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# Comparative reinfection rate of one-stage versus two-stage revision in the management of periprosthetic joint infection following total hip arthroplasty: a meta-analysis

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#### **Abstract**

**Background** Debates persist on the optimal surgical approach for treating Periprosthetic joint infection (PJI) following total hip arthroplasty (THA). This meta-analysis aimed to compare the reinfection rate of one-stage revision versus two-stage revision for PJI after THA.

**Methods** A comprehensive search was performed in four databases (PubMed, Embase, Web of Science, and Cochrane Library) to locate articles that assessed the reinfection rate of one-stage revision compared to two-stage revision. Meta-analyses of reinfection rate were performed.

**Results** A total of 14 articles including of 1429 patients were chosen for inclusion in this meta-analysis, with 561 patients in the one-stage group and 868 patients in the two-stage group. The meta-analysis of the 14 trials revealed that there was no statistically significant disparity in the reinfection rate between the two groups(OR=1.34, 95% CI  $0.92 \sim 1.93$ , P=0.12,  $I^2=0$ ). A subgroup analysis was conducted based on the presence of a well-defined algorithm for decision making in either a one-stage or two-stage revision. There was no statistically significant difference in reinfection rate between one-stage and two-stage revision if there was a decision algorithm(OR=0.83, 95% CI  $0.44 \sim 1.54$ , P=0.55,  $I^2=0$ ). If not, the reinfection rate of one-stage revision was significantly higher than that of two-stage revision(OR=1.79, 95% CI  $1.11 \sim 2.88$ , P=0.02,  $I^2=0$ ). Postoperative hip function score was significantly better in the one-stage revision group than that of the two-stage revision group(SMD=0.54, 95% CI  $0.31 \sim 0.78$ , P<0.05,  $I^2=79\%$ ).

**Conclusions** A strategy that is clearly defined and can be used for decision making in one-stage or two-stage revision is necessary for the treatment of PJI after THA. When there is significant damage to the soft tissue and/or the presence of strong microorganisms, a two-stage revision is recommended in order to decrease the reinfection rate. One-stage revision is recommended for patients with low-toxic infections and intact soft tissue.

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**Trial registration** PROSPERO (CRD42023450842, 17 August 2023) https://www.crd.york.ac.uk/prospero/display\_record.php?ID=CRD42023450842.

Keywords Total hip arthroplasty, Periprosthetic joint infection, Revision, Infection, Reinfection rate

#### Introduction

Hip replacement is among the most prevalent surgical interventions [1, 2]. Periprosthetic joint infection (PJI) is a frequent complication that can occur after joint replacement. PJI is classified as acute onset if it occurs within three months post-surgery, delayed onset if it occurs between three to twelve months post-surgery, and late onset if it occurs beyond twelve months post-surgery [3]. Acute periprosthetic joint infection is mostly treated with debridement, antibiotics, and implant retention, often known as DAIR [4]. However, the DAIR procedure may result in high revision and failure rate [5]. On the other hand, chronic PJI is typically treated with either one-stage revision or two-stage revision [6]. One stage revision involves the thorough removal of damaged tissue and the immediate placement of a new prosthesis in a single surgical procedure [7]. The two-stage revision procedure entails the complete removal of all suspected infections during the initial operation, followed by the subsequent implantation of a new prosthesis after a certain amount of time, which means the administration during this period of causative antimicrobial treatment [7]. CRP and ESR were assessed after six weeks of causative antimicrobial treatment. Repeat aspiration and debridement if symptoms return after discontinuing antibiotics. Second-stage surgery time depends on wound healing rate, inflammatory signs that return to normal or stable levels after antibiotics [8-10].

Currently, the majority of medical institutions employ two-stage revision surgery as the preferred method for addressing PJI following total hip arthroplasty (THA) [11–13]. This approach is widely considered to be the most effective and reliable therapeutic option [14]. A two-stage revision of infected total hip arthroplasty can yield elevated success rates in the management of chronic PJI [15]. The overall success rate of two-stage exchange arthroplasty rages from 75-100% [16]. However, two-stage revision not only complicates the surgical procedure, prolongs the duration of treatment and hospitalization, and raises the cost of treatment, but also frequently leads to the depletion of bone mass after surgery and the development of excessive scar tissue around the hip joint, resulting in impaired hip joint mobility in the later stages [17]. There was a mortality rate of up to 4% after 90 days of treatment in 205 cases of PJI after THA that underwent a two-stage revision, according to Berend [18].

