**HK98: What is the optimal duration of antimicrobial treatment between stages for patients undergoing two stage exchange for implant associated infections?**

Frank Kolhoff, Koji Yamada, Armen Daniliyants, Daniel H Taupin, Svetlana A Bozhkova, Oscar Murillo, Martin Pietsch, Ashok Rajgopal, Vinay K Aggarwal

**Response/Recommendation:**
Unknown. There is limited to no evidence to help determines the optimal duration of antimicrobial treatment between stages for patients undergoing two stage exchange arthroplasty for the management of periprosthetic joint infection (PJI).

**Level of Evidence:** Limited

**Delegate Vote:**

**Rationale:**
Periprosthetic joint infection (PJI) is a serious complication following total joint arthroplasty (TJA), that requires individualized management.[1,2] Although two-stage exchange arthroplasty is a popular treatment option for patients with chronic periprosthetic joint infection (PJI), the optimal duration and route of antimicrobial administration between the two stages remain undefined and unstandardized. Existing guidelines recommend durations that vary from 4 to 12 weeks, with 6 weeks being the most commonly utilized duration for antimicrobial treatment. To address the posed question above, we conducted a comprehensive systematic review of the literature using MeSH terms developed by librarians. We followed the PRISMA protocol to review the optimal duration of antibiotic treatment between first and second stage of two-stage revisions for PJI in total knee arthroplasty (TKA) and total hip arthroplasty (THA). Following deduplication, 1620 records were available for title and abstract screening, with 104 advancing to full-text review. All one-armed observational studies were excluded due to high risk of bias and low-quality of evidence. One randomized controlled study and four retrospective studies directly compared different antibiotic durations and their impact on success rates at final follow-up were included [3–7]. Risk of bias was evaluated using the Cochrane risk of bias tool 2.0 and the ROBINS-I (Risk of Bias in Non-Randomized Studies of Interventions) (Table 1).

Bernard et al.[3], the only randomized control trial included, analysed 325 PJI cases (hip and knee) assigned to either a 6-week or 12-week antibiotic treatment group, with 1-2 weeks of intravenous (IV) therapy followed by oral administration. A subgroup analysis of 40 patients (6 weeks) and 41 patients (12 weeks) undergoing two-stage procedures showed a non-significant reinfection risk difference within 2 years post-treatment (RD: 10.1, 95% CI [-3.1 to 23.3]), with low risk of bias. Reinfection occurred in 6 of 40 patients (15.0%) in the 6-week group and 2 of 41 patients (4.9%) in the 12-week group.

Meanwhile, Ma et al. [4], reviewed 64 THA PJI cases comparing a systemic antibiotic treatment duration of ≤1 week (n=21) with 4 - 6 weeks (n=43) treatment duration, which included intravenous (IV) followed by oral antibiotics between first and second stage. The mean

follow-up was 75 months (range 24–133). An adjusted odds ratio for reinfection of 0.051 (95% CI [0.002–1.122], p=0.059) was reported for the short-course group compared to 4-6 weeks with serious risk of bias. Additionally, the 5-year implant survival rate, defined as absence of revision or chronic antibiotic use, was 85.2% in the short-duration group compared to 74.0% in the longer-duration group, though this difference did not reach statistical significance (p=0.317).

Similarly, Hsieh et al.[5] assessed 99 THA PJI cases, retrospectively comparing success rates of two-stage revisions between a 1-week IV antibiotic course and a 4–6-week IV treatment group with a mean follow-up of 43 months (range 24–60). Again, no statistically significant difference in overall success rate was found between the 1-week group (89%; 47/53) and the 4–6-week group (91%; 42/46) (p=0.67) with serious risk of bias.

El Helou et al.[6], reported the outcome of 4 weeks IV antibiotics versus 6 weeks IV antibiotics, reviewing 208 PJI cases (THA: n=99; TKA: n=109). Using the Cox Proportional Hazards model adjusted for propensity scores, they found no significant difference in treatment failure rates between patients treated with 6 weeks vs. 4 weeks (HR=1.4, 95% CI [0.7–2.7], p=0.31, moderate risk of bias). However, the results of this study should be interpreted with caution as not all confounders such as causative organism were controlled for, with all MRSA PJI's being assigned to the 6-week group.

Mittal et al.[7] observed 37 TKA PJI cases caused by Methicillin-resistant staphylococcus aureus (MRSA) or Methicillin-resistant staphylococcus epidermidis (MRSE) and retrospectively categorized them into two groups based on antibiotic treatment duration: < 42 days and ≥ 42 days of IV therapy. The success rate of infection control of the initial resistant microorganism was 86.7% (13/15) in the < 42 days group compared to 90.9% (20/22) in the ≥ 42 days group at a mean follow-up of 51 (range 24-111) months. However, success rate was 80.0% (12/15) in < 42 days group compared to 63.6% (14/22) in the ≥ 42 days group, when the definition of success was considered as free of infection including infections caused by new microorganisms and free of chronic antibiotics at follow-up.

Due to the lack of standardised definition of success and the variations in methodologies, we were not able to combine the data and perform a meta-analysis. From our review, none of the comparative studies reported statistically significant differences between shorter and longer duration of antimicrobial treatment. However, it is important to note that the definition of shorter duration and success varied among studies. Moreover, these results were based on limited sample size, with strong heterogeneity in study design, definition of outcomes, and patient populations, which complicates direct comparisons and restricts the feasibility of a robust meta-analysis.

## Conclusion

There is little to no high-quality evidence related to optimal duration of antimicrobial treatment between first and second stage of a two-stage exchange revision for patients with PJI of hip and knee. Although there are several comparative studies, the heterogeneity among available studies and lack of standardized definitions of success makes it difficult to perform meta-analysis. Future research should focus on prospective randomized trials comparing different antibiotic durations, with standardized and comprehensive definitions of success rates with long-term follow-up, to improve our understanding of this issue.

**Table 1. Cochrane risk of bias 2 and ROBINS-I Risk of bias assessment**

| Study | Bias arising from the randomization process | Bias due to deviations from intended interventions | Bias due to missing outcome data | Bias in measurement of the outcome | Bias in selection of the reported result | Overall Risk of Bias |
|---|---|---|---|---|---|---|
| **Bernard et al. (2021)** | Low | Low | Low | Low | Low | Low |
| | - Centralized, computer-generated randomization<br>- Comparable baseline characteristics | - Open-label design<br>- Outcomes assessed by blinded committee<br>- No protocol deviations reported | - Minimal loss to follow-up<br>- Handled with sensitivity analyses | - Objective outcome definitions used<br>- Reinfection assessed by blinded clinical experts using objective criteria | - Predefined protocol and outcomes reported<br>- No selective reporting detected | |

| Study | Bias due to Confounding | Bias in Selection of Participants | Bias in Classification of Interventions | Bias due to Deviations from Intended Interventions | Bias due to Missing Data | Bias in Measurement of Outcomes | Bias in Selection of Reported Results | Overall Risk of Bias |
|---|---|---|---|---|---|---|---|---|
| **Ma et al. (2020)** | Serious | Serious | Low | Serious | Low | Moderate | Moderate | Serious |
| **Hsieh et al. (2009)** | Serious | Serious | Low | Low | Moderate | Moderate | Moderate | Serious |
| **El Helou et al. (2011)** | Moderate | Moderate | Low | Low | Low | Low | Low | Moderate |
| **Mittal et al. (2007)** | Serious | Serious | Moderate | Serious | Moderate | Moderate | Moderate | Serious |

## References


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