EFORT open reviews

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

KNEE

# Systematic review and meta-analysis of single-stage versus two-stage revision for periprosthetic joint infection after knee arthroplasty: a call for a randomised trial

Chengxin Xie*, Wenjun Pan*, Shouli Wang*, Xueli Yan and Hua Luo

Department of Orthopedics, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, Taizhou, Zhejiang, China
*(C Xie, W Pan and S Wang contributed equally to this work).

Correspondence should be addressed to H Luo Email luoh5367@enzemed.com

- *Purpose:* Knee arthroplasty is an effective treatment for severe knee degeneration; however, periprosthetic joint infection (PJI) is one of its serious complications. Single- and two-stage revision are common treatments, but few studies have compared single- and two-stage revision for PJI after knee arthroplasty. This study aimed to compare the reinfection and reoperation rates of single- and two-stage revision through meta-analysis.
- *Methods:* The review process was conducted according to the PRISMA guidelines. We searched the PubMed, Medline, Embase and Cochrane Central Register of Controlled Trials databases for trials comparing single- and two-stage revision for PJI after knee arthroplasty from the respective inception dates to April 2023. Two researchers individually screened the studies, performed the literature quality evaluation and data extraction and used Stata 17 software for data analysis.
- *Results:* The meta-analysis showed that the reinfection rate was significantly lower in the single-stage revision group than in the two-stage revision group. While the reoperation rates demonstrated no statistically significant difference between the two groups. We presented descriptive results because the discrepancies in the knee function scores and data reported in the studies meant that these data could not be combined in the meta-analysis.
- *Conclusion:* Based on the available research, single-stage revision is a reliable option for PJI after knee arthroplasty. However, when developing the best treatment strategy, it is still necessary to consider the individual circumstances and needs of the patient, as well as the risks of postoperative rehabilitation and complications.

Keywords: periprosthetic joint infection; knee arthroplasty; single-stage revision; two-stage revision

## Introduction

Knee arthroplasty is widely used to treat severe knee degeneration and is considered an effective measure that improves the quality of life and restores the mobility of patients (1, 2). However, despite the excellent performance of knee arthroplasty in most patients, postoperative periprosthetic joint infection (PJI) (an infection that occurs in joint replacement) remains concerning as a rare but serious complication (3).

Published by Bioscientifica Ltd.
www.efortopenreviews.org

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

PJI is identified if: there is a sinus tract linked to the prosthesis, a pathogen is isolated from two separate joint samples, or four out of six specific criteria are met, including elevated blood markers, increased joint fluid cell counts, presence of joint purulence or positive culture or histologic findings from joint tissue (4). Infection can lead to prosthesis loosening, bone defects and even life-threatening conditions in severe cases (5). With advances in surgical techniques and improvements in surgical conditions, PJI currently occurs in less than 1% of patients with knee arthroplasty (6).

For patients with PJI after knee arthroplasty, it is critical to choose the most appropriate treatment strategy. Two-stage revision surgery was previously considered the gold standard for PJI (2); however, the ideal time interval between surgeries, choice of antimicrobial agent and timing of treatment remain controversial. Furthermore, the recurrence rate of PJI varies widely, and some patients are medically ill and may not tolerate a second surgery. In recent years, the single-stage revision technique has received widespread attention worldwide, and its application is increasing (7, 8). The shortcomings of two-stage revision can be avoided by performing single-stage revision, which is more conducive to the functional recovery of the affected limb, reduces the occurrence of complications, overall cost and surgical trauma, and improves the level of patient satisfaction (9). Blom *et al.* highlighted that single-stage revision showed cost-effectiveness over an 18-month follow-up period and is increasingly being adopted (10). Additionally, some centres report that single-stage revision has a success rate comparable to two-stage revision (11, 12, 13). However, there is a lack of clear evidence to identify the superior surgical modality between single- and two-stage revision for PJI after knee arthroplasty. Although some small clinical studies have explored this issue, their conclusions are inconsistent and limited by small sample sizes. Therefore, this review aimed to systematically pool and synthesise existing clinical research data by conducting a comprehensive meta-analysis to compare the efficacy of single- and two-stage revision for PJI after knee arthroplasty. Through this comprehensive analysis, we hope to provide more accurate and effective treatment recommendations for medical teams to optimise treatment strategies for patients with PJI after knee replacement, and contribute to the recovery and health improvement of patients.

## Materials and methods

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, this meta-analysis was performed in agreement. (14) The protocol for this meta-analysis was registered on PROSPERO (Registration No: CRD 42022384299).

### Inclusion criteria

(i) Study type: randomised controlled trial, cohort study or case–control study. (ii) Study population: patients with infected knee arthroplasty. (iii) Intervention and control: single-stage in the treatment group and two-stage in the control group. (iv) Outcome index: reinfection rate, reoperation rate and knee function.

### Exclusion criteria

(i) Letters, meetings, case reports, reviews or republished studies; (ii) studies lacking a control group; (iii) patients with septic arthritis or tuberculous arthritis; (iv) patients did not undergo second-stage in the two-stage group.

### Outcomes

The primary outcome was the incidence of reinfection. A secondary outcome was the incidence of reoperation and knee function.

### Search strategy

Two of the authors performed the search in PubMed, Medline, EMBASE and the Cochrane Central Register of Controlled Trials from the inception dates to April 30, 2023, using the keywords '(periprosthetic joint infection or prosthetic joint infection) and (Two-stage or 2-stage or two stage or second-stage or double-stage) and (Single-stage or one-stage or 1-stage) and knee and (unhealed or infection or reoperate* or revise or function or knee score or range of motion)'. No language restrictions were applied during the search.