From 1976, an alternate one-stage revision process was employed at the Endo-Klinik in Hamburg, wherein

the implant was removed and replaced in a single operation [19]. However, this procedure was once suspected because of the high recurrence rate of infection [20]. With advancements in perioperative antibiotic administration and surgical techniques, one-stage revision of infection following THA has shown improved infection control rates and enhanced functional recovery post-surgery [21]. One-stage revision has obvious advantages in the management of infected THA, especially when performed on selected patients [22]. The one-stage approach was determined to be an effective surgical intervention for treating THA infection, contingent upon the fulfillment of selection criteria (known pathogen preoperatively and little bone loss) [23, 24]. Some surgeons have chosen to use a one-stage revision surgery since it offers the advantages of shorter duration and lower costs for therapy [25]. Associated benefits also include avoidance of a second procedure with its associated morbidities, improved post operative mobility and pain [26, 27].

The choice between one-stage revision and two-stage revision for PJI after THA remains a highly contentious issue, especially in terms of its efficacy in managing the reinfection rate. Hence, the present meta-analysis was performed with the objective of comparing the reinfection rate of one-stage revision versus two-stage revision for PJI after THA. The secondary outcome was the post-operative hip function score.

# Materials and methods Search strategy

The meta-analysis has been registered at PROSPERO with the registration number CRD42023450842. The current study was carried out following the principles of the Preferred Reporting Project for Systematic Review and Meta-Analysis (PRISMA) 2020. This analysis utilized four literature databases: Medline (1946 to Aug 01,2023), Embase (1974 to Aug 01,2023), Web of Science (1966 to Aug 01, 2023), and CENTRAL(1995 to Aug 01,2023). Two separate investigators conducted searches for studies using the following search strategy: "total hip arthroplasty" and "infection" and "revision" and "one-stage" and "two-stage" and ("randomized controlled trial" or "prospective study" or "retrospective study"). The search records of the four databases are provided in the Supplementary Tables with comprehensive details. In addition, a manual search was conducted to locate further studies in the relevant referable literature.

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#### Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) patients diagnosed with PJI following THA; (2) patients in one group received two-stage revision, while patients in another group received one-stage revision; (3) reinfection rate was reported; (4)Study type was randomized controlled trial, prospective study or retrospective study.

Procedure of one-stage revision [9, 10, 23, 25, 28]: (1) Removal of implants and comprehensive debridement of all foreign materials, including cement, necrotic bone, and soft tissues. (2) Cement containing gentamicin or vancomycin was utilized, and supplementary antibiotic powders were incorporated based on the sensitivities of the organisms obtained from the biopsy specimens. (3) A newly sized femoral stem and cup were coated with cement and implanted, and autogenous bonegrafts were used for defects in the acetabulum or femur If needed.

Procedure of two-stage revision [9, 10, 23, 25, 28]: (1) Removal of implants and comprehensive debridement of all foreign materials, including cement, necrotic bone, and soft tissues. (2) An antibiotic-loaded spacer was implanted, and cement containing gentamicin or vancomycin was utilized, with supplementary antibiotic powders incorporated based on the sensitivities of the organisms obtained from the biopsy specimens. (3) Patients received antibiotic therapy for 6-8 weeks. (4) The determination to proceed with second-stage reimplantation was predicated on the patient's clinical reaction, encompassing wound healing and the normalization of inflammatory markers, signifying the resolution of PJI. (5) The spacer was removed, the surgical site is again debrided and irrigated, and newly sized femoral stem and cup were coated with antibiotic cement and implanted. Autogenous bonegrafts were used for defects in the acetabulum or femur If needed.

Literatures meeting the following criteria were excluded: (1) Other types of articles, such as animal studies, guideline, case reports, publications, meta-analyses, letters, reviews, editorials, pharmacological intervention, and protocols; (2)unable to obtain full-text; (3)data cannot be extracted; (4)sample size was smaller than ten; (5) duplicate patient cohort.

