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Meta-analysis
Oral Surgery

Antibiotic prophylaxis in the prevention of dry socket and surgical site infection after lower third molar extraction: a network meta-analysis

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Abstract. Clinicians frequently prescribe systemic antibiotics after lower third molar extractions to prevent complications such as surgical site infections and dry socket. A systematic review of randomised clinical trials was conducted to compare the risk of dry socket and surgical site infection after the removal of lower third molars with different prophylactic antibiotics. The occurrence of any antibiotic-related adverse event was also analysed. A pairwise and network meta-analysis was performed to establish direct and indirect comparisons of each outcome variable. Sixteen articles involving 2158 patients (2428 lower third molars) were included, and the following antibiotics were analysed: amoxicillin (with and without clavulanic acid), metronidazole, azithromycin, and clindamycin. Pooled results favoured the use of antibiotics to reduce dry socket and surgical site infection after the removal of a lower third molar, with a number needed to treat of 25 and 18, respectively. Although antibiotic prophylaxis was found to significantly reduce the risk of dry socket and surgical site infection in patients undergoing lower third molar extraction, the number of patients needed to treat was high. Thus, clinicians should evaluate the need to prescribe antibiotics taking into consideration the patient's systemic status and the individual risk of developing a postoperative infection.

Keywords: Antibiotics; Dry socket; Surgical site infection; Adverse drug event; Third molar; Network meta-analysis.

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The extraction of lower third molars (L3M) is a routine procedure for many dentists.[1–3] Despite being a common treatment, it bears the risk of postoperative complications such as swelling, pain, and trismus, among others.[4] Since third molar extraction is classified as a clean-contaminated surgery, there is ground to consider the use of antibiotic prophylaxis, due to the risk of surgical site infection (SSI) and dry socket (DS).[1–5] The overall incidence of SSI in all third molar extractions is within the range of 1–13%.[4] In some rare cases, these infections can affect the deep anatomical spaces, and affected patients may require hospitalisation and surgical treatment.[1] On the other hand, DS – also known as alveolar osteitis – is a painful but not potentially life-threatening complication seen in approximately 0.5–5% of all patients subjected to tooth extractions.[6]

Dentists have traditionally used prophylactic antibiotics to prevent DS and SSI. The most commonly used antibiotic for the prevention of postoperative infection after L3M extraction is amoxicillin alone or in combination with clavulanic acid.[7] Other antibiotics are clindamycin, doxycycline, erythromycin, and metronidazole.[3] However, the ideal active ingredient and dosage for prophylaxis remain unclear, since no studies have compared multiple antibiotic regimens for the prevention of DS and SSI after L3M extraction.[3]

Antibiotic prophylaxis is effective for the prevention of complications in high-risk patients,[2] and is also indicated in cases of active infection at the time of surgery.[4] However, controversy remains regarding the systematic use of antibiotic prophylaxis in healthy patients who require L3M extraction. A systematic review and meta-analysis published in 2016 suggested that the cost–benefit ratio for the indiscriminate administration of antibiotics was unfavourable,[5] and a growing number of clinicians discourage this strategy because the infection risk is low.[4] Nevertheless, in some countries, antibiotic prophylaxis is still routinely prescribed for most patients undergoing L3M extraction.[5]

Moreover, antibiotics can interact with other drugs, cause allergic reactions, and modify the microbiota, the latter of which may result in complications such as candidiasis or infection by *Clostridium difficile*. Additionally, antibacterial agents may cause gastrointestinal adverse effects (e.g., nausea, vomiting, diarrhoea, and abdominal pain), or even lead to haematological complications (e.g., thrombocytopenia, neutropenia, and haemolysis).[4] In addition to such side effects, multiple or long-lasting courses of antibiotics may result in bacterial resistance to these drugs.[3] Antibiotics may also disrupt the healthy microbiome and increase patient susceptibility to future infections.[7]

Considering that different antibiotic regimens are available and that there is no agreement as to whether healthy patients should receive antibiotic prophylaxis when undergoing L3M extraction, evidence-based recommendations are clearly needed. These should focus on specifying which patients need antibiotics, and also on the optimum drug and dosage regimen for this particular surgical procedure.

