

Re-revision Knee Arthroplasty in a Tertiary Centre: Infection and multiple previous surgeries were associated with poor early clinical and functional outcomes

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Abstract

BACKGROUND

The incidence of re-revision knee arthroplasty (RRKA) has increased over the past decade and is projected to rise further. RRKA is complex surgery associated with high rates of complications and failure. However, information on these outcomes is limited. The aim of this study was to investigate implant survivorship, complications and patient-reported outcomes following RRKA and factors associated with poor outcome.

METHODS

In this retrospective cohort study, 206 patients (250 knees) undergoing RRKA were recruited from a major revision centre from 2015-2018. PROMS were collected. Logistic regression was performed to identify risk factors for further reoperation. Implant survivorship was compared for aseptic and infected RRKA.

RESULTS

Mean age at RRKA was 69.2 years. Mean follow-up was 25.5 months. Main indications for RRKA were prosthetic joint infection (PJI) (n=171/250, 68.4%) and aseptic loosening (n=25/250, 10.0%). 58 knees (28.7%) required further revision surgery within 2 years. Knees revised for PJI had poorer reoperation-free survival at 2 years compared to aseptic indications (55.7% versus 78.1%, p=0.002). Median OKS was 26.0 (range 1-48). Median EQ-5D-index was 0.648 (range -0.511-1.000). Multivariable analysis demonstrated that PJI (OR 2.39, 95%CI 1.06-5.40, p=0.036), greater number of previous surgeries (OR 1.18, 95%CI 1.04-1.33, p=0.008) and higher Elixhauser score (OR 1.06, 95%CI 1.01-1.13, p=0.045) were independently associated to further surgery.

54 *CONCLUSION*

55 RRKA carried a high risk of early failure. Multiply revised joints and patients with greater
56 comorbidities had worse function. Patients undergoing RRKA for PJI should be counselled to
57 expect higher failure rates and complications than patients with aseptic indications.

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59 *KEY WORDS: Knee arthroplasty, PJI, revision*

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Introduction

Knee arthroplasty is a common and successful surgical intervention¹. The majority of patients experience large improvements in pain, function, and quality of life². However, after primary knee arthroplasty, around 4% of patients require revision surgery within ten years³ and around 10% of these patients require a further revision (re-revision) procedure within 3 years⁴.

Re-revision knee arthroplasty (RRKA) may be technically challenging (for example, due to scar tissue or loss of bone) and perioperative complications are common⁵. The management of this patient group is expensive, resource intensive⁶⁻⁹, and often not supported by high-quality evidence. Information on the clinical and functional outcomes of RRKA is needed to support informed consent and shared decision-making for this complex patient cohort. As such, the primary aim of this study was to investigate implant survivorship following RRKA at a high-volume centre. Secondary aims were to investigate functional outcomes and complication rates following RRKA and factors associated with further revision surgery.

Patients and Methods

Institutional Review Board approval was obtained for this study.

Study design

In this retrospective cohort study, consecutive RRKA procedures were identified at our institution between 1st of January 2015 and 31st of December 2018 using our institutional database and operating theatre logbooks.

Inclusion and exclusion criteria

Re-revision knee arthroplasty was defined as any procedure following a first revision procedure where a component was added, removed or modified, or the patient underwent a Debridement, Antibiotics, and Implant Retention (DAIR) procedure³. We excluded first stage procedures of a planned two-stage procedure.

Patient cohort

Patient demographics, indication for RRKA, procedural details, and outcome was collected for all cases using the electronic patient record system and our local database. The 30-item Elixhauser Comorbidity Score¹⁰ (ECS) was utilised to document comorbidities. This is an index originally developed to predict in-hospital mortality but its use in predicting other outcomes has previously been demonstrated¹¹. In this study, it was collected through the International Statistical Classification of Diseases and Related Health Problems, Version 10 (ICD-10) coding at discharge using the coding algorithm from Quan et al.¹² and updated using the weights suggested by van Walraven et al¹³. The indication for surgery was coded as a single, dominant diagnosis based on the Australian Orthopaedic Association hierarchical system¹⁴.