# Selection of studies

The procedure of selecting literature, which included eliminating duplicate entries, was carried out using End-Note (Version 20; Clarivate Analytics). Two independent reviewers conducted the initial search. They removed duplicate data, evaluated the titles and abstracts to determine their relevance, and classified each study as either included or excluded. We reached a resolution by achieving consensus. In the absence of consensus between the two independent reviewers, a third reviewer assumed the position of a mediator.

#### Data extraction

The data was extracted by two reviewers independently. The extracted data included: (1) Basic information of the study, including the first author, publication year, country, study design, sample size; (2) Baseline characteristics of study subjects, including number of patients, age, follow-up time after revision, type of infecting microorganism; (3)Reinfection rate, or number of reinfection cases. The discrepancy was resolved by consulting a third investigator for advice. "Reinfection" was defined as recurrence of infection by the same organism(s) and/or re-infection with a new organism [28]. (4) Postoperative hip function score.

#### **Quality assessment**

The quality evaluation of the included studies was evaluated by two independent reviewers. In this study, we utilized the Newcastle Ottawa quality evaluation scale (NOS) [29] to evaluate the quality of studies. If there were any discrepancies, the disputed conclusions were resolved through collaborative discussion.

#### **Data Analysis and Statistical Methods**

EndNote (Version 20; Clarification Analysis) was used to manage the selection of retrieved studies, including duplicate deletion studies. All study findings were analyzed using Review Manager 5.3 (Cochrane Collaboration, Oxford, UK). The odds ratio (OR) with a 95% confidence interval (CI) was used to compare the binary variables. Continuous variables were compared using a weighted mean difference (WMD) with a CI of 95%. Median and interquartile ranges of the continuous data were converted to mean and standard deviation. For all meta-analyses, Cochrane Q p-values and I<sup>2</sup> statistics were used to test for heterogeneity. If the heterogeneity was low or moderate (I<sup>2</sup><50%), the pooled data were analyzed using a random effects model (REM); if the heterogeneity was high (≥50%), the fixed effects model (FEM) was used. Statistical heterogeneity was assessed using a standard chi-square test and was considered significant at P<0.05. Potential publication bias was assessed by visually inspecting the funnel plot.

#### **Results**

#### Search results

Figure 1 depicts the process of choosing and integrating articles. We initially identified a total of 821 articles. After removing duplicate studies, there were 788 articles left. Upon careful examination of the titles and abstracts, a grand total of 21 publications were determined to be irrelevant and subsequently eliminated. After a comprehensive inspection of the full text, a total of 14 articles were chosen for inclusion in this meta-analysis.

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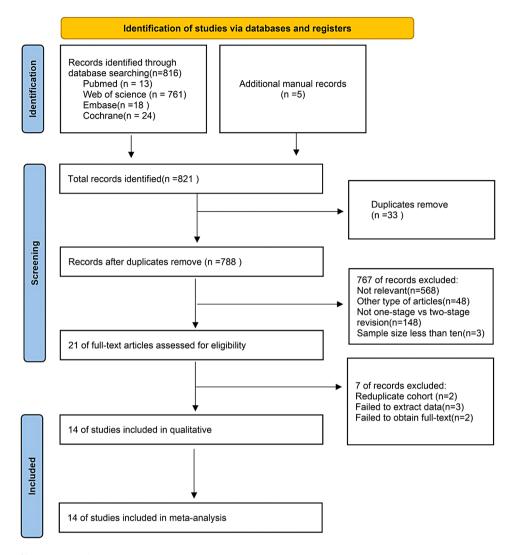


Fig. 1 Flow chart of literature search strategies

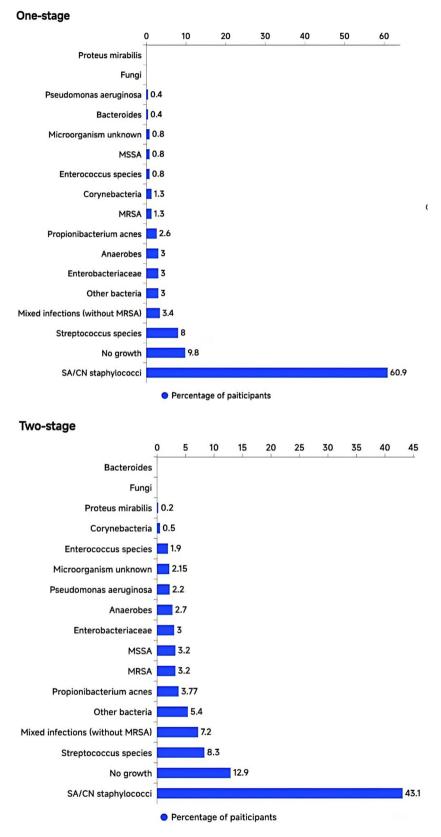
# Patient characteristics and quality assessment