The main aim of this systematic review and meta-analysis was to assess the role of different antibiotic prophylactic treatments in relation to the risk of developing DS and SSI after L3M extraction. The secondary aim was to identify the risk of adverse reactions related to antibiotic prophylaxis.

Materials and methods

Protocol and registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[8] The protocol has been registered in the PROSPERO database (CRD42020213678).

Study selection criteria

The PICOS framework (population, intervention, comparison, outcomes, study design) was applied in this systematic review. The inclusion criteria were randomised clinical trials (RCTs) (study design) published between 1999 and 2021, performed in a population of healthy patients (population) who underwent L3M extraction and took either oral antibiotic prophylaxis (intervention) or placebo/no treatment (comparison). Studies that employed other routes of administration (intramuscular, submucosal, or intravenous) were excluded. Whenever possible, the occurrence of DS, SSI, and adverse events (outcomes) was registered.

The PICOS question was: "In clinical trials with patients undergoing lower third molar extraction, does oral antibiotic prophylaxis lower the risk of developing dry socket and surgical site infection, compared with no treatment or placebo?".

The main outcomes were DS and SSI. DS was defined as persistent or increased postoperative pain in or around the extraction site, usually between the first and the third day postextraction, accompanied by a partially or totally disintegrated blood clot or an empty socket, with or without halitosis. SSI was identified from the presence of purulent drainage, sinus tracts, or space infection.

Additionally, adverse events occurring after the administration of antibiotics that might be related to the drug (e.g., gastric pain, allergic reactions, candidiasis) were registered as secondary outcomes.

Search strategy

Three independent researchers (H.S-B., N.V-R., and J.T-S) conducted an electronic search in MEDLINE (via PubMed), The Cochrane Library (Wiley), and Scopus (Elsevier) in December 2021. Relevant studies were identified using the search strategies provided in Supplementary Material Table S1.

The electronic search was complemented by a manual screening of the references cited in the selected articles.

Selection of studies

Three independent investigators (H.S-B., N.V-R., and J.T-S.) selected the articles according to the pre-established inclusion criteria. Any discordance among the authors was resolved by consensus between them or with the aid of two other researchers (E.V-C and O.C-F.). The PRISMA

guidelines were followed for the article screening process[8]; after initial screening of the titles and abstracts, the full-texts of the selected articles were evaluated. Studies removed at this stage and the reasons for their exclusion were recorded.

When multiple reports on the same patients were identified, the most recent was included. No restriction on publication language was applied.

Data extraction and method of analysis

The data extraction from the selected studies was conducted by two independent investigators (H.S-B. and J.T-S.) who recorded the following variables independently: (1) general article information (title, author, year of publication); (2) study characteristics (study setting, type of RCT, follow-up, number of patients); (3) patient information (age, sex, country of residence); (4) details of the intervention (number of extracted L3M, type of extraction (simple or surgical; with/without ostectomy, with/without tooth sectioning), duration of surgery); (5) use of antibiotics, including the dosage, dosing regimen, timing, and duration.

Authors were contacted when necessary for clarification of missing information.

Quality and risk of bias assessment

As part of the data extraction process, two investigators (H.S-B. and J.T-S.) evaluated the study quality and performed a risk of bias assessment by means of the Cochrane Collaboration tool, as suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (version 5.1.0).[9] The following items were evaluated: random sequence generation; allocation concealment; blinding of patients and personnel; blinding of outcome assessment; incomplete outcome data addressed; selective reporting; other bias. The publications were then grouped into the following categories: (1) low risk of bias (possible bias not seriously affecting the results) if all the criteria were met; (2) high risk of bias (possible bias seriously weakening the reliability of the results) if one or more criteria were not met; (3) unclear risk of bias when insufficient information was available for classification as 'high' or 'low' risk.