The presence of prosthetic joint infection (PJI) was determined based on the International Consensus Meeting on Musculoskeletal Infection (ICM) 2013 criteria¹⁵.

Outcome measures

Patient Reported Outcome Measures (PROMs): PROMs were collected at final follow up (FU). The Oxford Knee Score (OKS) has been validated and found to have good measurement properties for the assessment of pain and function after revision knee replacement^{16,17}. The OKS has a worst possible score of 0 and a best possible score of 48¹⁸. Health-related quality of life was assessed using the EQ-5D-5L¹⁹ where utilities for the UK population range from -0.594 (worst) to 1 (best). Its visual analogue scale (EQ-VAS) ranges from 0 (worst) to 100 (best).

Complications following re-revision. Electronic patient records were reviewed for medical or surgical complications (deep vein thrombosis, surgical site infection, wound problems, bleeding, implant related complications, pneumonia, or pulmonary embolism) in the 90-day period following discharge.

Statistical analysis

Statistical analyses were performed using SPSS (IBM Corp. Released 2018. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.) and R Version 4.1.2. A p-value of ≤ 0.05 was considered statistically significant. Demographics and procedural details were analysed using means and standard deviations (SD) or medians and ranges, as appropriate. Differences in age, sex, body mass index (BMI), ECS and number of previous procedures for patients having and not having returned PROMs were compared using a two-sided independent t-test or chi-square test to ensure no structural differences. When only one or two answers on

the OKS were missing, the average score of the remaining responses was utilized to calculate the sum score as has previously been suggested²⁰.

Kaplan-Meier survival analysis was used to investigate time to further revision for all RRKA. The survivorship of PJI RRKA compared to aseptic RRKA was then compared using the log-rank test. Deaths were censored as we expected them to fulfil the non-informative censoring assumption²¹. Analyses were curtailed when less than 10% of knees remained at-risk. Failure rates at 2 and 4 years were reported with 95% confidence intervals (95% CI).

To investigate risk factors for reoperation at 1 year, we used multivariable logistic regression. We excluded manipulation under anaesthesia (MUA) procedures. Subsequent procedures on the same patient were treated as independent and included in the model. Absolute risk reduction was calculated for significant, dichotomous risk factors.

Results

Patient cohort

263 re-revisions were performed between 1st of January 2015 and 31st of December 2018 at our institution. After reviewing patient notes, 13 knees were excluded for not meeting inclusion criteria (12 repeat first stage revision procedures for PJI, 1 total femoral replacement) (Figure 1). Mean follow-up was 25.5 months. Patient characteristics are described in Table 1. The mean age of all patients was 69.2 years (SD 10.6, range 31-91); 108/250 (43.2%) were female. Median number of all previous knee surgical procedures before undergoing the re-revision at our institution was 4.0 (range 2-15). 94.4% had 3 or fewer revisions before undergoing index RRKA (Table 2). The main indication for RRKA was infection (n=171/250 knees, 68.4%), followed by aseptic loosening (n=25/250 knees, 10.0%), dislocation/subluxation (n=12/250 knees, 4.8%), and instability (n=12/250 knees, 4.8%) (Table 3). A fifth of all cases (n=53/250 knees, 21.2%) needed plastic surgical input for soft tissue cover. A local flap was used in 20 cases (8.0%) (15 fasciocutaneous flaps [6.0%], 5 skin flaps [2.0%]), a regional flap in 25 cases (10.0%) (24 gastrocnemius flaps [medial or lateral] [9.6%], 1 myocutaneous flap [0.4%]), and a free flap in 1 case (1 latissimus dorsi flap [0.4%]). In 7 cases (2.8%) more than one flap was utilized or a flap was combined with a split skin graft.

Patient Reported Outcome Measures

Response rate for the PROMs was 55.6% (n=99/178 patients contacted). No statistical differences in age, sex, BMI, ECS or number of previous procedures between patients having and not having returned PROMs were found. Mean OKS was 25.9 (SD 12.6, range 1-48). The responses to each item of the EQ-5D-5L can be seen in Table 4. Patients reported the highest mean level of limitation for usual activities (2.72, SD 1.23). 63 different health states were generated. Mean QALY weight was 0.539 (SD 0.332, range -0.511 – 1.000). 11.2% had a score

regarded as “worse than death” (i.e. <0). Mean EQ-VAS score was 61.8 (SD 24.4, range 0-100).