### Study selection

Two researchers screened the retrieved literature strictly and individually against inclusion and exclusion criteria. In cases where two researchers do not agree during the literature screening process, it will be left to the senior researcher.

### Data collection process

Data on relevant outcome measures were extracted from the literature that met the inclusion criteria, including author year, country, age, study design, follow-up and outcomes by two researchers individually. If two researchers do not agree during the data collection, it will be left to the senior researcher.

### Assessment of risk of bias and quality of evidence

Two researchers independently assessed the quality of all included trials based on Cochrane risk-of-bias

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

criteria (15). The Newcastle–Ottawa scale (NOS) was used to evaluate the literature quality of the retrospective studies (16). We also examined the quality of evidence for outcomes using the grading of recommendations assessment, development, and evaluation (GRADE) approach (17).

## Data synthesis

The meta-analysis was performed using Stata (version 17; StataCorp, 2021) software. Heterogeneity was assessed by using the *Q* test and $I^2$ value calculation. If heterogeneity was not present ($P > 0.1$ and $I^2 < 50\%$), the data were combined using a fixed-effect model. The random-effects model was used if heterogeneity was present ($P < 0.1$ or $I^2 > 50\%$). In the investigation of potential publication bias, the Harbord test was employed to assess the presence of a small-study effect. Odds ratio (OR) (method of Mantel–Haenszel heterogeneity) and their associated 95% CIs were used to assess outcomes, with a *P*-value less than 0.05 indicating a statistically significant difference.

## Sensitivity analyses

We performed a sensitivity analysis on a case-by-case exclusion basis.

# Results

After identifying total of 279 studies, 142 duplicates were removed, and 99 irrelevant studies were excluded based on the titles and abstracts. The full text of 38 articles was read, and 27 retrospective studies were included in the systematic review (8, 11, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42). Due to six studies discussing hip and knee replacements (38, 38, 39, 40, 41, 42), we were unable to separate and extract knee-specific data for inclusion in our article. Consequently, we only included them in the systematic review, resulting in a final meta-analysis comprising 21 studies (8, 11, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36). The literature screening process is shown in Fig. 1. All included studies had NOS scores of greater than or equal to 6 points, indicating that they are high-quality studies. The basic characteristics of the included studies are shown in Table 1.

## Reinfection rate

The 18 trials included in this study reported the reinfection rates after the two surgical regimens (11, 19, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36). As there was no heterogeneity between the results

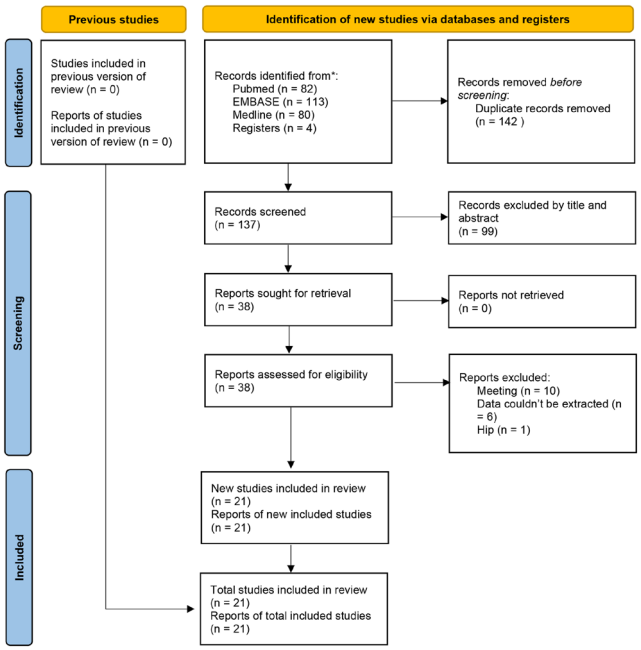


**Figure 1**

Flow diagram for search and selection of included studies.

($I^2$ = 0%), the fixed-effect model was used to pool the results. The reinfection rate was significantly lower after single-stage revision than two-stage revision (OR = 0.72, 95% CI: 0.55–0.96, *P* = 0.023, Fig. 2).

## Reoperation rate

A total of 10 studies reported the reoperation rates (8, 18, 21, 24, 26, 28, 30, 34, 35, 36). As there was no heterogeneity between study results ($I^2$ = 0%), the fixed-effect model was used to pool the results. There was no statistically significant difference in the rate of reoperation after single-stage revision compared with two-stage revision (OR = 0.95, 95% CI: 0.77–1.17, P = *0*.240, Fig. 3).

