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Much higher re-revision rates and mortality following septic revision total knee arthroplasty compared to meta-analyses

A REGISTRY STUDY

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Aims

This study investigates re-revision and mortality rates following septic revision of total knee arthroplasty (TKA) using registry data from Germany.

Methods

An observational cohort study was conducted using data from the German Arthroplasty Registry (EPRD), consisting of 15,372 revision TKAs. Cumulative incidences of re-revision and mortality for septic and aseptic revision-TKAs were analyzed over a seven-year follow-up (2015 to 2022). Kaplan-Meier estimates were employed to determine re-revision rates and cumulative mortality probabilities after revision TKA.

Results

The re-revision rate within the first year following septic revision TKA was 21.7% (95% CI 20.3 to 23.1), compared to only 7.1% (95% CI 6.6 to 7.6) for aseptic revisions. Notably, 74% of all re-revisions for septic revision TKA occurred within the first year. Cumulative mortality within the first year after septic revision TKA was 4.9% (95% CI 4.2 to 5.7), rising to 28.5% (95% CI 24.2 to 33.2) after seven years. In contrast, aseptic revision TKA had lower mortality rates, with 2% within the first year and 16% within seven years. After multiple previous knee revisions, re-revision rates increased to over 47%, and mortality to 30% for septic revisions.

Conclusion

Registry data revealed nearly twice the re-revision rates for septic revision TKA compared to single-centre studies, reflecting real-world outcomes in Germany. Septic revision TKA has a threefold higher re-revision rate in the first year and double the mortality rate compared to aseptic revisions. Given the high risk in the first postoperative year, optimizing perioperative procedures is crucial to reducing the burden of septic revision TKA.

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Introduction

With the substantial increase in the number of total knee arthroplasties (TKAs) and revision TKAs performed each year, the total number of periprosthetic joint infections (PJIs) following revision TKA is on the rise.[1] While primary TKAs show excellent 15-year survival rates of more than 90%,[2–5] revision TKAs have significantly higher failure rates and increased mortality due to component loosening, polyethylene wear, instability, and increasing frequency of PJIs, especially septic revision surgeries.[6–9] Meta-analyses and systematic reviews report that revision TKA has a five-year re-revision rate of approximately 14% with PJI as the most common aetiology for revision failure and an associated five-year mortality rate of 22% underscoring the high complexity and serious prognosis of PJI in revision TKA.[10,11]

Various approaches to evaluating treatment success have been used in the literature, like using endpoints such as re-revision rates, mortality, or the rate of infection eradication over time.[12] Moreover, most results for septic revision arthroplasty can be retrieved from single-centre or multicentre studies, but only registry data represent the widespread treatment reality of revision TKA beyond

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Table I. Demographic characteristics of knee revisions.

Characteristic	Initial revision (n = 14,191)		Multiple revision (n = 1,187)	
	Septic	Aseptic	Septic	Aseptic
Revisions, n	3,520	10,671	478	709
Median age, yrs (IQR)	69 (61 to 77)	66 (58 to 74)	68 (60 to 77)	66 (58 to 75)
Sex, n (%)				
Female	1,820 (52)	7,147 (67)	216 (45)	446 (63)
Male	1,700 (48)	3,524 (33)	262 (55)	263 (37)
BMI, n (%)				
Underweight	5 (0.3)	9 (0.2)	1 (0.3)	0 (0)
Normal	225 (14)	707 (13)	43 (11)	74 (12)
Pre-obese	499 (32)	1,769 (33)	122 (31)	185 (31)
Obese 1	405 (26)	1,522 (28)	99 (25)	185 (31)
Obese 2	255 (16)	868 (16)	65 (17)	91 (15)
Obese 3	184 (12)	505 (9.4)	60 (15)	60 (10)
Unknown	1,947	5,291	88	114
Elixhauser score, n (%)				
< 0	340 (18)	1,634 (25)	106 (22)	184 (26)
0	575 (30)	2,916 (44)	109 (23)	292 (41)
1 to 4	238 (12)	747 (11)	53 (11)	73 (10)
5+	758 (40)	1,260 (19)	210 (44)	160 (23)
Unknown	1,609	4,114		

large orthopaedic centres with high case numbers.[13,14] Nevertheless, most public registry data on revision TKA do not separately distinguish between the re-revision rate and mortality of aseptic and septic revision TKA,[15–20] which impairs the ability to draw a firm conclusion about septic and aseptic re-revision rate and mortality separately.

