Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Intrawound Vancomycin Powder for Infection Prophylaxis in Definitive Fixation of Complex Fractures: A Systematic Review and Meta-analysis of Efficacy and Safety

Diana Sarmiento
Hospital Universitario de la Samaritana
Juan Francisco Guio
Hospital Universitario de la Samaritana
Jaime A. Leal
Jalealcamacho@hotmail.com

Hospital Universitario de la Samaritana

Research Article

Keywords: Vancomycin, fracture-related infection, trauma surgery, topical antibiotics, meta-analysis

Posted Date: April 1st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9234973/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at European Journal of Orthopaedic Surgery & Traumatology on June 6th, 2026. See the published version at https://doi.org/10.1007/s00590-026-04813-y.

Intrawound Vancomycin Powder for Infection Prophylaxis in Definitive Fixation of Complex Fractures: A Systematic Review and Meta-analysis of Efficacy and Safety

Abstract

Objectives

To evaluate the effectiveness and safety of intrawound vancomycin powder in the definitive surgical management of high-risk fractures, with particular attention to postoperative infection, microbiological profile, and adverse events.

Methods

Data Sources: A systematic search of PubMed, EMBASE, Web of Science, and Scopus was conducted in February 2025, with a search cut-off date of January 31, 2025.

Study Selection: Randomized and observational comparative studies were included if they evaluated intrawound vancomycin powder in patients undergoing definitive fracture fixation and reported outcomes related to postoperative infection, microbiology, or adverse events.

Data Extraction: Two reviewers independently screened studies, extracted data, and assessed methodological quality using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials and ROBINS-I for non-randomized studies.

Data Synthesis: Random-effects models were used to estimate pooled odds ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic.

Results

Eight studies involving 3185 patients were included; 1149 received topical vancomycin powder. Vancomycin use was associated with a significant reduction in postoperative infection after fracture fixation (OR 0.59, 95% CI 0.42–0.82; p = 0.002; I^2 = 0%). Microbiological data were limited, but one study reported a lower proportion of gram-positive infections in the vancomycin group, with no similar pattern for gram-negative organisms. Two studies contributed to an exploratory pooled safety analysis, which showed no statistically significant difference in adverse events between groups (OR 1.39, 95% CI 0.95–2.02; p = 0.38; I^2 = 0%).

Conclusions

The certainty of evidence was limited by risk of bias, indirectness, and the inclusion of non-randomized studies. Intrawound vancomycin powder was associated with reduced postoperative infection in high-risk fracture fixation, without a statistically significant increase in reported adverse events. Microbiological findings remain sparse and should be interpreted cautiously. These results support selective consideration of intrawound vancomycin powder in orthopedic trauma surgery, while further high-quality studies are needed to clarify safety and microbiological consequences.

Keywords

Vancomycin, fracture-related infection, trauma surgery, topical antibiotics, meta-analysis

Level of Evidence: II

Introduction

Surgical site infections (SSIs) represent a significant complication in orthopedic trauma surgery, particularly in the management of lower limb fractures. The Centers for Disease Control and Prevention (CDC) define SSIs as infections that occur within 30 days after surgery (1). However, this definition is limited in orthopedic and trauma surgery due to the use of implants and the complexity of soft tissue involvement, which led to the introduction of the fracture-related infection (FRI) concept, proposed by Metsemakers et al. in 2018 (2).

Lower limb articular fractures often require extensive surgical approaches, increasing the risk of infection. The reported incidence of FRI is approximately 4% in distal femur fractures and 5–12% in tibial articular fractures(3,4). The economic burden associated with treating these infections is substantial, with an estimated cost between 10,504 USD per patient in China to 108,782 USD in USA, including hospitalization, reoperations, antibiotic therapy, rehabilitation, and work incapacity (5,6).

Several preventive strategies have been implemented to reduce infection rates, including both pharmacological and non-pharmacological measures. These include preoperative bathing, hair removal protocols, prophylactic intravenous antibiotics, and intraoperative glove changes (7). More recently, the use of topical antibiotics—particularly intrawound vancomycin powder (VP)—has emerged as an adjunctive strategy for SSI prevention. Although widely adopted in some practices, the application of VP in this context remains an off-label use, lacking formal approval from regulatory agencies.

The application of intrawound VP was first reported in spinal surgery, where its deep fascial application significantly reduced SSI rates in patients undergoing posterior fusion and scoliosis correction procedures (8).

Subsequent studies have explored the use of vancomycin in hip and knee arthroplasty, with systematic reviews and meta-analyses supporting its application in the field of orthopaedics (9). In the domain of orthopedic trauma, multiple investigations have yielded encouraging findings; however, the existing body of evidence includes trials, systematic reviews, and meta-analyses that often evaluate topical vancomycin within heterogeneous orthopedic populations—frequently amalgamating data from arthroplasty, spinal, and trauma procedures. Moreover, several studies assess vancomycin in conjunction with other antimicrobial agents or employ alternative formulations, such as antibiotic-loaded beads or hydrogels, thereby limiting the specificity of conclusions regarding the efficacy of VP alone in fracture-related applications (10–15).

Given these methodological limitations and the emerging evidence, there has been growing interest in the potential role of intrawound vancomycin powder in orthopedic trauma surgery, particularly in fractures requiring extensive surgical exposure and implant placement.

Considering the significant impact of infections in patients with lower limb fractures, it is crucial to evaluate both the effectiveness and safety of using intrawound vancomycin powder as a prophylactic strategy. This intervention may offer a promising advance in preventing fracture-related infections (FRI) and improving the surgical outcomes in complex trauma cases. Furthermore, it is essential to analyze whether the application of vancomycin alters the microbial profile of surgical site

infections and to assess the potential for selecting antibiotic-resistant organisms (16).

This systematic review and meta-analysis aim to comprehensively assess the effectiveness and safety of intrawound VP in preventing FRI among patients undergoing open reduction and internal fixation (ORIF) for complex upper and lower limb fractures.

