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### Use of Antibiotic-loaded Bone Cement in Knee Prosthesis: Infection Prevention and its Economic Impact on Hospitalization Costs

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#### Abstract

##### Background

Periprosthetic joint infection (PJI) remains one of the most serious complications following total knee arthroplasty (TKA), often requiring complex surgical revisions and prolonged antibiotic therapy. Antibiotic-loaded bone cement (ALBC) has been proposed as a preventive strategy by delivering high local concentrations of antibiotics at the implant site.

##### Objective

This review aims to critically analyze the clinical effectiveness of ALBC in preventing PJIs in TKA and to evaluate its impact on healthcare costs associated with infection-related hospitalizations and revisions.

##### Methods

A narrative review was conducted based on 22 peer-reviewed studies, including randomized trials, registry data, systematic reviews, and economic analyses. The selected literature focused on infection rates, resistance patterns, biomechanical performance, and cost-effectiveness of ALBC compared to plain bone cement (PBC) in primary and revision TKA.

##### Results

Evidence supports the selective use of ALBC in high-risk patients and revision procedures, showing reduced infection rates and favorable economic outcomes. However, its universal application in primary TKA remains controversial due to inconsistent findings and concerns regarding mechanical properties and antibiotic resistance. Dual-antibiotic formulations demonstrate enhanced antimicrobial efficacy, especially in biofilm-related infections. The mechanical performance of ALBC is preserved in low-dose industrial formulations, and cost analyses suggest long-term savings when used in targeted populations.

##### Conclusion

ALBC is a valuable adjunct in TKA for infection prevention, particularly in high-risk or revision cases. Its routine use in all primary procedures is not currently supported by conclusive evidence. Risk-based implementation, guided by microbiological and economic considerations, is recommended to optimize outcomes and ensure cost-effective care.

**Keywords:** Antibiotic-loaded Bone Cement, Total knee Arthroplasty, Periprosthetic Joint Infection, Cost-effectiveness, Biofilm

#### 1. Introduction

Periprosthetic joint infection (PJI) is one of the most devastating complications associated with total knee arthroplasty (TKA), with incidence rates ranging from 1% to 2% worldwide, imposing significant clinical and economic burdens on healthcare systems and patients alike <sup>[1, 2]</sup>. The consequences of PJI include prolonged hospitalization, decreased functional outcomes, psychological distress, and elevated treatment costs that can be up to double those of aseptic revisions <sup>[3]</sup>.

The current standard of care for chronic PJI includes a two-stage revision protocol, involving the removal of the infected prosthesis, thorough debridement, placement of an antibiotic-loaded bone cement (ALBC) spacer, and subsequent reimplantation after infection control <sup>[4]</sup>. ALBC plays a key role in this context by delivering high local concentrations of

antibiotics at the infection site, surpassing levels achievable through systemic therapy alone, and contributing to biofilm disruption on the implant surface<sup>[5]</sup>.

Introduced in the 1970s, ALBC has gained broad acceptance for both prophylaxis and treatment of PJIs. Nonetheless, there is ongoing debate about its effectiveness, particularly in primary TKA. Variability in antibiotic types, doses, and cement formulations has led to conflicting results regarding its impact on infection prevention and prosthetic survival<sup>[6]</sup>. In some European countries, ALBC is used routinely in primary TKA, whereas in others, such as the United States, its use remains more limited due to regulatory and cost considerations<sup>[7]</sup>.

Large-scale observational studies and registry data have shown that ALBC is associated with reduced risks of both septic and aseptic revisions, with enhanced prosthetic survival, particularly when dual-antibiotic formulations are used<sup>[2, 6]</sup>. Meta-analyses confirm that high-dose ALBC and the use of specific antibiotics, such as gentamicin or vancomycin, contribute to better outcomes in reducing deep infections in primary procedures<sup>[8]</sup>.

However, the success of ALBC may be compromised in cases where the causative pathogens exhibit resistance to the incorporated antibiotics. Studies have demonstrated that infections involving gentamicin- or teicoplanin-resistant organisms require more surgical interventions and are associated with higher overall treatment burdens<sup>[1, 3]</sup>. Tailoring the antibiotic composition in ALBC to the sensitivity profile of the infecting microorganisms has been suggested as a strategy to improve efficacy.

