Systematic Review and/or Meta-analysis

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Intrawound vancomycin powder for prevention of surgical site infections in primary joint arthroplasty: an umbrella review of systematic reviews and meta-analyses

Zhong Zhu, MS[a], Tao-Hsin Tung, MD[b], Yongwei Su, MM[c], Yimin Li, MS[a], Hua Luo, MM[a,*]

Objectives: The aim of this umbrella review is to explore the effect of intrawound vancomycin on the incidence of infection and wound complications in patients undergoing primary joint arthroplasty.

Methods: Two authors conducted a systematic search of PubMed, EMBASE, Medline, and the Cochrane Central Register of Controlled Trials from inception to 15 October 2023. All systematic reviews and meta-analyses examining the effect of intrawound vancomycin on the incidence of infection and wound complications in primary joint arthroplasty were included. Two authors independently screened and extracted the data from the studies, evaluated the methodological quality of the included studies using the Assessment of Multiple Systematic Reviews scale, and assessed the publication bias and small-sample effects.

Results: Our umbrella review includes a total of five systematic reviews, comprising 16 retrospective studies. The pooled results indicate that intrawound vancomycin significantly reduces overall infection rates [odds ratio (OR): 0.41; 95% confidence interval (CI): 0.30–0.54, $P < 0.001$], superficial infections (OR: 0.51; 95% CI: 0.26–0.97, $P = 0.04$), and periprosthetic joint infection rates (OR: 0.38; 95% CI: 0.28–0.52, $P < 0.001$) among patients undergoing primary joint arthroplasty. However, vancomycin did not increase the risk of aseptic wound complications (OR: 1.34; 95% CI: 0.88–2.04, $P = 0.17$) and prolong wound healing (OR: 1.40; 95% CI: 0.87–2.26, $P = 0.17$).

Conclusions: Based on the available research, our umbrella review demonstrates that intrawound vancomycin significantly reduces infection rates in primary joint arthroplasty, including periprosthetic joint and superficial infections, without increasing wound complications. However, given the inclusion of studies with varying quality, these findings should be interpreted with caution. Further high-quality studies are needed to better confirm its long-term safety, cost-effectiveness, and overall clinical utility.

Keywords: complication, primary joint arthroplasty, review, surgical site infection, vancomycin

[a]Department of Orthopedic, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, Linhai, Zhejiang, China, [b]Evidence-based Medicine Center, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, Linhai, Zhejiang, China and [c]Department of Orthopedic, The First Affiliated Hospital of Jinzhou Medical University, Jinzhou, Liaoning, China.

Z.Z., T.T., and Y.S. have contributed equally to this work and share first authorship.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Orthopedic, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, No. 150 Ximen Road, Taizhou 317000, Zhejiang, China. Tel.: +86 57687682115.
E-mail: 18732196660@163.com (Hua Luo).

International Journal of Surgery (2025) 111:3508–3524

Received 25 June 2024; Accepted 23 February 2025

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/international-journal-of-surgery.

Published online 3 March 2025

http://dx.doi.org/10.1097/JS9.0000000000002316

HIGHLIGHTS

- Intrawound vancomycin significantly lowers the rates of overall infections, superficial infections, and periprosthetic joint infections in patients undergoing primary joint arthroplasty, highlighting its potential as a preventative measure against post-surgical infections.
- The use of intrawound vancomycin does not correlate with an increased risk of wound complications, suggesting its safety for patients undergoing primary joint replacement surgeries.
- Despite the positive outcomes associated with intrawound vancomycin, the limitations in study quality noted in the umbrella review call for a cautious interpretation of these results and underline the necessity for more high-quality clinical trials to conclusively determine the benefits and risks of vancomycin in this context.

Introduction

Joint arthroplasty, including total knee arthroplasty and total hip arthroplasty, is recognized as the most effective treatment for end-

stage osteoarthritis[1]. This procedure addresses joint deformities, alleviates joint pain, restores function, and enhances patient quality of life by replacing the affected joint with an artificial one[2-4]. Although joint arthroplasty is highly effective, infections can lead to severe consequences, including persistent joint pain, deformity with limited mobility, disability, and even death[5]. Infections significantly prolong hospitalization, increase psychological and physical pain, and may even hasten death, thereby increasing a substantial economic burden on the health care system[6,7]. In the United States, patients with periprosthetic joint infection (PJI) reportedly incur an average treatment cost of $93,600[8], with the overall cost of PJI projected to reach $1.85 billion by 2030[9].

Rational and standardized use of prophylactic antibiotics has been shown to clinically reduce joint infections[10]. According to relevant literature, the most common pathogenic bacteria causing PJI are *Staphylococcus aureus* and coagulase-negative *Staphylococcus* species[11]. The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in joint arthroplasty has been increasing annually, leading to a growing frequency of clinical prophylactic use of narrow-spectrum, potent antibiotics such as vancomycin[12]. Intrawound vancomycin powder (VP) has minimal systemic side effects and can maintain high local concentrations for extended periods, effectively killing bacteria. Its efficacy in preventing surgical site infections has been well-demonstrated in spinal surgery[13]. Recent studies involving patients undergoing joint arthroplasty have shown that vancomycin significantly decrease the likelihood of infection[14-17]. However, some studies have reported that intrawound vancomycin was ineffective in reducing the incidence of infection[18-20]. Given the relatively low incidence of infection, the results of clinical studies on this topic have been inconsistent[21-26]. Although the article published by Movassaghi *et al.* included 16 trials[22], they had the following limitations: Firstly, only two databases were searched, and the language was limited to English. Secondly, the study was aimed at total joint arthroplasty. However, the trail of Hanada's reported unicompartmental knee arthroplasty was also analyzed as total joint arthroplasty, which increased the article's bias. Thirdly, for the trial of the Koutalos[27], we think this is unreasonable to merge two combinations of unused vancomycin. As the experimental group is tranexamic acid combined with vancomycin, the control group should be the tranexamic acid group so that other variables can be controlled. Fourthly, only the PJI was analyzed. The infection around the comparison operation is mainly caused by the colonization bacteria of the local skin, so the importance of superficial infection cannot be ignored. If the superficial infection aggravation, it will also lead to deep secondary infection. Fifthly, they included three trails from the same institution and merged their data for the analysis[28-30], which will increase the bias. Sixthly, the control group of Riesgo's study was the patient with PJI, which may not meet the inclusion criteria of the meta-analysis. While the study by Movassaghi *et al.* has made significant contributions, it is still limited by certain factors, as noted above. Moreover, conclusions across various systematic reviews are inconsistent. We believe there is a pressing need for umbrella reviews to systematically revisit previous research, address these limitations, and conduct a re-analysis to achieve more reliable conclusions.

To address this, we performed an umbrella review, evaluated the evidence level of each included review, synthesized the current understanding on the subject, and thoroughly evaluated the effectiveness and safety of intrawound vancomycin in patients undergoing joint arthroplasty. This umbrella review aims to provide a solid foundation for decision-making.

Methods

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and has been reported in line with the AMSTAR (Assessing the methodological quality of systematic reviews) Guideline[31,32]. The protocol for this meta-analysis was registered on PROSPERO.

Inclusion criteria

The eligibility criteria were as follows: (1) studies with a meta-analysis or systematic review design; (2) investigations examining the impact of topical VP on infection or wound complications among patients undergoing primary joint arthroplasty; (3) for updated systematic reviews, we assessed whether they included all the studies from prior reviews. If the updated review encompassed all studies from earlier reviews, it was included in our analysis, and the earlier review was excluded. If the updated review did not include all the studies from the earlier review, both the updated and prior reviews were included; and (4) systematic reviews published in any language that were accessible through the databases we searched.

Exclusion criteria

The exclusion criteria were as follows: (1) studies that were literature reviews or animal trials; (2) studies that did not report outcomes relevant to our analysis; and (3) studies lacking a quantitative synthesis.

Search strategy

The literature screening process was carried out by two independent investigators, each with extensive experience in systematic reviews and knowledge of the field of orthopedic surgery and infection management. The investigators hold advanced degrees in biomedical sciences and have previously been involved in systematic reviews and meta-analyses related to infection control in surgical procedures. Their familiarity with the subject matter, particularly in arthroplasty and the use of vancomycin, ensured that the screening was both comprehensive and accurate. Both investigators were trained in systematic review methodologies and were familiar with the PRISMA guidelines, ensuring adherence to best practices throughout the screening process. The databases (PubMed, EMBASE, Medline, and the Cochrane Central Register of Controlled Trials) were chosen for their extensive coverage of biomedical literature, ensuring a wide scope for relevant studies on vancomycin use in arthroplasty-related infections and complications. The search covered the period from inception to 15 October 2023. The search strategy employed a combination of keywords and Medical Subject Headings terms to maximize retrieval. The primary keywords included "Systematic review", "Vancomycin", "Arthroplasty", "infection", and "complication". Boolean operators (AND, OR) were used to combine these terms

effectively (For detailed search strategies for each database, see Supplementary materials. http://links.lww.com/JS9/D983). No language restrictions were applied.

Data extraction

The screening process was carried out by two independent investigators, both of whom have extensive experience in conducting systematic reviews and meta-analyses. Their expertise ensures a high level of accuracy and consistency in the selection and evaluation of studies. After the initial retrieval, duplicates were removed using EndNote reference management software. The remaining studies underwent a two-stage screening process. First, both investigators independently reviewed the titles and abstracts to identify studies that met the predefined inclusion criteria. The studies that passed the title and abstract screening were then subjected to a comprehensive full-text review to confirm eligibility. Any disagreements between the two investigators during the screening process were resolved through discussion. If consensus could not be reached, a senior researcher was consulted to make the final decision, ensuring unbiased and accurate selection of studies. Two investigators independently extracted data from the eligible studies using a standardized data extraction form. Extracted information included general details such as the author(s), year of publication, country; study design and the number of studies included in the meta-analysis; and outcome measures including overall infection rates, PJI, superficial infection and wound complications. Additionally, statistical data such as effect sizes with 95% confidence intervals (CIs), and heterogeneity measures such as the I^2 statistic. Any inconsistencies in data extraction were addressed by re-examining the original studies and consulting a third investigator when necessary.

Outcomes measured

The primary outcomes of this study focused on the overall infection rate, which encompassed any infection occurring after joint arthroplasty, including both superficial and PJI. Superficial infections were specifically defined as those confined to the subcutaneous tissue at the surgical site, and were typically identified based on clinical signs such as redness, swelling, warmth, and discharge, as well as positive cultures from superficial wound swabs. In contrast, PJI was a more severe outcome, involving the joint prosthesis itself and usually requiring surgical intervention. Additionally, we assessed the impact of vancomycin on wound-related complications, including prolonged wound healing and aseptic complications. Any assumptions made about missing or unclear information were documented.

Subgroup analysis

Subgroup analyses were performed based on surgical site (hip versus knee), vancomycin dosage (1 g versus 2 g), surgical method (cemented versus cementless), infection diagnostic criteria (e.g., international consensus guidelines, MSIS criteria, culture-based methods), and region to explore factors influencing the effectiveness of intrawound vancomycin.