## Knee function

Seven studies reported the postoperative knee function (18, 19, 20, 24, 30, 31, 34). The findings regarding the effects of single- and two-stage revision on knee function scores were heterogeneous and inconsistent and could not be combined in a meta-analysis. Therefore, we have presented the results descriptively and provided a brief summary of the study findings. Baker *et al.* found that the Oxford Knee Score did not significantly differ between the two groups (18). Bauer *et al.* also reported no significant difference between the two groups in the knee score but did not report the SD. and CIs (19). Capuano *et al.* found no difference in Knee Society Scores (KSS) between the two groups at the final follow-up (20). Haddad *et al.* showed that the

**Table 1** Characteristics of included studies.

| Study | Country | Date range | Design | FU | Age* | | | Subjects, *n* | | Outcomes | NOS score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | One stage | Two stage | One stage | Two stage | | |
| Baker *et al.* (18) | UK | 2008–2010 | RCS | 6–12 m | | 69.4 ± 10.7 | 70.3 ± 8.9 | 33 | 89 | Reoperation, knee score, satisfaction, complications | 8 |
| Bauer *et al.* (19) | France | NA | RCS | 2 Y | | 71.8 | 68.3 | 30 | 77 | Reinfection rate, knee score | 8 |
| Capuano *et al.* (20) | Italy | 2013–2015 | RCS | 29.3 M† | | - | - | 17 | 17 | Reinfection, length of hospital stay, KSS | 9 |
| Chalmers *et al.* (21) | USA | 2009–2017 | RCS | 1–9 Y | 51–87 | | | 1 | 4 | Reinfection, reoperation | 9 |
| Crego *et al.* (22) | Germany | NA | RCS | NA | | NA | NA | 20 | 45 | Reinfection | 9 |
| Cury *et al.* (23) | Brazil | 2008–2010 | RCS | NA | | NA | NA | 6 | 7 | Reinfection, functionality score, life scores | 6 |
| Haddad *et al.* (24) | UK | 2004–2009 | RCS | 3–9 Y | | 63 (48–87) | 68 (45–85) | 28 | 74 | Reinfection, reoperation, knee score, | 7 |
| Kheir *et al.* (25) | USA | 1991–2014 | RCS | 12 M | 66.3 (39–85) | | | 2 | 36 | Failure rate | 9 |
| Klemt *et al.* (26) | USA | 2015–2018 | RCS | NA | | 64.9 ± 9.2 | 65.4 ± 8.6 | 44 | 88 | Reinfection, reoperation, readmission, PROM | 8 |
| Laffer *et al.* (27) | Switzerland | 1988–2003 | RCS | 2–193 M | 70.1 (43.5–90.1) | | | 2 | 13 | Success rate | 8 |
| Lenguerrand *et al.* (8) | Multicentre | 2003–2014 | RCS | NA | | 68 ± 10 | 69 ± 9 | 489 | 2377 | Reoperation | 9 |
| Leta *et al.* (28) | Norway | 1994–2016 | RCS | 1 Y | | 69 ± 9.5 | 69 ± 9.7 | 72 | 243 | Reinfection, reoperation, survival rate, mortality rate | 9 |
| Li *et al.* (29) | China | 2003–2014 | RCS | 12–158 M | 64.4 ± 9.5 | | | 22 | 87 | Reinfection, complication | 9 |
| Massin *et al.* (30) | France | 2005–2010 | RCS | 2 Y | | 71 (63–76) | 67 (59–73) | 108 | 177 | Reinfection, reoperation, knee score | 8 |
| Matar *et al.* (11) | UK | 2003–2018 | RCS | 2.0–17.6 Y | | 71.8 ± 9.8 | 70.5 ± 10.2 | 82 | 161 | Success rate, survivorship rate | 8 |
| Ribes *et al.* (31) | France | 2009–2014 | RCS | 1 Y | | 72.6 ± 9.2 | 69.5 ± 9.1 | 21 | 41 | Reinfection, knee score | 9 |
| Ritter and Farris (32) | Indiana | 1969–2004 | RCS | 1 Y | 65.4 ± 12.2 | | | 3 | 51 | Success rate | 9 |
| Shanmugasundaram *et al.* (33) | Multicentre | 2008–2011 | RCS | NA | | NA | NA | 5 | 16 | Success rate | 6 |
| Siddiqi *et al.* (34) | USA | 2012–2017 | RCS | 2 Y | | NA | NA | 57 | 137 | Reinfection, reimplantation, reoperation rates, success rate, ROM | 9 |
| Tuecking *et al.* (35) | Germany | 2013–2019 | RCS | 18–92 M | | 65.0 ± 10.2 | 69.3 ± 11.1 | 15 | 48 | Reinfection, reoperation, implant survival | 9 |
| Van den Kieboom *et al.* (36) | USA | 2010–2018 | RCS | 2.5–22.9 Y | | 67.9 ± 10.6 | 65.0 ± 11.0 | 18 | 48 | Reinfection, reoperation, amputation, readmission, mortality, hospital stay | 9 |

*Data are mean ± s.d. or range; †Mean value.

NOS, Newcastle–Ottawa scale; FU, follow-up; M, month; Y, year; NA, not applicable; RCS, retrospective cohort study; KSS, knee society scores; PROM, patient-reported outcome measures; ROM, range of motion.

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

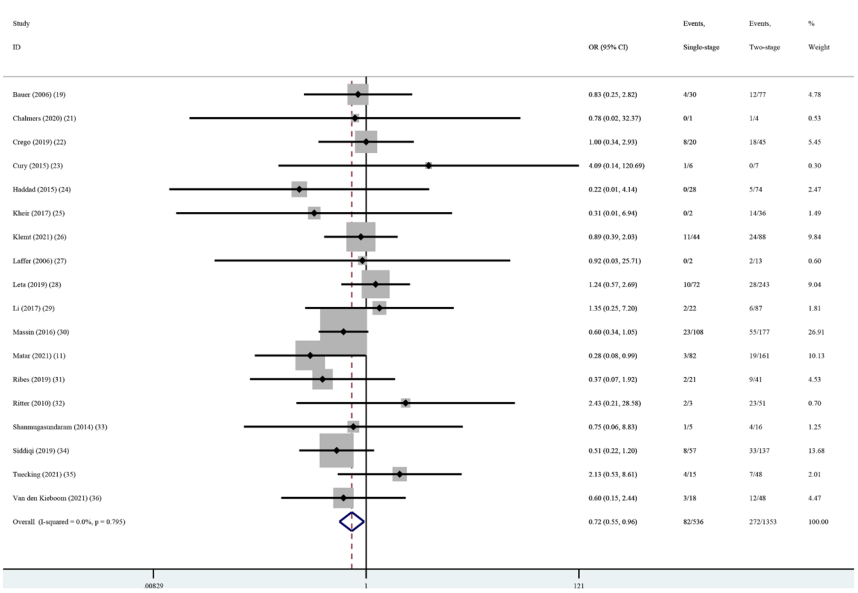


**Figure 2**

Reinfection rate in included studies.

