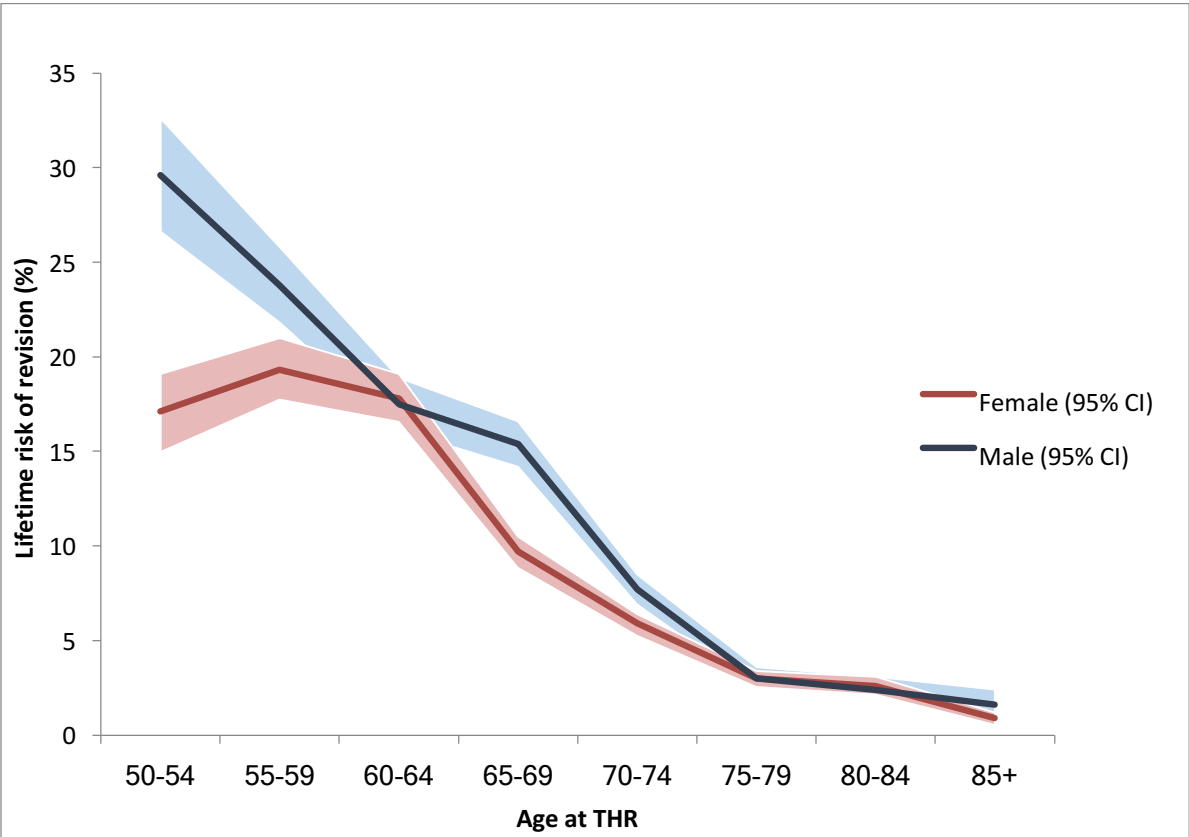
Graph 2: Lifetime risk of revision following TKR:

Plot showing estimates of lifetime risk of TKR revision against age at the time of primary TKR surgery (in 5-year age bands) and stratified by sex (results adjusted for LCP)
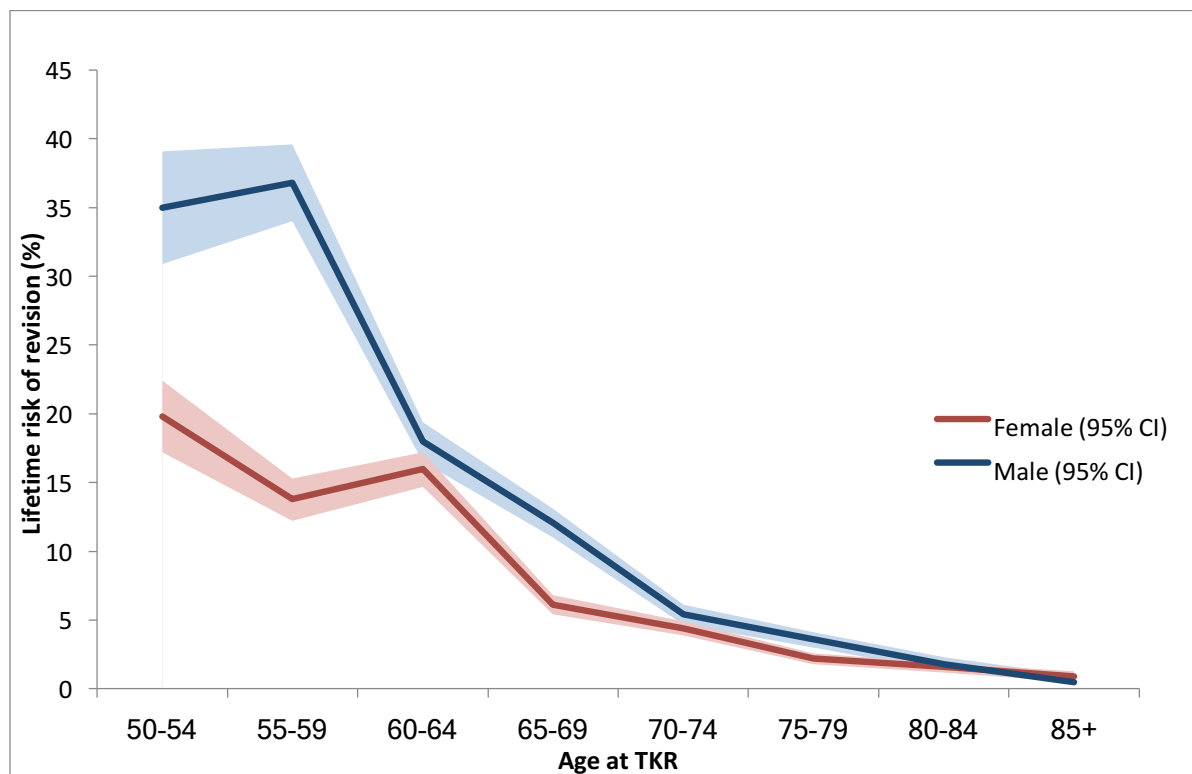