Assessment of methodological quality

The methodological quality of each included meta-analysis was assessed using the Assessment of Multiple Systematic Reviews (AMSTAR-2) tool by two independent investigators with expertise in systematic review methodology. One investigator is a senior researcher with extensive experience in evidence synthesis, while the other is a specialist in biostatistics, ensuring a robust evaluation process. In the event of any discrepancies between the two assessors, these were resolved through discussion and consensus, with input from a third expert if needed, to ensure impartiality and accuracy. The AMSTAR-2 ranks the quality of a meta-analysis from low to high according to 16 predefined items, providing a comprehensive evaluation of methodological rigor, including criteria such as the adequacy of literature search, assessment of risk of bias, and consideration of conflicts of interest. This tool is widely recognized for its ability to identify both strengths and weaknesses in systematic reviews, making it a reliable and informative measure for quality assessment.

Quality assessment

The Newcastle–Ottawa scale (NOS) was used to evaluate the literature quality of the Non-RCTs (Randomized Controlled Trials)[33]. This evaluation was carried out independently by two investigators. Any disagreements in the scoring of the studies were resolved by discussion, with a third expert brought in if needed. The NOS evaluates three broad domains: selection, comparability, and outcome assessment, which provides a well-rounded assessment of study design quality. This tool is advantageous in evaluating the potential for bias in observational studies, particularly in cohort and case-control studies, which were prevalent in our included studies. Based on the NOS scores, the studies were classified into three quality categories: high quality (score 7–9), moderate quality (score 4–6), and low quality (score 0–3). This classification allowed for a more precise understanding of the methodological strengths and limitations of the included studies, ensuring that the overall quality of evidence was appropriately considered when interpreting the results. Additionally, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was employed to assess the overall quality of evidence across studies by two independent researchers. Any disagreements between the researchers were addressed through discussion and resolved with input from a third expert if needed. GRADE takes into account factors such as study limitations, inconsistency of results, imprecision, indirectness, and publication bias[34]. Given that our analysis included more than five studies, this approach was particularly useful for providing a more nuanced judgment of the body of evidence, facilitating a clearer understanding of the strength of the recommendations derived from our findings.

Sensitivity analysis

To address concerns regarding the inclusion of low-quality studies, we conducted sensitivity analyses by excluding studies with high risk of bias (NOS 0-3). This helped assess the robustness of our findings and ensured that the conclusions drawn were not unduly influenced by any single study.

Data synthesis and analysis

The meta-analysis was performed using Reman (version 5.4; The Cochrane Collaboration) software. The heterogeneity was assessed by using the Q test and I^2 value calculation. Suppose the heterogeneity was not present ($P > 0.1$ and $I^2 < 50\%$), the data were combined with a fixed effect model. If the heterogeneity was present ($P < 0.1$ or $I^2 > 50\%$), the random effects model was used. The odds ratio (OR) and their associated 95% CI were used to assess

outcomes, and a *P* value less than 0.05 suggested that the difference was statistically significant.

Reporting bias assessment

We assessed the risk of bias due to missing results in the synthesis, particularly arising from reporting biases. This was evaluated using funnel plots and Egger's test.

Results

Ninety-two relevant studies were retrieved using the established search strategy. After the removal of duplicates, 68 studies remained. Of these, 59 were not relevant to the topic, and three focused on discussing antibiotics in general, not solely vancomycin, so we were unable to extract specific results related to vancomycin . In addition, one meta-analysis[22] was an update of a previous meta-analysis[21]; therefore, we included only the most recent study. Finally, five studies met our inclusion criteria for this umbrella review[22-26]. The flow diagram is shown in Fig. 1. Among the five included studies, four were meta-analyses[22-24,26] and one was a systematic review[25], encompassing a total of 16 retrospective studies[15-20,27,28,35-42].

Study characteristics

The characteristics of included systematic reviews were shown in Table 1. A meta-analysis conducted by Movassaghi *et al.* (2022), which included three prospective studies and 13 retrospective studies, involving a total of 33,731 patients who underwent primary and revised joint arthroplasty, with 28,508 of them being primary joint replacement patients, revealed that intrawound vancomycin significantly reduced the overall infection rate[22]. In the subgroup analysis, intrawound vancomycin significantly reduced knee infection rates compared to the control group, but the difference was not statistically significant for the hip. Peng *et al.* (2021), analyzing six retrospective and three prospective studies[23], concluded that vancomycin reduces the incidence of overall infection and PJI in primary joint arthroplasty. The subgroup analysis further indicated

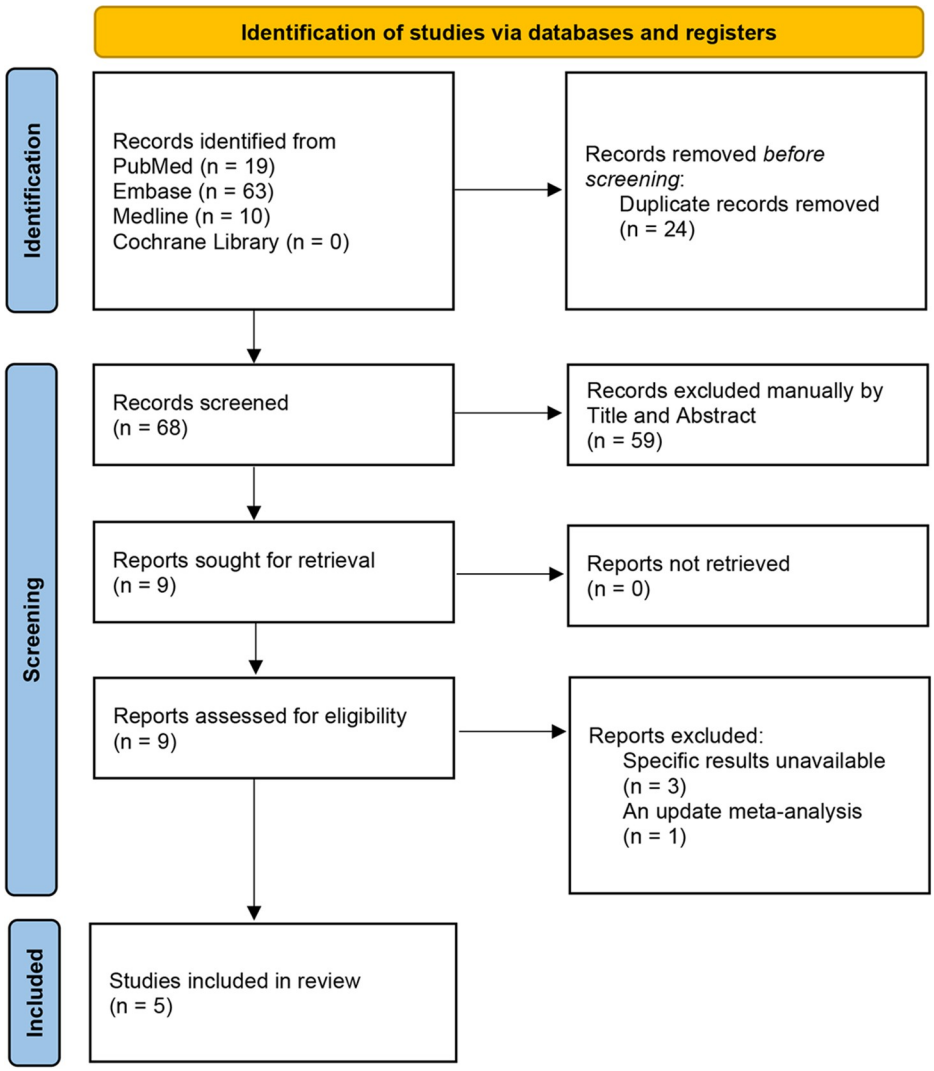

Figure 1. Flow diagram of the study search and selection processes.

Table 1

Characteristics of the included systematic reviews

Study	Country	Range of years of included studies	No. of primary studies in review	Duration	Outcomes	I^2	Statistical significance	Summary effect size	Funding
Movassaghi 2022[22]	USA	2010–2021	16	Minimum 3 month	Overall infection; Aseptic wound Complications	0%; NS	$P < 0.05$; NS	OR 0.44 (95% CI: 0.32, 0.60); NS	NS
Peng 2021[23]	China	2010–2020	9	Not limited	Overall infection; PJI	0%; 0%	$P < 0.0001$; $P < 0.0001$	RR 0.40 (95% CI: 0.27, 0.61); RR 0.37 (95% CI: 0.23, 0.60)	Yes
Saidahmed 2020[24]	Canada	2010–2019	9	Not limited	PJI; Superficial infection; Aseptic wound complications	0%; 0%; 12%	$P = 0.0007$; $P = 0.43$; $P = 0.03$	RR 0.44 (95% CI: 0.28, 0.71); RR 0.61 (95% CI: 0.17, 2.12); RR 2.36 (95% CI: 1.10, 5.03)	NS
Wong 2021[25]	Canada	2017–2020	9	Minimum 3 month	PJI; Aseptic wound complications	NS; NS	NS; NS	NS; NS	NS
Xu 2020[26]	China	2010–2019	9	Not limited	PJI; Superficial infection; Aseptic wound complications	0%; 0%; 16.2%	$P < 0.05$; $P > 0.05$; $P < 0.05$	OR 0.44 (95% CI: 0.28, 0.69); OR 0.60 (95% CI: 0.17, 2.12); OR 2.44 (95% CI: 1.12, 5.34);	Yes

PJI, periprosthetic joint infection; NS, not Specified; OR: Odds Ratio; RR: Relative Risk.

that vancomycin can also reduce the incidence of overall infection and PJI in both hip and knee joints. The study highlighted that the most common bacterial infection following joint arthroplasty was caused by *S. aureus*. Saidahmed *et al.* (2021), in their examination of nine studies[24], found that topical antibiotics significantly reduced the incidence of PJI after joint arthroplasty, but the effect on superficial infections was not statistically significant. Additionally, they noted that the use of topical antibiotics was associated with an increased incidence of wound complications. Wong *et al.* (2021) recalculated the ORs of nine included studies and found that only one study suggested vancomycin reduced the incidence of PJI, whereas the other eight studies showed no significant intergroup difference[25]. Furthermore, there was no significant difference in the risk of wound complications. Xu *et al.* (2020) summarized nine studies and found that while intrawound vancomycin did not significantly affect the rates of superficial infections or acute renal impairments, it did reduce the risk of PJI[26]. However, they also observed that intrawound vancomycin increases the incidence of wound complications. We conducted a NOS scoring for the 16 included studies, and all studies scored ≥7 points (Table 2), indicating that the quality of the included studies is relatively high.

Assessment of methodological quality

Three of the included studies restricted their publication language to English[22-24], which resulted in one key item not being met. One study did not mention the risk of bias assessment tool[22], and none of the studies provided further methodological explanations for the risk of bias for allocation concealment, blinding, and other outcomes. In addition, in the calculation of pooled results, the results were combined directly without adjusting for confounders[22-24,26], leading to non-compliance with key item 11. Furthermore, three studies did not discuss the risk of bias at the time of outcome analysis[24-26], resulting in non-compliance with key item 13. As a result, all five included studies were assessed to have critically low methodological quality (Table 3).