knee function was better after single-stage revision than after two-stage revision based on the KSS but only showed the mean and range (24). Massin *et al.* reported that international KSS were similar between the two groups (30). Ribes *et al.* found that the international KSS and Knee Injury and Osteoarthritis Outcome Score were better in the single-stage revision group than the two-stage revision group (31). Siddiqi *et al.* showed that the postoperative knee range of motion did not significantly differ between the two groups (34). The detail of knee joint function scores for each study are shown in Table 2.

## Sensitivity analysis

The remaining studies were combined using the OR values when any individual study was excluded. No individual study had a significant impact on the results (Fig. 4).

## Risk of bias

As shown in Fig. 5, the funnel plots showed some asymmetry, which may suggest the presence of publication bias. However, the Harbord test showed no evidence of a small study effect regarding reinfection ($P = 0.66$) and reoperation ($P = 0.24$).

# Discussion

Our meta-analysis results suggest that the reinfection rate is significantly lower after single-stage revision than after two-stage revision for PJI after knee arthroplasty. Two-stage revision has long been considered the gold standard for PJI, but it significantly reduces the activity time of patients, predisposing them to bone degeneration and periprosthetic fractures (43). Our

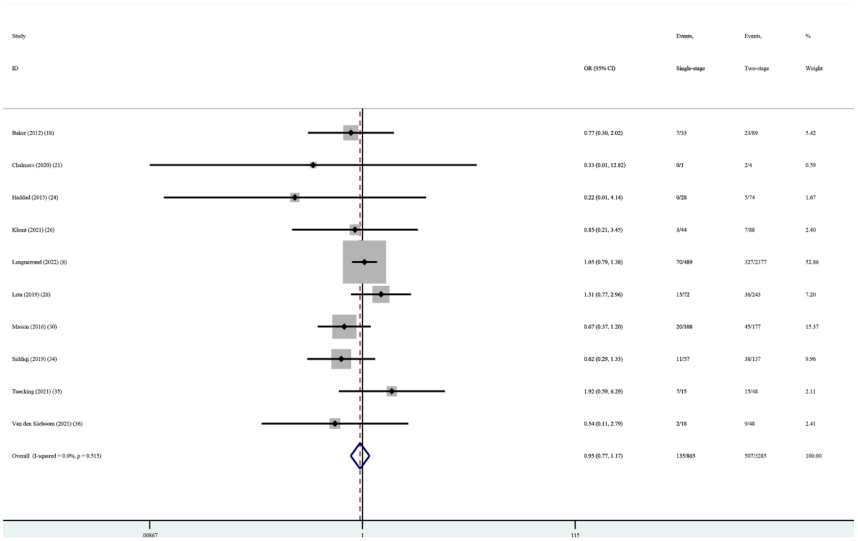


**Figure 3**

Reoperation rate in included studies.

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

**Table 2** The results of the studies about knee function. Data are presented mean ± s.d. or as mean (range).

| | Study | | | | | | |
|---|---|---|---|---|---|---|---|
| | (18) | (19) | (20) | (24) | (30) | (31) | (34) |
| OKS | | | | | | | |
| One stage | 24.9 ± 13.1 | | | | | | |
| Two stage | 22.8 ± 12.4 | | | | | | |
| KSS | | | | | | | |
| One stage | | 75.5 | 78 ± 6.1 | 88 (38–97) | | | |
| Two stage | | 74.8 | 77.3 ± 6.4 | 76 (29–93) | | | |
| IKS | | | | | | | |
| One stage | | | | | 88.6 ± 9.4 | 51.05 | |
| Two stage | | | | | 89.7 ± 2 | 39.75 | |
| KOOS | | | | | | | |
| One stage | | | | | | 10 | |
| Two stage | | | | | | 8.75 | |
| SF-12 | | | | | | | |
| One stage | | | | | | 39.1 | |
| Two stage | | | | | | 34.41 | |
| Flexion range | | | | | | | |
| One stage | | 92.5 (10–125) | | | 97 ± 18 | | 106.6 ± 23.2 |
| Two stage | | 93 (20–125) | | | 91 ± 24 | | 104.0 ± 18.1 |

OKS, Oxford Knee Score; IKS, International Knee Society; KSS, Knee Society Score; KOOS, Knee Injury and Osteoarthritis Outcome Score; SF-12, Short form-12 questionnaire.

results suggest that single-stage revision is no less effective than two-stage revision and has a lower rate of infection recurrence. However, the studies included in our review were retrospective studies with some bias in the process of patient allocation, as the decision whether to perform single- or two-stage revision is made at the discretion of the surgeon after considering all the details of the patient and the surgical site. The need for larger-scale, randomised clinical trials to validate our conclusions and to comprehensively address potential biases in future investigations. Besides, single-stage revision can avoid the shortcomings of two-stage revision, reduce the hospitalisation time and cost, reduce the number of surgeries and improve patient satisfaction and quality of life (44, 45). Although recurrent infection seriously decreases quality of life, not all recurrent infections require reoperation; mild infections can be improved with anti-infective treatment. Our analysis found no difference in the reoperation rate after the two treatment modalities. Due to differences in reporting across studies, we were unable to pool the knee function data; therefore, we could only describe the results. Although descriptive results are still useful to understand trends in knee function scores in the single- and two-revision groups, future studies should increase the sample sizes and add data from more independent studies to fully assess the knee function of patients with PJI after knee arthroplasty.