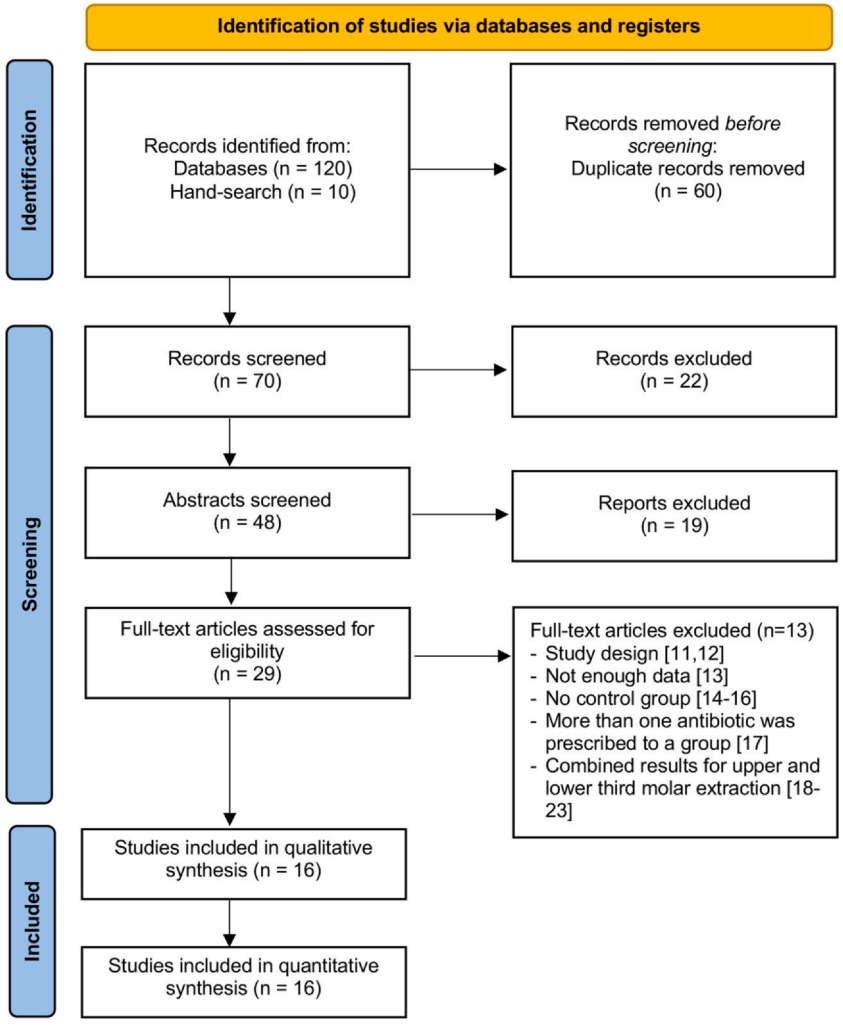

Fig. 1. Flowchart of the review process according to the PRISMA statement.

Statistical analysis

The main information obtained from the articles was recorded in tables. Outcome measures were calculated as per protocol. A pairwise meta-analysis (PMA) was performed to combine the studies with the same equivalent treatment comparisons. Since all variables were dichotomous (DS, SSI, and adverse events), odds ratio (ORs) with the 95% confidence interval (95% CI) were used to summarise the effect of an intervention. A random-effects model was selected, as methodological and clinical heterogeneity was expected from studies comparing the same pair of treatments. Heterogeneity was assessed by means of χ^2 (Q-value) and I^2, with a P-value of < 0.10 and an I^2 value of $> 50\%$ being interpreted as representing significant heterogeneity. Additionally, the number needed to treat (NNT) was also calculated.

If the meta-analysis included at least 10 RCTs, publication bias was explored through visual inspection of funnel plots and Egger and Peters tests at the $P < 0.05$ level of significance.

