SYSTEMATIC REVIEW

Effects of Antibiotic-Loaded Bone Cement on the Risk of Periprosthetic Joint Infection in Total Knee Arthroplasty: A Systematic Review and Meta-Analysis

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Abstract

Objectives: The use of antibiotic-loaded bone cement (ALBC) is a common strategy for preventing periprosthetic joint infection (PJI) after total knee arthroplasty (TKA); however, its effectiveness remains controversial. This study aimed to provide a clear, evidence-based recommendation regarding the use of ALBC versus plain bone cement (PBC) for the prevention of PJI after TKA.

Methods: This systematic review and meta-analysis was conducted in accordance with the PRISMA 2020 reporting guidelines. PubMed, Embase, and Scopus were searched to identify relevant studies evaluating PJI in patients who received ALBC versus PBC. Eligible studies were screened, selected, and assessed for risk of bias using appropriate checklists. Random-effects meta-analyses were performed to calculate odds ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic. The effects of antibiotic type and dose were examined through subgroup analyses. Meta-regression was performed to evaluate the effects of age, sex, follow-up duration, and diabetes mellitus on the occurrence of PJI.

Results: Eighteen studies including 72,928 TKAs (20,201 in the ALBC group and 52,727 in the PBC group) were included. The overall analysis showed no significant difference in PJI rates between the ALBC and PBC groups (OR, 0.92; 95% CI, 0.67–1.27; p = 0.6). However, cefuroxime-loaded cement was associated with a significantly lower risk of PJI (p = 0.01). In contrast, cement containing gentamicin (p = 0.08), vancomycin (p = 0.3), or tobramycin (p = 0.6) did not show a similar protective effect. Antibiotic dose, age, sex, diabetes mellitus, and follow-up duration did not appear to influence the results.

Conclusion: Most ALBC formulations were not associated with a significant reduction in the risk of PJI. Larger, dedicated trials are needed to further evaluate the effect of ALBC on PJI risk in selected patient populations.

Level of evidence: II

Keywords: Antibiotic-loaded bone cement, Bone cement, Cefuroxime, Periprosthetic joint infection, Total knee arthroplasty, Vancomycin

Introduction

Periprosthetic joint infection (PJI) remains one of the most serious complications associated with total knee arthroplasty (TKA) (1), despite advances in surgical techniques and perioperative care .[1, 2] With an incidence typically ranging from 0.5% to 2%, PJI is a major cause of patient morbidity and mortality and remains the leading indication for revision TKA. [3,4]

The use of antibiotic-loaded bone cement (ALBC) has become a common strategy for reducing the incidence of PJI and the need for revision TKA. The theoretical advantage of ALBC lies in its ability to deliver high local concentrations of antibiotics to the surgical site, thereby preventing initial

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bacterial colonization of the implant and the subsequent formation of difficult-to-treat biofilms. [5]

Although the prophylactic use of antibiotic-loaded bone cement (ALBC) is well established in some regions, its efficacy in primary TKA remains controversial. Recent studies, including large-scale registry analyses and meta-analyses, have reported conflicting findings, making it difficult for clinicians to draw firm conclusions. [6-9] This lack of consensus, together with the potential drawbacks of ALBC—such as increased cost,[10,11] the risk of altered cement mechanical properties,[12] and a possible contribution to antibiotic resistance[13] highlights an important gap in the current literature. Therefore, this study aimed to conduct an updated systematic review and meta-analysis to synthesize the available evidence and provide a clear, evidence-based recommendation regarding the use of ALBC versus plain bone cement (PBC) for the prevention of PJI after TKA. In addition to comparing outcomes according to study design (RCTs vs observational studies), we also assessed the effects of specific antibiotics—vancomycin and cefuroxime—alongside the more commonly used gentamicin and tobramycin

Materials and Methods

This study was conducted in accordance with the PRISMA 2020 reporting guidelines for systematic reviews and meta-analyses,[14] although the study protocol was not prospectively registered.

Search strategy

A comprehensive literature search was conducted in PubMed, Embase, and Scopus, covering all available records from database inception to July 4, 2025. Search terms included database-specific keywords and Medical Subject Headings (MeSH), including bone cements, Arthroplasty, Replacement, Knee, total knee arthroplasty, and periprosthetic joint infection. No restrictions were applied regarding language, country of origin, study design, or publication date. Detailed search strategies are provided in the Supplementary Materials. In addition, to ensure a comprehensive search, the reference lists of all studies included after full-text screening were manually reviewed.