This meta-analysis included a total of 14 articles [8–10, 14, 23, 25, 28, 30–36], which consisted of one prospective study and 13 retrospective studies. Eight studies [8-10, 14, 23, 25, 31, 33] presented a surgical treatment algorithm that outlined the decision-making process for choosing between a one-stage or two-stage revision. In these studies, two-stage revision was conducted if there was moderate or severe damage to soft tissue and/or the presence of microorganisms that are difficult to cure. If these conditions were not present, one-stage revision was performed. In contrast, another six studies [28, 30, 32, 34-36] did not make any reference of this algorithm. A subgroup analysis was conducted based on the presence of a well-defined algorithm for decision making in either a one-stage or two-stage revision. Subgroup A consisted of the eight studies that provided a surgical treatment algorithm. Subgroup B comprised an additional six studies. Nine studies [8, 9, 14, 23, 25, 28, 30, 31, 34] reported the types of infecting microorganism. Figure 2 presented the types of infecting microorganism by type of revision strategy. The most cultured microorganism associated with a PJI following the index operation in both groups was staphylococcus aureus or coagulase-negative (SA/CN) staphylococci. Table 1 provides detailed information about the basic characteristics of the patients. For assessing the quality, we utilized the NOS scale to analyze the included studies. All studies were assessed as having a high level of quality. Table 2 provides detailed information pertaining to the evaluation of quality.

# Reinfection rate

Figure 3 displayed aggregated findings regarding the rate of reinfection. The meta-analysis of the 14 studies revealed that there was no statistically significant disparity in the reinfection rate between the two groups(OR=1.34, 95% CI  $0.92 \sim 1.93$ , P=0.12, I<sup>2</sup>=0). A subgroup analysis was conducted based on the presence

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**Fig. 2** Type of infecting microorganism by type of revision strategy. SA/CN staphylococci: Staphylococcus aureus/Coagulase-negative staphylococci; MRSA: Methicillin-resistant Staphylococcus aureus; MSSA: Methicillin-Ausceptible Staphylococcus Aureus

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 Table 1
 Basic characteristics and quality assssment of included studies and patients

Number	Autor	Year	Study type	Surgical treatment	Subgroup	Sample size		Mean age(SD)	
				algorithm		one stage	two stage	one stage	two stage
1	Born [9]	2016	retrospective	Yes	A	28	53	70	70
2	Choi [30]	2013	retrospective	No	В	17	44	66	65
3	De Man [31]	2011	retrospective	Yes	Α	22	50	69	70
4	Engesater [32]	2011	retrospective	No	В	192	283	72	71
5	Giulieri [33]	2004	retrospective	Yes	Α	16	31	72	72
6	Hope [34]	1989	retrospective	No	В	72	8	64	65
7	Klouche [23]	2012	prospective	Yes	Α	38	46	63.6	66.9
8	Kieboom [25]	2021	retrospective	Yes	Α	12	27	67.9	65
9	Morscher [35]	1990	retrospective	No	В	47	27	72	72
10	Oussedik [8]	2010	retrospective	Yes	Α	11	39	65	65
11	Sotiriou [28]	2022	retrospective	No	В	9	46	73	68
12	Tirumala [14]	2021	retrospective	Yes	Α	46	92	68.9	68.2
13	VAN DIJK [10]	2022	retrospective	Yes	Α	14	67	70	72
14	Wolf [36]	2014	retrospective	No	В	37	55	64.5	64.5