A network meta-analysis (NMA) was then performed to compare each outcome variable (DS, SSI, and adverse events) simultaneously for the different treatments. Treatments were represented as nodes, and direct comparisons between them were represented as lines between the nodes. Line width was proportional to the number of studies. The NMA was based on a multivariate random-effects meta-regression analysis.

Inconsistencies were evaluated substantially and statistically by comparing the results obtained across PMAs and NMAs and adapting both

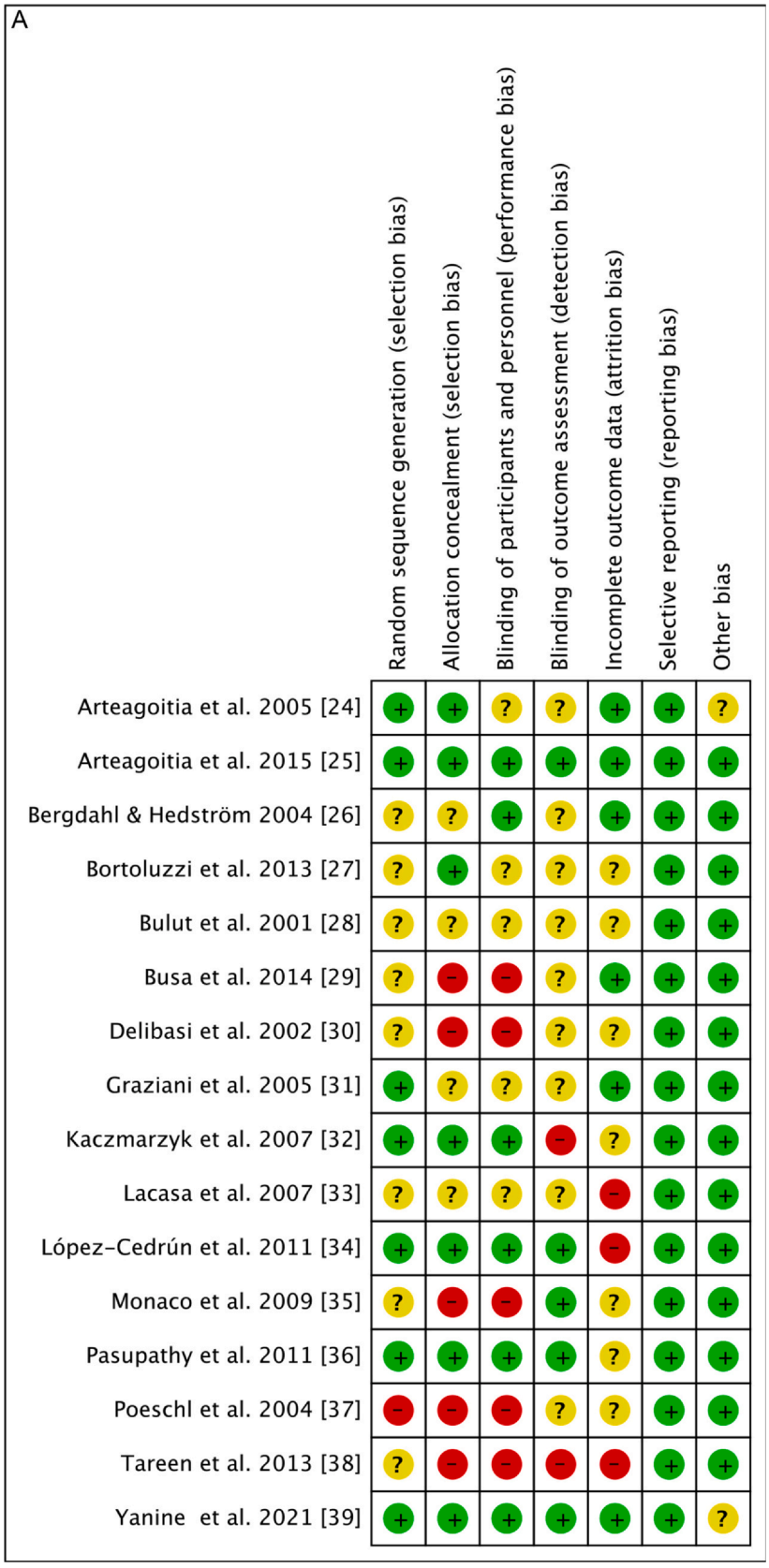

Fig. 2. Risk of bias of (A) each study and (B) across the studies, according to the Cochrane tool.