Previous meta-analyses of single- and two-stage revision for PJI after knee arthroplasty have been reported, but most have been single-arm meta-analyses that systematically reviewed the recurrence of infection after both surgical modalities (46, 47, 48). In contrast, we included studies that compared single- versus two-stage revision, providing more specific and reliable estimates of the outcomes of single- and two-stage revision for PJI after knee arthroplasty. Nagra *et al.* also compared the efficacy of single- and two-stage revision in the treatment of PJI in 2015 (49), but their study included only five cohort studies of 231 patients. Based on the included studies, their conclusion was

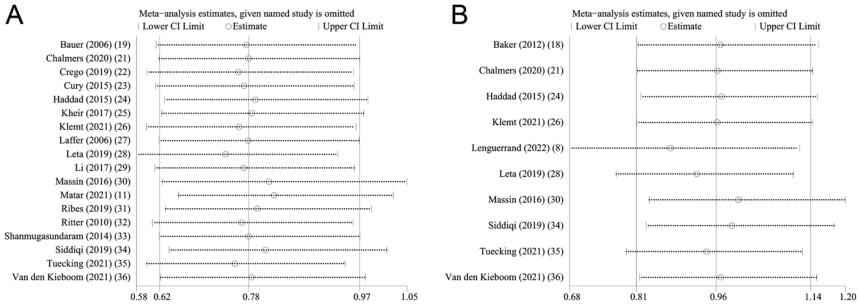


**Figure 4**

The result of sensitivity analysis of reinfection (A) and reoperation (B).

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

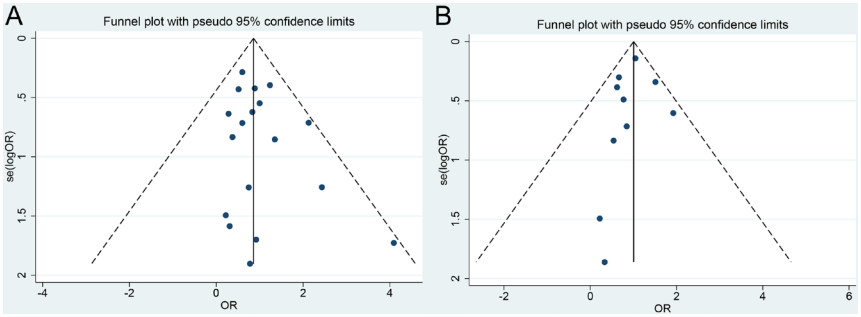


**Figure 5**

Funnel plot of the included studies in this meta-analysis for the incidence of reinfection (A) and reoperation (B).

that there was no difference in the re-infection rates between single-stage and two-stage revisions. However, their subgroup analysis revealed a divergence: among studies published before 2000 (including two studies), no difference was observed between single-stage and two-stage revisions. Contrastingly, among studies published after 2000 (comprising three studies), the re-infection rate was significantly lower in single-stage revisions compared to two-stage revisions. Since then, more studies comparing single- and two-stage revision have been published. As our results are based on a larger number of studies (21 studies, 4911 patients), our conclusion indicates that the re-infection rate in single-stage revisions is significantly lower than in two-stage revisions. Our study possesses stronger statistical power, robustly demonstrating these findings. Technological advancements, accumulated expertise and further optimisation of surgical techniques might contribute to the increased success rates in single-stage revisions. Additionally, we conducted a comparative analysis of reoperation rates between the two procedures, which was not performed in the study by Nagra *et al.*

### Strengths and limitations

The present study has some strengths. First, we included a large number of studies (four times more than were included in the previous meta-analysis (49)) and compared the effectiveness of single- and two-stage revision in more detail. Secondly, in contrast to previous reviews (46, 47, 48), we used a two-arm meta-analysis approach that enabled the use of quantitative estimates to compare the effectiveness of the two revision strategies. Thirdly, our results remained robust in several sensitivity analyses.

Our study also had certain limitations. First, there was bias in the selection of the revision strategy. Capuano *et al.* used implants coated with an antibiotic-loaded hydrogel for single-stage revision but used uncoated implants for two-stage revision (20). Li *et al.* performed single-stage revision in cases with negative cultures and performed two-stage revision in cases with positive cultures (29). Secondly, the included studies were retrospective, and there was a lack of randomised controlled trials with large samples, resulting in reduced confidence in the study results. Thirdly, when discussing the advantages and disadvantages of single- and two-stage revisions, we only considered reinfection rates, reoperation rates and knee function scores, and did not perform a comprehensive analysis of other relevant indicators such as patient satisfaction, quality of life and complication rates. Future studies should consider more factors to fully assess the advantages and disadvantages of the two surgical modalities.