Therefore, the current study aimed to elaborate on the differences between septic and aseptic revision TKA regarding re-revision and mortality rates using the German Arthroplasty Registry (EPRD).

Methods

Data source. This study is based on data from the EPRD. Data are generated by register documentation from three independent sources. First, participating clinics document the surgery with the consent of the patients. Second, the implanted materials are recorded by barcode scanning and transmitted from the manufacturer. Third, health insurance companies provide information about endoprosthetic services, follow-up operations, comorbidities, and patient deaths. Combining these three sources, a near-complete follow-up of all patients is generated, with the rare exceptions of patients who have revision surgery outside of Germany, who change to a health insurance company which does not report to the EPRD and at the same time undergo revision surgery in a hospital that does not report. The EPRD covers around 70% of all operations in Germany and receives data on 754 German hospitals.[21] As comorbidities and indications for surgery are provided by health insurance companies, the ERPD is able to distinguish between septic and aseptic revision TKA.

Anthropometric and demographic measures including age, sex, and BMI were documented. Comorbidities are classified by Elixhauser score using a weighted algorithm based on the association between comorbidity and death.[22]

The EPRD defines a revision arthroplasty as the exchange of any component of the knee arthroplasty, which includes mobile parts such as the insert. Secondary patellar resurfacing without replacement of an additional prosthesis component are not recorded as a revision in the underlying dataset. Revision TKAs were defined as septic in the EPRD if the diagnosis T84.5 (infection and inflammatory reaction due to internal joint prosthesis) according to the International Classification of Diseases and Related Health Problems was transmitted, or 'infection' was documented by the surgeon as the reason for revision in the register.[23] In the case of a two-stage revision surgery, re-revision is counted after reimplantation of exchanged or removed components. Re-revision knee surgery and death of the patient were determined as endpoints.

The EPRD received general institutional review board approval from the University of Kiel (approval number D 473/11).

Patient cohort and endpoint selection. As seen in Figure 1, from 2015 to 2022, the EPRD conveyed data of 15,378 revision TKAs, of which 14,191 were first-time revision TKAs (92%) and 1,187 were multiple (> 1) revision TKAs (8%). Of the 14,191 first-time revision TKAs, 3,520 patient cases were identified as septic (25% of first-time revision TKAs) and 10,671 as aseptic (75% of first-time revision TKAs). In the 1,187 multiple-revision TKAs, 478 patient cases were identified as septic (40% of multiple-revision TKAs) and 709 as aseptic (60% of multiple-revision TKAs).

Patient characteristics and comorbidities. The population characteristics, BMIs, and Elixhauser scores of the cohorts are shown in Table I.

Statistical analysis. All statistical analyses were performed using R (version 4.2.2; R Foundation for Statistical Computing, Austria), with RStudio (Posit, USA) as the integrated develop-