Eligibility Criteria

Studies were eligible for inclusion if they reported data on TKAs performed using ALBC versus PBC. The primary outcome of interest was the incidence of periprosthetic joint infection, including deep joint infection, in the ALBC and PBC groups. To be included, studies were required to report the total number of joints and the number of infections in each group. Studies involving animal models, case series, conference abstracts, editorials, and review articles were excluded.

Selection process

Initial screening of titles and abstracts was performed independently by two reviewers according to predefined eligibility criteria. Any discrepancies were resolved through consultation with a third reviewer to reach consensus. Subsequently, the same two reviewers independently assessed the full texts of all potentially eligible studies and manually screened the reference lists of relevant systematic reviews.

Data extraction

An Excel-based data extraction form was developed for this study and included study design, publication year, country, number of joints, sex, age, surgical indication, antibiotic type and dose, and the outcomes of interest. Thereafter, two authors independently extracted the data. Any discrepancies in data extraction were resolved through discussion and consensus.

Quality appraisal

Two independent reviewers assessed the quality of nonrandomized studies using the Newcastle–Ottawa Scale (NOS). This scale uses an 8-point checklist and assigns stars to evaluate study quality across three domains: (1) selection of the study cohorts; (2) comparability of the groups; and (3) ascertainment of the outcomes of interest. Studies scoring seven or more stars were considered to be of good quality. The quality of randomized studies was assessed using the RoB 2 tool, a widely used instrument for evaluating the risk of bias in randomized trials.

Statistical Analysis

All analyses were conducted using R software, version 4.3.2 (R Foundation for Statistical Computing), with the Meta package, version 6.5-0. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated using a random-effects model to pool the data. Heterogeneity was assessed using the Q statistic and the I^2 statistic, with $I^2 > 50\%$ or $p < 0.05$ considered indicative of significant heterogeneity. Egger's regression test was used to assess publication bias, with $p < 0.10$ considered statistically significant. Three subgroup analyses were performed to evaluate the effects of study design and antibiotic type and dose on the study endpoints. In addition, meta-regression was performed to assess the effects of sex, diabetes mellitus, age, and follow-up duration on the occurrence of PJI.

Results

Search and Screening Results

After removal of 168 duplicate records, 694 articles were retrieved from the database search for further screening. During title and abstract screening, 657 records were excluded, and 37 were retained for full-text review. An additional three reports were identified through citation searching. Ultimately, 18 studies met the eligibility criteria and were included in the analysis, [11, 15-31] as shown in [Figure 1]. One study was excluded [32] because a more recent publication with a longer follow-up from the same patient cohort was available. [27]