Risk factors for a poor outcome after RRKA

13 pre-operative factors predicting a poor outcome after knee arthroplasty were identified. Results from the univariable and multivariable regression analyses can be seen in Table 5. Univariable analyses revealed significant risk of a poor outcome (as assessed by further surgical intervention excluding MUA at 1 year after re-revision) for infected vs. not infected cases (OR 3.26; 95%CI: 1.49-7.10; p=0.002), the number of previous operations to the knee joint (OR 1.20; 95%CI: 1.07-1.35; p=0.002), the weighted Elixhauser score (OR 1.07; 95%CI: 1.01-1.13; p=0.027), and cardiac arrhythmia (OR 2.62; 95%CI: 1.27-5.42; p=0.015). Arrhythmia was omitted from the multivariable model to avoid collinearity as it is an item in the ECS. In the multivariable analysis infection as indication for re-revision (OR 2.39; 95%CI: 1.06-5.41; p=0.036), the number of previous operations (OR 1.18; 95%CI: 1.04-1.33; p=0.008), and the weighted Elixhauser sum score (OR 1.06; 95%CI: 1.00 to 1.13; p=0.045) showed to be significant predictors of reoperation at 1 year from index re-revision. Calculated absolute risk reduction for infected versus not infected cases was -0.20 (95%CI: -0.31 to -0.09).

Readmission rate and implant survival

90-day readmission rate was 14.0%. There were 19 (7.6%) cases which had a surgical site infection (4 superficial, 15 deep) and 3 (1.2%) with wound dehiscence (two treated with a washout, one treated conservatively). The remaining complications are listed in Table 6. One patient who had undergone a RRKA and soft tissue cover with a gastrocnemius flap underwent an arthrodesis due to wound breakdown.

190 The estimated revision rate at 2 years was 28.7% (95%CI: 22.7-35.9) and 42.0% (95%CI: 32.8-
191 52.6) at 4 years (Figure 2). PJI cases had a significantly worse reoperation rate than aseptic
192 cases ($p=0.003$) (Figure 3).

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Discussion

This study investigated the outcome of 250 RRKA cases undertaken within a tertiary major revision centre. It demonstrated that infection was the main indication for RRKA and was associated to poorer earlier implant survivorship compared to aseptic revisions with a 3.3-fold increased risk of needing a further surgical intervention. Disease-specific and overall health related PROMs after RRKA were fair. It also demonstrated the 90-day complication rate and the short to mid-term survival of this complex cohort of patients. In addition to infection, we demonstrated that a higher Elixhauser comorbidity score and higher number of previous procedures are independent risk factors for further operations and a poor outcome.

The National Joint Registry for England, Wales, Northern Ireland, and the Isle of Man (NJR) has only recently started to report on re-revisions. Deere et al. analysed 3575 re-revision cases from the NJR. Main indication was infection with 34.9%⁴. Yu et al. published a series of 66 re-revision cases, but excluded patients who had previously been revised for PJI²². The main indications for re-revision in the latter study were arthrofibrosis (23%), PJI (21%), and aseptic component loosening (20%). In a study from 2008, Bae et al. looked at a series of 18 cases with the main indication was polyethylene wear (50%)²³. This failure mechanism as a cause of re-revision will become less frequent with the introduction of better implant materials and improved manufacturing processes²⁴. Kirschbaum et al. reported on a single-centre cohort of 157 TKA re-revisions²⁵. Main indications for RRKA were PJI (48%) and instability (12%). In the present study, the main indication for RRKA was infection (68.4%) and this finding is in keeping with the results of other contemporary studies. Mortazavi et al. reported that PJI as an indication for re-revision was present in 44.1% of cases²⁶, whilst Suarez et al. reported a rate of 46.0%²⁷. The NJR 2020 annual report analysed all re-revisions with a linked primary and first revision knee replacement in the registry. In 30.7% of cases infection was the leading indication for re-revisions³. Geary et al. reported 38.9% of all re-revisions to be septic²⁸. Even