Graph 3: Smoothed Hazard Curve of Revision Risk in Female Patients by age.

Instantaneous risk of revision for a given length of implant survival, stratified by age at time of primary THR or TKR (in 10-year age-bands).
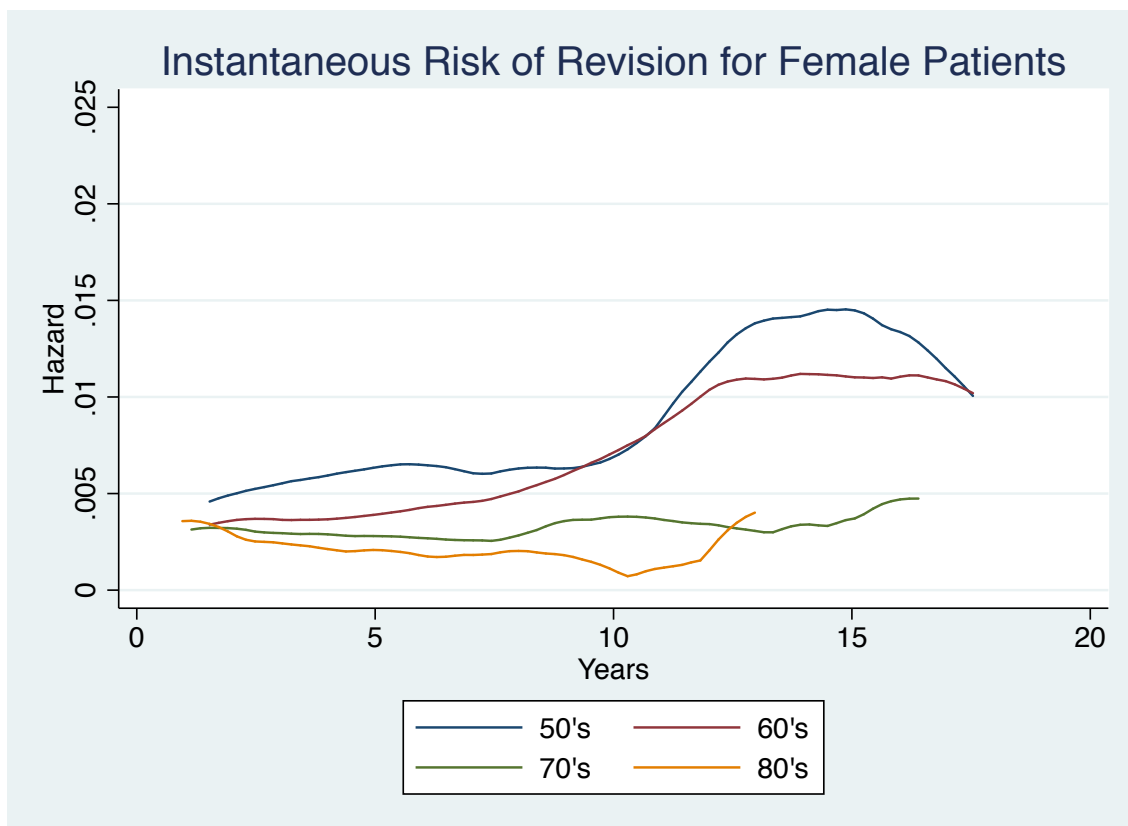
Graph 4: Smoothed Hazard Curve of Revision Risk in Male Patients by age.

