

# Re-Infection Outcomes Following Irrigation and Debridement and Revision of Deep Site Periprosthetic Joint Infection: A Meta-Analysis of 12 Studies

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**Citation:** Wang X, Zhong X, Tu B, Zhang Y, Hong D, et al.(2017) Re-Infection Outcomes Following Irrigation and Debridement and Revision of Deep Site Periprosthetic Joint Infection: A Meta-Analysis of 12 Studies. J OrthopTher. JORT133. DOI: 10.29011/JORT-133.000033

**Received Date:** 15 April, 2017; **Accepted Date:** 19 April, 2017; **Published Date:** 26 April, 2017

## Abstract

**Purpose:** Irrigation and debridement (I&D) with retention of the components and revision are both current mainstream treatments of periprosthetic joint infection. However, the optimal management of the infection after arthroplasty is still controversial. We conducted this meta-analysis to assess the efficacy of I&D and revision strategy in patients with infected arthroplasty.

**Methods:** A complete search of PubMed, Web of Science, The Cochrane Library and EMBASE was performed for studies published prior to Feb 20, 2017. All observational comparative studies were included to compare the retention and revision strategy in patients with periprosthetic joint infection.

**Results:** Twelve studies with a high quality of methodology were included in the analysis, a significant difference was found in the comparison of the re-infection rates between revision and I&D treatments. (RR=0.37, 95% CI: 0.29-0.49, P = 0.027, fixed effects model) Moreover, we found that patients with revision got higher KSS scores and KSS function scores but lower ROM and WOMAC. The length of hospital stay and the treatment duration after the two treatments were inconsistent among different studies.

**Conclusion:** The re-infection rate of revision strategy was significantly lower than that of retention. Moreover, the patients with revision got better joint function after the treatment. The length of hospital stay and the treatment duration between the two treatments were uncertain.

**Keywords:** prosthesis, infection, irrigation, debridement, revision

thetic joint infection (PJI) is between 0.5- 1.2% after THA[2] and 1-3% after TKA [3].

The current mainstream treatment of PJI may involve irrigation and debridement (I&D) with retention of the components, exchange arthroplasty either as a one- or two-stage procedure and salvage procedures such as resection arthroplasty, arthrodesis, or amputation [4].

In clinical practice, irrigation and debridement (I&D) with component retention is often preferred for early postoperative or acute haematogenous infection while revision is often preferred for chronic infection [5]. For superficial infection, there is a consensus on the management of I&D. However, the optimal management of the deep site infection after arthroplasty is still controversial.

According to the uncertain evidence, further work needs to be done to compare the effectiveness of the two strategies. We therefore sought to find if there was a difference in re-infection rates and other clinical outcomes when comparing I&D strategy to the revision strategy using a systematic meta-analytic approach. Our aim was to evaluate the effectiveness of prosthesis retention or prosthesis removal strategies using re-infection rate and other clinical outcomes as measured by WOMAC score, KSS knee, KSS function, ROM, the length of hospital stay and the treatment duration.

## Method

### Data sources and search strategy

We systematically searched for longitudinal studies (retrospective, prospective or randomized controlled trials) reporting re-infection outcomes following revision or debridement of infected prosthesis of hip, knee, shoulder and elbow in PubMed, Web of Science, The Cochrane Library and EMBASE from ten years ago to February 2017. The search strategy included free, MeSH and keywords search terms, which related to total knee arthroplasty, total hip arthroplasty, total shoulder arthroplasty, total elbow arthroplasty, infection, revision, irrigation and debridement. No language restrictions were employed. We also manually scanned all the reference lists for relevant articles.

### Eligibility criteria

We included studies which consisted of unselected patients which the groups of patients can represent the population of this kind of patient. These patients were treated exclusively by surgical revision or debridement with the reason of prosthetic joint infection after total knee arthroplasty, total hip arthroplasty, total shoulder arthroplasty or total elbow arthroplasty, and followed up for at least 20 months for reinfection outcomes (recurrent or new infections) after treatment. We excluded: (1) studies that reported case series of methods in selected group of patients (such as patients with a specific infection); (2) studies that did not include patients with less than 20 months of follow-up; (3) studies with less than ten participants.