220 though revision for infection appears to be the main indication for re-revision across most
221 studies, the rate in our study was considerably higher. This could be due to the fact, that our
222 unit is a tertiary referral centre with a specialized Bone Infection Unit which receives cases
223 from around the country. Furthermore, we included not only first-time re-revisions, but also
224 subsequent re-revisions. As infection has previously been shown to be a predictor for a poor
225 outcome²⁹, selection bias causing a higher number of revisions is likely. In keeping with
226 existing literature, we also observed that septic cases had a higher risk of further re-operation²⁸.
227 Compared to aseptic cases, the risk of needing a further reoperation at 1 year was 3.3-fold
228 increased and highlights detrimental effects of a septic diagnosis as an indication for RRKA.
229 This provides further evidence to support the notion that patients with suspected or confirmed
230 PJI should be treated by a multidisciplinary team (MDT) within dedicated units in order to
231 mitigate the risk of treatment failure in this high-risk cohort.

232 Mean OKS score after re-revision was 25.9. The national average OKS for primary TKA and
233 revisions, reported by the National Health Service in the United Kingdom (NHS) in 2020, is
234 36.0 and is 10 points above the average found in this study³⁰. Other studies report similar
235 PROMs scores to national figures. Beard et al. reported an OKS of 33.8 in 94502 cases and
236 Sabah et al. reported a mean OKS of 29 in 14.316 cases^{31,32}. Mean QALY weight was 0.539
237 with more than every tenth patient reporting a score below 0. The national average QALY,
238 according to data from the NHS, is 0.748 for primary and revision procedures and 0.691 for
239 revisions only^{2,16}. Mean VAS in this study was 61.8 compared to 75.2 (for primary and revision
240 cases) and 67.0 (for revision only cases) reported by the NHS^{2,30}. In order to improve shared
241 decision making with patients, it is important to communicate the potential outcomes of re-
242 revision surgery to patients pre-operatively. This study demonstrates that PROMs for RRKA
243 are lower compared to 1st time revisions, and so patients should be informed of this potential
244 outcome during the consent procedure. In particular, for diagnoses that do not require an

immediate treatment, e.g. stiffness or instability, the expected functional improvement needs to be carefully weighed against the risks of surgery. Older patients and those with significant frailty may benefit from conservative treatment options such as physiotherapy.

We observed a relatively low readmission rate of 14% in the 90-days following discharge which is comparable to first time revision surgery. Schairer et al. found a rate of 13% after revision TKA³³ whilst Nichols and Vose reported that one in five patients required readmission⁶. We found a high failure rate following RRKA with 2 out of 5 patients undergoing further revision by 4 years. It is difficult to contextualize these findings, as a paucity of literature on re-revision exits. In the aforementioned study by Yu et al. they reported a survival rate free of further surgical intervention at 2 years of 73%²². Deere et al. estimated a revision rate of 25% after the second revision at 4 years⁴. The high failure rates observed in this study further emphasis the complex nature of re-revision surgery and as such, the decision to undertake re-revision surgery should be carefully considered and discussed within an MDT setting. These complex cases should be managed within units which have the necessary expertise and infrastructure in place in order to optimise outcomes. High number of previous procedures performed on the knee and a high weighted ECS carry a higher risk of failure and such cases should prompt an early referral to specialised centres.

We acknowledge the limitations of this study. The retrospective nature carries the standard limitation of such studies, and the population has a high clinical heterogeneity. Furthermore, all patients were managed within an MDT setting in a high-volume centre by surgeons with expertise in revision knee arthroplasty. As a result, the results of the current study may not be applicable to all centres. The moderate sample size also places the results at risk of a type-2 error.