**Table 2** Quality assessment of the studies based on the NOS

Study	Selection				Comparability of cases	Outcomes	Score		
	Is the case definition adequate?	Represen- tativeness of the cases	Selec- tion of Controls	Defini- tion of Controls	and controls on the basis of the design or analysis	Ascertain- ment of exposure	Same method of ascertainment for cases and controls	Non- Re- sponse rate	
Born [9]	*	*	*		*	*	*	*	7
Choi [30]	*	*	*		**	*	*	*	8
De Man [31]	*	*	*		**	*	*	*	8
Engesater [32]	*	*	*	*	*	*	*	*	8
Giulieri [33]	*	*	*		**	*	*	*	8
Hope [34]	*	*	*		**	*	*	*	8
Klouche [23]	*	*	*	*	**	*	*	*	9
Kieboom [25]	*	*	*	*	**	*	*	*	9
Morscher [35]	*	*	*		**	*	*	*	8
Oussedik [8]	*	*	*		**	*	*	*	8
Sotiriou [28]	*	*	*		*	*	*	*	7
Tirumala [14]	*	*	*	*	**	*	*	*	9
VAN DIJK [10]	*	*	*		**	*	*	*	8
Wolf [36]	*	*	*		**	*	*		7

of a well-defined algorithm for decision making in either a one-stage or two-stage revision. Subgroup A consisted of eight studies that provided a surgical treatment algorithm detailing the decision-making process for selecting either a one-stage or two-stage revision. Subgroup B comprised an additional six studies. There was no statistically significant difference in reinfection rate between one-stage and two-stage revision in subgroup A(OR=0.83, 95% CI  $0.44 \sim 1.54$ , P=0.55,  $I^2=0$ ). In subgroup B, the reinfection rate of one-stage revision was significantly higher than that of two-stage revision(OR=1.79, 95% CI  $1.11 \sim 2.88$ , P=0.02,  $I^2=0$ ).

# Postoperative hip function score

Figure 4 displayed aggregated findings regarding the postoperative hip function score. Since hip function were

measured by different scores (Harris hip score or hip disability and osteoarthritis outcome score), standardized mean difference (SMD) was calculated with the corresponding 95% CIs. Only five studies reported postoperative hip function score, and the result revealed that the postoperative hip function score was significantly better in the one-stage revision group than that of the two-stage revision group(SMD=0.54, 95% CI 0.31 ~ 0.78, P<0.05,  $I^2$ =79%). Subgroup analysis was not performed since the limited sample.

# **Publication bias**

Publication bias of the reinfection rate was assessed by a funnel plot. No obvious evidence of publication bias was observed in the bilaterally symmetrical funnel plot of reinfection rate (Fig. 5).

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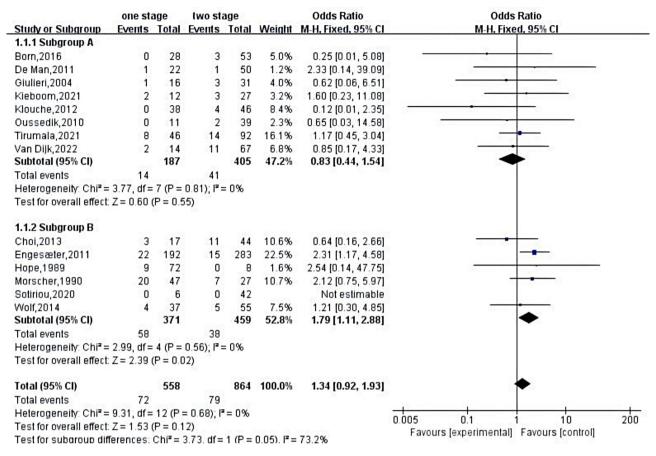


Fig. 3 Forest plot for reinfection rate

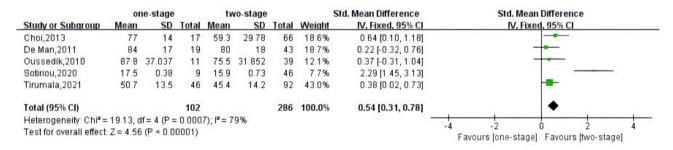


Fig. 4 Forest plot for hip function score

# **Discussion**

This study compared the reinfection rate of PJI after THA between one-stage revision and two-stage revision. The findings of this study indicate that there was no statistically significant disparity in the reinfection rate between one-stage and two-stage revision. None of the 14 studies included in the analysis were randomized controlled trials, and eight studies devised a decision algorithm to choose the surgical approach based on the severity of PJI, as indicated in Table 1. In these studies, two-stage revision was conducted if there was moderate or severe damage to soft tissue and/or the presence of microorganisms that are difficult to cure. If these conditions were not

present, one-stage revision was performed. A subgroup analysis was conducted to evaluate the influence of the presence of a well-defined algorithm. The findings of this subgroup analysis revealed that the reinfection rate did not change significantly between one-stage and two-stage revision procedures when a decision algorithm was utilized. When a decision algorithm was not present, the reinfection rate of one-stage revision was considerably higher than that of two-stage revision. The result indicated that two-stage revision arthroplasty is a safe and efficacious treatment particularly if there was moderate or severe damage to soft tissue and/or the presence of resistant organisms. Likewise, prior study suggested