Materials and Methods

This systematic review and meta-analysis was conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Eligible studies included randomized controlled trials and observational comparative studies (prospective or retrospective cohorts and case-control designs) involving patients with traumatic diaphyseal or articular fractures of the upper or lower extremities, whether open or closed, treated with open reduction and internal fixation (ORIF). To be eligible, studies had to compare patients receiving topical vancomycin powder in addition to standard intravenous antibiotic prophylaxis with a control group managed without topical vancomycin powder.

We included studies published through January 31, 2025, without language restrictions, provided they reported at least one of the following outcomes: postoperative infection, fracture-related infection (FRI), microbial isolates, or

antibiotic resistance patterns. Studies focused on spinal procedures, oncologic bone surgery, arthroplasty, revision surgery for pre-existing infection, or the use of local vancomycin formulations other than powder (e.g., beads, sponges, or hydrogels) were excluded. Animal studies, in vitro experiments, and non-original reports such as case reports, narrative reviews, and other secondary literature were also excluded.

A comprehensive literature search was conducted in February 2025 in PubMed, EMBASE, Web of Science, and Scopus, with a search cut-off date of January 31, 2025. The search strategy combined terms related to vancomycin powder, orthopedic trauma, and infection outcomes, while excluding spinal surgery and arthroplasty. The following search string was used and adapted as appropriate for each database: ("vancomycin powder" OR "intralesional vancomycin" OR "local vancomycin" OR "pixie powder" OR "intrawound vancomycin powder" OR "topical vancomycin powder") AND ("fracture-related infection" OR "surgical site infection" OR "SSI" OR "deep infection") AND ("trauma" OR "fracture" OR "orthopedic trauma") NOT ("spine" OR "arthroplasty"). No language or study design filters were applied at the search stage. All retrieved records were uploaded to Rayyan, where duplicates were removed and studies were screened for eligibility according to predefined inclusion and exclusion criteria. Data analysis and forest plot generation were performed using Cochrane Review Manager (RevMan), version 5.4.1.

Study Selection and Data Extraction

Two independent reviewers screened titles and abstracts using the Rayyan platform, followed by full-text assessment of potentially eligible studies. Disagreements were resolved through discussion and, when necessary, adjudication by a third senior reviewer. Data were extracted using a standardized form that captured study design, population characteristics, fracture type and anatomical location, vancomycin dosage and administration plane, comparator intravenous antibiotic regimen, follow-up duration, infection definitions, microbiological findings, and outcomes of interest.

Outcomes Assessed

The primary outcome was postoperative infection after fracture fixation, preferentially classified according to the fracture-related infection (FRI) framework. Whenever feasible, infection outcomes were interpreted using diagnostic criteria consistent with the international consensus definition of FRI. In studies reporting postoperative infection according to Centers for Disease Control and Prevention (CDC) surgical site infection (SSI) criteria, superficial and deep SSI events were retained within the broader infection outcome framework to maximize sensitivity of event capture, while recognizing the resulting indirectness relative to strictly defined FRI.

Secondary outcomes included the microbiological profile of infection, with particular attention to multidrug-resistant organisms, and the safety profile of topical vancomycin powder. Resistant organisms were assessed descriptively according to the pathogens reported in each study. Safety outcomes were extracted as reported in the original studies and analyzed separately from the primary infection outcome.

Statistical Analysis

Meta-analyses were performed using Review Manager (RevMan), version 5.4.1. Only studies providing sufficient comparative data on postoperative infection outcomes were included in the quantitative synthesis. Given the expected clinical and methodological heterogeneity across studies, pooled analyses were conducted using random-effects models a priori. For dichotomous outcomes, effect sizes were expressed as odds ratios (ORs) with 95% confidence intervals (CIs) to maintain a consistent measure across randomized and observational study designs. Statistical heterogeneity was assessed using the I^2 statistic.

Because the number of eligible comparative studies was limited and included both randomized controlled trials and observational cohorts, an overall pooled analysis was performed using a common effect measure. Study design was explicitly considered during risk-of-bias assessment and interpretation of the certainty of evidence. When feasible, sensitivity analyses were considered to explore the influence of studies at higher risk of bias and studies using SSI-based definitions as proxies for FRI.

Safety outcomes were analyzed separately from the primary infection outcome. Given the limited number of studies contributing safety data and the clinical heterogeneity of reported adverse events, pooled safety estimates were considered exploratory and interpreted with caution.

Risk of bias in individual studies was independently assessed by three reviewers. Randomized trials were evaluated using the revised Cochrane Risk of Bias 2 (RoB

2) tool, whereas non-randomized comparative studies were assessed using the ROBINS-I tool. Discrepancies were resolved through discussion and consensus among the reviewers.

Ethical Considerations

This study was based exclusively on previously published data and did not involve direct contact with human participants or access to identifiable patient-level information. Institutional review board approval was obtained under protocol number 08-2024.

Results

Study Selection

The initial search strategy identified 382 records across four databases. After removal of 148 duplicates, 234 unique records underwent title and abstract screening. Sixteen studies were assessed in full text, of which eight met the predefined eligibility criteria and were included in the systematic review. The study selection process is summarized in the PRISMA 2020 flow diagram (Figure 1) (3,10,17–22).

Characteristics of Included Studies

Eight studies were included: three randomized controlled trials (RCTs) and five retrospective cohort studies. No prospective observational studies or case-control studies met the eligibility criteria. Seven studies evaluated lower-extremity long-bone fractures, whereas one focused exclusively on acetabular fractures. None provided analyzable data specifically for upper-extremity fractures. Although Gandhi et al. included some patients with upper-limb injuries, these cases were not reported separately, and the anatomical site of infection could not be determined; therefore, no subgroup analysis of upper-extremity fractures was possible.

Across all included studies, 3185 patients were analyzed, of whom 1149 received topical vancomycin powder (VP) in addition to standard intravenous antibiotic prophylaxis and 2036 served as comparators without adjunctive topical VP. In the intervention group, VP was generally applied to the deep fascial plane during wound closure at a dose of 1,000 mg; only one study used a 2,000 mg dose in a small subgroup (n = 44).