Nevertheless, to our knowledge, this is the largest single-centre study on the outcome of re-revision knee arthroplasty. We provide evidence on achievable functional and clinical outcome

for RRKA – a procedure which many knee surgeons may encounter given the rising incidence of revision knee arthroplasty. Further evidence and treatment algorithms are needed to optimize the management of patients with a multiply failed knee. As relations of volume and outcome in knee arthroplasty have previously been demonstrated^{34,35}, a broad discussion on the benefits of minimal volume thresholds and national referral structures is required. A movement towards such revision networks in England was noted by the “Getting It Right First Time” (GIRFT) report in 2020 and is now underway with a proposed hub-and-spokes model which has shown to improve efficiency and quality^{36,37}.

Conclusion

This study demonstrated that the failure rate following RRKA is high and that the PROMs for this patient cohort are fair. Decision-making prior to such procedures is key and should involve the MDT as well as the patients themselves. Conservative treatment options should always be explored prior to surgery due to the risks involved with re-operation. An infective diagnosis, high number of comorbidities and a high number of previous procedures performed on the knee should predict worse outcome. These results should form an evidence-base for informed decision making with patients who are being considered for RRKA.

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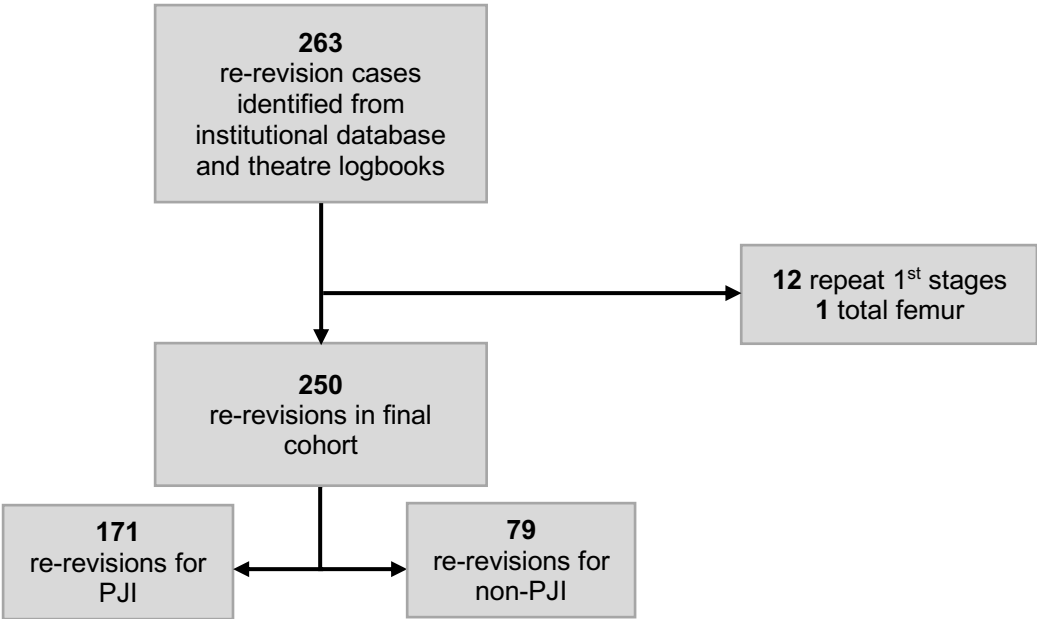


Figure 1. Patient inclusion flowchart

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Table 1. Basic demographics for the re-revision cohort. Data aggregated on a procedure level from the perspective of the surgical unit. *n*=number, *SD*=standard deviation, %=percentage, *ECS*=Elixhauser comorbidity score

	n (%)	mean	SD	range
Age (years)		69.2	10.6	31.2 - 90.5
Gender				
female	108 (43.2)			
male	142 (56.8)			
Side				
right	142 (56.8)			
left	108 (43.2)			
Height (cm)		169.7	10.6	144 - 198
Weight (kg)		90.5	19.7	46 - 165
Body Mass Index (kg/m²)		31.4	6.0	17 - 49
Positive items on ECS		2.5		0 - 7
Weighted ECS		0.14	5.0	-14 - 19