consistency and inconsistency to treatment-designated interaction models. The efficacy (DS and SSI) and safety of the different treatments was calculated using the surface under the cumulative ranking (SUCRA) curve, which was represented graphically using a cluster grading graph. SUCRA provides a value that ranges from 0% to 100% and represents the overall ranking of each treatment. A value close to 100% indicates that a particular antibiotic is very likely to be the best, or one of the best. Conversely, lower values suggest that the antibiotic is probably the worst.

The statistical analysis was performed using the Stata 14 package (StataCorp, College Station, TX, USA).

Assessment of the certainty of the evidence

The GRADE (Grading of Recommendations Assessment, Development, and Evaluation) tool, GRADEpro GDT, was used to evaluate the level of evidence of the included articles. The overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, and the precision of the estimates were all taken into consideration when evaluating the degree of certainty of the body of evidence. The level of certainty in the body of evidence for each of the primary and secondary outcomes was rated as high, moderate, low, or very low.[10]

Results

Study selection and description

The electronic and manual searches yielded 130 references in total (51 through PubMed, 50 through Scopus, 19 through Cochrane Library, and 10 through the hand-search). After duplicate removal and assessment of both the title and the abstract, a total of 29 articles were eligible for full-text analysis. Inter-rater agreement was 94.12%, with a Cohen's kappa of 0.85 (almost perfect).

Thirteen papers were discarded for the following reasons: study design,[11,12] insufficient data,[13] there was no control group,[14–16] more than one antibiotic was prescribed to a group,[17] and combined results for upper and lower third molar extractions.[18–23]

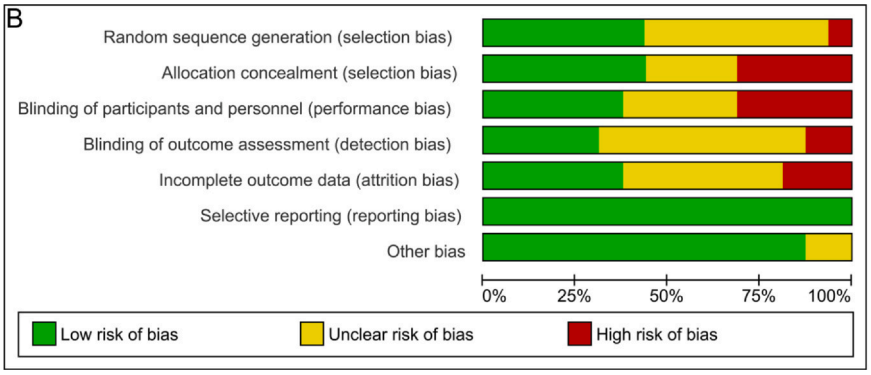

Fig. 2. (*continued*)

As shown in Fig. 1, 16 RCTs met the inclusion criteria and were selected for the qualitative and quantitative synthesis.[24–39]

Risk of bias assessment

Fig. 2 shows that most of the included studies had an unclear or high risk of bias, mainly owing to non-compliance with some sections of the Cochrane Collaboration tool,[24,26–39] while only two articles had a low risk of bias.[25]

Qualitative synthesis

Sixteen studies with 2158 patients and 2428 L3M were included. All of the included RCTs had parallel groups except one, which had a crossover design.[28] It was possible to compare amoxicillin + clavulanic acid,[24,25,29,30,33,37,38] amoxicillin,[27,28,34–36,39] metronidazole,[26,36] azithromycin,[31] and clindamycin[32,37] against a no treatment/placebo group. The characteristics of the included studies, including details of the specific dosages of each antibiotic and the dosing regimens applied, are given in Supplementary Material Table S2.