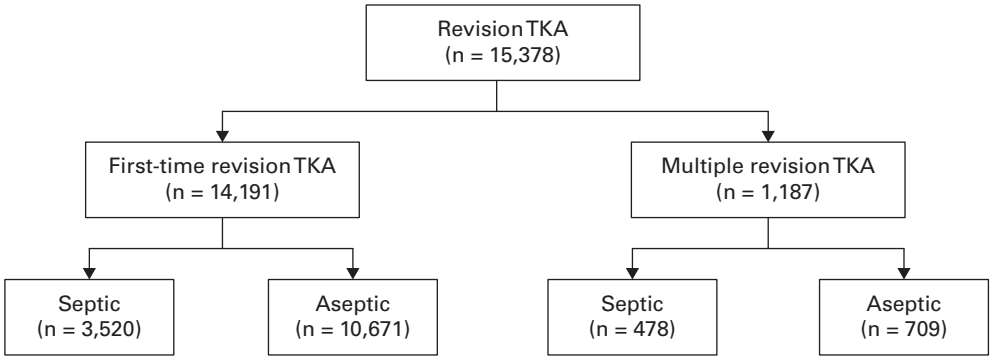

Fig. 1

Revision total knee arthroplasty (TKA) data overview from the German Arthroplasty Registry from 2015 until 2022.

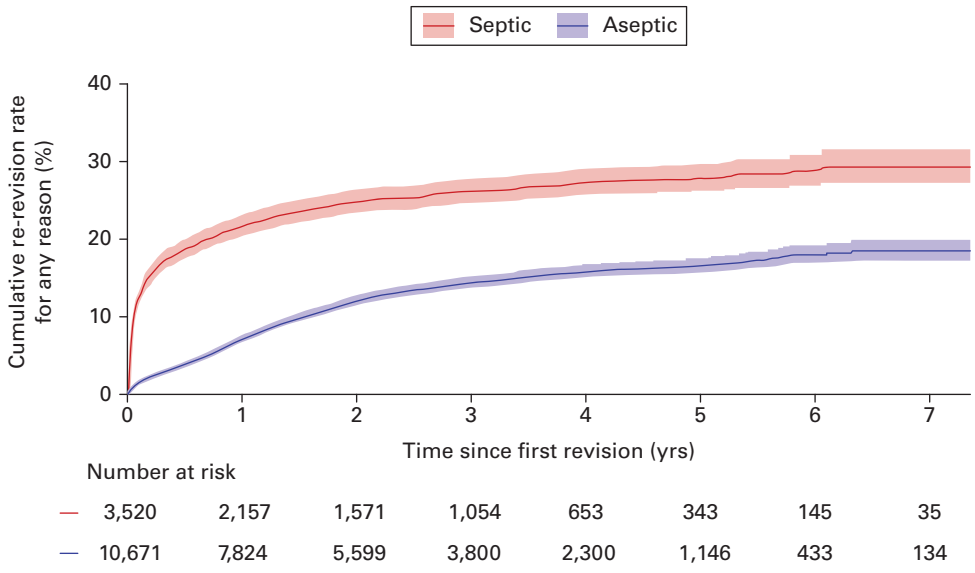

Fig. 2

Cumulative re-revision rate after first revision in total knee arthroplasty.

ment environment. The continuous demographic variables are presented as median and IQR, while categorical variables are presented in number of observations and percentages. The weighted Elixhauser score by van Walraven was calculated using the R package 'comorbidity'. Kaplan-Meier estimates with log-log CIs were used for determining cumulative re-revision and mortality rates up to seven years. Log-rank tests were used to compare the survival distributions of aseptic and septic groups and survival rates at one and seven years.

Results

Re-revision rate after revision TKA. Septic revision TKAs shows a cumulative re-revision rate of 21.7% (95% CI 20.3 to 23.1) within one year, and aseptic of 7.1% (95% CI 6.6 to 7.6). The re-revision rate of the septic patient group rises to 29.3% (95% CI 27.1 to 31.6) in the seventh year, whereas a maximum of 18.4% (95% CI 17.1 to 19.8) is reported in the aseptic patient group. Considering the difference between septic and aseptic patients in distribution over time, 74% of re-revisions occur within the first year for septic patients, and 39% for aseptic patients. After the first year, the re-revision rate increases almost in parallel, as seen in Figure 2. Data are given in Supplementary Table i.