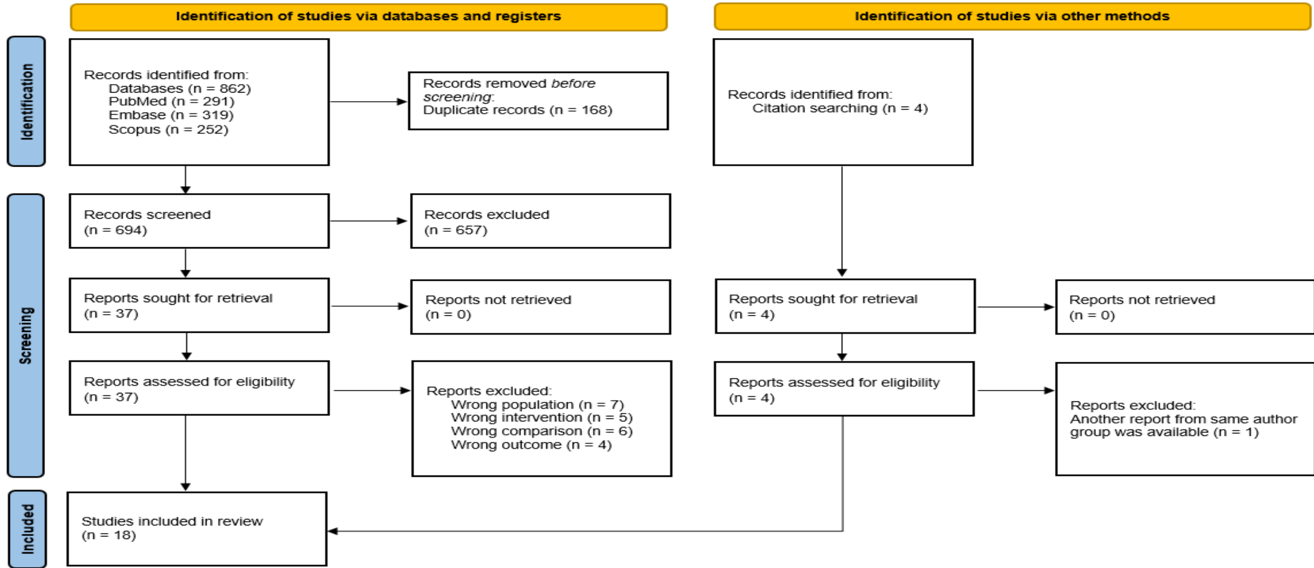

Figure 1. PRISMA flowchart of study selection

Study and patient characteristics

[Table 1] summarizes the characteristics of the 18 included studies published between 2001 and 2024. Most studies were conducted in the United States (n = 7) or China (n = 4). Overall, 12 retrospective studies, five randomized controlled trials (RCTs), and one prospective study were included. The total sample comprised 72,928 knee arthroplasties, of which 20,201 received ALBC and 52,727 received PBC.

Table 1. Baseline study characteristics

Author, Publication year	Country	Study design	Joints (ALBC vs PBC)	M/F	Age, mean ± SD (ALBC vs PBC)	Antibiotic, dose (per 40 g of cement)	PJI definition criteria	Indication to use ALBC vs PBC	Follow up (month)
Chiu et al., 2001[15]	China	RCT	41 vs 37	52/26	72±7.6 vs 69±5.9	Cefuroxime, 2 g	Superficial or deep infection based on McQueen criteria	Patients with odd number on their medical records received ALBC	50 (26 to 88)
Chiu et al., 2002[14]	China	RCT	178 vs 162	136/104	70±7.4 vs 68±6.9	Cefuroxime, 2 g	Superficial or deep infection based on McQueen criteria	Patients with odd number on their medical records received ALBC	49 (23 to 80)
Li et al., 2014[18]	China	RCT	70 vs 66	-	-	Vancomycin, 1 g	Not mentioned	Not mentioned	20.6 (4 to 24)

Table 1. Continued

Cobra et al., 2021[25]	Brazil	RCT	128 vs 158	53/233	Median (IQR): 68 (61-73) vs 66 (61-72.3)	Vancomycin, 2 g	MSIS	Patients with even number on their medical records received ALBC	24
Pardo-Pol et al., 2024[26]	Spain	RCT	1441 vs 1452	652/2241	72.79±7.0 vs 72.60±7.3	Erythromycin+colistin, 0.5 g	Zimmerli criteria	Randomized with a computer-generated list	104.4 (12 to 168)
Namba et al., 2009[27]	USA	Retrospective	2030 vs 20859	8120/14487	67.5 vs 68.1	Gentamicin or Tobramycin, -	CDC criteria for deep infection	Not mentioned	-
Anis et al., 2019[29]	USA	Retrospective	4337 vs 8164	4721/7820	68±10 vs 69±9	Gentamicin or Tobramycin, -	Deep infection based on positive cultures and/ or requiring reoperations	Not mentioned	24 (6 to 54)
Hoskins, et al., 2020[28]	USA	Retrospective	344 vs 2677	-	-	-	Deep infection (no criteria mentioned)	Based on the surgeon's discretion	-
Yayac et al., 2019[10]	USA	Retrospective	1077 vs 1434	-	65.7±8.3 vs 64.6±8.5	Gentamicin or Tobramycin, -	MSIS	Not mentioned	>12 m
Gutowski et al., 2014[30]	USA	Retrospective	4830 vs 3048	-	65.7 vs 65.9	Tobramycin, -	MSIS	After 2003, ALBC was used routinely in all primary TKA in this center. Before 2003, only PBC was used	>24 m
Gandhi et al.,2009[16]	Canada	Prospective	814 vs 811	552/1073	65.1±15.4 vs 67.2±10.8	Tobramycin, -	CDC criteria for deep infection	Based on the surgeon's discretion	>12 m