### Study selection and quality assessment

Two investigators independently screened titles and abstracts for eligibility. Each article was assessed using the inclusion criteria above and any disagreement of an article was discussed, and consensus reached with a third reviewer. One author indepen-

dently extracted data and performed quality assessments using a standardized data collection form. A second reviewer checked data in original articles. We extracted data from studies, including first author, year of publication, geographical location, mean age, proportion of males follow-up mean month, number of participants, of episodes which take part in surgical revision or debridement and the number of re-infection. Methodological quality of included studies was assessed based on the Methodological Index for Non-Randomized Studies (MINORS).

### Outcome measure

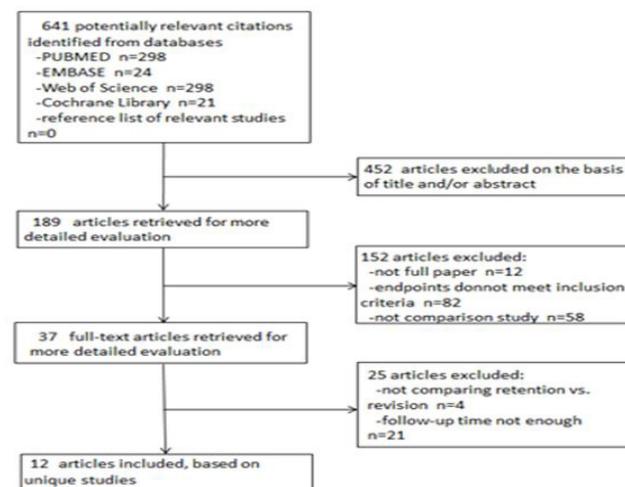
The primary outcomes were comparisons of re-infection rates between revision and I&D treatments. Subgroup analysis was performed according to the location of joints (hip, knee and shoulder/elbow). The secondary outcomes included total length of hospital stay, treatment duration, WOMAC score, KSS knee, KSS function and ROM.

### Statistical analysis

We carried out the meta-analysis using Stata software (version 12.0) (Stata Corp, College Station, TX, USA). The statistics were analysed using fixed effect models. The risk ratio (RR) with 95% confidence intervals (CI) was selected to compare the binary variables. Besides, the statistical heterogeneity among studies was assessed with a standard chi<sup>2</sup> test and inconsistency (I<sup>2</sup>) statistic. The publication bias was assessed by using Egger's regression symmetry test. The consistency of the results was assessed by a sensitivity analysis. P value $\leq$ 0.05 or I<sup>2</sup> $\geq$ 50% suggested significant heterogeneity. P value $\leq$ 0.05 suggested statistical significance.

## Results

Overview of the included studies (Figure 1).



**Figure 1:** Flow chart for Systematic Reviews and Meta-Analysis presenting the search strategy results.

There were total 641 potentially relevant citations identified from databases. 452 articles were excluded when we read the titles or abstracts, then 189 articles were retrieved for more detailed evaluation. 152 articles were excluded from the source. From these articles, 12 articles were excluded because of con not get full text, 82 articles' endpoints didn't meet inclusion criteria, 58 articles were not comparison studies. Then, 37 full-text articles were left for further selection. As a result, 25 articles were excluded for that there were 4 articles were not comparing Irrigation and debridement (I&D) and revision, the follow-up time was not enough in 21 articles. Finally, there remained 12 articles based on unique studies for us to do the meta-analysis [6-17].

The characteristic of the included studies and quality assessment (Table 1).