The number of re-revisions is far higher in the multiple-revision TKAs than in first-time revisions. While the re-revision rates in septic multiple-revision TKAs (26.6% (95% CI 22.7 to 31.0)) and aseptic multiple-revision TKAs (12.4% (95% CI 9.9 to 15.3)) are similar to the numbers of first-time revisions in the first year, the maximum of re-revision rate is 46.5% (95% CI 39.5 to 54.1) in septic patients and 36.6% (95% CI 25.5 to 50.6) in aseptic patients. Therefore, the re-revision rate for septic multiple-revision TKAs is much higher than for septic first-time revision TKAs. However, when examining the distribution over time, septic multiple-revision TKAs do not show the steep rise

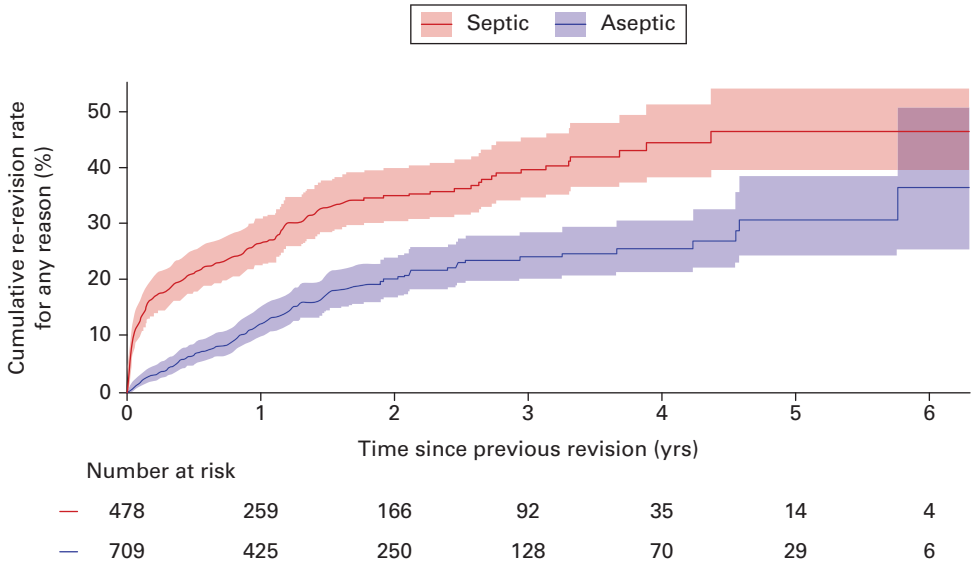

Fig. 3

Cumulative re-revision rate after multiple revision total knee arthroplasties.

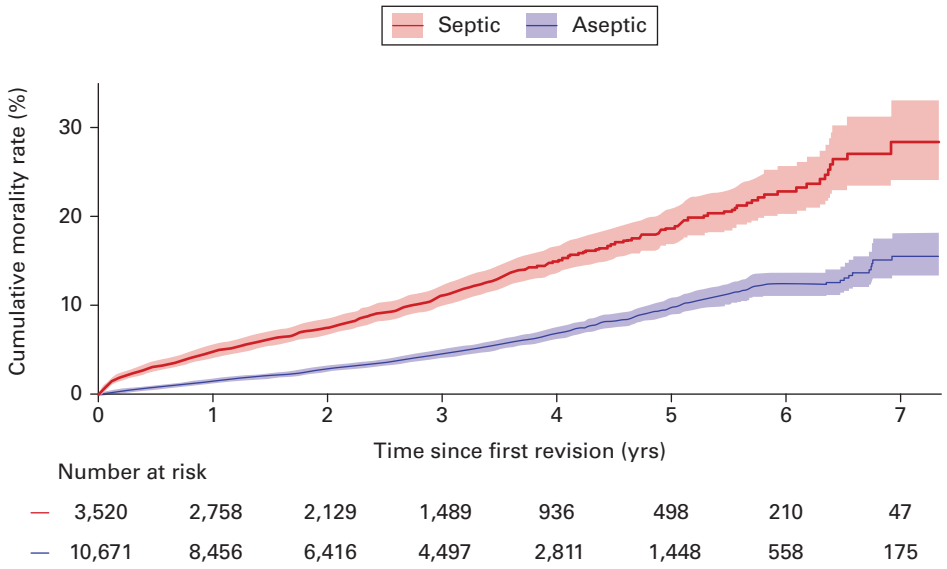

Fig. 4

Cumulative mortality rate after first revision total knee arthroplasty.

in re-revision rates within the first year seen in septic first-time revision TKAs. Instead, they exhibit a steadier increase in re-revision rates up to the fifth year (Figure 3). Data are presented in Supplementary Table ii.