Overall infection rate

Two systematic reviews evaluated the effect of intrawound vancomycin on the incidence of overall infection in patients who underwent primary joint arthroplasty[22,23]. These Reviews indicated that vancomycin significantly reduced overall infection rates. A total of 15 original studies, as reported in the included systematic reviews, contributed to the pooled analysis. The pooled result from these studies indicates that local administration of vancomycin significantly reduces the overall infection rate (OR: 0.41; 95% CI: 0.30–0.54, $P < 0.001$, $I^2 = 0\%$, Fig. 2). We conducted subgroup analyses on different doses of vancomycin to observe its impact on the overall infection rate. The result of subgroup analysis on the dose of 1 g and 2 g VP revealed that VP sprayed on the wound, at a dose of 1 g (OR: 0.36, 95% CI: 0.23–0.55; $P < 0.001$, $I^2 = 0\%$, Fig. 3A) and 2 g (OR: 0.48, 95% CI: 0.31–0.74, $P = 0.0008$, $I^2 = 0\%$, Fig. 3B), respectively, could reduce the occurrence of infection rate after joint arthroplasty. These effect sizes indicate that 1 g and 2 g of vancomycin can reduce the infection risk by approximately 64% and 52%, respectively, which is clinically significant. In the study by Xu *et al.*[41], 0.5 g of VP was applied intraoperatively, with results indicating that local use of VP effectively reduced infection rates. Similarly, Assor *et al.*[15] utilized a dosage of 1–2 g of VP during surgery, which also demonstrated a significant reduction in infection rates. Subgroup analysis based on the type of joint replacement (hip versus knee) also demonstrated significant reductions in infection rates. The pooled results for hip arthroplasty indicated a reduced infection rate when vancomycin was used (OR: 0.41, 95% CI: 0.23–0.71; $P = 0.002$, $I^2 = 0\%$, Fig. 4A), and similar significant reductions were observed for knee arthroplasty (OR: 0.41, 95% CI: 0.29–0.57; $P < 0.001$, $I^2 = 0\%$, Fig. 4B). These effect sizes suggest that vancomycin application can lower the infection risk by approximately 59% for both hip and knee replacements, highlighting its substantial clinical value. Subgroup analysis based on the type of fixation used in joint arthroplasty (cemented versus cementless) demonstrated significant reductions in infection rates

Table 2

Characteristics of included studies

Study	Country	During	Gender (M/F)		Age (Mean ± SD)		Design	Participants	Intervention		Outcomes	NOS
			VP	Control	VP	Control			VP	Control		
Aljuhani 2021[18]	Saudi Arabia	2018.01-2020.03	13/36	3/46	NS	NS	Retrospective	TKA	2 g VP	No-VP	Surgical site infection, PJI	8
Assor 2010[15]	France	2002–2006	16/46	17/56	73 ± 8.2	72 ± 7.6	Prospective	TKA	1–2 g VP	No-VP	Superficial infection, PJI, IKS score	9
Buchalter 2021[28]	USA	2012.01-2013.12 2016.01-2019.09	NS	NS	63.74 ± 9.54	63.82 ± 10.28	Retrospective	TKA	2 g VP	No-VP	PJI	8
Cohen 2019[19]	USA	2015.04-2016.12	149/160	109/137	66 ± 10.2	67.3 ± 12.6	Retrospective	THA	1 g VP	No-VP	PJI	7
Crawford 2018[35]	USA	2011 and 2015	524/546	391/424	64.8 ± 10.2	63.3 ± 11.9	Retrospective	THA	1 g VP	No-VP	Overall infection, PJI	7
Dial 2018[36]	USA	2013.06-2016.02	65/72	64/64	61.2 ± 11.1	61.5 ± 10.5	Retrospective	THA	1 g VP	No-VP	Superficial infections, PJI, sterile wound complication, acute renal failure	8
Hanada 2019[37]	Japan	2010–2017	27/83	22/70	74.6 ± 8.4	73.3 ± 6.6	Prospective	TKA and UKA	1 g VP	No-VP	PJI, wound complications	8
Khatri 2017[20]	India	2014.02-2016.01	32/19	44/20	NS	NS	Retrospective	TKA	1 g VP	No-VP	Overall infection, superficial infections, PJI	7
Koutalos 2020[27]	Greece	2016.01-2017.02	41/101	37/111	67	68	Prospective	THA and TKA	2 g VP	No-VP	Overall infection, superficial infections, PJI	9
Matziolis 2020[16]	Germany	2013–2018	416/666	3145/4718	69 ± 10	68 ± 9	Retrospective	THA and TKA	1 g VP	No-VP	PJI	9
Otte 2017[38]	USA	2012.05-2014.04	NS	NS	66.0 ± 10.7	67.6 ± 11.0	Retrospective	THA and TKA	1 g VP	No-VP	PJI	8
Patel 2018[39]	USA	2016.04-2017.10	138/210	48/64	63.6	64.9	Retrospective	THA and TKA	1 g VP	No-VP	Overall infection rate, PJI, superficial infections, acute renal failure	9
Tahmasebi 2021[17]	Iran	2007.03-2018.12	317/1393	62/252	64.99 ± 11.49	66.37 ± 8.9	Retrospective	TKA	1 g VP	No-VP	Suspected superficial incisional infection, PJI	9
Winkler 2018[40]	USA	2012.01-2015.12	131/193	95/154	70	46	Retrospective	THA and TKA	2 g VP	No-VP	PJI	8
Xu 2020[41]	China	2015.05-2017.10	121/316	129/289	66.9 ± 9.9	67.1 ± 9.3	Retrospective	TKA	0.5 g VP	No-VP	Superficial infection, PJI, wound complications	9
Yavuz 2020[42]	Turkey	2012–2016	148/326	154/348	65.5 ± 10.7	63.4 ± 12.1	Retrospective	TKA	2 g VP	No-VP	PJI	9

M, male; F, female; VP, vancomycin powder; KA, Total Knee Arthroplasty; THA, Total Hip Arthroplasty; UKA, Unicompartmental Knee Arthroplasty; PJI, Periprosthetic Joint Infection; IKS, International Knee Society; NOS, Newcastle-Ottawa Scale; NOS, New Castle–Ottawa Scale

Table 3

AMSTAR 2 assessments of all Systematic Reviews

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Overall Confidence
Movassaghi 2022	Yes	Yes	No	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Critically low
Peng 2021	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Critically low
Saidahmed 2020	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Critically low
Wong 2021	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No MA	No MA	No	No	No MA	Yes	Critically low
Xu 2020	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Critically low

MA, meta-analysis

with the use of VP. The pooled results for cemented arthroplasty indicated a reduced infection rate when vancomycin was used (OR: 0.43, 95% CI: 0.23–0.79; P = 0.007, I^2 = 0%, Fig. 5A). Similarly, significant reductions were observed for cementless arthroplasty (OR: 0.28, 95% CI: 0.13–0.57; P = 0.0005, I^2 = 0%, Fig. 5B). These effect sizes indicate that vancomycin can reduce infection risk by approximately 57% in cemented and 72% in cementless fixations, further supporting its widespread clinical application. Besides, we conducted a subgroup analysis based on different diagnostic criteria for infections, encompassing a range of established standards, including international consensus guidelines such as the WHO criteria and the Meeting on PJIs Definitions (International consensus), the Musculoskeletal Infection Society (MSIS) criteria, which utilize a combination of major and minor criteria, and culture-based methods, where bacterial cultures and joint fluid cultures were used to detect pathogens. The subgroup analysis revealed that intrawound vancomycin significantly reduced infection rates across various diagnostic criteria [culture-based methods (OR: 0.40, 95% CI: 0.20–0.78; P = 0.008, I^2 = 0%, Fig. 6A]; International consensus (OR: 0.45, 95% CI: 0.29–0.70; P = 0.0004, I^2 = 0%, Fig. 6B); MSIS (OR: 0.42, 95% CI: 0.22–0.81; P = 0.010, I^2 = 0%, Fig. 6C); not specified (OR: 0.34, 95% CI: 0.18–0.64; P = 0.0009, I^2 = 0%, Fig. 6D), demonstrating consistent efficacy regardless of the method used to diagnose infections. The subgroup analysis based on different regions (Asia, North America, and Europe) further supported the efficacy of intrawound vancomycin. The results indicated that, in all regions (Asia (OR: 0.50, 95% CI: 0.29–0.87; P = 0.01, I^2 = 0%, Fig. 7A), North America (OR: 0.38, 95% CI: 0.26–0.56; P < 0.001, I^2 = 0%, Fig. 7B), and Europe (OR: 0.35, 95% CI: 0.15–0.78; P = 0.01, I^2 = 0%, Fig. 7C), vancomycin significantly reduced the occurrence of infections compared to the control group, reinforcing the consistent effectiveness of vancomycin in reducing postoperative infections across various geographic regions.

Superficial infection and PJI rate

Two systematic reviews, by Saidahmed *et al.* and Xu *et al.* both reported on superficial infections. Their findings indicated that intrawound vancomycin did not effectively reduce the occurrence of superficial infections[24,26]. PJI was investigated in four systematic reviews[23-26]. Wong et al. considered that many studies used Pearson's chi-squared test to overestimate the effect of small sample sizes, so they used Fisher's exact test to recalculate the study results considering that the included studies were retrospective, so they only performed a systematic review without pooling analysis. Three others systematic reviews found that vancomycin reduces

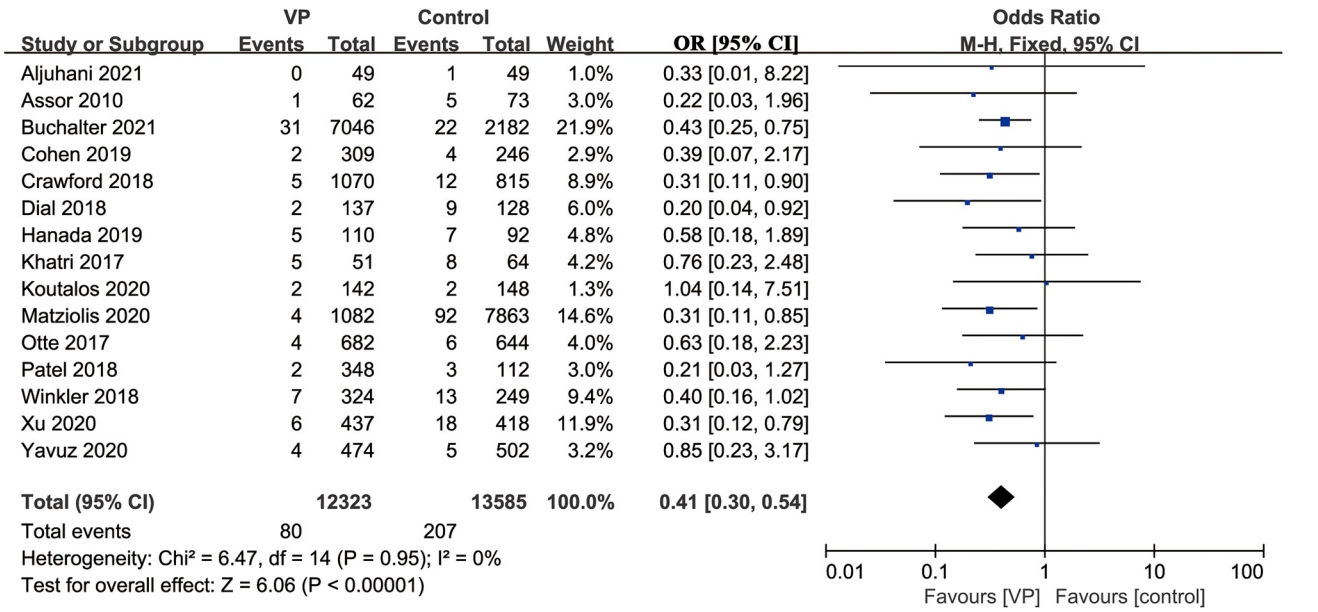

Figure 2. Forest plot of comparison: VP versus No-VP; outcome: incidence of overall infection.