Infection outcomes were reported using heterogeneous definitions across studies, including either consensus-aligned fracture-related infection (FRI) criteria or Centers for Disease Control and Prevention (CDC) surgical site infection (SSI) definitions. As specified a priori, SSI-based outcomes were retained within the broader postoperative infection framework, while acknowledging their indirectness relative to strictly defined FRI.

Risk of Bias Assessment

Methodological quality was assessed using established tools. Randomized controlled trials were evaluated with the Cochrane Risk of Bias 2 (RoB 2) tool, whereas observational studies were assessed using ROBINS-I. The corresponding judgments and their relationship to the certainty-of-evidence assessment are summarized in Figure 2. Overall, the RCTs were judged to have low to moderate risk of bias, with the main concerns related to deviations from intended interventions and missing outcome data. In contrast, the observational studies showed greater methodological variability, with several domains frequently rated as serious, particularly selection of participants and classification of interventions. These limitations were taken into account when interpreting pooled estimates and rating the certainty of evidence.

Certainty of evidence (GRADE)

Certainty of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for the primary infection outcome (reported as fracture-related infection or surgical site infection, according to each study's definitions) and, when available, for safety outcomes potentially attributable to topical vancomycin. Evidence from randomized trials was initially rated as high certainty and evidence from nonrandomized studies as low certainty, with downgrading applied according to prespecified GRADE domains: risk of bias, inconsistency, indirectness, imprecision, and suspected publication bias.

GRADE assessments were performed separately for randomized and observational evidence whenever both informed a given outcome. When a combined pooled estimate was presented, the overall certainty rating reflected the lowest-certainty body of evidence contributing to that inference, as well as the potential influence of limitations inherent to the nonrandomized studies.

Primary Outcome – Postoperative Infection (FRI/SSI-based definitions)

A total of eight studies were included in the meta-analysis of postoperative infection outcomes after fracture fixation. Across all studies, 58 infection events were reported in the intervention group and 182 in the control group. The pooled random-effects analysis showed a statistically significant reduction in infection risk associated with topical vancomycin powder, with an odds ratio (OR) of 0.59 (95% CI, 0.42–0.82; $p = 0.002$) (Figure 3). No statistical heterogeneity was observed ($I^2 = 0\%$), and the direction of effect was consistent across the included studies.

Most studies used a similar prophylactic approach, consisting of 1 g of topical vancomycin powder applied to the deep fascial plane during wound closure in addition to standard intravenous antibiotic prophylaxis. This relative procedural consistency may have reduced clinical variability across studies.

Subgroup Analysis – Open vs. Closed Fractures

Although subgroup analyses were planned to explore potential differences in infection risk between open and closed fractures, only two of the eight included

studies reported outcomes stratified by fracture type. Consequently, the available data were insufficient to support a reliable pooled subgroup analysis.

A numerical trend favoring topical vancomycin powder was observed in both open and closed fracture strata; however, the low number of studies, limited event counts, and wide confidence intervals precluded any definitive inference. Accordingly, the available evidence does not allow firm conclusions regarding whether the effect of topical vancomycin powder differs between open and closed fractures.

Secondary Outcome – Microbiological Outcomes

Among the eight included studies, only one study (Zingas et al.) reported stratified microbiological outcome data, precluding quantitative synthesis for this domain. In that study, no gram-positive infections were observed in patients who received topical vancomycin powder (0/115), whereas gram-positive organisms were identified in 15 of 344 control patients (4%), corresponding to an adjusted odds ratio (OR) of 0.12 (95% CI, 0.04–0.32; $p < 0.01$). By contrast, no significant association was found for infections caused exclusively by gram-negative pathogens (adjusted OR 3.01, 95% CI 0.29–31.7; $p = 0.38$).(17)

In the vancomycin group, the two reported infections consisted of one culture-negative case and one infection caused by *Pseudomonas aeruginosa*. In the control group, most infections involved gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *Staphylococcus aureus* (MSSA), and vancomycin-sensitive *Enterococcus*; additional infections

included *Pseudomonas aeruginosa*, one polymicrobial infection involving *Proteus* with concurrent MRSA and *Enterococcus*, and two culture-negative cases. These findings suggest that topical vancomycin powder may preferentially reduce gram-positive postoperative infections; however, this observation derives from a single retrospective cohort study and should be interpreted cautiously.

Safety Outcome - Adverse Events

Two studies—Cichos et al. and the METRC randomized clinical trial—reported adverse events in sufficient detail to permit pooled analysis within the safety domain. The reported events included acute kidney injury (AKI), seroma/hematoma, all-cause mortality, below-knee amputation (BKA), and non-union. Wound dehiscence or wound breakdown was not analyzed as an independent adverse event because, according to the 2018 fracture-related infection consensus definition, it constitutes a confirmatory criterion for FRI rather than a separate safety outcome (10,21).

The pooled exploratory analysis did not show a statistically significant difference in adverse events between patients treated with topical vancomycin powder and controls (OR 1.39, 95% CI 0.95–2.02; p = 0.38) (Figure 4). No statistical heterogeneity was observed (I^2 = 0%). However, this safety estimate should be interpreted cautiously because it was derived from only two studies and combined clinically heterogeneous outcomes that are not all equally plausibly attributable to topical vancomycin itself.

Although the point estimate numerically favored a higher event rate in the vancomycin group, the included studies reported these complications as part of broader postoperative outcome assessment and did not establish a direct causal relationship with intrawound vancomycin powder. Events such as renal dysfunction, mortality, amputation, and non-union are likely influenced by multiple factors, including injury severity, systemic illness, limb viability, and perioperative management.

Risk-of-bias assessments for this outcome domain, performed using RoB 2 for randomized trials and ROBINS-I for observational studies, are presented in Figure 5.

Discussion

This appears to be the first systematic review and meta-analysis focused exclusively on orthopedic trauma surgery evaluating the prophylactic use of intrawound vancomycin powder. In contrast to previous reviews that included mixed or elective surgical populations, this analysis centered solely on patients undergoing fracture fixation for high-energy injuries. Most included studies attempted to replicate the surgical indications defined in the VANCO trial, contributing to a relatively consistent high-risk profile across cohorts. Three clinically relevant outcomes were assessed—postoperative infection, microbiological profile, and safety—offering a broad perspective on the intervention’s potential impact.