From an economic standpoint, although ALBC increases the initial procedural cost, it may reduce the total cost of care by decreasing the incidence of reinfection and subsequent revision surgeries<sup>[3]</sup>. Still, the literature reports substantial heterogeneity in clinical outcomes and cost-effectiveness, reflecting differences in surgical protocols, microbiological patterns, and healthcare system practices.

Given the increasing number of TKA procedures globally and the anticipated rise in revision surgeries due to PJIs, consolidating the evidence on the clinical and economic implications of ALBC is imperative to guide orthopedic decision-making and resource allocation. The objective of this review article is to critically analyze the use of antibiotic-loaded bone cement in knee arthroplasty procedures, focusing on its effectiveness in preventing periprosthetic joint infections (PJIs) and evaluating its impact on hospitalization-related healthcare costs. The study aims to synthesize current evidence from clinical and economic perspectives to inform best practices in orthopedic surgery and hospital resource management.

## 2. Methodology

This study was designed as a narrative literature review with the aim of evaluating the clinical effectiveness and economic impact of antibiotic-loaded bone cement (ALBC) in the prevention of periprosthetic joint infection (PJI) in total knee arthroplasty (TKA). The review adhered to methodological standards for structured evidence synthesis in orthopedic surgery and infection control research. The process was carried out in the following stages:

### 2.1 Definition of Research Objective and Scope

The central objective was to critically analyze the role of ALBC in TKA procedures, particularly in relation to its efficacy in preventing PJI and its influence on

hospitalization-related healthcare costs. The review also included secondary aims such as assessing ALBC's impact on antibiotic resistance, mechanical properties, and its applicability in different healthcare contexts.

### 2.2 Eligibility Criteria

The selection of studies for this review followed rigorously defined eligibility criteria to ensure the inclusion of high-quality and clinically relevant evidence. Eligible studies were limited to peer-reviewed publications released between 2004 and 2025. The types of studies considered included randomized controlled trials, prospective and retrospective observational studies, meta-analyses, registry-based cohort analyses, systematic reviews, and economic evaluations. Inclusion was restricted to studies that specifically examined the use of antibiotic-loaded bone cement (ALBC) in the setting of total knee arthroplasty (TKA), and which reported measurable outcomes related to infection prevention, microbial resistance development, biomechanical properties of the cement, or economic implications associated with its use.

Exclusion criteria were applied to maintain thematic specificity and methodological rigor. Studies that focused on arthroplasty procedures unrelated to the knee joint, such as those concerning the hip or shoulder, were excluded unless findings were directly applicable to TKA. Non-English publications were also excluded to ensure consistency in data interpretation and methodological assessment. Additionally, opinion-based literature, including narrative editorials, expert commentaries, and letters to the editor lacking original clinical data, were not considered in this review.

### 2.3 Search Strategy and Data Sources

Although the search was not limited to database access, all primary articles included in this review were selected from a pre-established set of 22 scientific papers provided by the authors of the study. These articles were drawn from reputable journals including *The Journal of Arthroplasty*, *Knee Surgery Sports Traumatology Arthroscopy*, *Antibiotics*, *BMJ Open*, *EFORT Open Reviews*, *World Journal of Orthopaedics*, and others. Sources span registry data from Europe, retrospective cohort analyses, randomized controlled trials, biomechanical studies, and cost-effectiveness models.

### 2.4 Screening and Selection Process

All 22 articles were read in full by the lead reviewer. A checklist was applied to assess relevance to the topic, quality of data, clarity of outcomes, and applicability to the context of TKA and ALBC use. Duplicate information across studies was cross-referenced and categorized under thematic subtopics: Clinical efficacy, comparison with plain bone cement (PBC), antibiotic resistance, mechanical properties, and economic impact.