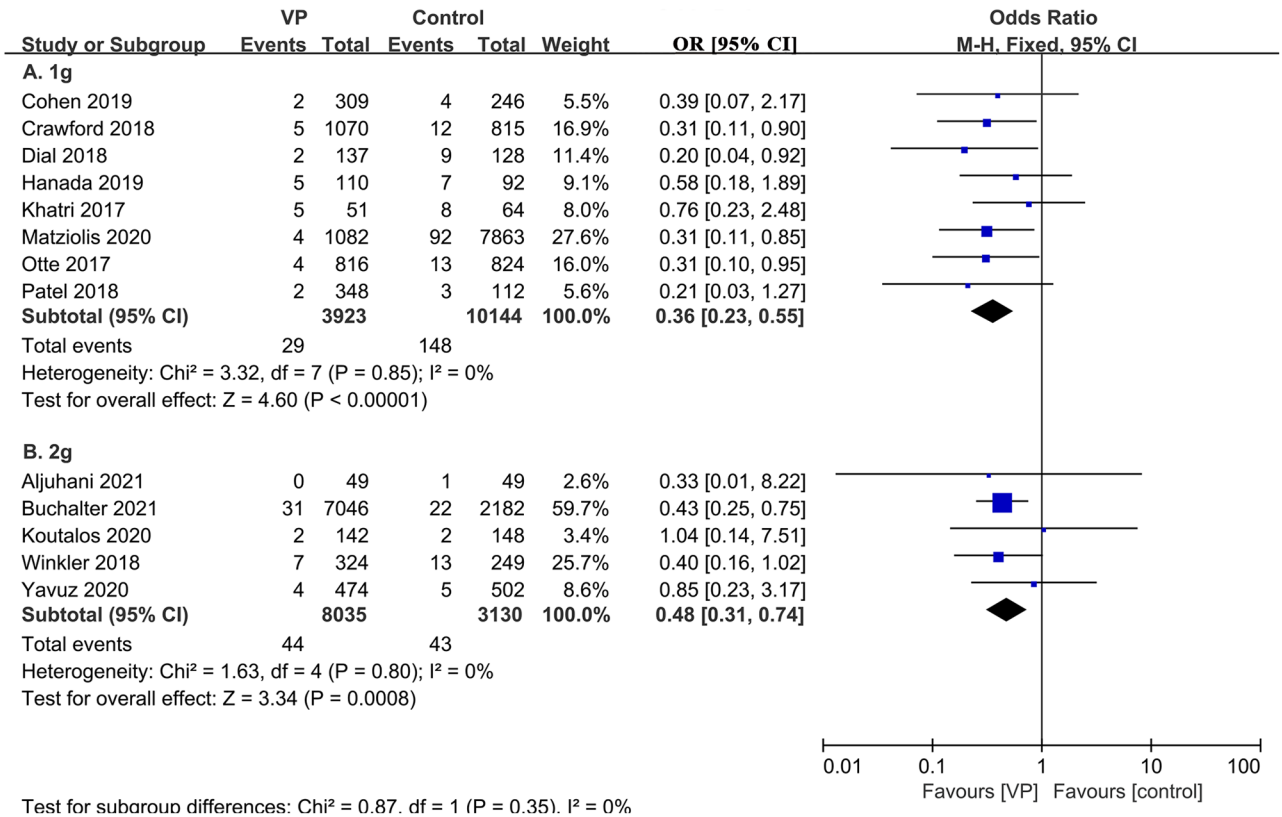

Figure 3. Subgroup analysis based on the dosage of vancomycin powder used (A) 1 g, (B) 2 g.

the incidence of PJI[23,24,26]. A total of seven original studies, as reported in the included systematic reviews, addressed superficial infection, and 16 studies addressed PJI. After pooling the results from these studies, we found that intrawound vancomycin significantly reduces the occurrence rate of superficial infection (OR: 0.51; 95% CI: 0.26–0.97, $P = 0.04$, $I^2 = 0\%$, Fig. 8A) and PJI (OR: 0.38; 95% CI: 0.28–0.52, $P < 0.001$, $I^2 = 0\%$, Fig. 8B). These effect sizes indicate that vancomycin can reduce the risk of superficial infections by approximately 49% and PJI by 62%, demonstrating significant preventive value in clinical practice.

Complications

Wound complications were described by four systematic reviews[22,24-26]. These wound complications did not meet the criteria of infection but required an additional operation for debridement and closure without replacement of joint prostheses or postoperative antibiotics. These include prolonged wound healing, stitch abscesses or erythema, and bleeding. Two of the systematic reviews reported an increase in incision complications following topical vancomycin treatment[24,26], while the other two reviews described incision complications only and without conducting meta-analyses[22,25]. In total, four original studies addressed aseptic wound complications, and three studies reported on prolonged wound healing. Our pooled results indicate that intrawound vancomycin does not increase the occurrence of aseptic wound complications (OR: 1.32; 95% CI: 0.86–2.02, $P = 0.20$, $I^2 = 0\%$, Fig. 9A) and prolonged wound healing (OR: 1.38; 95% CI: 0.42–4.51, $P = 0.59$, $I^2 = 64\%$, Fig. 9B). Despite some heterogeneity ($I^2 = 64\%$), the overall findings suggest that vancomycin application maintains a favorable safety profile in clinical settings.

Publication bias

The assessment of publication bias differed among the included systematic reviews. Peng did not use funnel plots to assess publication bias in their meta-analysis due to limited number of included studies[23]. Saidahmed did not mention the details of publication bias[24]. Xu *et al.* detected no observable publication bias across all included studies according to funnel plot analysis and Egger's test results[26]. Heckmann and Movassaghi detected no observable publication bias based on a funnel plot analysis[21,22]. In our umbrella review, we specifically assessed publication bias for outcomes where more than 10 studies were included, such as the overall infection rate. The funnel plot (Fig. 10) displayed a generally inverted funnel shape with a reasonable degree of symmetry, indicating some variability in the study results but a relatively low likelihood of significant publication bias. This conclusion was supported by the Egger's test, which produced a non-significant result ($P = 0.908$), suggesting that publication bias is unlikely to have substantially influenced the findings in our analysis.

Small study effects and excess significance bias

As none of the included studies provided the results of Egger's test, small-study effects were not evaluated.

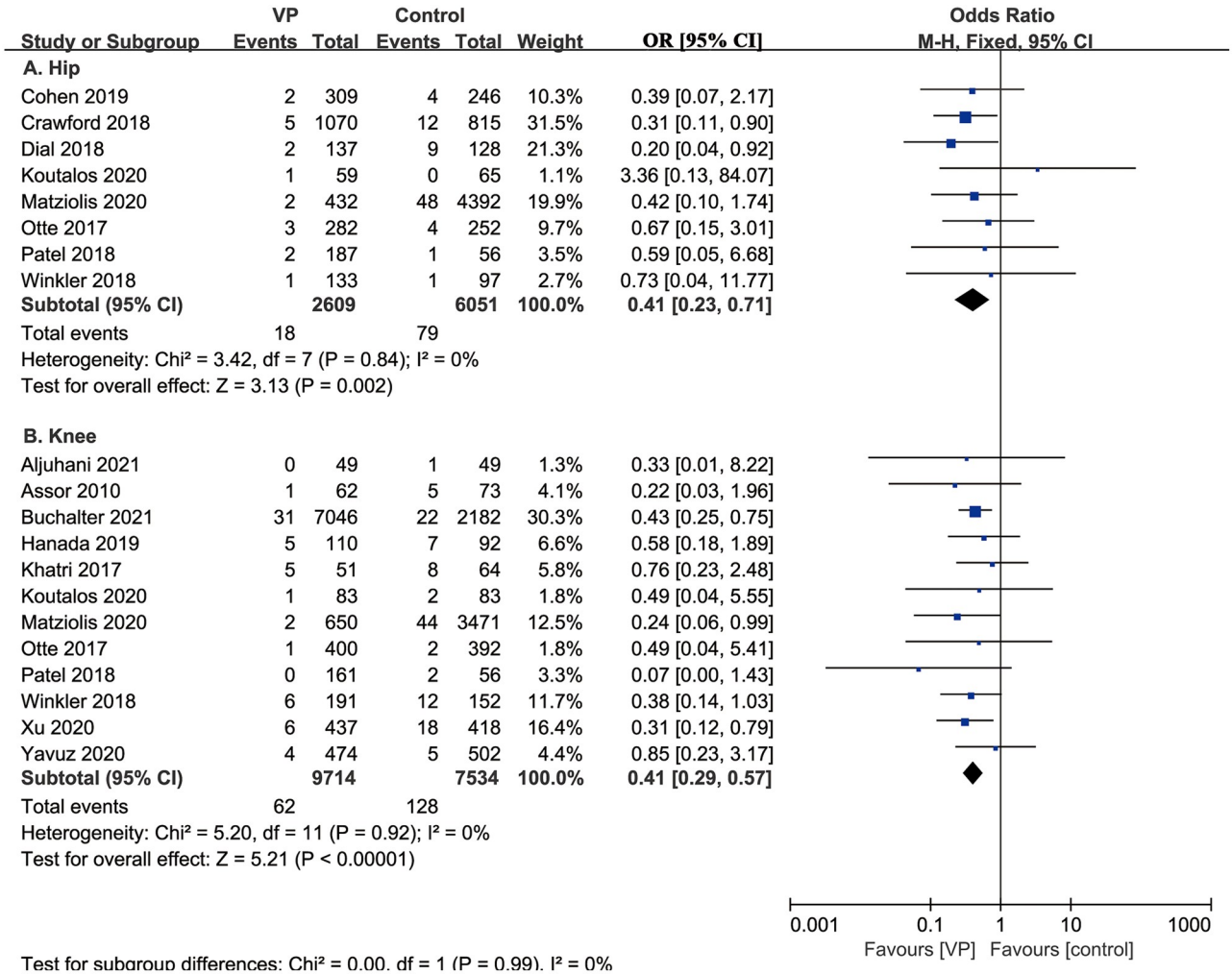

Figure 4. Subgroup analysis based on the surgical site (A) hip, (B) knee.

GRADE

For outcomes derived from studies where five or more were included, we utilized the GRADE approach to assess the quality of evidence. The analysis indicated that the use of VP consistently demonstrated a significant reduction in overall infection rates, superficial infections, and PJIs across various subgroups. The quality of evidence ranged from moderate to high, with most outcomes achieving a high level of certainty (Table 4). This robust evidence supports the clinical application of vancomycin in reducing postoperative infections.