Regarding the primary outcome, the pooled analysis showed a statistically significant reduction in postoperative infection risk in patients who received topical vancomycin compared with standard care. This finding supports the potential clinical relevance of the intervention in this setting. Although the search strategy was not anatomically restricted, none of the eight included studies clearly or specifically focused on upper extremity fractures. As a result, the analyzed cohort consisted almost entirely of patients with acetabular or lower limb long-bone fractures, predominantly involving periarticular regions of the tibia. This likely contributed to the relative clinical homogeneity of the study population and may have improved comparability across studies.

Safety analyses did not show a statistically significant difference in adverse events in the vancomycin group. However, the reported complications—acute kidney injury, mortality, non-union, seroma/hematoma, and amputation—were clinically heterogeneous and were not directly attributed by the original studies to topical vancomycin application. These events were more likely influenced by injury severity, patient comorbidities, and perioperative factors than by the local antibiotic itself.

Additional recent studies have explored the safety of vancomycin powder in spine and arthroplasty settings. Zimmerly S. and Schar R.T. published preliminary results from the VANCO Trial in 2022, reporting a 0.3% incidence of systemic adverse events—mainly in retrospective studies—including two cases of transient hearing loss and one case of nephropathy; however, a direct causal relationship with vancomycin could not be established (23).

In 2024, Xie C. et al. published a systematic review and meta-analysis indicating an increased incidence of aseptic wound complications in patients undergoing joint arthroplasty who received topical vancomycin (24).

In contrast, Han B. et al. (2025) conducted a prospective, double-blind randomized controlled trial and found no adverse events associated with vancomycin powder use (25).

Microbiological outcomes could not be synthesized due to limited stratified data. Nonetheless, one study reported a significantly lower incidence of gram-positive infections in the vancomycin group, suggesting a possible selective protective effect, although no similar pattern was observed for gram-negative organisms.

This study has several methodological strengths. It followed the PRISMA 2020 guidelines, included a sample of more than 3,000 patients, and focused on a relatively homogeneous clinical population undergoing a broadly similar intervention. Most included studies shared surgical indications comparable to those defined in the VANCO trial for high-risk injuries. These included at least one of the following criteria: initial management with temporary external fixation due to swelling that prevented early definitive fixation (performed more than three days post-injury); Gustilo-Anderson (GA) type I, II, or IIIA open fractures; or fractures associated with ipsilateral compartment syndrome treated with fasciotomy. Notably, GA type IIIB and IIIC fractures were explicitly excluded (10).

Most studies also used similar prophylactic protocols, combining standard intravenous first-generation cephalosporins with topical VP applied during wound closure. Outcome assessment was sufficiently comparable to permit pooled analysis, although some studies relied on SSI-based definitions as proxies for FRI, which introduces indirectness. Risk of bias was rigorously assessed using the Cochrane RoB 2 tool for randomized controlled trials and the ROBINS-I tool for non-randomized studies. Confidence intervals for the primary outcome did not cross the null value, supporting the precision of the pooled estimate. At the same time, the inclusion of both randomized and observational evidence should be considered when interpreting the strength of the inference.

Nonetheless, important limitations must be acknowledged. First, the number of eligible studies focused exclusively on orthopedic trauma remains limited. Second, as previously mentioned, none of the studies clearly or independently reported upper extremity fractures, which limits the generalizability of the findings to this anatomical region. Third, subgroup analyses comparing open versus closed fractures could not be performed robustly because only two studies provided outcomes stratified by fracture type. Fourth, limited microbiological data precluded meaningful evaluation of the intervention’s potential influence on antibiotic resistance patterns or pathogen selection. Finally, although pooled analysis was feasible, the overall estimate combined randomized and observational studies and incorporated infection outcomes that were not uniformly defined as strictly consensus-based FRI.

Despite these limitations, this review supports the selective and clinically reasoned use of intrawound vancomycin powder as a prophylactic adjunct in the surgical

management of high-risk lower extremity fractures. The observed reduction in postoperative infection risk, together with the absence of a statistically significant increase in reported adverse events, suggests that topical vancomycin powder may have a role in selected trauma populations. However, further well-designed studies are needed to clarify unresolved issues such as the long-term impact on antimicrobial resistance, the emergence of more virulent pathogens, and effectiveness in underrepresented fracture types, including those of the upper limb.

Conclusion

This systematic review and meta-analysis provides focused evidence regarding the prophylactic use of intrawound vancomycin powder in orthopedic trauma surgery. In a high-risk and relatively homogeneous trauma population broadly aligned with the VANCO trial indications, topical vancomycin powder was associated with a significant reduction in postoperative infection, without a statistically significant increase in reported adverse events. Although microbiological data and upper extremity fracture representation remain limited, these findings support selective consideration of vancomycin powder in chosen lower extremity and pelvic fracture cases. Future research should clarify its role across broader fracture patterns, long-term safety, and microbiological consequences.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, not-for-profit sectors or any institution.

Bibliography

1. Borchardt RA, Tzizik D. Update on surgical site infections: The new CDC guidelines. J Am Acad Physician Assist. 2018;31(4):52–4. doi:10.1097/01.JAA.0000531052.82007.42 PubMed PMID: 30973535.

2. Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, et al. Fracture-related infection: A consensus on definition from an international expert group. Injury. 2018;49(3):505–10. doi:10.1016/j.injury.2017.08.040 PubMed PMID: 28867644.

3. Wang H, Liu Y, Shi Z, Wang D, Zhang H, Diao S, et al. Intrawound application of vancomycin reduces the proportion of fracture-related infections in high-risk tibial plateau fractures. Injury. 2023;54(4):1088–94. doi:10.1016/j.injury.2023.01.055 PubMed PMID: 36740472.