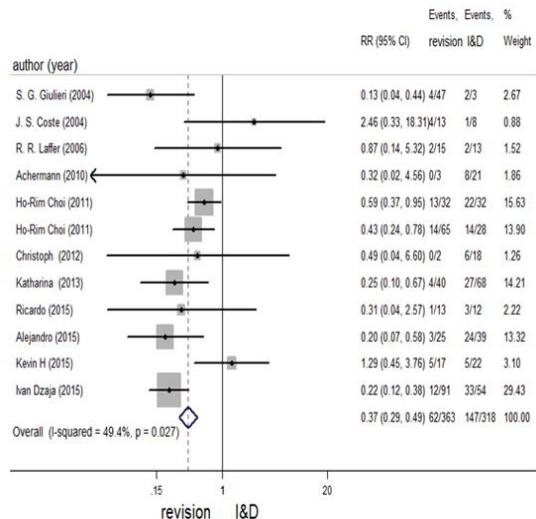
Lead author, publication data	Country	Location	Qualify score	Mean age	male%	Follow up mean month	Number of episodes	Management strategy			
								Irrigation and Debridement		Revision	
								Number of episodes	Number of reinfection	Number of episodes	Number of reinfection
3. S. Costeer 81.2004	France	Shoulder	15	64	54.8	34	42	8	1	13	4
S.C. Giulieri et al. 2004	Switzerland	Hip	11	72	52.4	28	63	3	2	47	4
R. R. Laffer et al. 2006	Switzerland	Knee	19	70.1	48.6	28	40	13	2	15	2
Y. Achermann et al. 2010	Switzerland	Elbow	19	61	31	32.4	21	21	8	3	0
Ho-Rim Choi et al. 2011	USA	Knee	20	65.2	48.3	36	64	32	22	32	13
Ho-Rini Choi et al. 2011	USA	Hip	20	66	52	59	93	28	14	65	14
Chnstopb Spormann et al. 2012	Switzerland	Elbow	19	61.2	121	622	20	18	6	2	0
Kathahna MDMerallini et al. 2013	Australia	Hip	25	NS	46.5	NM	114	68	21	40	4
Ricardo de Paula LeiteCury et al. 2015	Brazil	Knee	19	10.3	68.4	403	29	12	3	13	1
Ivarr Bzaja et al. 2015	UK	Knee	20	59	642	NM	145	54	33	91	12
Alejandro Lizaur-Utrila et al. 2015	Spain	Knee	20	71.8/73.8	33	NM	64	39	24	25	3
Kevill H et al. 2015	USA	Knee	20	NM	NM	NM	39	22	5	17	5

**Table 1:** Characteristics of Studies Included in Meta-Analysis.

Twelve studies involving 740 episodes were included in our analysis from 2004 to 2015. The baseline characteristics of the included studies were shown in Table 1. One article studied shoulder arthroplasty, two elbow arthroplasty, three total hip arthroplasty and six total knee arthroplasty. All of these articles compared the re-infection rate between the group of irrigation and debridement and the group of revision. These articles were evaluated by MINORS (Methodological index for non-randomized) and all had a score higher than 15( $19 \pm 1.54$ ). They were all considered with high quality.

### Primary outcomes

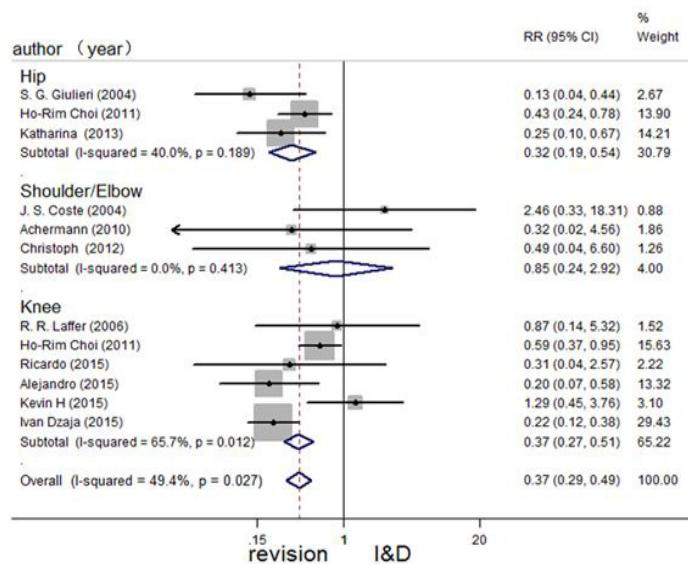
A significant difference was found in the comparison of the re-infection rates between revision and I&D treatments ( $RR=0.37$ , 95% CI: 0.29-0.49,  $P = 0.027$ , fixed effects model, (Figure 2).