Discussion

The main finding of our study is that vancomycin significantly reduces the overall rate of infection, superficial infection, and the incidence of PJI, without increasing wound complications. According to Cichos *et al.*, vancomycin exhibits a minimum inhibitory concentration (MIC) of 1.56 μg/ml against seven microorganisms, including MRSA, *S. epidermidis, Haemophilus influenzae, Pseudomonas aeruginosa, Burkholderia cepacia, Escherichia coli*, and *dry-phase bacteria*[43]. Given that *Staphylococcus* is the primary cause of infections following joint replacement[1], it is noteworthy that local application of a 2-g dose of vancomycin can maintain a local concentration of 200 μg/ml even 24 hours postoperatively[44]. In our included studies, vancomycin was administered at doses ranging from 0.5 to 2 g. Notably, even at the lowest dose of 0.5 g, the local concentration remained significantly higher than the MIC required to inhibit *Staphylococcus*, indicating that even lower doses are likely to be effective. Future research should aim to explore the optimal dosing strategies to balance efficacy with the potential risks associated with higher antibiotic concentrations. Typically, bone cement is impregnated with antibiotics, such as gentamicin, which are gradually released postoperatively to reduce infection rates[45,46]. This raises a critical question: in cases where antibiotic-laden bone cement is already used, is there still a need to apply additional VP? Our study suggests that the prophylactic effect of VP extends beyond what is achieved with antibiotic-loaded cement alone. In cementless joint arthroplasties, the impact of VP on reducing infection rates was even more pronounced. This highlights the essential role of VP in infection control, particularly in scenarios lacking mechanical fixation with antibiotic protection. Consequently, our findings strongly support the continued use of intrawound VP in joint arthroplasty, regardless of whether

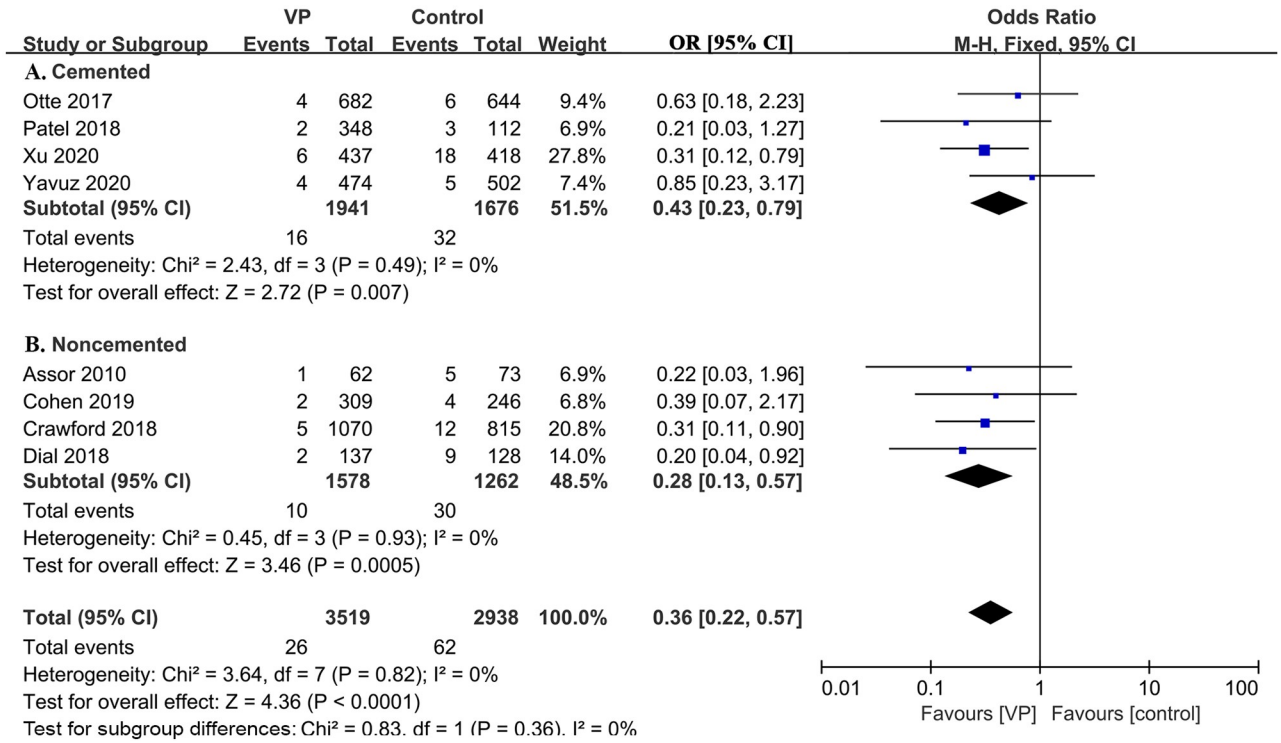

Figure 5. Subgroup analysis based on the surgical method (A) cemented, (B) cementless.

antibiotic-loaded cement is used. The additional reduction in infection rates, even in cases where antibiotic-loaded cement is employed, underscores the significant protective benefits of incorporating VP into standard prophylactic protocols. This approach may be especially beneficial in high-risk patients or complex procedures, providing an extra layer of defense against postoperative infections. Functional recovery of the joint is a key indicator of success after joint arthroplasty, and the increased pressure within the joint compartment during repeated movements may elevate the risk of wound complications[47]. In addition, the introduction of a crystalline substrate (such as vancomycin) between artificial joints could potentially increase prosthetic wear rates. Although *in vitro* experiments have indicated that topical vancomycin does not increase prosthesis wear rate[48], it has not been confirmed by *in vivo* studies. Future research should focus on evaluating both the efficacy of vancomycin at preventing infection and its impact on prosthesis wear rate. While intrawound vancomycin may not reduce the risk of superficial infection, it significantly reduces the risk of PJI. However, the side effects caused by its application are a problem that cannot be ignored. Previous studies have suggested that topically high concentrations of vancomycin may irritate local tissues, potentially leading to skin irritation, redness, swelling, and rupture of the skin, potentially leading to form subcutaneous effusions and increase local exudation, thereby raising concerns about an increased risk of complications from aseptic incisions[36,37]. However, our pooled analysis did not find a statistically significant increase in the occurrence of aseptic wound complications associated with vancomycin use. This suggests that while it is important to consider the potential risks highlighted in earlier studies, our findings support the safe use of intrawound vancomycin for reducing infection risk without a significant increase in incision-related complications.

While intrawound vancomycin has shown promise in reducing infection rates in joint arthroplasty, it is crucial to consider the potential risks associated with its clinical use. One significant concern is the emergence of antibiotic resistance. It is an established fact that exposure to antibiotics increases the likelihood of drug resistance[49,50]. However, given that the use of intrawound vancomycin in joint arthroplasty is typically a single-dose, localized application with a high dose and short exposure time, this approach contrasts with the typical long-term, systemic antibiotic use that often leads to resistance[51]. As a result, the risk of developing resistance from intrawound vancomycin is relatively low. Unlike long-term systemic antibiotic therapy, the systemic subinhibitory levels generated by localized vancomycin application are unlikely to lead to the emergence of resistant strains[51]. Furthermore, there is currently no evidence to suggest that the use of intrawound vancomycin contributes to the development of antibiotic resistance. Nevertheless, we emphasize the need for further long-term studies to more thoroughly assess this potential risk. Another potential risk is adverse tissue reactions. While vancomycin is generally well tolerated when used locally, there are concerns regarding its potential to cause tissue irritation or damage, particularly when applied in high concentrations. In the studies we included, three reported wound-related complications[27,37,41], particularly delayed wound healing. For example, the study by Hanada *et al.*[37] found that the incidence of delayed wound healing in the VP group was significantly higher than in the control group, although the other two studies did not show significant differences between the groups. These discrepancies may be attributed to individual patient factors or differences in surgical technique. Therefore, careful monitoring of the wound healing process during clinical application is essential to identify and address any potential adverse reactions, thus minimizing the occurrence of tissue damage and complications.

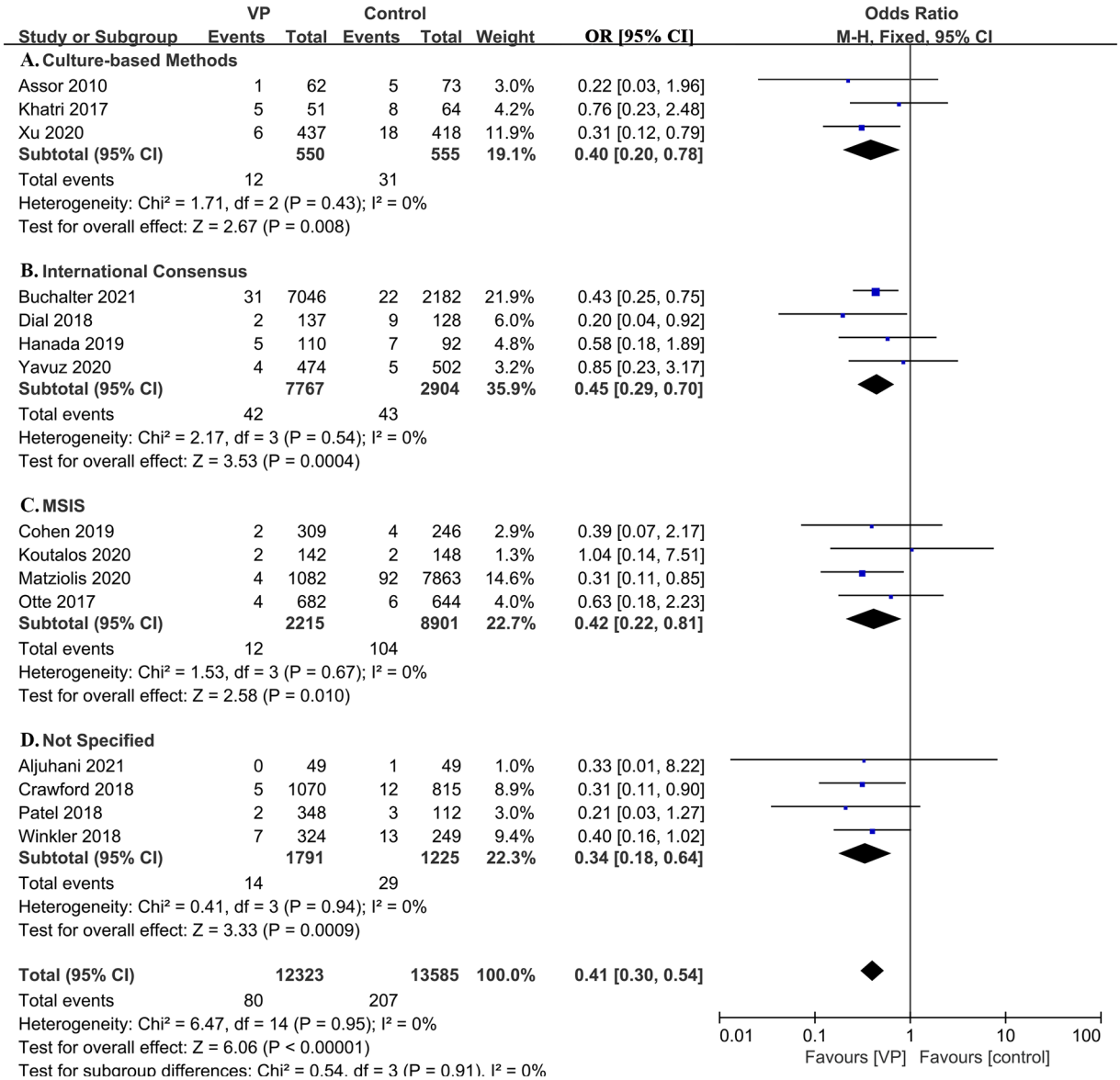

Figure 6. Subgroup analysis based on infection diagnostic criteria (A) culture-based methods, (B) international consensus, (C) MSIS, (D) not specified.