Mortality rate after revision TKA. In the first year, a three-times higher mortality rate was detected in septic (4.9% (95% CI 4.2 to 5.7)) than in aseptic patients (1.5% (95% CI 1.3 to 1.8)), and the difference between the groups increased from year to year. The mean difference in cumulative mortality rate between septic and aseptic revision TKA was 7.9%. The greatest difference in mortality was identified in the seventh year, at 12.8%. In the seventh year, septic patient cases showed a mortality rate of 28.5% (95% CI 24.2 to 33.2) and aseptic 15.7% (95% CI 13.4 to 18.2) (Figure 4). Data are presented in Supplementary Table iii.

Looking at the mortality rate in multiple-revision TKA, we see a similar distribution of the septic and aseptic curves as in first-time revision TKA. In the first year, septic cases have a mortality rate of 5.8% (95% CI 4.0 to 8.5) and aseptic 2.5% (95% CI 1.5 to 4.1). The gap between these two curves increases up to the fifth year and septic cases (29.7% (95% CI

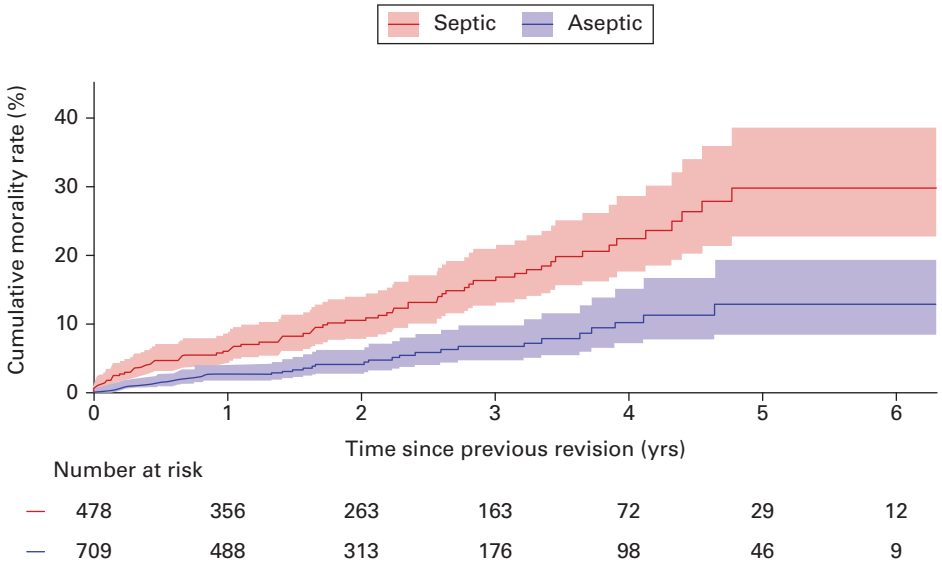

Fig. 5

Cumulative mortality rate after multiple revision total knee arthroplasties.

