

Review Article

Two-Stage Revision for Periprosthetic Joint Infection: Eradication Rates and Functional Recovery

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Abstract

Background: Periprosthetic joint infection (PJI) remains one of the most feared complications of hip and knee arthroplasty, and two-stage exchange has long been considered the reference standard for chronic infection.

Objective: To synthesise evidence on spacer selection, antibiotic delivery, interstage timing, eradication and reinfection rates, comparison with one-stage revision, functional recovery, and risk factors for failure.

Methods: Narrative review of systematic reviews, meta-analyses, registry studies, randomised trials, and cohort literature.

Findings: Pooled reinfection rates after two-stage revision are approximately 8% for both hip and knee, statistically indistinguishable from one-stage revision in aggregate data and in the INFORM randomised trial. Articulating spacers preserve range of motion and function without compromising eradication compared with static spacers. Roughly one in ten to one in four patients never reaches reimplantation.

Conclusions: Two-stage revision achieves reliable infection control, but attrition, mortality, and variable functional recovery remain substantial unresolved burdens.

Keywords: Periprosthetic joint infection; Two-stage revision; Antibiotic spacer; Reinfection rate; Functional outcomes

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Introduction

Periprosthetic joint infection complicates an estimated 0.6-1.0% of primary and up to 4% of revision hip and knee arthroplasties, and already a multi-hundred-million-dollar annual cost to the United States healthcare system a decade ago [1], with its projected economic burden expected to exceed one billion dollars annually as arthroplasty volumes rise [2]. Beyond cost, PJI carries a substantial mortality burden in its own right, with a matched cohort analysis reporting a significantly higher one-year mortality among patients diagnosed with PJI than among aseptic revision controls,

underscoring that infection-related morbidity extends well beyond the operating room [3]. The 2018 International Consensus Meeting definition, validated against a large multicentre cohort, established major and minor criteria combining serum, synovial, and intraoperative findings that now underpin diagnosis and enrolment in comparative outcome studies [4]. Since the classic description of staged reimplantation for infected total knee arthroplasty, two-stage exchange—resection of all components and cement, an interval of antibiotic-loaded spacer treatment, and delayed reimplantation—has been regarded by many surgeons as the most reliable strategy for eradicating chronic PJI [5]. The Infectious Diseases Society of America guideline formalised the surgical and antimicrobial framework for staged exchange alongside debridement-and-retention and one-stage alternatives [6]. Two-stage exchange is technically demanding and resource-intensive, requiring two major operations, a prolonged period of antibiotic-loaded spacer treatment, and close multidisciplinary coordination between orthopaedic surgery and infectious disease services; it is against this backdrop that one-stage revision has re-emerged as a candidate alternative in appropriately selected patients. This review synthesises the comparative literature on spacer type, antibiotic delivery, interstage interval, eradication and reinfection outcomes, one- versus two-stage comparisons, functional recovery, and risk factors for failure, drawing on systematic reviews, meta-analyses, a large pragmatic randomised trial, and national registry data.

Spacer Types: Static versus Articulating

Antibiotic-loaded cement spacers serve as temporary interstage constructs, broadly categorised as static (a cement block or mould providing no joint motion) or articulating (contoured or preformed to permit continued flexion-extension) [7]. A meta-analysis of trials and

cohorts comparing the two approaches in the knee found no significant difference in pooled infection eradication (odds ratio 1.18) but significantly greater postoperative range of motion with articulating spacers (mean difference 12.2°), together with higher Knee Society function scores (mean difference 9.2 points) and Hospital for Special Surgery scores (mean difference 7.0 points) (Table 1) [8]. A minimum five-year comparison likewise found comparable reinfection-free survival between static and articulating spacer cohorts, with the articulating group retaining a functional advantage into mid-term follow-up [9]. Contemporary spacer options—all-cement moulded, metal-on-cement, and preformed articulating designs—each carry trade-offs between mechanical durability, antibiotic elution surface area, and ease of extraction at reimplantation [10]. Historic description of the PROSTALAC functional spacer demonstrated that a mobile, antibiotic-eluting construct could preserve soft-tissue tension and simplify reimplantation while controlling infection [11]. Practically, static spacers are generally reserved for extensive bone loss, ligamentous incompetence, or extensor mechanism disruption, where an articulating construct cannot be reliably retained.