**Figure 2:** Forest plot showing the meta-analysis results of all studies.

The results suggested that the re-infection rate of revision was significantly lower than those of I&D.

We considered  $I^2=49.4\%$  as a reasonable heterogeneity, but it was still close to 50%. Therefore, we conducted a subgroup analysis to further investigate the source of heterogeneity. As for subgroup analysis according to locations, significant differences were found in the re-infection rates between revision and I&D treatments for hip ( $RR = 0.32$ , 95% CI: 0.19-0.54,  $p = 0.189$ , fixed effects model, (Figure 3) and knee ( $RR = 0.37$ , 95% CI: 0.27-0.51,  $p = 0.012$ , fixed effects model, Figure 3). However, no difference was found in the re-infection rates for shoulder and elbow ( $RR = 0.85$ , 95% CI: 0.24-2.92,  $p = 0.413$ , fixed effects model, (Figure 3).



**Figure 3:** Forest plot of the subgroup analysis by location.

### Secondary outcome

(Table 2) showed that patients with revision got higher KSS scores, higher KSS function scores, lower WOMAC and lower ROM compared to I&D.

Clinical Outcome	Lead author, publication data	Irrigation and Debridement		Revision	
		Number of episodes	score	Number of episodes	score
WOMAC score	Ricardo de Paula Lode Dory et al.2015	12	85.9	13	69.8
ROM	Alejandro Lizaur-Utrilla et al.2015	39	96.2	25	93.3
KSS knee	Alejandro Lizaur-Utrilla et al.2015	39	65	25	73.5
KSS function	Alejandro Lizaur-Utrilla et al.2015	39	45.3	25	63.6

**Table 2:** Summary of Secondary Outcome (score).

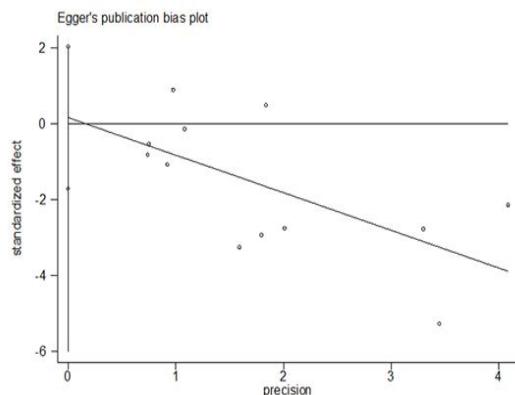
Clinical Outcome	Lead author, publication data	Irrigation and Debridement		Revision	
		Number of episodes	Total length	Number of episodes	Total length
Total length of hospital stay (days)	Ho-Rim Choi et al. 2011 Alejandro Liza-uttrilla et al. 2015	32	16	32	20
		12	54.2	13	41.3
Treatment duration (days)	Ho-Rim Choi et al. 2011 Alejandro Lizaur-Utrilla et al 2015	32	120	32	180
		12	241	13	163

**Table 3:** Summary of Secondary Outcome (time).

the length of hospital stay and the treatment duration were compared between the two groups. Alejandro Lizaur-Utrilla et al [14] reported that the total length of hospital stay and treatment duration of I&D group were longer than that of revision group. But Ho-Rim Choi et al [16] found that the total length of hospital study and treatment duration of I&D group were shorter than that of revision group.

### Egger's Test

Funnel plots with the Egger test is shown in (Figure 4).