4. Coelho A, Parés-Alfonso I, Companys R, Sánchez-Soler JF, Torres-Claramunt R, Alier A, et al. Factores de riesgo de infección de fracturas de meseta tibial. Rev Esp Cir Ortop Traumatol. 2024;68(1):44–9. doi:10.1016/j.recot.2023.07.002

5. O'Connor O, Thahir A, Krkovic M. How Much Does an Infected Fracture Cost? Archives of Bone and Joint Surgery. 2022;10(2):135–40. doi:10.22038/abjs.2021.53590.2665

6. Thakore R V., Greenberg SE, Shi H, Foxx AM, Francois EL, Prablek MA, et al. Surgical site infection in orthopedic trauma: A case-control study evaluating risk factors and cost. J Clin Orthop Trauma. 2015;6(4):220–6. doi:10.1016/j.jcot.2015.04.004

7. Calderwood MS, Anderson DJ, Bratzler DW, Dellinger EP, Garcia-Houchins S, Maragakis LL, et al. Strategies to prevent surgical site infections in acute-care hospitals: 2022 Update. Infect Control Hosp Epidemiol. 2023;44(5):695–720. doi:10.1017/ice.2023.67 PubMed PMID: 37137483.

8. Sweet FA, Roh M, Sliva C. Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: Efficacy, drug levels, and patient outcomes. Spine (Phila Pa 1976). 2011;36(24):2084–8. doi:10.1097/BRS.0b013e3181ff2cb1 PubMed PMID: 21304438.

9. Peng Z, Lin X, Kuang X, Teng Z, Lu S. The application of topical vancomycin powder for the prevention of surgical site infections in primary total hip and knee arthroplasty: A meta-analysis. Orthopaedics and Traumatology: Surgery and Research. 2021;107(4):102741. doi:10.1016/j.otsr.2020.09.006 PubMed PMID: 33257290.

10. O'Toole R V., Joshi M, Carlini AR, Murray CK, Allen LE, Huang Y, et al. Effect of Intrawound Vancomycin Powder in Operatively Treated High-risk Tibia

Fractures: A Randomized Clinical Trial. JAMA Surg. 2021;156(5):1–12. doi:10.1001/jamasurg.2020.7259 PubMed PMID: 33760010.

11. Kirchner GJ, Smith NP, Garner MR. Intra-wound vancomycin and tobramycin powder for infection prophylaxis in orthopaedic trauma surgery: Economically justifiable? Injury. 2021;52(11):3340–3. doi:10.1016/j.injury.2021.08.028 PubMed PMID: 34509285.

12. Marchand LS, Sprague S, O'Hara NN, Li CS, O'Toole R V., Joshi M, et al. Local administration of vancomycin powder in orthopaedic fracture surgery: current practice and trends. OTA International. 2023;6(1):E223. doi:10.1097/OI9.0000000000000223

13. Lameire DL, Soeder J, Abdel Khalik H, Pinsker E, Atri N, Khoshbin A, et al. Local vancomycin administration in Orthopaedic Surgery - A systematic review of comparative studies. J Orthop. 2024;55(April):44–58. doi:10.1016/j.jor.2024.03.040

14. Awad ME, Chung JY, Griffin N, Stoneback JW, Alfonso NA. Prophylactic Intrawound Antibiotics Significantly Reduce the Risk of Deep Infections in Fracture Fixation: Subgroup Meta-analyses of the Type of Fracture, Antibiotics, and Organism. J Orthop Trauma. 2023;37(10):E400–9. doi:10.1097/BOT.0000000000002641 PubMed PMID: 37296086.

15. Saka N, Yamada K, Ono K, Iwata E, Mihara T, Uchiyama K, et al. Effect of topical vancomycin powder on surgical site infection prevention in major orthopaedic surgery: a systematic review and meta-analysis of randomized controlled trials with trial sequential analysis. Journal of Hospital Infection. 2024;150:105–13. doi:10.1016/j.jhin.2024.04.028 PubMed PMID: 38825190.

16. Joshi M, O'Toole R V., Carlini AR, Gary JL, Obremskey WT, Murray CK, et al. Does Topical Vancomycin Powder Use in Fracture Surgery Change Bacteriology and Antibiotic Susceptibilities? An Analysis of the VANCO Trial. J Orthop Trauma. 2024;38(4):183–9. doi:10.1097/BOT.0000000000002767 PubMed PMID: 38206761.

17. Zingas N, Hannan ZD, Healey KM, Mckibben NS, Burke CE, Mckegg PC, et al. The Use of Vancomycin Powder in Tibial Plateau Fractures at Lower Risk of Infection. J Orthop Trauma. 2023;37(6):282–6. doi:10.1097/BOT.0000000000002555 PubMed PMID: 36729009.

18. Singh K, Bauer JM, LaChaud GY, Bible JE, Mir HR. Surgical site infection in high-energy peri-articular tibia fractures with intra-wound vancomycin powder: a retrospective pilot study. Journal of Orthopaedics and Traumatology. 2015;16(4):287–91. doi:10.1007/s10195-015-0352-0 PubMed PMID: 25957509.

19. Qadir R, Costales T, Coale M, Mulliken A, Zerhusen T, Joshi M, et al. Vancomycin Powder Use in Fractures at High Risk of Surgical Site Infection. J Orthop Trauma.

2021;35(1):23–8. doi:10.1097/BOT.0000000000001863 PubMed PMID: 32898082.

20. Gandhi M, Balaji G, Menon J, Thomas RR. Does topical vancomycin prevent fracture-related infections in closed fractures undergoing open reduction and internal fixation? A randomised controlled trial. Chinese Journal of Traumatology - English Edition. 2024;27(2):71–6. doi:10.1016/j.cjtee.2023.11.006 PubMed PMID: 38071168.

21. Cichos KH, Spitler CA, Quade JH, Ponce BA, McGwin G, Ghanem ES. Intrawound Antibiotic Powder in Acetabular Fracture Open Reduction Internal Fixation Does Not Reduce Surgical Site Infections. J Orthop Trauma. 2021;35(4):198–204. doi:10.1097/BOT.0000000000001943 PubMed PMID: 32890070.