Although current evidence suggests that the local application of vancomycin is generally safe, further research is necessary to evaluate its long-term effects on tissue health, especially with increased frequency of use or over extended periods of clinical practice. A further concern associated with the local use of vancomycin is its potential impact on microbiome diversity. While long-term systemic antibiotic use has been shown to alter the microbiome and promote the development of resistance[49,50], the effects of localized vancomycin application are different. The results from the VANCO trial indicate that intrawound vancomycin significantly reduces the incidence of gram-positive bacterial infections[52]. Moreover, Joshi *et al.*[51] did not observe a significant increase in gram-negative rod (GNR) infections or changes in resistance patterns. Notably, although vancomycin's local application effectively targets gram-positive cocci, no increase in gram-negative infections was observed. Specifically, in Joshi et al.'s study, the incidence of MSSA (methicillin-susceptible *Staphylococcus aureus*) infections was significantly lower in the treatment group compared to the control group. However, there was no significant difference in the rate of MRSA and coagulase-negative staphylococci infections between the two groups. Importantly, no increased risk of GNR infections or development of resistance patterns was observed following the use of intrawound vancomycin. Given these potential risks, further research is essential to assess the long-term safety of intrawound vancomycin, particularly its effects on antibiotic resistance, tissue reactions, and microbiome composition. These factors are critical to its clinical application and must be carefully weighed against the observed benefits in reducing infection rates. By addressing these concerns through continued research, we can ensure the safe and effective use of intrawound vancomycin in clinical settings.

Unfortunately, the methodological quality of all included systematic reviews was critically low according to AMSTAR-2,

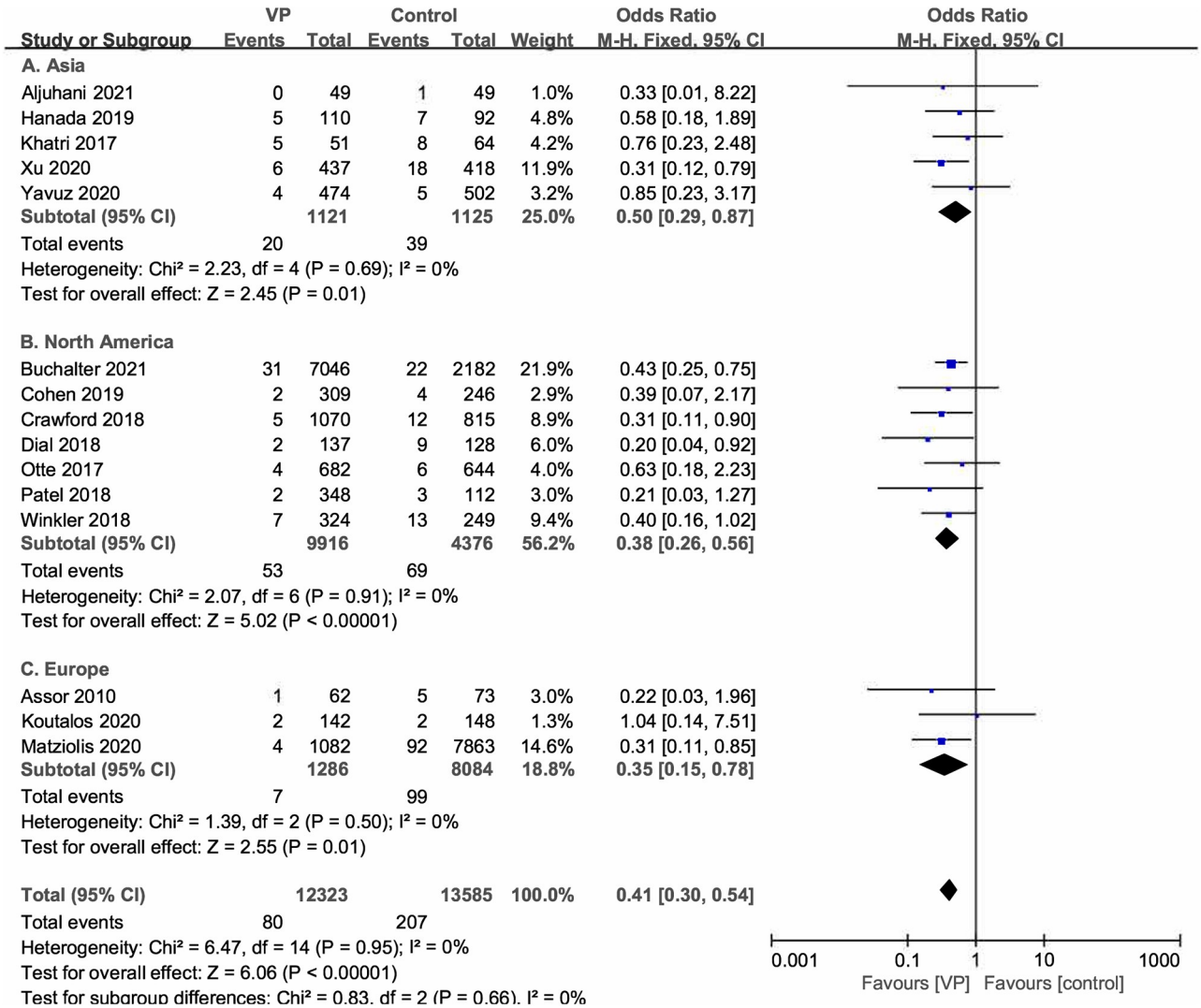

Figure 7. Subgroup analysis based on region (A) Asia, (B) North America, (C) Europe.

it is crucial to highlight the robustness of the underlying evidence. The individual studies included in our umbrella review were of high quality, as reflected by their strong NOS scores. Moreover, the GRADE assessment consistently demonstrated a high level of evidence across our key outcomes, reinforcing the validity and reliability of our conclusions. Despite the limitations inherent in the systematic reviews, the high-quality primary studies and the rigorous evaluation of evidence lend significant weight to our findings, making them a valuable resource for guiding clinical practice in joint arthroplasty.

Recent advancements in vancomycin delivery systems and diagnostic tools have contributed significantly to enhancing infection prophylaxis in joint arthroplasty[53]. Innovative delivery methods, such as thiol-mediated nanodrug systems, have been developed to improve vancomycin's penetration efficiency and intracellular antibacterial activities[54]. Additionally, liposome-encapsulated vancomycin carriers have shown potential in enhancing drug absorption at target tissues, thereby improving therapeutic outcomes. On the diagnostic front, novel biomarkers such as calprotectin and lipocalin have demonstrated promise as reliable markers for PJI, improving diagnostic accuracy and patient management[55]. Furthermore, advanced diagnostic techniques, including synovial fluid analysis using reporter gene assays and flow cytometry, are being explored for their value in detecting PJI with greater precision[56,57]. These developments represent cutting-edge advancements in infection prevention strategies for joint arthroplasty and highlight the potential for future innovations to optimize clinical outcomes. Looking ahead, a promising direction for future research lies in exploring different vancomycin administration methods and innovative delivery systems. Comparative studies on local application, oral, intravenous, intraosseous vancomycin, and advanced delivery systems such as sustained-release formulations and nano-carrier technologies could offer critical insights into optimizing infection prophylaxis while minimizing complications. Individualized infection prevention strategies, tailored to patient-specific risk factors, could further enhance clinical efficacy and safety. Additionally, the integration of advanced diagnostic tools, such as microbiome profiling and next-generation sequencing,

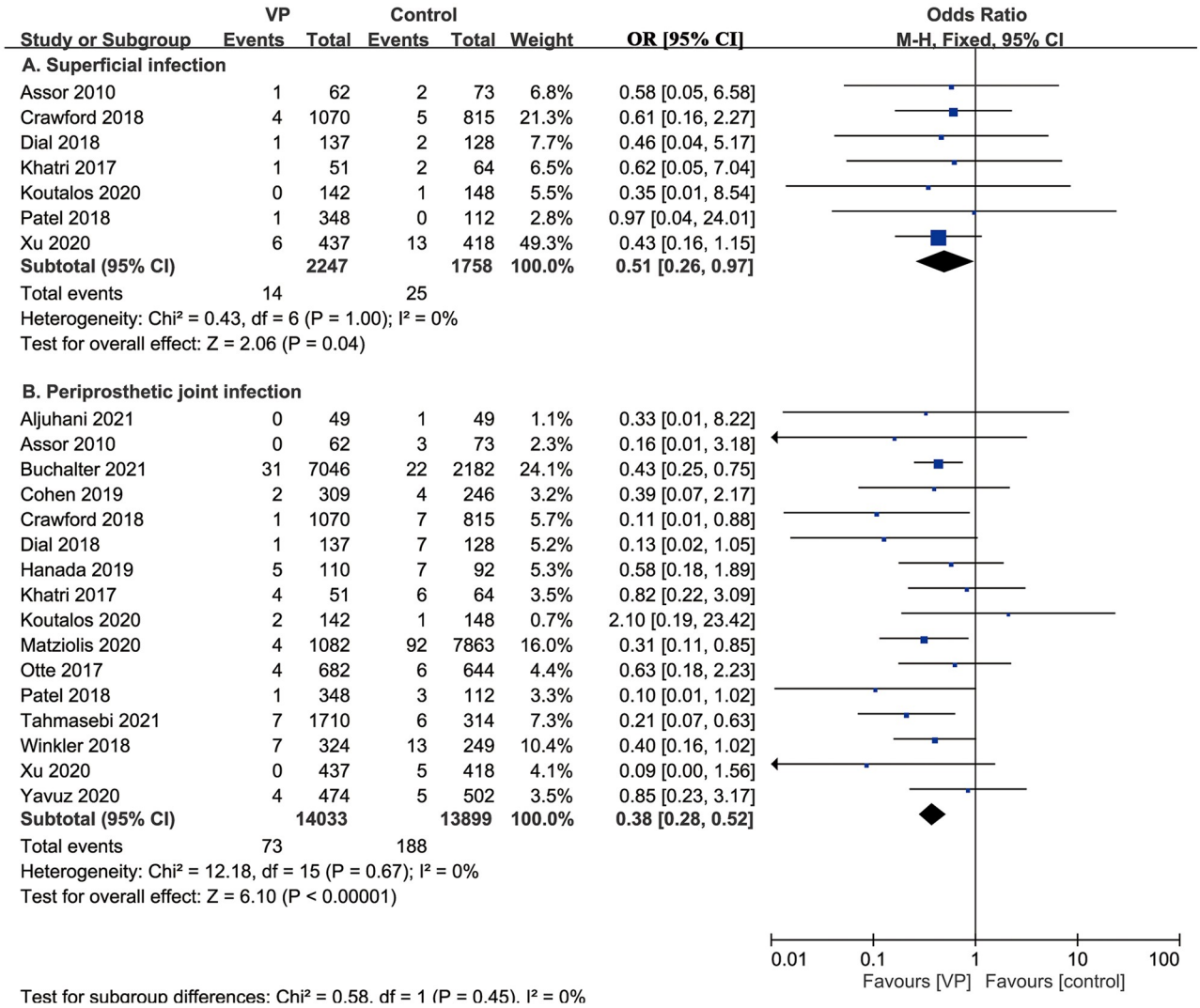

Figure 8. T Forest plot of comparison: VP versus No-VP; outcome: superficial infection (A) and periprosthetic joint infection (B).

holds promise for more targeted and effective infection prevention strategies. Comparative studies evaluating vancomycin against emerging antimicrobials, as well as extended follow-up studies assessing its long-term effects on prosthesis longevity and functional recovery, are essential. Furthermore, cost-effectiveness analyses would provide valuable insights into the economic implications of vancomycin use, supporting evidence-based decision-making and influencing health policy. By addressing these forward-looking aspects, future research can refine infection prevention strategies in joint arthroplasty and solidify the role of intrawound vancomycin as a cornerstone of surgical prophylaxis.