Table 1. Continued

Zhang et al., 2012[17]	China	Retrospective	945 vs 701	764/882	70.2±7.6 vs 70±7.9	Gentamicin,-	Deep infection (no criteria mentioned)	Not mentioned	>12 m
Eveillard et al., 2003[19]	France	Retrospective	83 vs 84	-	-	Gentamicin, -	Deep wound infection was identified if organisms were isolated in a deep operative tissue sample	Not mentioned	29.6 ± 11.7
Qadir et al., 2014[20]	USA	Retrospective	1486 vs 1025	1646/682	68.1±10.3 vs 68.1±9.8	Gentamicin -, Tobramycin, -	CDC criteria for deep infection	PBC: years 2000 to 2005 ALBC: years 2005 to 2010	>12 m
Wang et al., 2015[21]	China	Retrospective	256 vs 2037	389/1904	63.3±11.1 vs 64.9±10.6	Gentamicin, 0.5-0.8 g	CDC criteria for deep infection	Not mentioned	>12 m
Turhan, 2019[23]	Turkey	Retrospective	85 vs 421	92/414	62.8±10.3 (range: 51-82)	Gentamicin, 1 g	CDC criteria for deep infection	Based on the surgeon's discretion	12 m
Cieremans et al., 2023[24]	USA	Retrospective	1386 vs 7980	3044/6322	65.8±10.1 vs 65.8±9.7	Gentamicin or Tobramycin	MSIS	Not mentioned	60
Sanz-Ruiz et al. 2017[22]	Spain	Retrospective	555 vs 695	433/817	76.1 vs 76.4	Gentamicin, 0.5 g	MSIS	PBC: years 2009 to 2010 ALBC: years 2011 to 2012	>24 m

RCT: Randomized Clinical Trial; ALBC: Antibiotic Loaded Bone Cement; PBC: Plain Bone Cement; CDC: Centers for Disease Control; MSIS: MusculoSkeletal Infection Society; PJI: Periprosthetic Joint Infection

Quality assessment

Most observational studies were of good quality, with 10 of the 13 studies scoring ≥7 on the Newcastle–Ottawa Scale (NOS). The main reasons for lower NOS scores were lack of comparability due to baseline differences between patients

receiving ALBC and PBC and short follow-up duration (<12 months). All five RCTs were judged to have some concerns according to the RoB 2 assessment. Most concerns arose from the lack of appropriate blinding of participants and outcome assessors. Detailed assessments for each study are provided in [Supplementary Table 1], [Supplementary Figure 1], and [Supplementary Figure 2].

ALBC vs PBC and periprosthetic joint infection

This analysis included all eligible studies, comprising 72,928 knee arthroplasties (20,201 in the ALBC group and 52,727 in the PBC group). The incidence of periprosthetic joint infection (superficial or deep) did not differ significantly between the ALBC and PBC groups (OR, 0.92; 95% CI, 0.67–1.27; p = 0.6), with substantial heterogeneity across studies (I^2 = 57.8%; p = 0.002), as shown in [Figure 2]. A sensitivity analysis restricted to studies defining PJI as deep infection showed similar rates of deep infection between the two groups (OR, 1.10; 95% CI, 0.63–1.92; p = 0.7). No evidence of publication bias was detected based on visual inspection of the funnel plot or Egger's test (p = 0.7) [Supplementary Figure 3].

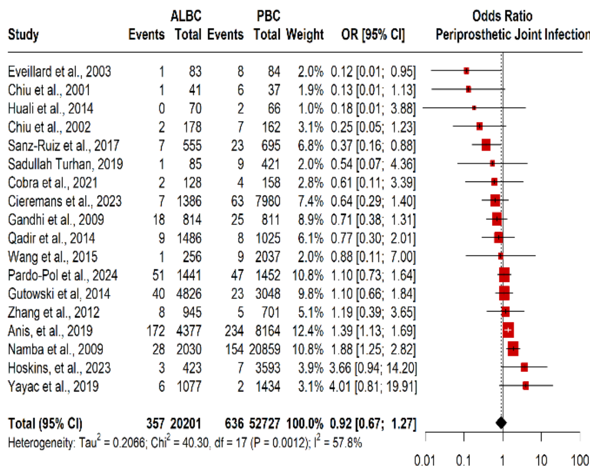

Figure 2. Forest plot of periprosthetic joint infection: PJI rate in ALBC vs PBC after TKA

Subgroup analysis by study design showed that both randomized controlled trials (RCTs) (OR, 0.48; 95% CI, 0.19–1.24; p = 0.13) and observational studies (OR, 1.02; 95% CI, 0.71–1.46; p = 0.9) reported similar rates of joint infection in the ALBC and PBC groups [Figure 3].

Subgroup analysis by antibiotic type included only studies in which the antibiotic used was clearly defined and consistent within the cohort. This analysis showed a lower rate of joint infection among patients who received cefuroxime-loaded cement (OR, 0.20; 95% CI, 0.06–0.72; p = 0.01). In contrast, no significant differences were observed for gentamicin- (p = 0.08), vancomycin- (p = 0.3), or tobramycin-loaded cement (p = 0.6) [Figure 4].