### 2.5 Data Extraction and Synthesis

From each selected article, a structured data extraction process was conducted to ensure consistency and comprehensive synthesis. The following variables were systematically collected: The type and year of publication; characteristics of the study population and sample size; the intervention implemented, including the formulation and dosage of antibiotic-loaded bone cement (ALBC); the

control or comparison group used, such as plain bone cement (PBC) or systemic antibiotic therapy alone; the clinical and economic outcomes evaluated, including rates of periprosthetic joint infection (PJI), emergence of antimicrobial resistance, procedure-related costs, and cement-related mechanical failure. Additionally, the principal conclusions and reported methodological limitations of each study were documented to aid in the critical appraisal and comparative analysis.

The extracted data were synthesized qualitatively through a thematic analysis framework. This approach enabled the identification of key concepts and trends across studies, which were subsequently organized into subtopics reflecting the main dimensions of the research objective—namely, clinical efficacy, antimicrobial resistance, biomechanical performance, cost-effectiveness, and implementation practices. These thematic categories served as the structural basis for the discussion and interpretation of the findings within the context of TKA and infection prevention.

## 2.6 Quality and Bias Assessment

Although this review did not employ formal risk-of-bias assessment tools such as GRADE or PRISMA—given its narrative and integrative design—a critical appraisal of the included studies was nonetheless conducted to ensure methodological soundness and interpretive reliability. Each study was evaluated based on the robustness of its design, including clarity of research questions, appropriateness of methodology, and internal validity. The statistical rigor of the analyses was also considered, particularly the adequacy of sample sizes, use of control groups, and transparency in data reporting.

Furthermore, potential sources of bias were examined, including risks of selection bias, reporting bias, and publication bias, especially in non-randomized or industry-funded studies. Finally, the clinical relevance and applicability of the findings to total knee arthroplasty (TKA) were assessed, ensuring that only studies with direct translational value to infection prevention strategies in TKA were retained for synthesis and discussion.

## 2.7 Ethical Considerations

As this study constitutes a narrative review of previously published literature, it did not involve the collection of new clinical data or direct interaction with human participants. Consequently, the research did not require approval from an institutional review board or ethics committee. All data analyzed were obtained from publicly accessible, peer-reviewed scientific sources, and were used in accordance with principles of academic integrity and ethical scholarship.

## 3. Results and Discussion

Preventing periprosthetic joint infection (PJI) remains a critical concern in total knee arthroplasty (TKA), given the significant morbidity, revision burden, and financial impact it imposes. In this context, antibiotic-loaded bone cement (ALBC) has been widely investigated for its potential to reduce infection rates both in primary and revision arthroplasties. This section explores the clinical efficacy, microbiological implications, mechanical properties, economic impact, and global variation in ALBC usage. Evidence is drawn from 22 peer-reviewed studies and is organized into five key subtopics.

### 3.1 Clinical Efficacy of ALBC in TKA

Antibiotic-loaded bone cement (ALBC) has been the focus of considerable clinical research regarding its role in reducing the incidence of periprosthetic joint infection (PJI) in total knee arthroplasty (TKA), especially in revision procedures. Its primary advantage lies in the ability to deliver high local concentrations of antibiotics directly to the surgical site, exceeding those achievable through systemic administration. When employed in conjunction with systemic antimicrobial therapy, ALBC demonstrated an enhanced capacity to reduce infection recurrence, making it a valuable tool in complex or high-risk cases<sup>[1, 2]</sup>.

Robust registry-based data, particularly from Scandinavian countries, have provided consistent evidence supporting the prophylactic benefit of ALBC in cemented TKAs. Notably, findings from the Catalan Arthroplasty Register highlighted a statistically significant reduction in both septic and aseptic revision rates in patients treated with ALBC compared to those receiving plain bone cement (PBC)<sup>[2]</sup>. These large-scale observational findings suggest that ALBC may contribute not only to infection control but also to improved prosthesis longevity in specific healthcare settings.

Nevertheless, controlled clinical trials and meta-analyses have produced more heterogeneous results, particularly in the context of primary TKA. Several randomized studies have indicated no significant difference in infection rates between patients receiving ALBC and those receiving PBC in populations considered to be at low risk for infection<sup>[4, 14]</sup>. These inconsistencies underscore the importance of patient stratification and raise questions about the generalizability of ALBC's prophylactic benefits across broader clinical contexts.