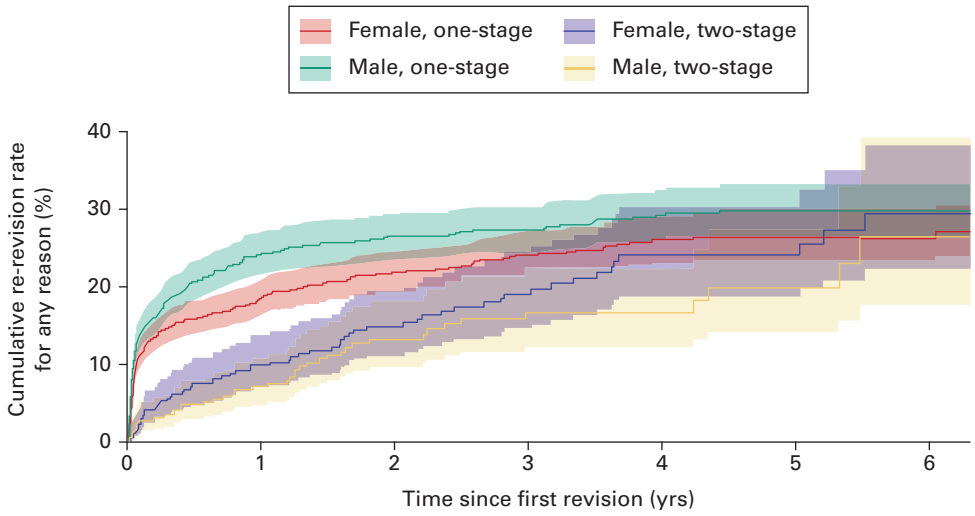

Fig. 6

Re-revision rate after one-stage and two-stage septic first revision total knee arthroplasties. Significant differences were seen between re-revision rate for one- and two-stage revision in males ($p < 0.001$), as well as in females ($p < 0.001$).

22.5 to 38.5)) show a mortality rate twice as high as aseptic cases (12.8% (95% CI 8.4 to 19.2)) (Figure 5). Data are given in Supplementary Table iv.

Re-revision rate after one-stage or two-stage septic revision. The one-stage revisions caused significantly higher re-revision rates in septic revision TKA, especially in the initial years. While female patients present a re-revision rate of 18.6% (95% CI 16.4 to 21.1) after one year following a one-stage revision, only 9.8% (95% CI 7.0 to 13.7) of them undergo a re-revision after septic two-stage revision TKA within the first year. The differences are even greater for male patients: while they have a re-revision rate of 24.3% (95% CI 21.7 to 27.2) in the first year after a one-stage revision, only 7.1% (95% CI 4.6 to 10.7) have undergone a re-revision within the first year after a two-stage revision. However, as shown in Figure 6, the differences in the long-term follow-up continue to converge, especially for female patients. After five years, female patients with one-stage revision show a re-revision rate of 26.4% (95% CI 23.5 to 29.6), compared to 24.1% (95% CI 18.8 to 30.6) for two-stage revision. In contrast, differences remain for males. While male patients with one-stage revision have a re-revision rate of 30.0% (95% CI 26.8 to 33.4) in the five-year follow-up,

male patients with two-stage revision show a re-revision rate of 19.9% (95% CI 14.2 to 27.5).

Discussion

The main finding of the current register-based study of the EPRD is a noteworthy disparity in re-revision rates and mortality between previously published review articles and meta-analyses mainly based on studies from high-volume orthopedic centres and the results from EPRD registry data.[10,11,24,25] More specifically, for septic revision TKA a re-revision rate of 22% within the first year was seen, compared to an aseptic re-revision rate of 7%. Following the first year, only a slight annual increase in cumulative re-revision rate is seen, with a re-revision rate of 29% in the seven-year follow-up for septic revision TKA and 18% for aseptic revision TKA. The five-year survival rate following septic primary revision TKA is 81.2% and 71.5% after seven years, whereas multiple-revision TKA has a survival rate of 70.3% after five years. The first year appeared as the most critical time interval for the survival of the prosthesis, as 74% of all documented revisions in the follow-up of seven years were performed in the first year in the patient group of septic revision TKA. Therefore, improvements in surgery as well as in perioperative care, such as an interdisciplinary approach, improved wound management, antibiotic regimens, preoperative patient health optimization, and treatment are needed, especially for septic revision TKA.