Table 1: Comparative characteristics of static and articulating antibiotic-loaded cement spacers in two-stage revision, drawn from comparative and meta-analytic literature [8,9,10,11].		
Characteristic	Static spacer	Articulating spacer
Joint motion during interval	None	Preserved flexion-extension
Typical indication	Extensive bone loss, extensor mechanism disruption	Adequate bone stock and soft tissue
Pooled infection eradication	Reference (no significant difference)	Odds ratio 1.18 vs static (not significant)
Postoperative range of motion	Reference	+12.2 degrees vs static
Knee Society function score	Reference	+9.2 points vs static
Minimum 5-year reinfection-free survival	Comparable to articulating	Comparable to static

Antibiotic-Loaded Cement and Local Delivery

Spacers are typically loaded with heat-stable antibiotics such as vancomycin, gentamicin, or tobramycin, chosen empirically or according to known organism sensitivities, delivering high local concentrations while limiting systemic exposure [7]. Elution kinetics vary with cement porosity, antibiotic load, and spacer surface area, and under-dosing or antibiotic-cement incompatibility can compromise local drug delivery even when the correct agent class is selected [10]. Local antibiotic delivery is adjunctive to, not a substitute for, pathogen-directed systemic antimicrobial therapy during the interstage period, as codified in the IDSA guideline, which recommends a minimum of four to six weeks of organism-directed intravenous or highly bioavailable oral therapy before consideration of reimplantation [6]. In practice, most surgeons combine a broad-spectrum agent effective against staphylococci with a second agent targeting gram-negative organisms, reserving higher-dose or dual-antibiotic loading for spacers used after culture-negative or polymicrobial resections where empirical coverage must be broader.

Timing Between Stages

The optimal interstage interval remains debated. A systematic review found inconsistent evidence that a longer interval reduces reinfection risk, with most series reporting no significant association between interval duration and treatment success once host and organism factors were accounted for [12]. An Asian cohort study identified a threshold beyond which further delay conferred no added benefit and only prolonged patient morbidity, favouring reimplantation once clinical and laboratory markers normalise rather than a fixed calendar interval [13]. Predictors-of-outcome data similarly suggest that a first stage completed promptly, and reimplantation performed once infection markers have normalised (commonly within four to six weeks in favourable cases),

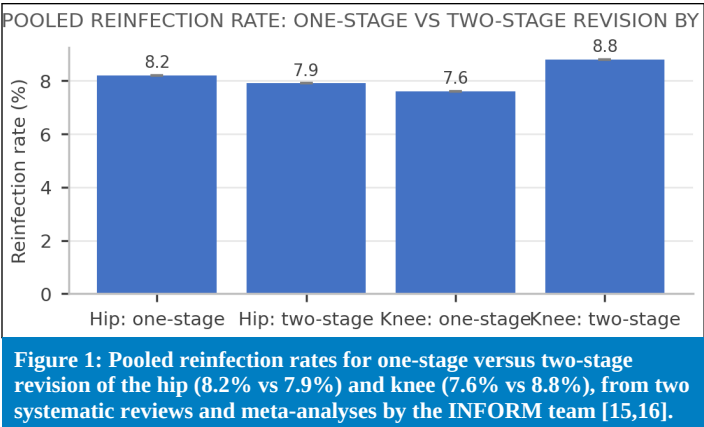
is associated with better long-term function and survivorship (Table 2) [14].

Table 2: Selected comparative and cohort studies of two-stage revision reviewed here [15,16,17,20,21,13,14,26].				
Study	Comparison	Design	Follow-up	Key outcome
Kunutsor 2015	One- vs two-stage, hip	Systematic review/meta-analysis	Variable	Reinfection 8.2% vs 7.9%, not significant
Kunutsor 2016	One- vs two-stage, knee	Systematic review/meta-analysis	Variable	Reinfection 7.6% vs 8.8%, not significant
Nagra 2016	One- vs two-stage, knee	Systematic review	Variable	No overall difference; narrowing gap in recent series
Blom 2022 (INFORM)	One- vs two-stage, hip	Pragmatic RCT	18 months	No difference in hip-related quality of life; fewer operations with one-stage
Lenguerra and 2023	One- vs two-stage, hip	National registry cohort	Up to several years	Comparable mortality; higher early re-revision hazard with one-stage
Tsai 2024	Interstage timing	Observational cohort	Not stated	Reinfection risk plateaus beyond an optimal interval
Rajgopal 2024	Predictors of outcome	Retrospective cohort	10 years	Prompt staging and sensitive organisms predict better function
Wang 2019	Attrition after first stage	Retrospective cohort	Not stated	Substantial proportion never reach reimplantation

Infection Eradication and Reinfection Rates

Aggregate data support two-stage exchange as reliably effective: a systematic review and meta-analysis of hip PJI reported a pooled reinfection rate of 7.9% after two-stage revision, statistically similar to 8.2% after one-stage revision [15]. The equivalent knee analysis reported 8.8% reinfection after two-stage exchange versus 7.6% after one-stage revision, again without a significant difference (Figure 1) [16]. A knee-specific systematic review reached a concordant conclusion, noting that more recent one-stage series achieved lower reinfection rates than earlier cohorts, narrowing the historical gap attributed to two-stage superiority [17]. Long-term follow-up of staged hip reimplantation confirmed durable pathogen control

beyond five years in most successfully reimplanted patients, though repeat infection episodes still occurred in a meaningful minority [18]. Reported success also depends heavily on the outcome definition applied, and repeat two-stage revision after a failed first attempt achieves lower eradication rates than a primary staged exchange [19].