Strength

To the best of our knowledge, this is the first umbrella review to investigate the association between vancomycin and infection in primary joint arthroplasty. The included studies combined data on infection and wound complications in patients who underwent primary joint arthroplasty, offering insights of high clinical value. Given the severe consequences of PJI, the scientific prevention of PJI and its associated complications warrants further exploration. Moreover, we believe that this study will garner significant public interest.

Limitation

Our study has the following limitations. First, the pooled results from the included meta-analysis did not adjust for effect size; instead, the raw data were directly combined statistically, which may have increased bias in the results. Second, many of the included studies are retrospective in nature, which introduces inherent limitations in terms of data quality and the ability to control for confounding factors. This reliance on retrospective data may affect the generalizability and strength of the conclusions drawn. . Third, three of the included studies did not search the literature in all relevant languages[22-24]; instead, they restricted their searches to English-language publications without providing a rationale, which may have limited the accuracy and comprehensiveness of the systematic reviews. Fourth, Movassaghi *et al.* did not differentiate between infection types, and in the trials

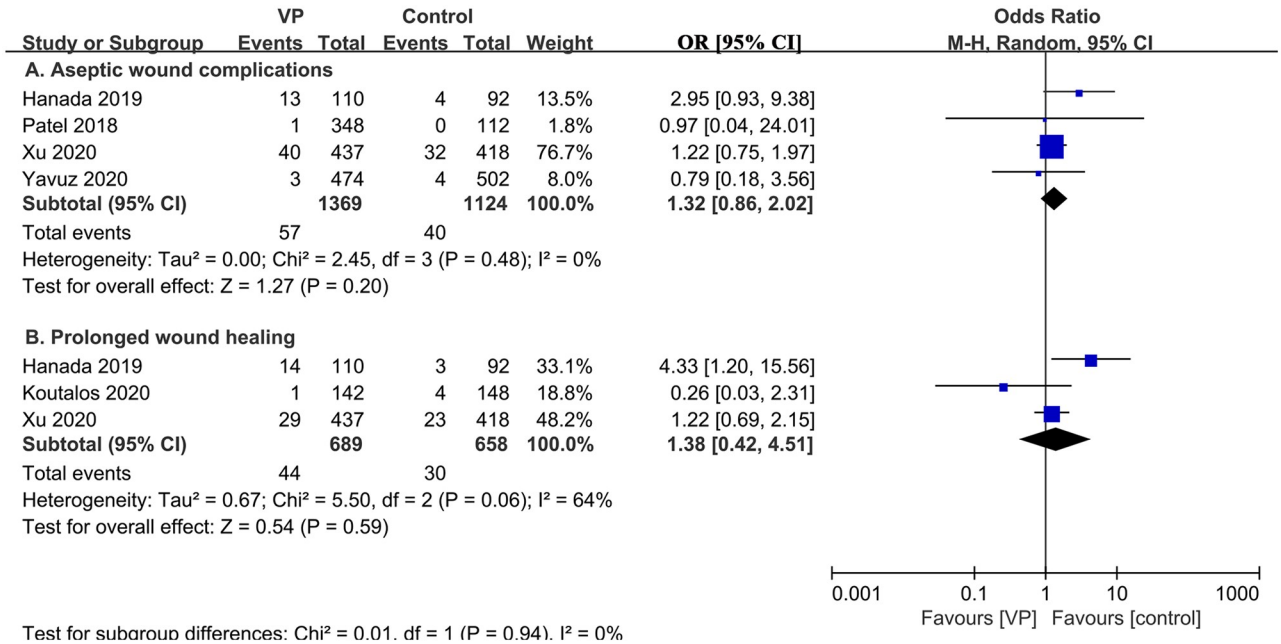

Figure 9. The effect of intrawound vancomycin on aseptic wound complications (A) and prolonged wound healing (B).

included in their meta-analysis, they combined trials with PJI as the overall infection, which may have increased the bias of the results[22]. Fifth, due to the limited data availability in the included studies, we were unable to perform subgroup analyses for different patient populations, such as age groups, high-risk patients, compliance, or medication use. As a result, the generalizability of our findings across all patient groups may be limited. Future studies with more detailed patient-level data are needed to explore the effectiveness of intrawound vancomycin in diverse populations. Sixth, this study was unable to perform a cost-effectiveness analysis due to the lack of economic outcome data from the included studies, which did not provide sufficient data on economic outcomes. This omission limits our ability to assess the economic benefits of vancomycin use in joint arthroplasty. Future research should focus on this aspect to better understand the cost-effectiveness of intrawound vancomycin in this context. Seventh,

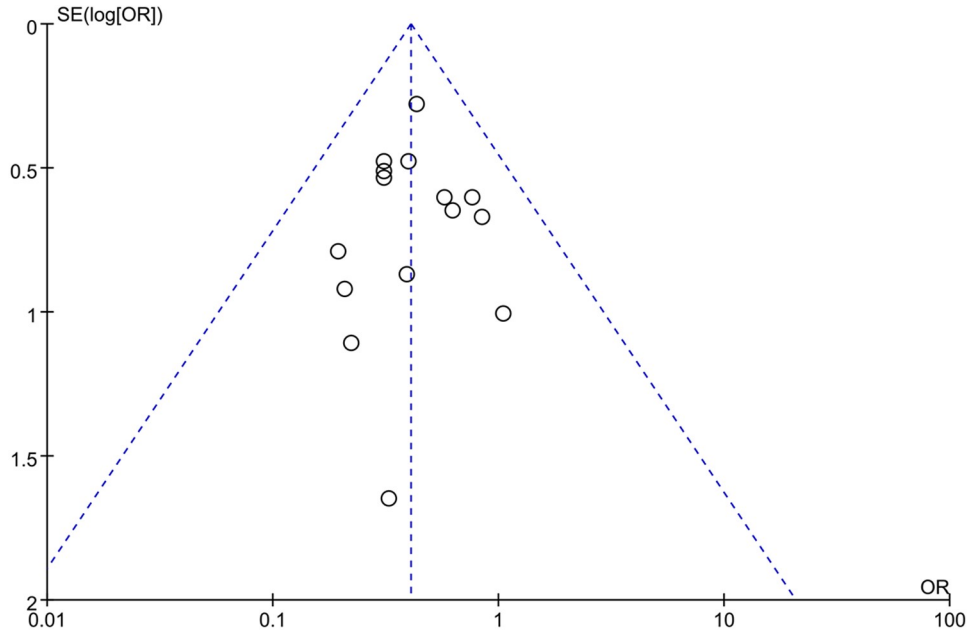

Figure 10. Funnel plots for publication bias (overall infection rate).

Table 4

GRADE summary of findings

VP compared to No-VP for prevention of surgical site infections in primary joint arthroplasty

Patient or population: prevention of surgical site infections in primary joint arthroplasty
Setting:
Intervention: VP
Comparison: No-VP

	Anticipated absolute effects* (95% CI)				
Outcomes	**Risk with No-VP**	**Risk with VP**	**Relative effect (95% CI)**	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
Overall infection rate	15 per 1000	6 per 1000 (5 to 8)	OR 0.41 (0.30 to 0.54)	25 908 (15 non-randomized studies)	⊕⊕⊕⊕ High[a]
Overall infection rate (2 g VP)	14 per 1000	7 per 1000 (4 to 10)	OR 0.48 (0.31 to 0.74)	11 165 (5 non-randomized studies)	⊕⊕⊕⊕ High[a]
Overall infection rate (1 g VP)	15 per 1000	5 per 1000 (3 to 8)	OR 0.36 (0.23 to 0.55)	14 067 (8 non-randomized studies)	⊕⊕⊕⊕ High[a]
Overall infection rate (Hip)	13 per 1000	5 per 1000 (3 to 9)	OR 0.41 (0.23 to 0.71)	8660 (8 non-randomized studies)	⊕⊕⊕⊕ High[a]
Overall infection rate (Knee)	17 per 1000	7 per 1000 (5 to 10)	OR 0.41 (0.29 to 0.57)	17 248 (12 non-randomized studies)	⊕⊕⊕⊕ High[a]
Superficial infection rate	14 per 1000	7 per 1000 (4 to 14)	OR 0.51 (0.26 to 0.97)	4005 (7 non-randomized studies)	⊕⊕⊕◯ Moderate[a]
Periprosthetic joint infection rate	14 per 1000	5 per 1000 (4 to 7)	OR 0.38 (0.28 to 0.52)	27 932 (16 non-randomized studies)	⊕⊕⊕⊕ High[a]

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.
*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
CI: confidence interval; OR: odds ratio
[a]unclear risk of bias

due to the limited number of studies (only three) reporting on prolonged wound healing, substantial heterogeneity was observed, and we were unable to conduct subgroup analyses to explore potential sources of this variability. Eighth, there is considerable variability in perioperative protocols across studies, including differences in the choice of antibiotics, their dosing regimens, and the timing of administration. For example, some studies used intravenous vancomycin in patients allergic to cefazolin, while others may have employed different antibiotics or dosages. Additionally, the timing of antibiotic administration, such as whether antibiotics were given preoperatively, intraoperatively, or postoperatively, varied across the studies. These differences in perioperative antibiotic protocols could introduce significant heterogeneity in the results, influencing infection outcomes. Ninth, given the limitations in study design, there may be publication bias, as studies with positive results are more likely to be published, skewing the findings. Finally, the methodological quality of all included studies was critically low, and, to some extent, our confidence in the results was low. A high-quality systematic review is an important source of evidence for optimal clinical use in evidence-based medicine, and further high-quality RCTs are needed to confirm these findings.

Conclusion

Based on our extensive umbrella review, intrawound vancomycin has emerged as a potent intervention for significantly reducing infection rates in patients undergoing primary joint arthroplasty, regardless of the diagnostic criteria or type of joint involved. The findings consistently indicate a marked reduction in overall infection rates, including PJI and superficial infections, without an associated increase in aseptic wound complications or delays in wound healing. Despite some heterogeneity across the included studies, the robust nature of our analysis underscores the potential of intrawound vancomycin as an effective strategy for preventing infections in joint arthroplasty. The low likelihood of publication bias further strengthens the reliability of these results. Nonetheless, to fully validate these findings and to better understand the long-term safety and cost-effectiveness of this approach, further high-quality, prospective research is essential.

Author contributions

H.L. conceived and designed the project. Z.Z. performed the literature retrieval. H.L. drafted the article. Y.S. and T.T. conceived the project and provided suggestions to improve it, H.L. and Y.L. developed the idea for the study and finally revised the paper.

Conflicts of interest disclosure

Not applicable.