## Conclusion

The existing research suggests that single-stage revision surgery is a reliable option for PJI after knee arthroplasty. In clinical practice, medical professionals should carefully select the appropriate surgical method based on factors such as the individual characteristics of the patient, severity of infection and available surgical technology. We hope that our results will provide useful guidance for clinical decision-making and contribute to further improving the treatment outcomes and quality of life of patients with PJI after knee arthroplasty. Through continuous in-depth research, we have the potential to provide patients with safer and more effective treatment options, thereby promoting their recovery and wellbeing.

**ICMJE Conflict of Interest Statement**
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

**Funding Statement**
This work did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

**Author contribution statement**
CX and HL collected data, performed data analysis, interpreted results, and wrote the first draft of the manuscript. WP and SW reviewed the protocol, screened articles, extracted data, and reviewed the results and manuscript. XY and HL contributed to the systematic review protocol and critically reviewed the results and manuscript. HL contributed to the protocol development and reviewed the manuscript. All authors contributed to the conception and design of the study and reviewed all documents and materials.

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

## References


1 Garner AJ, Dandridge OW, van Arkel RJ & Cobb JP. The compartmental approach to revision of partial knee arthroplasty results in nearer-normal gait and improved patient reported outcomes compared to total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy* 2023 **31** 1143–1152. (https://doi.org/10.1007/s00167-021-06691-9)

2 Mahendira L, Jones C, Papachristos A, Waddell J & Rubin L. Comparative clinical and cost analysis between surgical and non-surgical intervention for knee osteoarthritis. *International Orthopaedics* 2020 **44** 77–83. (https://doi.org/10.1007/s00264-019-04405-y)

3 Nelson SB, Pinkney JA, Chen AF & Tande AJ. Periprosthetic joint infection: current clinical challenges. *Clinical Infectious Diseases* 2023 **77** e34–e45. (https://doi.org/10.1093/cid/ciad360)

4 Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, Garvin KL, Mont MA, Wongworawat MD & Zalavras CG. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clinical Orthopaedics and Related Research* 2011 **469** 2992–2994. (https://doi.org/10.1007/s11999-011-2102-9)

5 Chuang CA, Lee SH, Chang CH, Hu CC, Shih HN, Ueng SWN & Chang Y. Application of structural allogenous bone graft in two-stage exchange arthroplasty for knee periprosthetic joint infection: a case control study. *BMC Musculoskeletal Disorders* 2022 **23** 325. (https://doi.org/10.1186/s12891-022-05228-6)

6 Finley R, Glass-Kaastra SK, Hutchinson J, Patrick DM, Weiss K & Conly J. Declines in outpatient antimicrobial use in Canada (1995–2010). *PLoS One* 2013 **8** e76398. (https://doi.org/10.1371/journal.pone.0076398)

7 Li Y, Zhang X, Ji B, Wulamu W, Yushan N, Guo X & Cao L. One-stage revision using intra-articular carbapenem infusion effectively treats chronic periprosthetic joint infection caused by Gram-negative organisms. *Bone and Joint Journal* 2023 **105–B** 284–293. (https://doi.org/10.1302/0301-620X.105B3.BJJ-2022-0926.R1)

8 Lenguerrand E, Whitehouse MR, Kunutsor SK, Beswick AD, Baker RP, Rolfson O, Reed MR & Blom AW. Mortality and re-revision following single-stage and two-stage revision surgery for the management of infected primary knee arthroplasty in England and Wales: evidence from the National Joint Registry. *Bone and Joint Research* 2022 **11** 690–699. (https://doi.org/10.1302/2046-3758.1110.BJR-2021-0555.R1)

9 Kildow BJ, Della-Valle CJ & Springer BD. Single vs 2-stage revision for the treatment of periprosthetic joint infection. *Journal of Arthroplasty* 2020 **35** S24–S30. (https://doi.org/10.1016/j.arth.2019.10.051)

10 Blom AW, Beswick AD, Burston A, Carroll FE, Garfield K, Gooberman-Hill R, Harris S, Kunutsor SK, Lane A, Lenguerrand E, *et al*. *Programme Grants for Applied Research. Infection after Total Joint Replacement of the Hip and Knee: Research Programme Including the INFORM RCT*. Southampton, UK: National Institute for Health and Care Research; 2022. (https:doi.org/10.3310/HDWL9760)

11 Matar HE, Bloch BV, Snape SE & James PJ. Outcomes of single- and two-stage revision total knee arthroplasty for chronic periprosthetic joint infection: long-term outcomes of changing clinical practice in a specialist centre. *Bone and Joint Journal* 2021 **103–B** 1373–1379. (https://doi.org/10.1302/0301-620X.103B8.BJJ-2021-0224.R1)

12 Tibrewal S, Malagelada F, Jeyaseelan L, Posch F & Scott G. Single-stage revision for the infected total knee replacement: results from a single centre. *Bone and Joint Journal* 2014 **96–B** 759–764. (https://doi.org/10.1302/0301-620X.96B6.33086)

13 Ji B, Li G, Zhang X, Xu B, Wang Y, Chen Y & Cao L. Effective single-stage revision using intra-articular antibiotic infusion after multiple failed surgery for periprosthetic joint infection: a mean seven years' follow-up. *Bone and Joint Journal* 2022 **104–B** 867–874. (https://doi.org/10.1302/0301-620X.104B7.BJJ-2021-1704.R1)

14 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J & Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Medicine* 2009 **6** e1000100. (https://doi.org/10.1371/journal.pmed.1000100)

15 Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP & Thomas J. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database of Systematic Reviews* 2019 **10** ED000142. (https://doi.org/10.1002/14651858.ED000142)