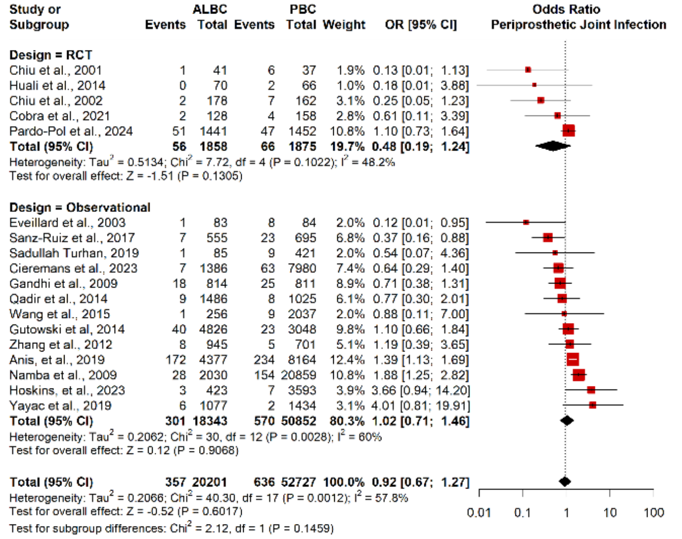

Figure 3. Subgroup analysis based on study type: PJI rate in ALBC vs PBC after TKA

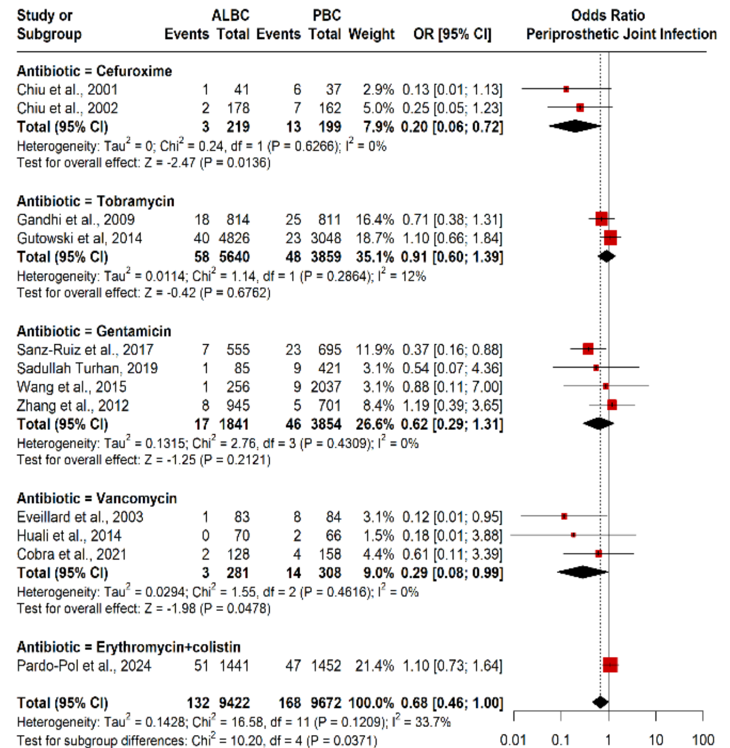

Figure 4. Forest plot of periprosthetic joint infection based on type of antibiotic

Subgroup analysis by antibiotic dose showed no significant difference between the <1 g/40 g and ≥1 g/40 g groups [Supplementary Figure 4].

Meta-regression showed that neither age (intercept = -0.057; p for moderator = 0.27) nor follow-up duration (intercept = -0.0007; p for moderator = 0.88) significantly affected the results. Similarly, no significant effects were observed for the percentage of female patients (intercept = 1.6; p for moderator = 0.9) or diabetes mellitus (intercept = 0.3; p for moderator = 0.12).

Discussion

In this study, we conducted a comprehensive analysis of the efficacy of different antibiotics incorporated into bone cement for the prevention of PJI. Based on the overall analysis of all included studies, no significant reduction in PJI rates was observed between the ALBC and PBC groups. This finding was consistent across both randomized controlled trials (RCTs) and observational studies, suggesting no overall benefit when all available data were pooled. However, subgroup analysis showed that antibiotic type was an important determinant of PJI prevention, whereas antibiotic dose (<1 g vs >1 g per 40 g of cement) did not demonstrate a comparable effect.

A review of the existing literature shows that seven previous meta-analyses have examined the effectiveness of ALBC in knee arthroplasty [6,8,33-37] The most recent of these, published by Kato et al. in 2024, [8] included evidence available up to August 2022. However, the present analysis incorporates several important updates to this body of evidence. We identified three additional studies published after the final search date of the meta-analysis by Kato et al., collectively contributing data from more than 10,000 additional patients. Furthermore, we identified a more recent study from the same Spanish research group with a longer follow-up period. This enabled us to replace an earlier, less comprehensive report from the same group, thereby strengthening the robustness of the dataset.