22. Acosta-Olivo CA, Hernández-Alejo A, Rangel-Alanís AK, Elizondo-Rodríguez JA, Zertuche-Garza HM, Tamez-Mata YA, et al. Effect of Topical Vancomycin on Surgical Site Infections in Ankle Fractures: A Randomized, Double-Blind, Controlled Trial. Cureus. 2024;16(7):14–20. doi:10.7759/cureus.63694

23. Schär RT, Zimmerli S. VANCO Trial—Preliminary Results on the Safety Profile of Intrawound Vancomycin Powder in Complex Spine Surgery. World Neurosurg. 2022;162:7–8. doi:10.1016/j.wneu.2022.03.041 PubMed PMID: 35390649.

24. Xie C, Zhang L, Zhang D, Tao L, Zhao Y, Luo H. Efficacy and safety of vancomycin for local application in the prevention of surgical site infection after joint arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2024;9(10):953–68. doi:10.1530/EOR-23-0023

25. Han B, Lu H, Pan A, Guan L, Cheng F, Zhao M, et al. Safety and efficacy of intrawound vancomycin powder in the prevention of lumbar surgical site infection: a prospective, double-blind, randomized controlled study. Int J Surg. 2025;111(1):589–96. doi:10.1097/JS9.0000000000001846 PubMed PMID: 38913429.

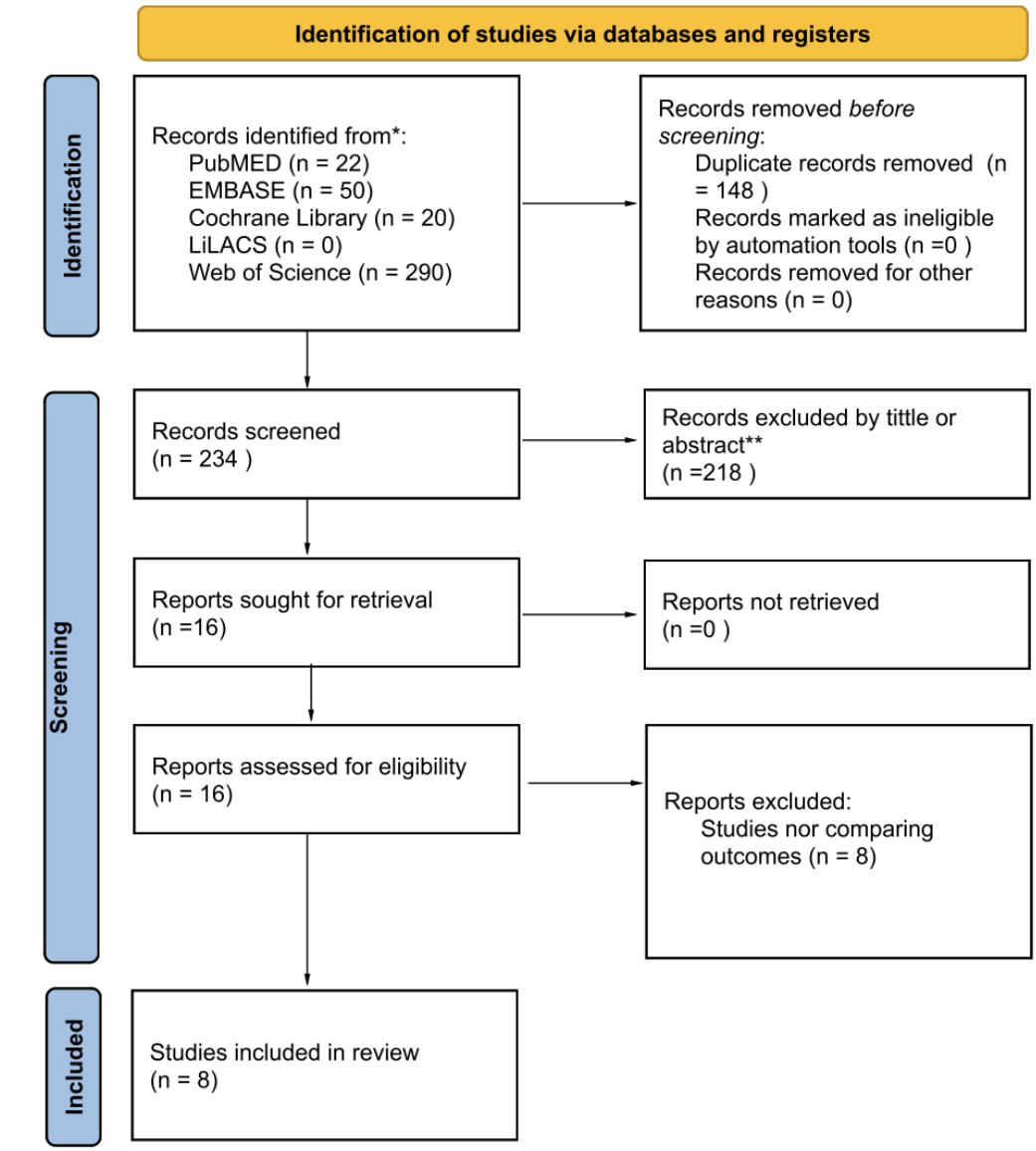
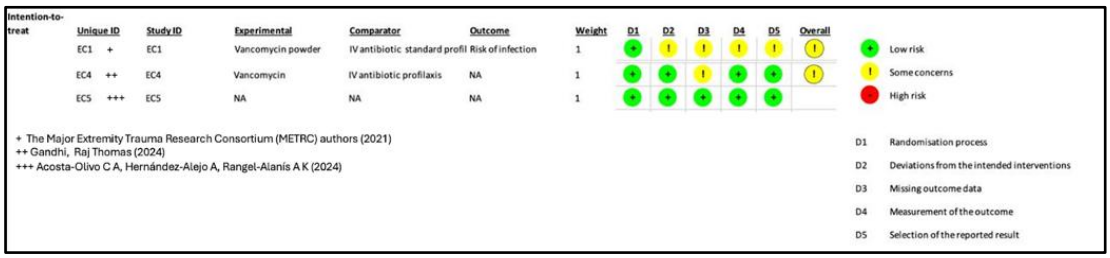


Figure 1. PRISMA Flow Diagram of Study Identification Through Databases and Registries.