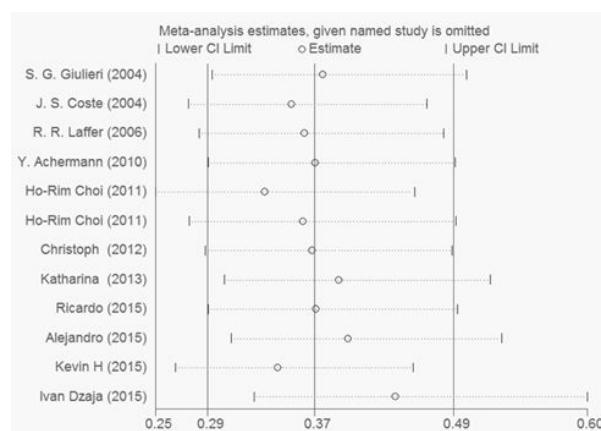


**Figure 4:** Egger's funnel plot for publication bias. The diameter of each circle represents the weight in the meta-analysis.

Visual inspection of the Egger funnel plot did not identify substantial asymmetry ( $P = 0.856$ ), indicating that there was no evidence of publication bias detected in this study.

### Sensitivity analysis

The sensitivity analysis evaluated the influence of each study on the overall effect size and indicated that the result was not dominated by single study (Figure 5).



**Figure 5:** Sensitivity analysis.

### Discussion

Our meta-analysis summarized all eligible studies comparing the effect of I&D strategy and revision strategy for patients with deep site PJI. Twelve observational comparative studies were collected, involving 734 patients. The pooled data revealed that the re-infection rates of revision was significantly lower than those of retention ( $RR=0.37$ , 95% CI: 0.29-0.49,  $P = 0.027$ , fixed effects model). As for subgroup analysis according to location, significant differences were found in the re-infection rates between revision and retention treatments for hip ( $RR = 0.32$ , 95% CI: 0.19-0.54,  $p = 0.189$ , fixed effects model) and knee ( $RR = 0.37$ , 95% CI: 0.27-0.51,  $p = 0.012$ , fixed effects model). However, no difference was found in the re-infection rates for shoulder and elbow ( $RR = 0.85$ , 95% CI: 0.24-2.92,  $p = 0.413$ , fixed effects model). Moreover, the results showed that patients with revision got lower WOMAC, higher KSS scores and KSS function scores and lower ROM. The length of hospital stay and the treatment duration between the two treatments were uncertain. The data suggested that revision had a lower re-infection rate and better functioning compared to I&D for

deep site PJI and the revision strategy might bring more benefits than I&D with prosthesis retention.

There have long been controversies on the optimal treatment for patients with deep site infection after PJI. So far there has been no meta-analysis on this topic. Our findings suggested a lower re-infection rate of prosthesis revision strategy compared to prosthesis retention strategy for treating periprosthetic hip infection and periprosthetic knee infection, which was consistent with the results of some previous reviews [18-21] Gallo J and colleagues in their review of a total of 77 studies, reported a two-stage protocol for PJI treatment had the lowest risk for PJI recurrence((hips, 7.4%; knees, 11%), followed by less reliable approach of one-stage pre-implantation and worse option of irrigation and debridement.[18]A review reported success rates ranging from 31%-75% in prosthesis retention (8 studies) and 72%-100% in prosthesis removal (14 studies) groups respectively [18]. Our result was also consistent with current consensus that two-stage revision is the established gold standard for treating infected hip and knee replacements [22].

Daniel J in their review suggested that a two-stage approach with an antibiotic spacer was a better treatment for periprosthetic shoulder infection [23]. However, our results of subgroup analysis suggested the I&D strategy as an equivalent strategy to the revision strategy in terms of effectiveness for treating periprosthetic shoulder infection and periprosthetic elbow infection.