Guarantor

Hua Luo

Acknowledgements

None.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] Lei X, Xiang J, Yang H, *et al*. Intraosseous regional prophylactic antibiotics decrease the risk of infection in total knee arthroplasty compared with intravenous antibiotics: a systematic review and meta-analysis. EFORT Open Rev 2023;8:127–34.
[2] Kulm S, Kolin DA, Langhans MT, *et al*. Characterization of genetic risk of end-stage knee osteoarthritis treated with total knee arthroplasty: a genome-wide association study. J Bone Joint Surg Am 2022;104:1814 Am.
[3] Ramos-Guarderas P, Arteaga-Guerrero G, Vargas-Morante M, *et al*. Total hip arthroplasty with second generation dual mobility system as a treatment for primary coxarthrosis, medium-term results. Rev Esp Cir Ortop Traumatol Artroplastia total de cadera con sistema doble movilidad de segunda generación como tratamiento de coxartrosis primaria, resultados a mediano plazo. 2024;68:4384op.
[4] Salimy MS, Paschalidis A, Dunahoe JA, *et al*. Time to achieve the minimal clinically important difference in primary total hip arthroplasty: comparison of anterior and posterior surgical approaches. J Arthroplasty 2024;39:S314throp.
[5] Xie C, Pan W, Wang S, Yan X, *et al*. Systematic review and meta-analysis of single-stage versus two-stage revision for periprosthetic joint infection after knee arthroplasty: a call for a randomised trial. EFORT Open Rev 2024;9:4794T .
[6] Vertesich K, Puchner SE, Staats K, *et al*. Distal femoral reconstruction following failed total knee arthroplasty is accompanied with risk for complication and reduced joint function. BMC Musculoskelet Disord 2019;20:47.
[7] Kuo FC, Hsu CW, Tan TL, *et al*. Effectiveness of different wound dressings in the reduction of blisters and periprosthetic joint infection after total joint arthroplasty: a systematic review and network meta-analysis. J Arthroplasty 2021;36:2612thr.
[8] Kurtz SM, Lau E, Watson H, *et al*. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty 2012; 27:6112thr.
[9] Premkumar A, Kolin DA, Farley KX, *et al*. Projected economic burden of periprosthetic joint infection of the hip and knee in the United States. J Arthroplasty 2021;36:1484throplas.
[10] Stevoska S, Behm-Ferstl V, Zott S, *et al*. The impact of patient-reported penicillin or cephalosporin allergy on the occurrence of the periprosthetic joint infection in primary knee and hip arthroplasty. Antibiotics (Basel) 2022;11:1345.
[11] Kapadia BH, Berg RA, Daley JA, *et al*. Periprosthetic joint infection. Lancet 2016;387:3866et.
[12] Arunshankar A, Chandy VJ, Elangovan D, *et al*. Microbiological profile of infections of the hip joint: an Indian perspective. Indian J Med Microbiol 2019;37:5099an.
[13] Luo H, Ren Y, Su Y, *et al*. Intraoperative vancomycin powder to reduce surgical site infections after posterior spine surgery: a systematic review and meta-analysis. EFORT Open Rev 2022;7:1092T .
[14] Chiu F-Y, Lin C-FJ. Antibiotic-impregnated cement in revision total knee arthroplasty a prospective cohort study of one hundred and eighty-three knees. J Bone Joint Surgery-Am Volume 2009;91A:6289ne.
[15] Assor M. Noncemented total knee arthroplasty with a local prophylactic anti-infection agent: a prospective series of 135 cases. Can J Surg 2010;53:4710J.
[16] Matziolis G, Brodt S, Böhle S, *et al*. Intraarticular vancomycin powder is effective in preventing infections following total hip and knee arthroplasty. Sci Rep 2020;10:13053.
[17] Tahmasebi MN, Vaziri AS, Vosoughi F, *et al*. Low post-arthroplasty infection rate is possible in developing countries: long-term experience of local vancomycin use in Iran. J Orthop Surg Res 2021;16:199.
[18] Aljuhani WS, Alanazi AM, Alghafees MA, *et al*. The efficacy of vancomycin powder in total knee arthroplasty: a single-center study. Saudi Med J 2021;42:5501i .
[19] Cohen EM, Marcaccio S, Goodman AD, *et al*. Efficacy and cost-effectiveness of topical vancomycin powder in primary cementless total hip arthroplasty. Orthopedics 2019;42:e430–e436.
[20] Khatri K, Bansal D, Singla R, Sri S. Prophylactic intrawound application of vancomycin in total knee arthroplasty. J Arthroscopy Joint Surg 2017;4:6117t.
[21] Heckmann ND, Mayfield CK, Culvern CN, *et al*. Systematic review and meta-analysis of intrawound vancomycin in total hip and total knee arthroplasty: a call for a prospective randomized trial. J Arthroplasty 2019;34:1815thr.
[22] Movassaghi K, Wang JC, Gettleman BS, *et al*. Systematic review and meta-analysis of intrawound vancomycin in total hip and total knee arthroplasty: a continued call for a prospective randomized trial. J Arthroplasty 2022;37:1405throplas.
[23] Peng Z, Lin X, Kuang X, *et al*. The application of topical vancomycin powder for the prevention of surgical site infections in primary total hip and knee arthroplasty: a meta-analysis. Orthop Traumatol Surg Res 2021;107:102741.
[24] Saidahmed A, Sarraj M, Ekhtiari S, *et al*. Local antibiotics in primary hip and knee arthroplasty: a systematic review and meta-analysis. Eur J Orthop Surg Traumatol 2021;31:6691 T.
[25] Wong MT, Sridharan SS, Davison EM, *et al*. Can topical vancomycin prevent periprosthetic joint infection in hip and knee arthroplasty? a systematic review. Clin Orthop Relat Res 2021;479:1655t R.
[26] Xu H, Yang J, Xie J, *et al*. Efficacy and safety of intrawound vancomycin in primary hip and knee arthroplasty. Bone Joint Res 2020;9:7780 J.
[27] Koutalos AA, Drakos A, Fyllos A, *et al*. Does intra-wound vancomycin powder affect the action of intra-articular tranexamic acid in total joint replacement? Microorganisms 2020;8:671.
[28] Buchalter DB, Kirby DJ, Teo GM, *et al*. Topical vancomycin powder and dilute povidone-iodine lavage reduce the rate of early periprosthetic joint infection after primary total knee arthroplasty. J Arthroplasty 2021;36:2861thropl.
[29] Iorio R, Yu S, Anoushiravani AA, *et al*. Vancomycin powder and dilute povidone-iodine lavage for infection prophylaxis in high-risk total joint arthroplasty. J Artic; Randomized Controlled Trial J Arthroplasty 2020;35:1933tic; .
[30] Riesgo AM, Park BK, Herrero CP, *et al*. Vancomycin povidone-iodine protocol improves survivorship of periprosthetic joint infection treated with irrigation and debridement. J Arthroplasty 2018;33:8478th.
[31] Shea BJ, Reeves BC, Wells G, *et al*. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. Bmj 2017;358:j4008.
[32] Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj 2021;372: n71.
[33] Stang A. Critical evaluation of the newcastle-ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:6030J .
[34] Guyatt G, Oxman AD, Akl EA, *et al*. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol Apr 2011;64:3831in.
[35] Crawford D, Berend K, Adams J, Lombardi A. Decreased incidence of periprosthetic joint infection in total hip arthroplasty with use of topical vancomycin. Reconstr Rev 2018;8:2018nst.
[36] Dial BL, Lampley AJ, Green CL, Hallows R. Intrawound vancomycin powder in primary total hip arthroplasty increases rate of sterile wound complications. Hip Pelvis 2018;30:3718i.
[37] Hanada M, Nishikino S, Hotta K, *et al* Intrawound vancomycin powder increases post-operative wound complications and does not decrease periprosthetic joint infection in primary total and unicompartmental knee arthroplasties. Knee Surg Sports Traumatol Arthrosc 2019;27: 2322 Su.
[38] Otte JE, Politi JR, Chambers B, Smith CA. Intrawound vancomycin powder reduces early prosthetic joint infections in revision hip and knee arthroplasty. Surg Technol Int 2017;30:2847 T.
[39] Patel NN, Guild GN, Kumar AR. Intrawound vancomycin in primary hip and knee arthroplasty: a safe and cost-effective means to decrease early periprosthetic joint infection. Arthroplasty Today 2018;4:47 98ro.
[40] Winkler C, Dennison J, Wooldridge A, *et al*. Do local antibiotics reduce periprosthetic joint infections? A retrospective review of 744 cases. J Clinl Orthopaedics Trauma 2018;9:S348inl.

[41] Xu X, Zhang X, Zhang Y, *et al*. Role of intra-wound powdered vancomycin in primary total knee arthroplasty. Orthop Traumatol Surg Res 2020;106:4170ma.
[42] Yavuz IA, Oken OF, Yildirim AO, *et al*. No effect of vancomycin powder to prevent infection in primary total knee arthroplasty: a retrospective review of 976 cases. Knee Surg Sports Traumatol Arthrosc 2020;28:3055 Su.
[43] Cichos KH, Andrews RM, Wolschendorf F, *et al*. Efficacy of intraoperative antiseptic techniques in the prevention of periprosthetic joint infection: superiority of betadine. J Arthroplasty 2019;34: S312throp.
[44] Johnson JD, Nessler JM, Horazdovsky RD, *et al*. Serum and wound vancomycin levels after intrawound administration in primary total joint arthroplasty. J Arthroplasty 2017;32:9247th.
[45] Hamoudi C, Hamon M, Reiter-Schatz A, *et al*. Cement loaded with high-dose gentamicin and clindamycin does not reduce the risk of subsequent infection after aseptic total hip or knee revision arthroplasty: a preliminary study. J Orthop Traumatol 2024;25:37.
[46] Sebastian S, Liu Y, Christensen R, *et al*. Antibiotic containing bone cement in prevention of hip and knee prosthetic joint infections: a systematic review and meta-analysis. J Orthop Translat 2020;23:5320s.
[47] Şükür E, Öztürkmen Y, Akman YE, *et al*. The effect of tourniquet and knee position during wound closure after total knee arthroplasty on early recovery of range of motion: a prospective, randomized study. Arch Orthop Trauma Surg 2016;136:1773ma .
[48] Qadir R, Ochsner JL, Chimento GF, *et al*. Establishing a role for vancomycin powder application for prosthetic joint infection prevention-results of a wear simulation study. J Arthroplasty 2014;29:1449thr.
[49] Zhao Q, Guo W, Luo H, *et al*. Deciphering the transfers of antibiotic resistance genes under antibiotic exposure conditions: driven by functional modules and bacterial community. Water Res 2021;205:117672.
[50] Yang X, Guo R, Zhang B, *et al*. Retrospective analysis of drug resistance characteristics and infection related risk factors of multidrug-resistant organisms (MDROs) isolated from the orthopedics department of a tertiary hospital. Sci Rep 2023;13:2199.
[51] Joshi M, O shiep RV, Carlini AR, *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;38:1834ma.
[52] O'Toole RV, Joshi M, Carlini AR, *et al*. Effect of intrawound vancomycin powder in operatively treated high-risk tibia fractures: a randomized clinical trial. JAMA Surg 2021;156:e207259.
[53] Luo Y, Su L, Yang H, *et al*. A disulfide molecule-vancomycin nanodrug delivery system efficiently eradicates intracellular bacteria. J Mater Chem B 2024;12:2334ter.
[54] Dubnika A, Egle K, Skrinda-Melne M, *et al*. Development of vancomycin delivery systems based on autologous 3D platelet-rich fibrin matrices for bone tissue engineering. Biomedicines 2021;9:814.
[55] Schindler M, Walter N, Maderbacher G, *et al*. Novel diagnostic markers for periprosthetic joint infection: a systematic review. Front Cell Infect Microbiol 2023;13:1210345.
[56] Sallai I, Marton N, Szatmn5e A, *et al*. Activated polymorphonuclear derived extracellular vesicles are potential biomarkers of periprosthetic joint infection. PLoS One 2022;17:e0268076.
[57] Yermak K, Karbysheva S, Perka C, *et al*. Performance of synovial fluid D-lactate for the diagnosis of periprosthetic joint infection: a prospective observational study. J Infect 2019;79:1239fe.