A.



B.

Study	Bias due to confounding	Bias in selection of participants into the study	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 the reported result	Overall Bias
Nicolas Zingas, Robert V. O'Toole, MD. 2023	Low	Moderate	Moderate	Low	Moderate	Low	Low	Moderate
H. Wang, Y. Liu, Z. Shi et al	Low	Serious	Serious	Low	Moderate	Moderate	Low	Moderate
Singh, K., Bauer, J. M., LaChaud, G. Y., Bible, J. E., & Mir, H. R	Low	Serious	Moderate	Moderate	Serious	Low	Low	Serious
Qadir, R., Costales, T., Coale, M.,	Low	Serious	Moderate	Moderate	Serious	Low	Low	Serious
Mulliken, A., Zerhusen, T., Jr, Joshi, Cichos, S. Ghanem, et a	Low	Serious	Moderate	Moderate	Serious	Moderate	Low	Moderate

C.

Author(s): Jaime A. Leal

Question: Topic Vancomycin Powder compared to Non Topic Vancomycin Powder for be used for SSI prophylaxis in Orthopaedic Trauma Surgery

Setting: Hospital Universitario de La Samaritana - Bogotá

Bibliography: Randomized Controlled Trials (RCTs)O'Toole RV, METRC Investigators. Effect of intrawound vancomycin powder in operatively treated high-risk tibia fractures: a randomized clinical trial. JAMA Surg. 2021;156(5):e207259. doi:10.1001/jamasurg.2020.7259Gandhi M, Balaji G, Menon J, Thomas RR. Does topical vancomycin prevent fracture-related infections in closed fractures undergoing open reduction and internal fixation? A randomised controlled trial. Chin J Traumatol. 2024;27:71–76. doi:10.1016/j.cjtee.2023.11.006Acosta-Olivo CA, Hernández-Alejo A, Rangel-Alanís AK, Elizondo-Rodríguez JA, Zertuche-Garza HM, Tamez-Mata YA, et al. Effect of topical vancomycin on surgical site infections in ankle fractures: a randomized, double-blind, controlled trial. Cureus. 2024;16(7):e63694. doi:10.7759/cureus.63694Non-randomized Studies (Non-RCTs)Zingas N, Hannan ZD, Healey KM, McKibben NS, Burke CE, McKegg PC, et al. The use of vancomycin powder in tibial plateau fractures at lower risk of infection. J Orthop Trauma. 2023;37(6):282–286. doi:10.1097/BOT.0000000000002555Wang H, Liu Y, Shi Z, Wang D, Zhang H, Diao S, et al. Intrawound application of vancomycin reduces the proportion of fracture-related infections in high-risk tibial plateau fractures. Injury. 2023;54:1088–1094. doi:10.1016/j.injury.2023.01.055Singh K, Bauer JM, LaChaud GY, Bible JE, Mir HR. Surgical site infection in high-energy peri-articular tibia fractures with intra-wound vancomycin powder: a retrospective pilot study. J Orthop Traumatol. 2015;16(4):287–291. doi:10.1007/s10195-015-0352-0Qadir R, Costales T, Coale M, Mulliken A, Zerhusen T Jr, Joshi M, et al. Vancomycin powder use in fractures at high risk of surgical site infection. J Orthop Trauma. 2021;35(1):23–28. doi:10.1097/BOT.0000000000001863Cichos KH, Spitler CA, Quade JH, Ponce BA, McGwin G Jr, Ghanem ES. Intrawound antibiotic powder in acetabular fracture open reduction internal fixation does not reduce surgical site infections. J Orthop Trauma. 2021;35(4):198–204. doi:10.1097/BOT.0000000000001943

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topic Vancomycin Powder	Non Topic Vancomycin Powder	Relative (95% CI)	Absolute (95% CI)		
SSI (follow-up: 12 weeks)												
3	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	31/590 (5.3%)	51/607 (8.4%)	**RR 0.63** (0.41 to 0.97)	**31 fewer per 1000** (from 50 fewer to 3 fewer)	⨁◯◯◯ Very low[a,b,c]	CRITICAL
SSI (follow-up: 12 weeks)												
5	non-randomised studies	serious[d]	not serious	not serious	serious[e]	none	27/559 (4.8%)	138/1429 (9.7%)	**RR 0.53** (0.34 to 0.83)	**45 fewer per 1000** (from 64 fewer to 16 fewer)	⨁⨁◯◯ Low[d,e]	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. Among the three RCTs, only one (O'Toole et al., 2021) was multicenter and well-designed. The other two (Gandhi and Acosta-Olivo) had small sample sizes, unclear allocation concealment, and lacked power.

b. There was inconsistency across studies in the magnitude of effect. The large multicenter trial showed no statistically significant effect, while the smaller trials were underpowered and showed variable point estimates.

c. The confidence interval includes a wide range of effects, from a clinically important benefit to a minimal or no effect. The number of events is low, leading to serious imprecision.g. Therefore, the certainty of evidence was downgraded one level due to serious imprecision.

d. All included studies were non-randomised and therefore subject to residual confounding and selection bias. In particular, the decision to use topical vancomycin was determined by clinical judgement and fracture characteristics, and one study used historical controls, increasing the risk of bias.

e. The number of events was relatively small in several studies, and the pooled estimate was influenced by a limited number of cohorts. Despite the confidence interval not crossing the line of no effect, the estimate remains fragile and encompasses a wide range of plausible effects across different clinical contexts.

Figure 2. Risk of Bias and GRADE Assessment for Studies Included in the Meta-Analysis of Infection Risk.

A. Risk of Bias Assessment for Randomized Controlled Trials Evaluated Using the Cochrane RoB 2 Tool.
This panel displays the domain-specific and overall risk of bias judgments for randomized controlled trials that contributed to the meta-analysis of the primary outcome, fracture-related infection. Each domain is rated as low risk (green), some concerns (yellow), or high risk (red), following the Cochrane Risk of Bias 2.0 framework.