Table 2. Number of previous revisions before index re-revision. The cumulative % shows the cases that had this many or fewer revisions before undergoing index re-revision. n = number, % = percentage

n of previous revisions	1	2	3	4	5	6	total
n	132	68	31	9	4	1	245
%	53.9	27.8	12.7	3.7	1.6	0.4	100.0
cumulative %	53.9	81.7	94.4	98.1	99.7	100.0	100.0

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Table 3. Indications for all re-revisions. *n* = number, % = percentage, ¹progression of the disease in the remaining knee, where a unicompartmental prosthesis was in place

Indication	n	%
infection	171	68.4
aseptic loosening	25	10.0
dislocation/subluxation	12	4.8
instability	12	4.8
stiffness	6	2.4
periprosthetic fracture	5	2.0
implant fracture	5	2.0
polyethylene wear	3	1.2
progression of disease ¹	3	1.2
unexplained pain	3	1.2
lysis	2	0.8
component dissociation	2	0.8
malalignment	1	0.4
Total	250	100.0

Table 4. Percentage of respondents rating their limitations from level 1 to 5 in the 5 categories of the EQ-5D-5L. Level 1 means low or no limitation, level 5 high limitation. The modus for each category has been highlighted. % = percentage, SD = standard deviation

category	level of limitation (%)					mean (SD)
	1	2	3	4	5	
Mobility	12.1	38.4	24.2	21.2	4.0	2.67 (1.07)
Self-care	49.5	25.3	12.1	11.1	2.0	1.91 (1.12)
Usual activities	14.3	35.7	26.5	10.2	13.3	2.72 (1.23)
Pain/discomfort	17.2	37.4	29.3	10.1	6.1	2.51 (1.08)
Anxiety/depression	51.5	27.3	9.1	8.1	4.0	1.86 (1.13)

Table 5. Results of univariable and multivariable regression analyses for pre-operative risk factors identified from literature. Endpoint for analyses was reoperation, including amputation and fusion, excluding manipulation under anesthesia, at 1 year after index re-revision. OR=odds ratio, CI=confidence interval, BMI=body mass index, p=p-value, ACR=absolute risk reduction

predictor	univariable		multivariable		absolute risk reduction
	OR (95%CI)	p	OR (95%CI)	p	ACR (95%CI)
Age at index surgery	1.01 (0.98-1.04)	.424	N/A		
Gender			N/A		
male	reference				
female	0.68 (0.37-1.26)	.282			
Infected vs. not infected					
not infected	reference		reference		
infected	3.26 (1.49-7.10)	.002	2.39 (1.06-5.41)	.036	-0.20 (-0.31 to -0.09)
Number of previous operations	1.20 (1.07-1.35)	.002	1.18 (1.04-1.33)	.008	N/A
Weighted Elixhauser score	1.07 (1.01-1.13)	.027	1.06 (1.00-1.13)	.045	N/A
Diabetes			N/A		
no	reference				
yes	1.41 (0.64-3.12)	.402			
BMI	1.02 (0.97-1.07)	.547	N/A		
Depression			N/A		
no	reference				
yes	1.37 (0.67-2.83)	.445			
Chronic lung disease			N/A		
no	reference				
yes	1.73 (0.81-3.72)	.213			
Renal disease			N/A		
no	reference				
yes	1.36 (0.45-4.16)	.560			
Fluid and electrolyte disorders			N/A		
no	reference				
yes	0.81 (0.25-2.58)	1.00			
Arrhythmia			N/A		
no	reference				
yes	2.62 (1.27-5.42)	.015			
Rheumatic arthritis			N/A		
no	reference				
yes	1.66 (0.74-3.75)	.269			

Table 6. Indication for readmissions within the first 90 days following discharge after re-revision.
n = number, % =percentage

Readmission indication	n	% of all readmissions	% of all index re-revisions
Surgical site infection	19	54.3	7.6
Wound problems	3	8.6	1.2
Haemarthrosis	2	5.7	0.8
Dislocation	2		
Fall	2		
Pneumonia	2		
Loss of graft	1	2.9	0.4
Cellulitis	1		
Implant fracture	1		
Pulmonary embolism	1		
Unexplained pain	1		
Total	35	100	14.0