A recent umbrella review of systematic reviews and meta-analyses on the use of ALBC in primary joint arthroplasty, including both TKA and total hip arthroplasty, has been published.[38] After analysing 10 studies, the authors concluded that there was no difference in the overall infection rate between ALBC and PBC in total joint arthroplasty (TJA). However, the rates of superficial infection and revision were higher in the ALBC group, whereas the rates of deep infection and revision specifically due to PJI were lower with ALBC than with PBC. [38] In the present study, we specifically focused on PJI after TKA and found no difference in PJI rates between ALBC and PBC. However, the subgroup analyses were informative. A key finding was that the type of antibiotic used in the cement may play an important role. Specifically, cefuroxime-loaded cement (p = 0.01) was associated with a significantly lower rate of PJI. In contrast, cement loaded with gentamicin (p = 0.08), vancomycin (p = 0.3), or tobramycin (p = 0.6) did not show a statistically significant protective effect. These findings suggest that the choice of antibiotic, rather than the use of ALBC itself, may be a critical determinant of PJI prevention. The effect of antibiotic type in bone cement was previously examined in a meta-analysis by Xu et al. [33] in 2022; The apparent effectiveness of cefuroxime may be related to its broader antimicrobial activity against common pathogens associated with PJI after TKA, including coagulase-negative staphylococci and *Staphylococcus aureus*. [39] Nevertheless, this finding should be interpreted with caution because the conclusion regarding cefuroxime is based on a very small number of studies and events. The analysis is therefore underpowered, and the confidence interval is wide. This important methodological limitation means that the statistically significant finding for cefuroxime should be considered hypothesis-generating and requires confirmation in larger, dedicated trials.

Interestingly, subgroup analysis according to antibiotic dose (i.e., <1 g/40 g versus ≥1 g/40 g) showed no significant difference in PJI rates. This finding is particularly relevant given concerns that higher antibiotic doses may compromise the mechanical properties of bone cement and contribute to the development of antibiotic resistance. Tootsi et al. [13] reported that the use of ALBC was not associated with increased antibiotic resistance in any of the bacterial isolates identified in 218 patients with joint infection following TKA or hip arthroplasty. [13]

Another important consideration is the cost-effectiveness of using antibiotics in bone cement to prevent a single case of infection. Yayac et al. [11] reported that, for ALBC to be cost-justified, it would need to prevent one PJI for every 101 patients treated. [11] King et al. showed that, in hospitals performing 1,000 TKAs annually, switching to PBC could save between $155,000 and $310,000 per year. [10] Given the inconsistent evidence regarding the efficacy of ALBC in preventing PJI and the substantial economic burden associated with its use, some authors have recommended restricting ALBC to selected situations, such as high-risk surgeries or revision arthroplasties. [9] Although the economic argument against routine ALBC use is compelling, other studies and professional bodies have suggested that the long-term benefits of infection prevention, even if the absolute event rate is low, may outweigh the initial costs. The burden of PJI is not solely economic; it also has a major impact on patient morbidity and quality of life, factors that are difficult to quantify financially. Oliver and Brown also highlighted the limited statistical power and risk of selection bias in previous studies of ALBC in TKA as possible explanations for the lack of significant differences observed between ALBC and PJI outcomes. They concluded that larger studies with higher-quality evidence may better clarify the cost-effectiveness of ALBC use in TKA. [40]

The ambiguity surrounding the indications for ALBC versus PBC use [Table 1] represents an important

methodological limitation across the reviewed literature and creates a substantial risk of confounding by indication. In most included observational studies, the clinical factors underlying the surgeon's decision to use ALBC—such as older age or known high-risk characteristics, including diabetes, immunocompromised status, or obesity—were not explicitly reported. This lack of clarity suggests that the ALBC group may have included patients with different, and potentially less favourable, baseline prognostic characteristics than the PBC group, given that ALBC is often selectively used in patients considered to be at higher risk of infection or fixation failure. Consequently, the observed comparative outcomes are highly vulnerable to channelling bias, whereby any true benefit or harm attributable to ALBC itself may have been obscured or exaggerated by underlying differences in patient risk profiles.

Overall, the available evidence highlights the complexity of this issue, as different studies and professional organizations weigh economic costs, clinical benefits, and patient outcomes differently. Ultimately, the decision to use ALBC is likely to depend on a combination of factors, including institution-specific PJI rates, individual patient risk factors, and the surgeon's clinical judgment.