In meta-analysis as well as in other registry studies, a significantly lower re-revision rate of revision TKA compared to the septic revision TKA data from the German registry has been reported.[10,11,24,25] Most of the registry data which are reported on re-revision rates and mortality following revision TKA do not distinguish between septic and aseptic revisions, so our data are only comparable to these numbers to a limited extent. Even if meta-analyses differentiated between septic and aseptic revision TKA, our registry data report much higher failure rates following septic revision TKA than most single-centre studies.[5,24,25] Registry results from the 2024 report of the National Joint Registry, which uses data from England, Wales, Northern Ireland, the Isle of Man, and the States of Guernsey, give an 11.5% re-revision rate after five years for revision TKA, whereas a 15-year re-revision rate of 18.2% is reported.[18,26] In the New Zealand Joint Registry, a yearly re-revision rate of 2.95 per 100 component-years is reported, which is in a seven-year follow-up with 20% in line with the EPRD aseptic revision data.[15] Additionally, the Dutch Joint Registry reports a re-revision rate of 18.3% in the eight-year follow-up.[16] In the report from the American Joint Registry, the re-revision rate of revision TKA is reported with a ten-year re-revision rate between 7% and 12%, depending on age.[19] In other major registries such as Sweden or Australia, no re-revision rate for revision TKA rate is reported in recent annual reports.[17,20] In meta-analysis, reinfection rates of 7% to 19% have been reported,[24,25] whereas only selected single-centre studies such as the results from Theil et al[27] match the reported re-revision rate in the EPRD for septic revision.[24,25]

Re-revision rates in single-centre studies following septic revision TKA reported in the literature show considerable heterogeneity; one single-surgeon study reports an extraordinary five-year re-revision rate of 2.7%,[5] whereas others report a five-year re-revision rate of 39%.[27] Varying prothesis survival rates for revision TKA are reported in the literature, with a 90.6% ten-year survival rate by Hossain et al[28] and a 81.7% survival rate with an average follow-up of 64.8 months by Mortazavi et al.[29]

These differences in re-revision rates might be influenced by multiple factors. Other registries may disproportionately represent high-volume centres with specialized expertise in septic revision TKA, such as the CRIOAC centres in France, potentially leading to more favourable outcomes.[30] Meanwhile, the EPRD captures a broad spectrum of hospitals, including lower-volume centres performing septic revisions, which may contribute to higher reported re-revision rates. Furthermore, differences in infection control strategies, perioperative antibiotic protocols, surgical techniques, and prosthesis selection can impact outcomes.[31,32] The German registry also distinctly categorizes septic and aseptic revisions, whereas some international registries do not consistently differentiate between these categories, leading to variability in reported failure rates. Additionally, access to healthcare services and thresholds for re-revision surgery may differ between countries, influencing the reported rates of failure. Varied data collection methods and practices can lead to differences in reported outcomes,[33] including how complications and revisions are defined and how treatment success is evaluated.[12] Some count a revision surgery due to soft-tissue infection or wound-healing problems as a revision surgery, while others only report a revision surgery if some parts of the prosthesis are changed.[34] Countries with shorter waiting list times may have more timely revisions, leading to differing registry data.[35] Furthermore, structural disparities, differences in healthcare practices, implant supply, underlying regional differences in resistance of bacteria, concomitant comorbidities, health insurance coverage, as well as demographic data of treated patients may also contribute to differences in registry data.[36–38] As an example, Clement et al[39] have shown that male sex, younger age, and revision TKA for septic indication have been associated with greater risk for re-revision. This is consistent with our results, as the proportion of male patients in the cohort of the septic revisions is greater than in the aseptic revisions, and septic revisions also indicate a much higher re-revision rate overall. Despite the aforementioned differences, another main factor is the distribution of septic or aseptic prosthetic failure as a cause for revision TKA. As can be inferred from the reported data, a higher proportion of septic revision TKA compared to aseptic leads to a higher re-revision rate, especially in the first year. This increase in re-revision rate within the first year necessitates the formation of interdisciplinary centres with high case numbers to optimize the crucial perioperative management of PJIs.[40] Moreover, early detection of PJI with the help of appropriate technical procedures in infection, diagnosis, and definition criteria is crucial for adequate treatment in septic revision surgery.[41,42]

PJI is the most common indication for early revision, and it is also associated with a higher risk of re-revision following septic revision TKA.[29] These results are reflected in the EPRD data, as septic revisions account for 25% at the first revision TKA and 40% at the multiple-revision TKA.