B. Risk of Bias Assessment for Non-Randomized Studies Evaluated Using the ROBINS-I Tool.

This panel summarizes the risk of bias assessment for non-randomized studies included in the same meta-analysis domain. Bias was assessed across seven domains, including confounding, selection of participants, classification of interventions, and measurement of outcomes. The ROBINS-I tool was used to classify the overall risk as low, moderate, serious, or critical.

C. Grade (Grading of Recommendations Assessment, Development, and Evaluation).

The GRADE tool used to assess the certainty of evidence and strength of recommendations in the selected papers.

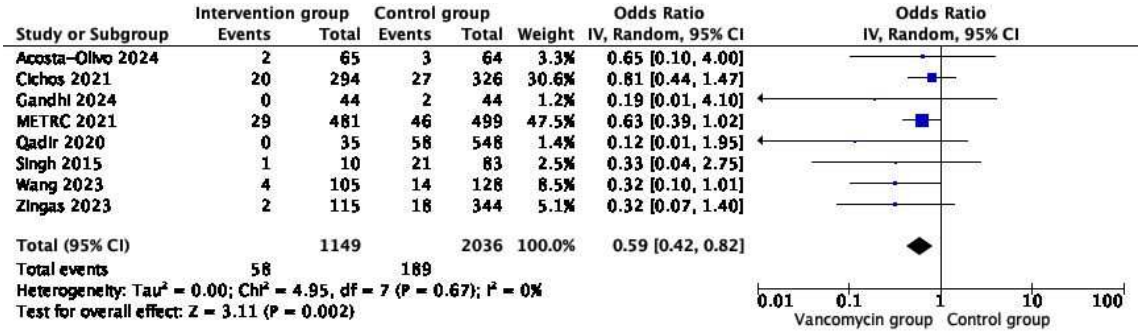


Figure 3. Forest Plot for Primary Outcome.

This Forest Plot displays the pooled odds ratio for fracture-related infection (FRI) comparing patients treated with adjunctive topical vancomycin powder versus standard intravenous antibiotic prophylaxis alone.

A significant reduction in infection risk was observed in the overall analysis (OR: 0.59; 95% CI: 0.42–0.82; p = 0.002), with no statistical heterogeneity (I^2 = 0%). Subgroup analyses for open and closed fractures did not reach statistical significance, largely due to the limited number of studies reporting stratified data.

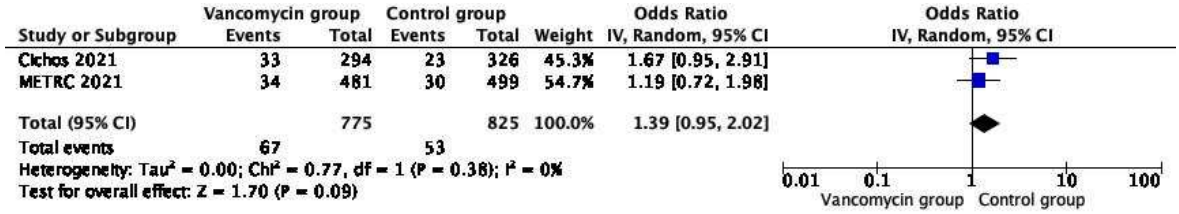
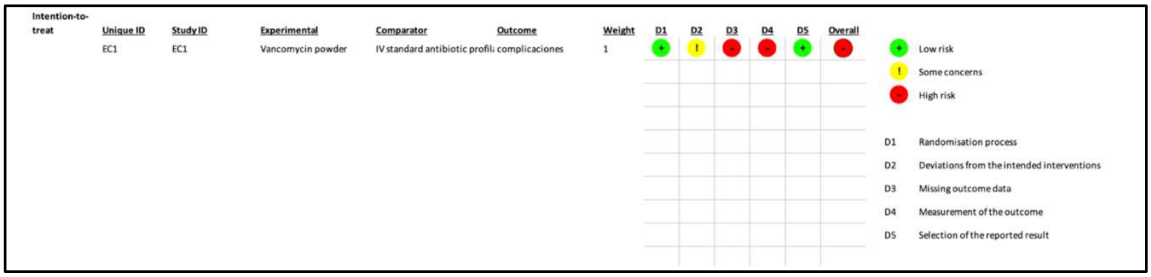
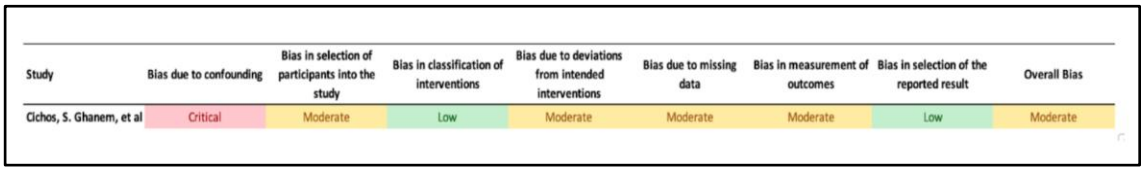


Figure 4. Forest plot for the safety outcome: adverse events

This figure summarizes the pooled estimate for adverse events reported in patients receiving topical vancomycin powder compared with controls, including acute kidney injury, seroma/hematoma, all-cause mortality, below-knee amputation, and non-union. The pooled exploratory analysis did not show a statistically significant difference between groups. This estimate should be interpreted cautiously because it is based on only two studies and combines clinically heterogeneous events.



B.



Study	Bias due to confounding	Bias in selection of participants into the study	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 the reported result	Overall Bias
Cichos, S. Ghanem, et al	Critical	Moderate	Low	Moderate	Moderate	Moderate	Low	Moderate

Figure 5. Risk of Bias Assessment for the Meta-Analysis of the Third Outcome Domain: Safety Associated with Topical Vancomycin Administration.

A. Risk of Bias Assessment for Randomized Controlled Trials Evaluated Using the Cochrane RoB Tool. This panel presents the risk of bias assessment for randomized studies included in the meta-analysis of adverse events associated with topical vancomycin powder.
B. Risk of Bias Assessment for Non-Randomized Studies Evaluated Using the ROBINS-I Tool. This panel presents the results for non-randomized studies included in the same outcome domain, reflecting overall methodological quality and specific sources of bias.