Beyond registries and randomized trials, evidence has emerged underscoring the particular utility of ALBC in revision arthroplasties. In these cases, the presence of mature bacterial biofilms presents a considerable therapeutic challenge. ALBC, particularly in high-concentration or dual-antibiotic formulations, has been shown to improve outcomes by delivering potent localized antimicrobial action capable of penetrating biofilms and addressing a broader spectrum of pathogens<sup>[1, 5, 17, 21]</sup>.

Expanding upon its role in revisions, ALBC has also shown promising results in specific high-risk groups undergoing primary TKA. Patients with diabetes, immunosuppression, or other systemic vulnerabilities have demonstrated a decreased incidence of superficial and deep postoperative infections when treated with ALBC<sup>[6, 8]</sup>. These findings point to the importance of individualized prophylaxis strategies and suggest that a one-size-fits-all approach may not be appropriate in TKA infection prevention.

However, not all investigations corroborate these findings. A multicenter randomized controlled trial conducted in Norway found no statistically significant difference in infection outcomes between ALBC and PBC groups in primary arthroplasty procedures, despite the use of standardized protocols<sup>[7]</sup>. Such findings contribute to ongoing debates about the universal application of ALBC and reinforce the need for contextual interpretation based on patient-specific and institutional factors.

Further support for ALBC's protective effect comes from long-term outcome analyses. Research conducted in Northern Europe has suggested a decrease in PJI-related revisions among patients who received ALBC, implying that its benefits may accrue over time and contribute to extended

prosthetic survival [2, 20]. These observations highlight the potential for cumulative prophylactic effects, especially in settings where surgical techniques and perioperative protocols are rigorously standardized.

Importantly, the success of ALBC implementation appears to be strongly influenced by the healthcare system and clinical infrastructure. Variables such as antibiotic stewardship programs, operative environment control, and post-discharge surveillance impact the overall efficacy of infection prevention measures, including ALBC [2, 20]. Therefore, international variations in outcomes may reflect differences in practice patterns as much as in the biological efficacy of the cement itself.

Taking it together, current evidence suggests that ALBC can play a significant role in infection prevention strategies in TKA. However, its benefits are most clearly demonstrated in revision surgeries and among patients with identifiable infection risk factors. Broad, routine use in all primary arthroplasty cases may not provide substantial clinical or economic advantages and should be evaluated on a case-by-case basis. While ALBC is undeniably valuable in selected patient populations, its universal application in primary TKA remains controversial. Tailoring its use according to clinical risk profiles, microbial sensitivity, and institutional capabilities appears to be the most prudent approach to maximizing its benefits while mitigating unnecessary risks and costs [8, 12].

### 3.2 Comparison Between ALBC and Plain Bone Cement (PBC)

Comparative analyses between antibiotic-loaded bone cement (ALBC) and plain bone cement (PBC) in total knee arthroplasty (TKA) have yielded inconsistent results across literature. While numerous retrospective studies report favorable outcomes with ALBC, particularly lower postoperative infection rates and reduced need for reoperation, these findings have not been consistently replicated in randomized controlled trials [2, 6, 13]. The discordance highlights the complexity of evaluating infection prevention strategies in varied clinical settings.

A comprehensive systematic review published in 2022, encompassing more than 6,000 primary TKA cases, concluded that there was no statistically significant difference in overall infection rates between ALBC and PBC groups. However, several studies within the review identified subgroups of patients, especially those with comorbid conditions—in whom ALBC use conferred a measurable benefit [20]. These results suggest that ALBC may be effective in selected populations but not universally across all surgical candidates.

Variations in surgical technique, types of cement used, antibiotic dosage, and follow-up duration likely contribute to the heterogeneity of findings. In addition, inconsistency in the definitions and diagnostic criteria for periprosthetic joint infection (PJI) further complicates the direct comparison of outcomes between studies [16]. This underscores the need for standardized reporting frameworks and outcome measures in future trials assessing cement types.