16 Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M & Tugwell P, eds. *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses*. 2014. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

17 Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ & GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008 **336** 924–926. (https://doi.org/10.1136/bmj.39489.470347.AD)

18 Baker P, Petheram TG, Kurtz S, Konttinen YT, Gregg P & Deehan D. Patient reported outcome measures after revision of the infected TKR: comparison of single versus two-stage revision. *Knee Surgery, Sports Traumatology, Arthroscopy* 2013 **21** 2713–2720. (https://doi.org/10.1007/s00167-012-2090-7)

19 Bauer T, Piriou P, Lhotellier L, Leclerc P, Mamoudy P & Lortat-Jacob A. Results of reimplantation for infected total knee arthroplasty: 107 cases. *Revue de Chirurgie Orthopédique et Reparatrice de l'Appareil Moteur* 2006 **92** 692–700. (https://doi.org/10.1016/s0035-1040(06)75930-x)

20 Capuano N, Logoluso N, Gallazzi E, Drago L & Romanò CL. One-stage exchange with antibacterial hydrogel coated implants provides similar results to two-stage revision, without the coating, for the treatment of peri-prosthetic infection. *Knee Surgery, Sports Traumatology, Arthroscopy* 2018 **26** 3362–3367. (https://doi.org/10.1007/s00167-018-4896-4)

21 Chalmers BP, Kapadia M, Chiu YF, Henry MW, Miller AO & Carli AV. Treatment and outcome of periprosthetic joint infection in unicompartmental knee arthroplasty. *Journal of Arthroplasty* 2020 **35** 1917–1923. (https://doi.org/10.1016/j.arth.2020.02.036)

22 Crego-Vita D, Sánchez-Pérez C, Espigares-Correa A & Aedo-Martín D. Total knee arthroplasty infection, what is the best strategy for better functional outcomes?. *Acta Ortopédica Mexicana* 2019 **33** 297–302. (https://doi.org/10.35366/OR195G).

23 Cury Rde P, Cinagawa EH, Camargo OP, Honda EK, Klautau GB & Salles MJ. Treatment of infection after total knee arthroplasty. *Acta Ortopédica Brasileira* 2015 **23** 239–243. (https://doi.org/10.1590/1413-785220152305138774)

24 Haddad FS, Sukeik M & Alazzawi S. Is single-stage revision according to a strict protocol effective in treatment of chronic knee arthroplasty infections? *Clinical Orthopaedics and Related Research* 2015 **473** 8–14. (https://doi.org/10.1007/s11999-014-3721-8)

25 Kheir MM, Tan TL, Higuera C, George J, Della Valle CJ, Shen M & Parvizi J. Periprosthetic joint infections caused by enterococci have poor outcomes. *Journal of Arthroplasty* 2017 **32** 933–947. (https://doi.org/10.1016/j.arth.2016.09.017)

26 Klemt C, Tirumala V, Oganesyan R, Xiong L, van den Kieboom J & Kwon YM. Single-stage revision of the infected total knee arthroplasty is associated with improved functional outcomes: a

*EFORT Open Reviews* (2024) **9** 479–487
https://doi.org/10.1530/EOR-23-0147

propensity score-matched cohort study. *Journal of Arthroplasty* 2021 **36** 298–304. (https://doi.org/10.1016/j.arth.2020.07.012)

27 Laffer RR, Graber P, Ochsner PE & Zimmerli W. Outcome of prosthetic knee-associated infection: evaluation of 40 consecutive episodes at a single centre. *Clinical Microbiology and Infection* 2006 **12** 433–439. (https://doi.org/10.1111/j.1469-0691.2006.01378.x)

28 Leta TH, Lygre SHL, Schrama JC, Hallan G, Gjertsen JE, Dale H & Furnes O. Outcome of revision surgery for infection after total knee arthroplasty: results of 3 surgical strategies. *JBJS Reviews* 2019 **7** e4. (https://doi.org/10.2106/JBJS.RVW.18.00084)

29 Li H, Ni M, Li X, Zhang Q, Li X & Chen J. Two-stage revisions for culture-negative infected total knee arthroplasties: a five-year outcome in comparison with one-stage and two-stage revisions for culture-positive cases. *Journal of Orthopaedic Science* 2017 **22** 306–312. (https://doi.org/10.1016/j.jos.2016.11.008)

30 Massin P, Delory T, Lhotellier L, Pasquier G, Roche O, Cazenave A, Estellat C & Jenny JY. Infection recurrence factors in one- and two-stage total knee prosthesis exchanges. *Knee Surgery, Sports Traumatology, Arthroscopy* 2016 **24** 3131–3139. (https://doi.org/10.1007/s00167-015-3884-1)

31 Ribes C, Masquefa T, Dutronc H, De Seynes C, Dupon M, Fabre T & Dauchy FA. One-stage versus two-stage prosthesis replacement for prosthetic knee infections. *Médecine et Maladies Infectieuses* 2019 **49** 519–526. (https://doi.org/10.1016/j.medmal.2019.01.013)

32 Ritter MA & Farris A. Outcome of infected total joint replacement. *Orthopedics* 2010 **33**. (https://doi.org/10.3928/01477447-20100129-09)

33 Shanmugasundaram S, Ricciardi BF, Briggs TW, Sussmann PS & Bostrom MP. Evaluation and management of periprosthetic joint infection-an international, multicenter study. *HSS Journal* 2014 **10** 36–44. (https://doi.org/10.1007/s11420-013-9366-4)