I&D with retention of the prosthesis is aimed to preserve the implanted prosthesis and treat the patient with surgical irrigation of the prosthesis and regularly antibiotics use. The indication for I&D may vary according to the duration of symptoms, loosening of the prosthesis and presence of functioning joint. Generally, the previous scientific evidence suggested that I&D should be preferred over the revision of the existing implant in patients with a short duration of symptoms within 30 days, which is defined as acute infection [24]. However, the confirmation of “acute” infection was difficult while some studies suggested that I&D should be used over patients with a duration of symptoms within 90 days. The advantages of open debridement with retention of prosthetic components over an exchange procedure for an acute prosthetic joint infection include fewer surgeries, less expense. However, the effectiveness of this strategy to avoid re-infection is still debated [20]. The success rates of I&D were reported to be inconsistent and varied greatly with average infection control rate of 45.9% and 52% following a single or repeated debridement and irrigation procedures with highest success rate for early treatment (within 30 days of onset) [21]. This meta-analysis suggested that the re-infection rate of I&D was various and had lower success rate in eradication of infection, which indicated that revision may be a better choice when there was not certain indication for I&D.

The revision of the existing implant includes both one-stage revision and two-stage revision. Compared to I&D, the revision strategy is generally reported to have lower re-infection rates of between 0 to 41% for two-stage studies and 0 to 11% for one-stage studies [25]. It has been reported that the one-stage strategy may be associated with better economic benefits and better joint functioning [26]. Two-stage revision has for several decades been the established gold standard for treating PJI with high success rate in eradication of infection [22]. In the meantime, the two-stage strategy can result in significant functional impairment and higher cost. The comparison between one and two stage revision was controversial. One meta-analysis suggested that the one-stage revision strategy may be as effective as the two-stage revision strategy in treating infected knee prostheses in generally unselected patients [27]. And it's hard to extract the data respectively from the included studies. Therefore, in this meta-analysis, we applied the pooled results of both one-stage and two-stage revision and suggested a higher efficacy of revision strategy in controlling PJI. In clinical practice, two-stage revision is more often used. Most of the patients included in this study undergone two-stage revision rather than one-stage revision.

The results showed that patients with revision got higher KSS scores and KSS function scores and lower ROM and WOMAC, which indicated that patients with revision got better joint function with less pain and better recovery after the treatment. And the results suggested that the length of hospital stay and the treatment duration between the two treatments were inconsistent among studies. Alejandro Lizaur-Utrilla et al [14] reported that the total length of hospital stay and treatment duration of I&D group were longer than that of revision group but Ho-Rim Choi et al [16] found them shorter. There might be some explanation for this because In the I&D group of Alejandro Lizaur-Utrilla et al' study, most (72%) patients had acute hematogenous infection, but in revision group, most (81%) patients had chronic infection which may need more time for treatment and recovery.

The current meta-analysis also had some limitations that must be considered. First, there were no RCT included in this meta-analysis. Second, heterogeneity was found between studies and there are several possible explanations for this. There may also be some heterogeneity among baseline characteristics of the included patients, with different timing of infection, geographical locations, ages at baseline and infectious organisms. Third, we could not conduct detailed subgroup analysis by relevant subgroups such timing of infection, history of diabetes, and infection caused by different microbes because the data was limited. Although we tried to identify the factors that contribute to the choice of treatment for

patients with PJI, we could not conduct the analysis because of limited data. Fourth, we failed to use a quantitative approach to evaluate secondary outcome because of lack of data. Two studies [12,16] reported the mean of total length of hospital stay and the treatment duration of both I&D and revision strategy but did not mention the standard deviation. There was only one study which reported the data of WOMAC score, KSS knee, KSS function, and ROM after I&D and revision strategy.

In general, our study is relatively comprehensive and timely, but should be interpreted with caution in the context of the level of evidence. Indeed, to robustly compare the effect of I&D and revision strategies, a well-designed randomized clinical trial will be needed in the future.

## Conclusion

This meta-analysis provided some evidences that significant differences were found in the re-infection rates between revision and I&D treatments for PJI. The results suggested that revision strategy might bring more benefits to patients with deep site PJI with better joint function. The length of hospital stay and the treatment duration between the two treatments were inconsistent among studies.

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