One-Stage versus Two-Stage Revision

The INFORM pragmatic randomised controlled trial, the largest trial directly comparing strategies for infected hip arthroplasty, found no significant difference between one-stage and two-stage revision in patient-reported hip-related quality of life at eighteen months, while one-stage revision required fewer total operations and was less costly to the health system [20]. A linked national registry analysis of English and Welsh hip revisions found comparable medium-term mortality between strategies (29 versus 33 deaths per 10,000 person-years) but a higher early re-revision hazard after one-stage revision in the first three postoperative months (hazard ratio 1.98), converging with two-stage results thereafter [21]. A systematic review of a hybrid "1.5-stage" approach—an articulating spacer intended as a potential definitive implant—reported eradication rates comparable to conventional two-stage exchange while avoiding a formal second major operation in a subset of patients [22].

Proponents of one-stage revision emphasise reduced cumulative surgical burden, shorter overall hospitalisation, and avoidance of a prolonged interstage period during which patients are immobile and functionally compromised; proponents of two-stage exchange emphasise a longer track record, applicability across a broader range of bone loss and soft-tissue compromise, and the option to confirm eradication before committing to definitive components. Collectively, these data suggest that surgical strategy should be individualised to host, organism, and soft-tissue factors rather than assumed to favour either approach universally.

Functional Recovery After Reimplantation

Functional recovery after two-stage revision is generally favourable but incomplete relative to primary arthroplasty. In a cohort followed to ten years, Knee Society knee and function scores improved substantially after reimplantation (knee score 64.0 to 77.2; function score 44.4 to 79.8), with better outcomes among patients with single, antibiotic-sensitive organisms and shorter, well-timed interstage intervals [14]. Articulating spacer use itself confers a measurable functional advantage during the interim period, translating into less muscle contracture and stiffness at the time of reimplantation (Figure 2) [8]. Nonetheless, mean scores after two-stage revision typically remain below those achieved after aseptic revision or primary arthroplasty, reflecting cumulative soft-tissue and bone loss across resection, spacer, and reimplantation stages.

Risk Factors for Treatment Failure

Failure after two-stage exchange clusters around host, organism, and surgical factors. Polymicrobial infection, gram-negative and drug-resistant organisms (including methicillin- and vancomycin-resistant isolates), and culture-negative status have each been associated with reduced survivorship free of reinfection [14,23]. A

dedicated risk-factor analysis of knee PJI treated by two-stage exchange confirmed that resistant or polymicrobial infection, elevated inflammatory markers persisting into the interstage period, and prior failed debridement independently predicted treatment failure [23]. A separate cohort study of early septic failure after reimplantation similarly identified persistently elevated C-reactive protein before reimplantation and unplanned repeat debridement as independent predictors of early recurrence [24]. Culture-negative PJI, which typically follows recent antibiotic exposure or fastidious organisms not recovered by standard culture, does not appear to carry an inherently worse prognosis: a comparative cohort found broadly similar treatment success after two-stage exchange in culture-negative and culture-positive infection, suggesting that empirical antimicrobial coverage guided by clinical suspicion can still achieve durable eradication when a pathogen is never isolated [25]. A substantial proportion of patients never reach reimplantation at all: cohort data indicate that roughly one in ten to one in four patients who undergo resection arthroplasty are unable to proceed to the second stage because of medical deterioration, persistent infection, or death, and that mortality and attrition after the first stage are considerably higher than commonly appreciated [26,27].

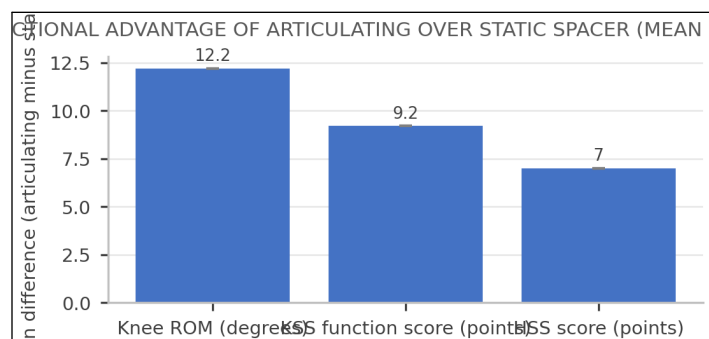


Figure 2: Mean functional advantage of articulating over static spacers in two-stage knee revision: postoperative range of motion (+12.2 degrees), Knee Society function score (+9.2 points), and Hospital for Special Surgery score (+7.0 points), from a meta-analysis of comparative studies [8].

Conclusion

Two-stage exchange remains an effective and widely used strategy for eradicating chronic periprosthetic joint infection, with pooled reinfection rates near 8% for both the hip and the knee that are statistically comparable to contemporary one-stage revision, as corroborated by the INFORM randomised trial and linked registry data [20,21]. Articulating spacers offer a clear functional advantage over static constructs without sacrificing infection control, and interstage timing should be guided by clinical and laboratory trajectory rather than a fixed interval. The principal unresolved burdens are the substantial minority of patients who never reach reimplantation, elevated interstage mortality, and functional outcomes that, while improved, generally fall short of primary arthroplasty—underscoring the need for individualised strategy selection and continued methodological standardisation of outcome reporting.

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