A major strength of this study is its comprehensive approach, combining meta-analysis and meta-regression to synthesize a large body of evidence. This approach incorporated a broad range of study designs, from randomized controlled trials (RCTs) to observational studies, thereby providing a robust overview of the topic. The subgroup analyses are another important strength, as they help clarify conflicting findings in the literature. However, several limitations should be acknowledged. The substantial heterogeneity among the included studies—for example, differences in the definition of PJI, follow-up duration, and patient characteristics—is a major concern, as pooling results from studies with different methodologies and populations can be challenging. In addition, most included studies were retrospective and therefore inherently susceptible to channelling, selection, and reporting biases. Furthermore, the limited number of RCTs in some subgroups, such as the erythromycin subgroup, may have reduced the statistical power of these analyses and limited the ability to draw firm conclusions. The study also did not evaluate the long-term effects of ALBC or its potential contribution to antibiotic resistance, both of which are important considerations in clinical practice. In addition, the lack of available data precluded analyses according to different follow-up durations and geographic regions. Finally, the potential for confounding by indication remains an important limitation and underscores the need for larger RCTs to address this issue.

Future implications:

Our findings highlight the need for future research to move beyond a simple comparison between ALBC and PBC. The focus should shift toward identifying which specific antibiotics are most effective, at what doses, and in which patient populations. Future studies should also investigate the potential role of combination therapies and other antimicrobial agents in further optimizing infection prevention strategies in TKA.

Conclusion

In conclusion, the findings of this meta-analysis suggest that the routine use of ALBC in primary TKA does not reduce the incidence of PJI. However, a more targeted approach using specific antibiotics may be more effective in reducing PJI rates. These findings underscore the need to move beyond a one-size-fits-all approach and to consider the specific antibiotic incorporated into the cement. Further high-quality randomized controlled trials, particularly those evaluating the efficacy of different antibiotics and their optimal dosing, are needed to provide greater clarity and inform evidence-based guidelines for PJI prevention.

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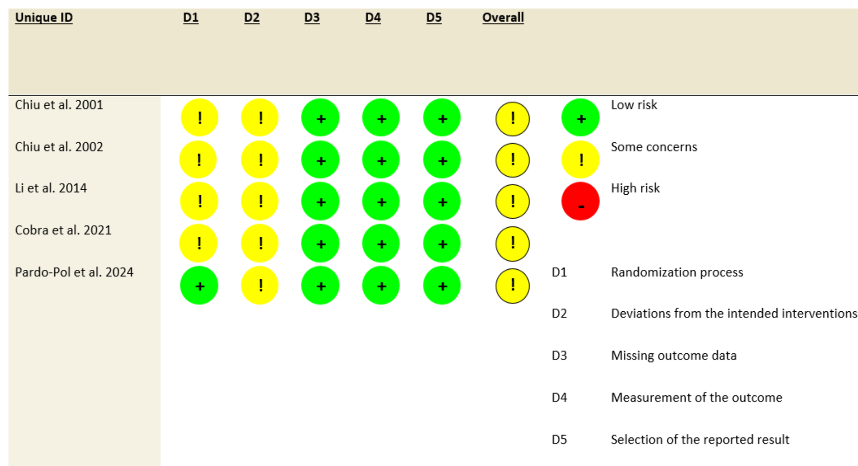
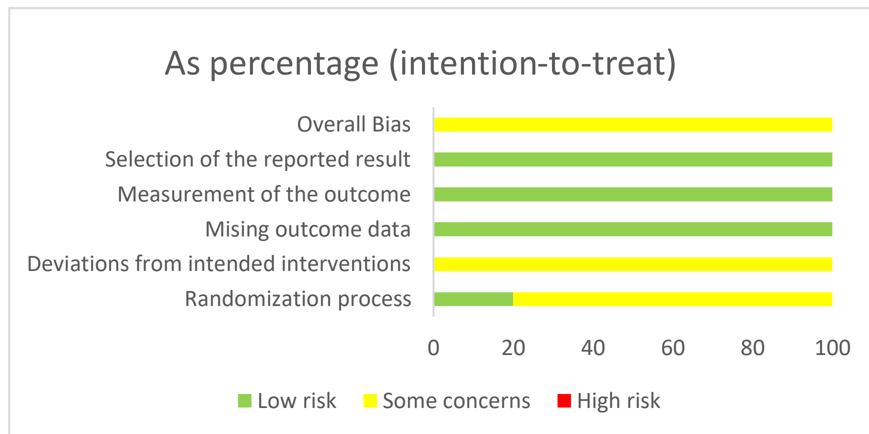
Supplementary Table 1. New Castle Ottawa scale scores for observational studies