Looking at mortality, the results indicate a higher cumulative mortality rate for septic revision TKA compared to aseptic revision TKA. In contrast to the re-revision rate, a linear increase of cumulative mortality rather than an accumulation within the first year was recorded. A study by Boddapati et al[43] reflects a higher risk of complications, sepsis, and death for septic compared to aseptic revision TKA. These findings are reflected in the EPRD data and are in line with the literature.[44,45] Whereas an almost linear increase in cumulative mortality is reported for both septic and aseptic re-revision, cumulative mortality for septic revision is nearly twice that for aseptic revision TKA. These results might partially be explained by demographic differences in the two cohorts. The patients with septic revision TKA are on average three years older, a higher percentage of them are male, and they have more comorbidities, as reflected in a higher Elixhauser score. These differences in the cohorts are known risk factors for higher re-revision rate as well as higher cumulative mortality.[44,46] Despite demographic differences, PJI is a severe medical condition which could be accompanied by immunodeficiency and may lead to sepsis, multiorgan dysfunction, and septic shock, all of which are life-threatening conditions. These complications, if not managed promptly and effectively, can result in a significant increase in mortality risk.[47] In contrast to the observed five-year survival rate of 70.3% after septic revision TKA, the expected five-year survival probability for the general German male population at the age of 69 years is approximately 87.7%, and for the female population 92.8%, based on the German Period Life Table 2021/2023.[48] When comparing the five-year survival rate of septic revision arthroplasty (70.3%) with that of the most common tumours, the impact of PJI becomes even more apparent, as the five-year survival rate for prostate cancer is 98.6%, 90% for breast cancer, 77% for bladder cancer, 64% for colon cancer, and 60% for leukaemia.[49] These findings underline the importance of rigorous infection prevention strategies, meticulous surgical techniques, early detection, and adequate therapy algorithms for PJIs in order to mitigate the risk of re-revision and mortality for revision TKA.

One limitation of this study is that the EPRD only covers approximately 70% of prosthetic surgeries and revision surgeries performed annually in Germany. This is due to the voluntary participation of hospitals and the fact that not all health insurance companies are involved. However, it is worth noting that almost all hospitals with a high number of cases are included in the EPRD, which may have led to reduced complication rates in the presented results. Diseases and comorbidities that only manifested after the implantation of the arthroplasty could not be recorded. Only revision TKAs related to the implant were included, but no periprosthetic fractures without implant exchange. A strength of this study is the comprehensive data collection process of the EPRD, the result of which is that the data generated allowed for nearly 100% follow-up of 15,378 patients who underwent revision TKA over a period of up to seven years.

In conclusion, the re-revision rates after septic revision TKA published to date are significantly lower compared to our retrieved re-revision rates, whereas published data for mortality following revision TKA are consistent with our results. To prevent early re-revisions after septic revision TKA, it is crucial to optimize perioperative treatment, as 74% of septic re-revisions occur within the first year.

Take home message

- Septic revision total knee arthroplasty (TKA) is associated with substantially higher re-revision rates and mortality compared to aseptic revision TKA.
- Notably, 74% of septic re-revisions occur within the first postoperative year, emphasizing this period as the most critical.
- The observed five-year survival after septic revision TKA (70.3%) is significantly lower than expected population survival, underscoring the urgent need for optimized perioperative care and infection prevention strategies.

Supplementary material

Tables providing Kaplan-Meier estimates with 95% CIs for cumulative re-revision and mortality rates after first and multiple revision total knee arthroplasties, stratified by septic and aseptic indications.

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