Importantly, a growing body of literature supports the notion that ALBC's protective effect becomes more apparent in higher-risk scenarios. For example, dual-antibiotic formulations or high-dose preparations have shown increased effectiveness in patients undergoing revision

surgeries or those with comorbidities such as diabetes or obesity [5, 21]. In contrast, the routine use of ALBC in otherwise healthy patients undergoing primary TKA does not appear to confer significant advantages and may not be cost-effective [6, 19].

A large-scale registry analysis from North America echoed these findings, reporting no reduction in deep infection rates associated with ALBC in standard-risk populations. This reinforces the importance of individualized treatment planning based on preoperative risk stratification, rather than adopting a one-size-fits-all approach [19].

From a biomechanical perspective, several studies comparing PBC and ALBC have demonstrated comparable outcomes in terms of implant fixation, long-term stability, and rates of aseptic loosening. These results suggest that, when properly formulated and applied, ALBC does not compromise the mechanical integrity of the prosthesis [13, 17]. Patient-reported outcomes further support this equivalency. Satisfaction levels, postoperative pain control, and functional recovery were found to be similar in matched cohorts receiving either ALBC or PBC, indicating that the key differentiator remains the potential for infection prophylaxis rather than improvements in subjective recovery metrics [14].

Moreover, some subgroup analyses from multicenter trials have noted a potential reduction in superficial wound complications and local inflammatory responses with ALBC use, although these findings have not consistently reached statistical significance [20]. Such observations suggest a possible adjunctive benefit of ALBC in soft tissue healing, warranting further investigation.

Ultimately, the choice between ALBC and PBC should be guided by a combination of clinical judgment, patient-specific risk factors, microbiological considerations, and institutional protocols. Given the variability in reported outcomes and the multifactorial nature of PJI prevention, a universal recommendation is not currently justified. Selective use of ALBC, particularly in high-risk or revision cases, appears to offer the most rational and evidence-based approach [12, 19].

### 3.3 Bacterial Resistance and Microbiological Concerns

Although antibiotic-loaded bone cement (ALBC) enables the delivery of high local concentrations of antibiotics directly at the implant site, concerns have been raised regarding the potential for prolonged subinhibitory antibiotic levels during the elution phase. These low yet persistent concentrations may exert selective pressure on microbial populations, potentially contributing to the emergence of resistant strains over time [3, 10, 16].

Both *in vitro* experiments and clinical observations have documented a higher prevalence of resistant pathogens—such as gentamicin-resistant *Staphylococcus aureus*—in revision arthroplasties previously managed with ALBC. This association underscores the risk of monotherapy, particularly when antibiotic elution is incomplete or prolonged at subtherapeutic levels [18, 21]. Nevertheless, recent studies suggest that the use of dual-antibiotic formulations may mitigate this effect by expanding antimicrobial coverage and minimizing resistance selection pressure through synergistic activity [4, 17].

Despite these microbiological concerns, epidemiological data indicate that the widespread use of ALBC has not yet translated into a demonstrable increase in antimicrobial



resistance at the population level. This appears particularly true when ALBC is used judiciously, in conjunction with systemic antibiotics, and with carefully controlled dosing protocols<sup>[11]</sup>.

The pharmacokinetic advantage of ALBC lies in its ability to exceed the minimum inhibitory concentration (MIC) for most causative pathogens, often by several orders of magnitude. Such concentrations may effectively suppress or eradicate low-level resistant bacterial subpopulations, especially in the early postoperative period<sup>[19]</sup>. Nonetheless, clinicians are advised to exercise caution, particularly in revision surgeries, where bacterial burden and biofilm presence are typically higher. In these cases, culture-guided antibiotic selection remains essential to optimize outcomes and minimize resistance development<sup>[1, 12]</sup>.

Evidence supports the use of personalized ALBC formulations, tailored to microbiological findings, particularly in two-stage exchange protocols for chronic PJI. In such cases, incorporating antibiotics with proven efficacy against the identified pathogens has been associated with higher rates of infection eradication and prosthesis salvage<sup>[21, 22]</sup>. Biofilm-producing organisms continue to represent a formidable therapeutic challenge. Although ALBC may exhibit some activity against superficial layers of biofilm, its ability to penetrate mature biofilms or eliminate intracellular pathogens remains limited. As such, its effectiveness is significantly enhanced when combined with thorough surgical debridement and appropriate systemic therapy<sup>[3, 5]</sup>.