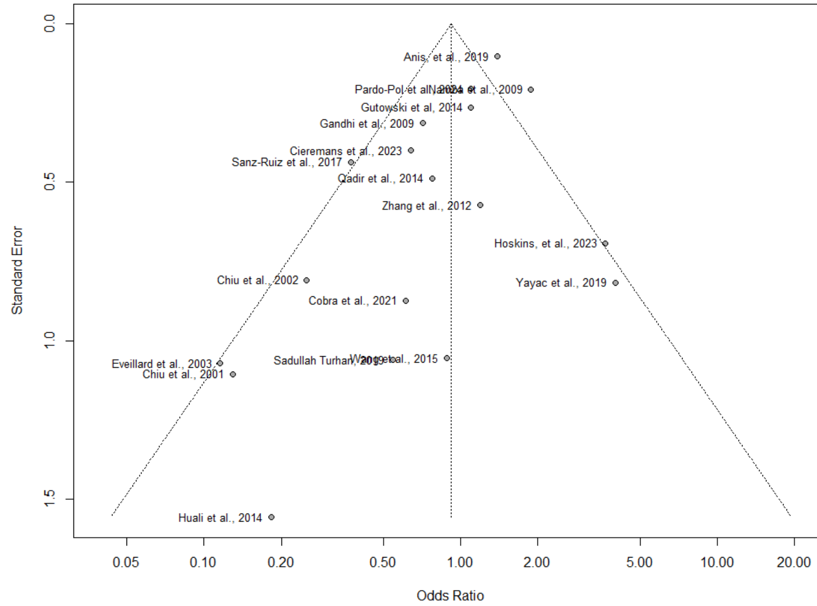
Study	Selection	Comparability	Outcome	Overall quality
Yayac et al. 2019	☆☆☆☆	☆	☆☆	7
Gutowski et al. 2014	☆☆☆☆	☆	☆☆	7
Hoskins, et al. 2020	☆☆☆☆	☆	☆☆	7
Namba et al. 2009	☆☆☆☆	☆	☆☆	7
Zhang et al. 2012	☆☆☆☆	☆☆	☆☆☆	9
Gandhi et al. 2009	☆☆☆☆	☆☆	☆☆☆	9
Qadir et al. 2024	☆☆☆☆	☆☆	☆☆	8
Wang et al. 2015	☆☆☆☆	☆	☆☆	7
Sanz-Ruiz et al. 2017	☆☆	☆	☆☆	5
Turhan et al. 2019	☆☆☆☆	--	☆☆	6
Cieremans et al. 2023	☆☆☆☆	☆	☆☆	7
Anis et al. 2019	☆☆☆	--	☆☆	5
Eveillard et al. 2003	☆☆☆☆	☆☆	☆☆	8



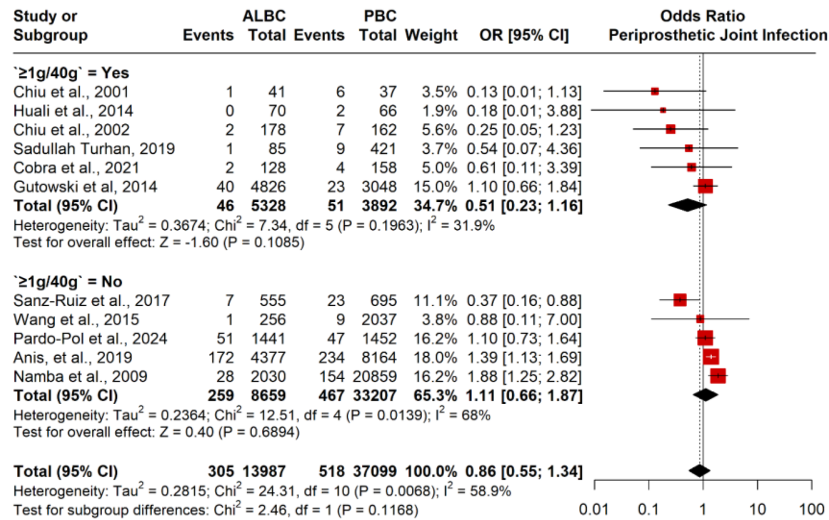
Supplementary figure 1. Quality of randomized clinical trials based on RoB2 tool



Supplementary figure 2. Overall quality of randomized clinical trials based on each domain of bias



Supplementary Figure 3. Funnel plot of periprosthetic joint infection in antibiotic-loaded bone cement vs plain bone cement for total knee arthroplasty. The figure shows no sign of publication bias.



Supplementary Figure 4. Forest plot of periprosthetic joint infection based on antibiotic dose