34 Siddiqi A, Nace J, George NE, Buxbaum EJ, Ong AC, Orozco FR, Ponzio DY & Post ZD. Primary total knee arthroplasty implants as functional prosthetic spacers for definitive management of periprosthetic joint infection: a multicenter study. *Journal of Arthroplasty* 2019 **34** 3040–3047. (https://doi.org/10.1016/j.arth.2019.07.007)

35 Tuecking LR, Silligmann J, Savov P, Omar M, Windhagen H & Ettinger M. Detailed revision risk analysis after single- vs. two-Stage Revision total knee arthroplasty in periprosthetic joint infection: a retrospective tertiary center analysis. *Antibiotics* 2021 **10**. (https://doi.org/10.3390/antibiotics10101177)

36 van den Kieboom J, Tirumala V, Box H, Oganesyan R, Klemt C & Kwon YM. One-stage revision is as effective as two-stage revision for chronic culture-negative periprosthetic joint infection after total hip and knee arthroplasty. *Bone and Joint Journal* 2021 **103–B** 515–521. (https://doi.org/10.1302/0301-620X.103B.BJJ-2020-1480.R2)

37 Betsch BY, Eggli S, Siebenrock KA, Täuber MG & Mühlemann K. Treatment of joint prosthesis infection in accordance with current recommendations improves outcome. *Clinical Infectious Diseases* 2008 **46** 1221–1226. (https://doi.org/10.1086/529436)

38 Castellani L, Daneman N, Mubareka S & Jenkinson R. Factors associated with choice and success of one- versus two-stage revision arthroplasty for infected hip and knee prostheses. *HSS Journal* 2017 **13** 224–231. (https://doi.org/10.1007/s11420-017-9550-z)

39 Mahieu R, Dubée V, Seegers V, Lemarié C, Ansart S, Bernard L, Le Moal G, Asseray N, Arvieux C, Ramanantsoa C, *et al.* The prognosis of streptococcal prosthetic bone and joint infections depends on surgical management-A multicenter retrospective study. *International Journal of Infectious Diseases* 2019 **85** 175–181. (https://doi.org/10.1016/j.ijid.2019.06.012)

40 Masood K, Redfern RE, Duggan JM, Georgiadis GM & Suleyman G. Clinical characteristics and outcomes of Staphylococcus lugdunensis prosthetic joint infections: a multicenter retrospective analysis. *Orthopedics* 2020 **43** 345–350. (https://doi.org/10.3928/01477447-20200923-03)

41 Van Dijk B, Nurmohamed FRHA, Hooning van Duijvenbode JFF, Veltman ES, Rentenaar RJ, Weinans H, Vogely HC & Van der Wal BCH. A mean 4-year evaluation of infection control rates of hip and knee prosthetic joint infection-related revision arthroplasty: an observational study. *Acta Orthopaedica* 2022 **93** 652–657. (https://doi.org/10.2340/17453674.2022.3975)

42 Wouthuyzen-Bakker M, Sebillotte M, Lomas J, Kendrick B, Palomares EB, Murillo O, Parvizi J, Shohat N, Reinoso JC, Sánchez RE, *et al.* Timing of implant-removal in late acute periprosthetic joint infection: a multicenter observational study. *Journal of Infection* 2019 **79** 199–205. (https://doi.org/10.1016/j.jinf.2019.07.003)

43 Engesater LB, Dale H, Schrama JC, Hallan G & Lie SA. Surgical procedures in the treatment of 784 infected THAs reported to the Norwegian Arthroplasty Register. *Acta Orthopaedica* 2011 **82** 530–537. (https://doi.org/10.3109/17453674.2011.623572)

44 Siddiqi A, George NE, White PB, Szczech BW, Thompson JV, Etcheson JI, Gwam CU, Caughran AT, Delanois RE & Nace J. Articulating spacers as a modified one-stage revision total knee arthroplasty: a preliminary analysis. *Surgical Technology International* 2018 **32** 239–248.

45 Okafor CE, Nghiem S & Byrnes J. Is 2-stage septic revision worth the money? A cost-utility analysis of a 1-stage versus 2-stage septic revision of total knee arthroplasty. *Journal of Arthroplasty* 2023 **38** 347–354. (https://doi.org/10.1016/j.arth.2022.09.003)

46 Masters JP, Smith NA, Foguet P, Reed M, Parsons H & Sprowson AP. A systematic review of the evidence for single stage and two stage revision of infected knee replacement. *BMC Musculoskeletal Disorders* 2013 **14** 222. (https://doi.org/10.1186/1471-2474-14-222)

47 Pangaud C, Ollivier M & Argenson JN. Outcome of single-stage versus two-stage exchange for revision knee arthroplasty for chronic periprosthetic infection. *EFORT Open Reviews* 2019 **4** 495–502. (https://doi.org/10.1302/2058-5241.4.190003)

48 Kunutsor SK, Whitehouse MR, Lenguerrand E, Blom AW & Beswick AD. Re-infection outcomes following one- and two-stage surgical revision of infected knee prosthesis: a systematic review and meta-analysis. *PLoS One* 2016 **11** e0151537. (https://doi.org/10.1371/journal.pone.0151537)

49 Nagra NS, Hamilton TW, Ganatra S, Murray DW & Pandit H. One-stage versus two-stage exchange arthroplasty for infected total knee arthroplasty: a systematic review. *Knee Surgery, Sports Traumatology, Arthroscopy* 2016 **24** 3106–3114. (https://doi.org/10.1007/s00167-015-3780-8)