In instances of ALBC treatment failure, postoperative cultures frequently reveal polymicrobial and multidrug-resistant flora. These cases are often more complex to manage and may necessitate escalation to broad-spectrum intravenous antibiotics or alternative local delivery strategies<sup>[12, 18]</sup>.

Surveillance data tracking resistance patterns among ALBC-treated patients indicate relatively stable susceptibility profiles for commonly used agents such as gentamicin and vancomycin. However, regional variations have been observed, likely influenced by local antimicrobial policies, prescribing habits, and cement formulations in use<sup>[10, 20]</sup>. Given these concerns, the routine prophylactic use of ALBC in low-risk primary arthroplasties remains controversial. In the context of increasing global efforts toward antimicrobial stewardship, its use should be reserved for well-justified clinical indications where the potential benefits clearly outweigh the risks<sup>[16, 22]</sup>.

### 3.4 Mechanical Properties and Elution Characteristics

The mechanical integrity of polymethylmethacrylate (PMMA) bone cement can be influenced by the incorporation of antibiotics, especially when used in high concentrations. Although antibiotic-loaded bone cement (ALBC) provides substantial antimicrobial advantages, excessive antibiotic loading has been associated with reduced compressive strength, diminished fatigue resistance, and compromised implant fixation—factors that can jeopardize the long-term stability of the prosthesis<sup>[5, 13, 17]</sup>.

Evidence from biomechanical studies suggests that low-dose ALBC formulations—generally defined as containing less than 2 grams of antibiotic per 40 grams of cement—preserve the structural properties of the cement matrix. This is particularly true when the cement is manufactured under controlled industrial conditions, which ensure consistent mixing, particle dispersion, and polymerization<sup>[16]</sup>.

Conversely, manual incorporation of antibiotics during surgery has been linked to heterogeneous distribution and increased porosity, both of which can undermine the mechanical performance of the cement<sup>[18]</sup>.

The ability of ALBC to release antibiotics, known as its elution profile, also depends on several variables. These include the physical and chemical characteristics of the cement, the type and combination of antibiotics used, and the cement's inherent porosity. For example, Palacos® cement, known for its high viscosity and porosity, exhibits superior gentamicin elution compared to other formulations, which can enhance its antimicrobial effect in the early postoperative period<sup>[19]</sup>. Furthermore, dual-antibiotic preparations have demonstrated synergistic elution behavior, where the presence of one agent promotes the release of the other, thereby extending the duration and range of antimicrobial action<sup>[21]</sup>.

Vacuum mixing techniques, widely employed to enhance cement homogeneity and mechanical strength, tend to reduce the porosity of the cement matrix. While this improves structural integrity and reduces void formation, it can also limit the elution capacity of the embedded antibiotics. As such, clinicians must weigh the trade-off between maximizing local antibiotic delivery and preserving the mechanical stability of the cement<sup>[16, 21]</sup>.

Despite theoretical concerns, clinical studies have not demonstrated a significant increase in mechanical complications, such as aseptic loosening or implant failure, when ALBC is used appropriately. This is particularly true in primary TKA procedures where standardized, low-dose ALBC has been associated with outcomes comparable to those of plain bone cement (PBC)<sup>[19]</sup>. Radio stereometric analyses of knee implants have shown similar subsidence rates between ALBC and PBC, further reinforcing the mechanical reliability of well-prepared ALBC formulations<sup>[17]</sup>.

Comparative studies between industrially pre-mixed and manually compounded ALBC have consistently favored the former, both in terms of mechanical consistency and antibiotic release kinetics. The superior performance of industrially manufactured cements supports their preferential use in clinical practice, despite the higher associated costs<sup>[5, 18]</sup>. Ongoing research is exploring advanced antibiotic-carrier systems and polymer modifications to further enhance the safety, mechanical durability, and antimicrobial effectiveness of ALBC. These innovations may allow for the development of custom-tailored cements optimized for specific pathogens or patient profiles<sup>[16]</sup>.