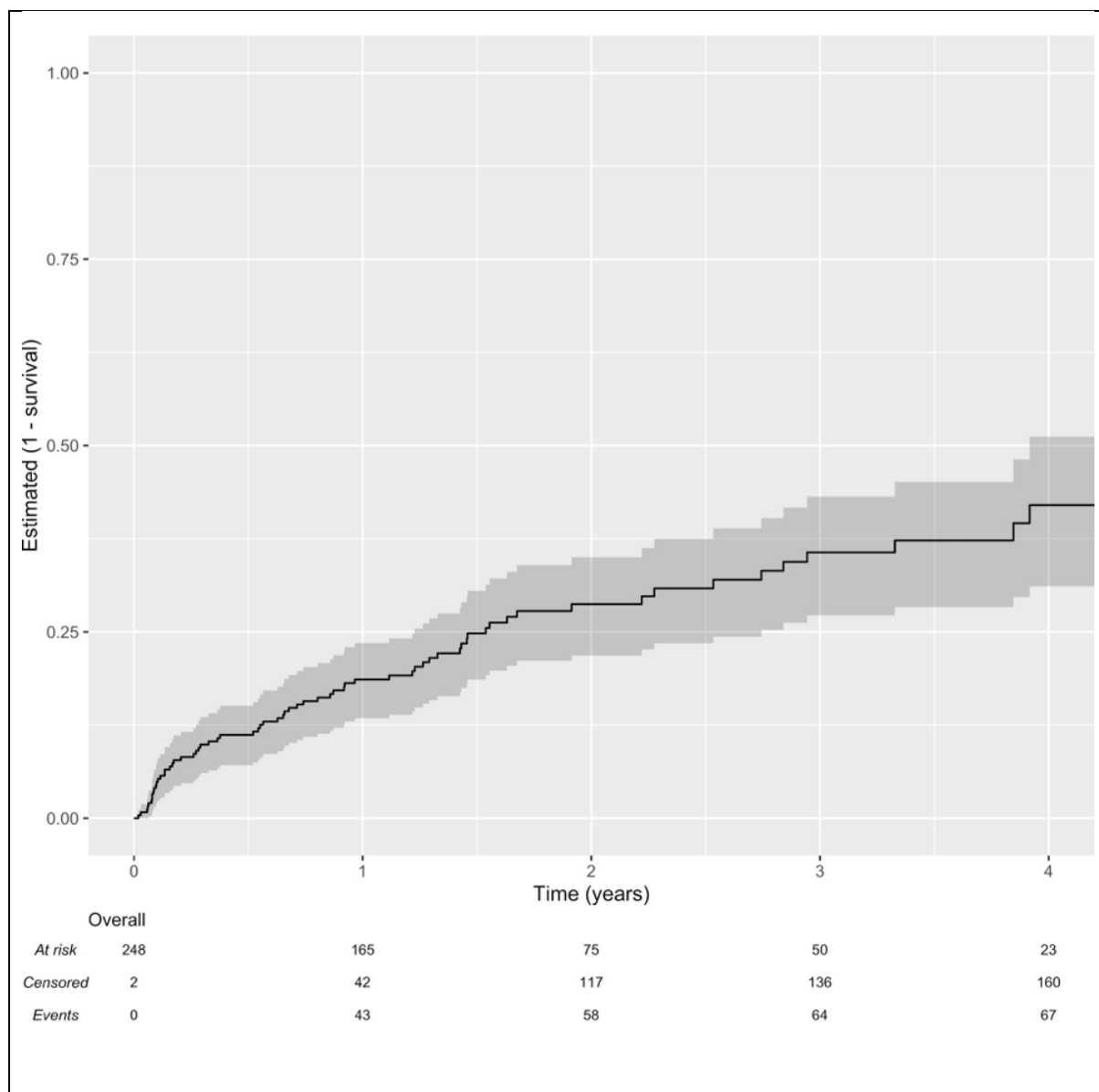


Figure 2. Estimated survival curves with 95% confidence interval for further revision for all re-revision cases. At 2 years 28.7% needed a further revision.