Instantaneous risk of revision for a given length of implant survival, stratified by age at time of primary THR or TKR (in 10-year age-bands).
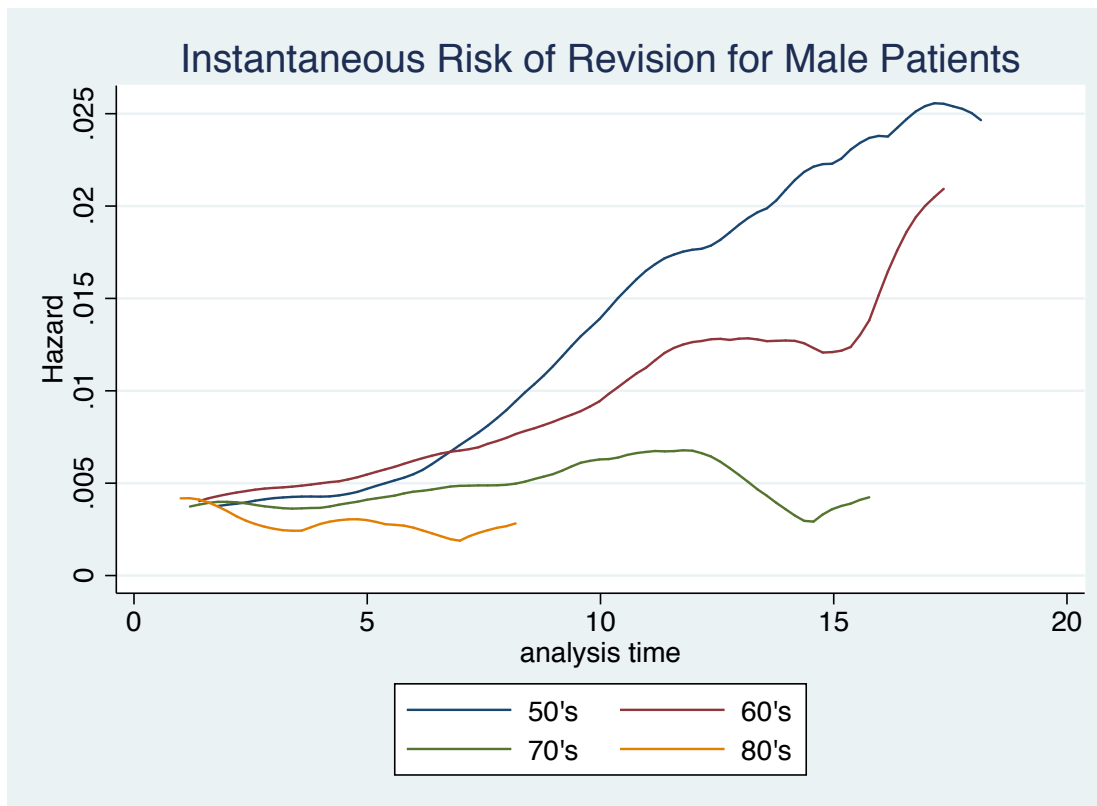
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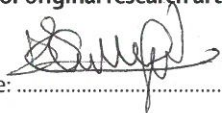
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