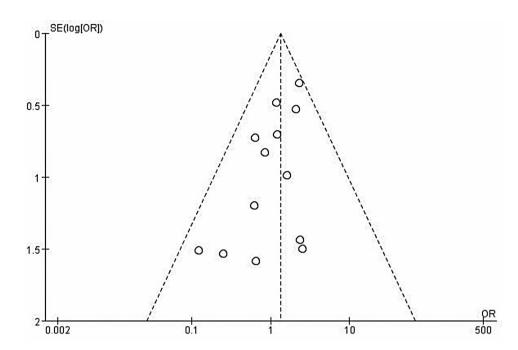


Fig. 5 Funnel plot for reinfection rate

that a two-stage revision is advisable for a loose prosthesis accompanied by a fistula, characterized by significant scar tissue, typically vascularized tissue, or compromised bone quality due to very toxic bacteria or mixed infection [35].

The one-stage revision offers significant advantages for patients, including a reduction in the number of surgical procedures, shorter hospital stays, decreased duration of antibiotic therapy, less time experiencing functional limitations and uncertainty, along with economic benefits [37]. Besides, the findings of this meta-analysis revealed that the postoperative hip function score was significantly better in the one-stage revision group than that of the two-stage revision group. However, the findings of this meta-analysis revealed that one-stage revision resulted in higher reinfection rate compared with two-stage revision if there was moderate or severe damage to soft tissue and/or the presence of resistant organisms. Therefore, one-stage revision should be restricted to organisms with relatively low toxicity have been found. Soft tissues must exhibit adequate vascularization, and bone beds must possess appropriate quality and quantity. Similarly, prior study suggested the criteria for a one-stage procedure encompassed the lack of severe immunocompromise, substantial soft-tissue or bone compromise, and concurrent acute sepsis [38]. Relative contraindications to onestage revision include significant severe bone loss, an unidentified pathogen and the presence of multiresistant bacteria [39, 40].

The removal of infected components and the administration of culture-directed antibiotics are crucial for the

effective management of chronic PJI [25]. The results of this study indicated that the most common pathogens involved in PJI were SA/CN staphylococci, which are consistent with the previous literature [41–43].

Toxic organisms like staphylococcus aureus typically induce acute red sepsis accompanied by toxemia and significant tissue necrosis; nevertheless, they may also lead to low-grade persistent infections. Organisms such as CN staphylococci, propionibacterium, and peptococcus exhibit lower toxicity; yet, they can still induce tissue damage and result in implantation failure [34]. The study results indicated that MRSA comprised 1.3% in the one-stage group and 3.2% in the two-stage group. With the advent of medicine and surgery, MRSA have emerged as a significant source of infections associated with numerous medical devices [44]. Infection due to MRSA poses a significant risk to joint infections associated with prostheses and is once regarded as a contraindication for one-stage revision [45]. However, Yoo et al. [46] documented successful infection control in four patients with MRSA using a one-stage revision, while Winkler et al. [47] reported five MRSA infections that were well treated with a one-stage revision. Nonetheless, the efficacy of one-stage modification remains unsubstantiated by extensive sample data.

It is worth noting that, the study results revealed that culture-negative PJI was the second most prevalent condition, comprising 9.8% in the one-stage group and 12.9% in the two-stage group. Due to the limitations of the data, we failed to conduct a subgroup analysis to compare the reinfection rate between one-stage revision and

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two-stage revision regarding culture-negative PJI after THA. J. van den Kieboom et al. indicated that the reinfection rate after one-stage revision was similar to those after two-stage revision for chronic culture-negative PJI [25]. Besides, several case series indicated that PJI could be successfully eliminated with one-stage revision, even in patients with culture-negative PJI [38, 48].