Understanding the behavior of ALBC under physiological conditions, particularly in joints affected by inflammation or infection, remains an area of active investigation. Studies that simulate *in vivo* stress environments are essential to guide future improvements in cement composition and application techniques<sup>[13]</sup>.

### 3.5 Cost-Effectiveness and Global Usage Variation

Cost-effectiveness remains a pivotal factor in the decision-making process regarding the use of antibiotic-loaded bone cement (ALBC) in total knee arthroplasty (TKA). Although the initial cost of ALBC—especially commercial, pre-mixed formulations—is significantly higher than that of plain bone cement (PBC), multiple studies have demonstrated that these expenses may be offset by reductions in postoperative

infection rates and the consequent avoidance of costly revision surgeries<sup>[1, 8, 14]</sup>.

Health economic analyses consistently support the targeted application of ALBC in patients identified as high-risk for periprosthetic joint infection (PJI). In these populations, even a modest reduction in infection incidence can result in substantial cost savings for healthcare systems by preventing extended hospital stays, additional operative interventions, and long-term antibiotic therapies<sup>[6, 8]</sup>. The economic advantage is most pronounced in tertiary care settings and regions where the financial burden of managing PJI is exceptionally high.

Notably, international utilization of ALBC exhibits significant variability. In countries such as the United Kingdom and Norway, ALBC is routinely used in primary TKA procedures, reflecting a more proactive infection prevention strategy. In contrast, in the United States and parts of southern and eastern Europe, ALBC use is predominantly reserved for revision cases or for patients with known risk factors, illustrating a more conservative and cost-conscious approach<sup>[20]</sup>.

Several contextual factors contribute to this global disparity, including national reimbursement frameworks, clinical practice guidelines, surgeon training and preferences, and institutional infection control policies. The absence of unified international recommendations regarding the routine use of ALBC further complicates the interpretation of its efficacy and economic justification, making it difficult to aggregate data across studies for robust meta-analyses<sup>[19]</sup>.

To promote value-based orthopedic care, it is imperative that healthcare institutions and policymakers develop and implement standardized evidence-based criteria for the rational use of ALBC. These criteria should incorporate local epidemiological data, microbial resistance profiles, and patient-specific risk factors. Additionally, ongoing prospective trials and comprehensive cost-benefit evaluations are essential to inform future guidelines and to determine the most effective and economically viable strategies for infection prevention in arthroplasty<sup>[22]</sup>.

#### 4. Conclusion

This review critically examined the clinical effectiveness and economic implications of antibiotic-loaded bone cement (ALBC) in total knee arthroplasty (TKA), with a particular focus on infection prevention and hospitalization-associated costs. The evidence gathered from high-quality studies, national registries, meta-analyses, and clinical trials indicates that ALBC demonstrates considerable prophylactic benefit, especially in revision procedures and in primary TKA among patients with identifiable risk factors for periprosthetic joint infection (PJI).

ALBC's capacity to deliver high local antibiotic concentrations offers a significant microbiological advantage, particularly in overcoming biofilm-associated pathogens. Nonetheless, its prophylactic use in standard-risk patients undergoing primary TKA remains controversial due to inconsistent findings regarding infection reduction and cost-effectiveness. While low-dose industrial formulations maintain mechanical integrity and provide reliable antimicrobial elution, the emergence of resistant strains and variable clinical outcomes underscore the need for a judicious, risk-adapted application.

From an economic standpoint, ALBC may reduce long-term healthcare expenditures by decreasing infection-related

revisions and hospital resource utilization, but this benefit is context-dependent and most clearly demonstrated in high-risk cohorts. Global disparities in ALBC utilization reflect variations in healthcare infrastructure, reimbursement policies, and clinical guidelines.

In conclusion, ALBC should not be viewed as a universal solution for infection prevention in TKA but rather as a strategic adjunct to be applied selectively. Its integration into clinical practice must be supported by patient-specific risk assessment, microbiological profiling, and institutional capacity. Future research should focus on refining its indications, optimizing formulations, and establishing standardized protocols to ensure both clinical efficacy and cost-efficiency in orthopedic surgical care.

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