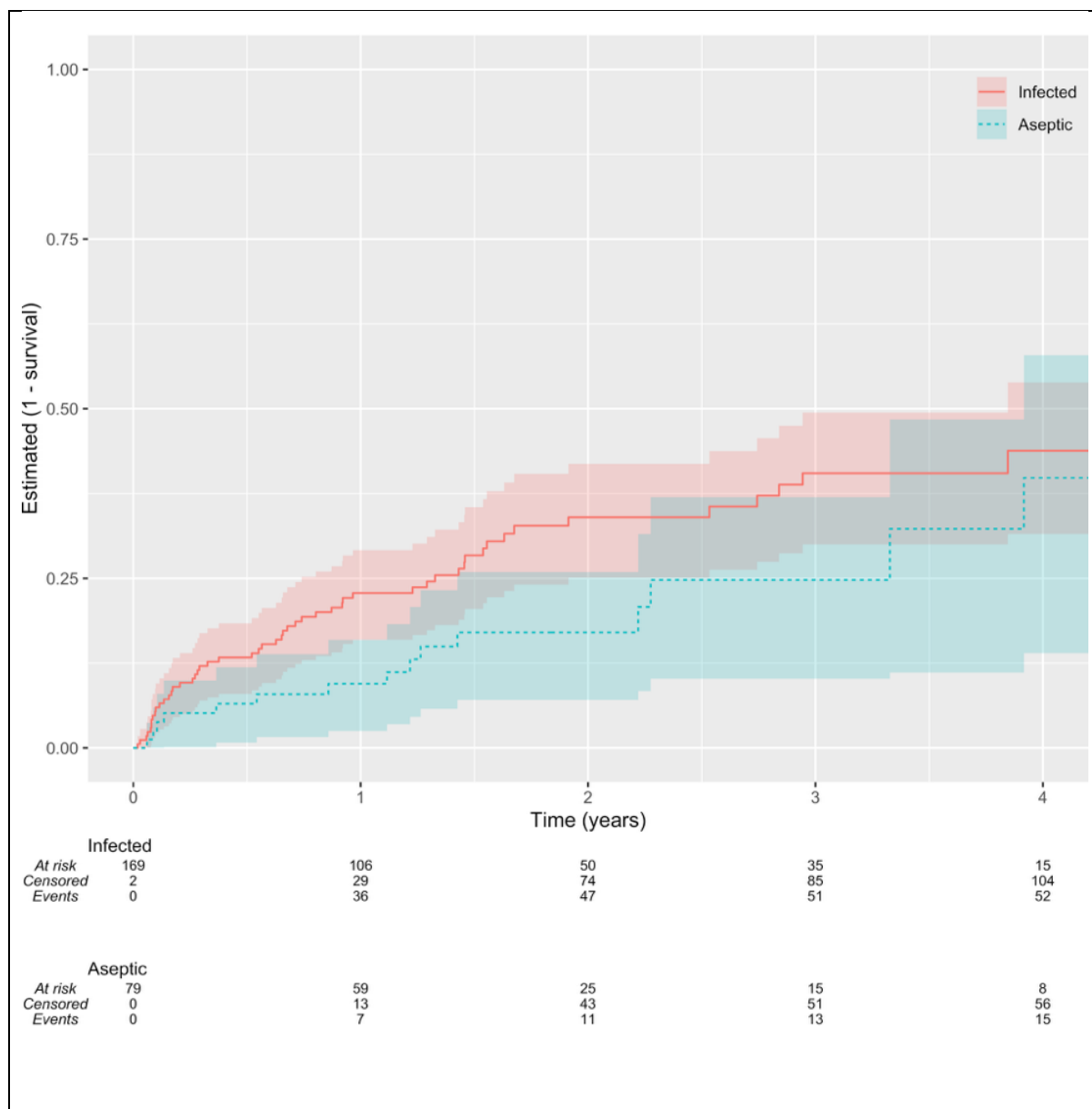


Figure 3. Estimated survival curves with 95% confidence interval for further reoperation for prosthetic joint infection (PJI) vs. aseptic cases. PJI has a significantly worse survival. Log-rank test: $p = 0.003$

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