The results of this meta-analysis revealed that streptococcal species was the third common pathogens in both group. Eradicating streptococcal infection of the hip appears to be more challenging with a one-stage exchange compared to other bacteria. Ohlmeier M reported that the re-revision for infection was 20% after one-stage revision for streptococcal PJI of the hip, which was extremely high [37]. Akgün et al. documented a treatment failure rate of 40% within their cohort, which included 10 out of 22 patients who underwent two-stage exchange operations for streptococcal PJI, indicating an infection control rate of merely 59% in this subgroup [49]. The unsatisfactory results of streptococcal PJI, irrespective of the surgical intervention employed, may be partially attributed to the characteristics of the organism [37]. The elimination of streptococcal periprosthetic joint infection of the hip is challenging. Multidisciplinary development of a particular management plan is still required.

Fungal infections of hip prosthesis joints (PJIs) are infrequent yet serious conditions [49]. This study found that fungal infection occurred in less than 1% of all cases of PJI after THA. The incidence has risen in recent decades owing to the aging population and the growing number of immunosuppressed individuals [3]. Candida species are the predominant fungi implicated with PJIs, succeeded by other fungal species [50, 51]. Treatment of candidal periprosthetic joint infections seemed to require a lengthy course of antifungal medication [49]. An effective approach for treating fungal periprosthetic infections was shown by Konstantinos Anagnostakos et al. to be a two-stage revision involving the implantation of cement spacers impregnated with biantibiotics [52]. Systemic antifungal medication may be confined to 6 weeks without an increased risk of chronic or recurrent infection [52]. The identification and therapy of fungal PJI in individuals who have undergone THA are fairly challenging. A multidisciplinary approach is crucial, since the integration of antifungal therapy and two-stage revision seems to be the appropriate therapeutic strategy [3].

Our study possesses multiple strengths. First, our study provided updated evidence in terms of the reinfection rate of one-stage versus two-stage revision in treating PJI following THA. Furthermore, a subgroup analysis was performed to evaluate the influence of the decision algorithm on the reinfection rate. However, our study has several limitations. First, all the studies

considered in the analysis consisted solely of retrospective or prospectibe studies and did not include any highquality randomised controlled trials. Furthermore, it is important to consider that loss to follow-up, which can occur due to patient mortality or other circumstances, has the potential to impact the infection recurrence rate as reported in certain studies. In addition, the varying durations of follow-up in different studies can introduce bias in the monitoring of the reinfection rate. Further more, The advancements in joint prosthesis design, surgical concepts, surgical technology, antibiotic research, population drug resistance rates, and variations in infectious bacterial flora will also influence the results of the two treatment methods to some degree. Additional randomised controlled trials are required to further validate the benefits and drawbacks of the two procedures.

In conclusion, the present meta-analysis compared the reinfection rate of one-stage revision versus twostage revision for PJI after THA. When the patients was selected, there was no statistically significant difference in reinfection rate between two groups. If not, the reinfection rate of one-stage revision was significantly higher than that of two-stage revision. Therefor, performing a two-stage revision is recommended when there is significant damage to the soft tissue and/or the presence of resistant microorganisms. Given the substantial benefits of one-stage revision, such as better hip function, fewer surgical interventions, reduced hospital stays, shorter antibiotic treatment durations, diminished functional limitations and uncertainties, as well as economic advantages, a one-stage revision is recommended when the pathogens demonstrate relatively low toxicity and the soft tissue remains intact.

# **Supplementary Information**

The online version contains supplementary material available at https://doi.or g/10.1186/s12891-024-08199-y.

Supplementary Material 1

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Everyone who contributed significantly to this study has been listed.

#### **Author contributions**

Y.Q. and Z.L. performed the data analyses and wrote the manuscript. L.L. made great contribution to the revision of the manuscript. Y.Y. and X.H. helped perform the analysis with constructive discussions. W.L. contributed to data presentation. L.L. is responsible for ensuring that the descriptions are accurate and agreed by all authors. All authors read and approved the final manuscript.

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#### **Availability of Data and Materials**

The datasets [GENERATED/ANALYZED] for this study can be found in the [figshare] [https://doi.org/10.6084/m9.figshare.25515076]

#### **Declarations**

# Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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