No statistically significant differences were found between the groups in terms of DS ($P > 0.05$). Regarding SSI, Arteagoitia et al.[24] and Lacasa et al.[33] reported a higher risk of SSI in the control group ($P < 0.05$). In three trials, the antibiotic groups showed more adverse events related to the use of antibiotics than the control groups ($P < 0.05$).[24,25,33] The most common among all of the adverse events were diarrhoea, nausea, vomiting, gastric pain, headache, and mycosis.

Quantitative synthesis

Dry socket

Twelve studies comparing antibiotic versus no treatment/placebo with a parallel design, representing 1995 L3M (1755 patients), were included in the analysis of DS[24–27,29–32,34,37–39] (Supplementary Material Tables S2 and S3). The network graph (Fig. 3A) shows comparisons of the placebo/no treatment groups with nine active substances.

The pooled results in the meta-analysis of the direct comparisons favoured antibiotics over placebo/no treatment to reduce the number of DS (OR 0.54, 95% CI 0.33–0.90, $P = 0.02$, $I^2 = 0\%$) (Fig. 4A). The NNT was 25. The NMA model did not reveal any significant differences between the different antibiotics (Table 1). The network inconsistency was low ($\chi^2 = 2.40$; $P = 0.30$).

The ranking of treatments according to the SUCRA results of the NMA, from best to worst, was as follows: clindamycin preoperative (73.7%), azithromycin preoperative (71.3%), amoxicillin preoperative (66.3%), amoxicillin–clavulanic acid pre- and postoperative (55.1%), clindamycin pre- and postoperative (50.2%), amoxicillin postoperative (49.1%), amoxicillin–clavulanic acid postoperative (43.7%), clindamycin postoperative (38.8%), metronidazole preoperative (34.0%), placebo/no treatment (17.8%) (Supplementary Material Fig. S1).

Regarding publication bias, visual inspection of the funnel plot showed relative asymmetry (Supplementary Material Fig. S2A), which means that publication bias cannot be ruled out.

According to the GRADE tool, the level of evidence was low because some of the included studies had a high risk of bias and the sample size was too small (Supplementary Material Table S4).

Surgical site infection

Twelve studies with a parallel design[24,25,27,29,31,33–39] and one crossover study,[28] including 1986 L3M and 1746 patients, were included in the analysis of SSI (Supplementary Material Tables S2 and S3). The network graph is depicted in Fig. 3B, which compares placebo/no treatment versus nine active substances.

The pooled results in the meta-analysis of the direct comparisons favoured antibiotics over placebo/no treatment to reduce the number of SSI (OR 0.36, 95% CI 0.22–0.57, $P < 0.001$, $I^2 = 4\%$) (Fig. 4B). The NNT was 18. The NMA revealed a statistically significant difference when comparing amoxicillin plus clavulanic acid given pre- and postoperatively with placebo/no treatment (Table 2). The network inconsistency was low ($\chi^2 = 6.75$; $P = 0.239$).

The ranking of treatments according to the SUCRA results of the NMA, from best to worst, was as follows: amoxicillin postoperative (77.7%), metronidazole preoperative (74.2%), amoxicillin–clavulanic acid preoperative and postoperative (72.7%), azithromycin preoperative (67.5%), amoxicillin–clavulanic acid preoperative (50.9%), amoxicillin–clavulanic acid postoperative (49.7%), amoxicillin preoperative (43.6%), clindamycin postoperative (25.1%), amoxicillin preoperative and postoperative (23.7%), placebo/no treatment (15.0%) (Supplementary Material Fig. S1).

The funnel plot showed a balanced distribution of the studies on visual inspection (Supplementary Material Fig. S2B), thus the presence of publication bias could be ruled out.

According to the GRADE tool, the level of evidence was low because some of the included studies had a high risk of bias and the sample size was too small (Supplementary Material Table S4).

Adverse events

Seven studies with a parallel design, including 1724 L3M in 1484 patients,

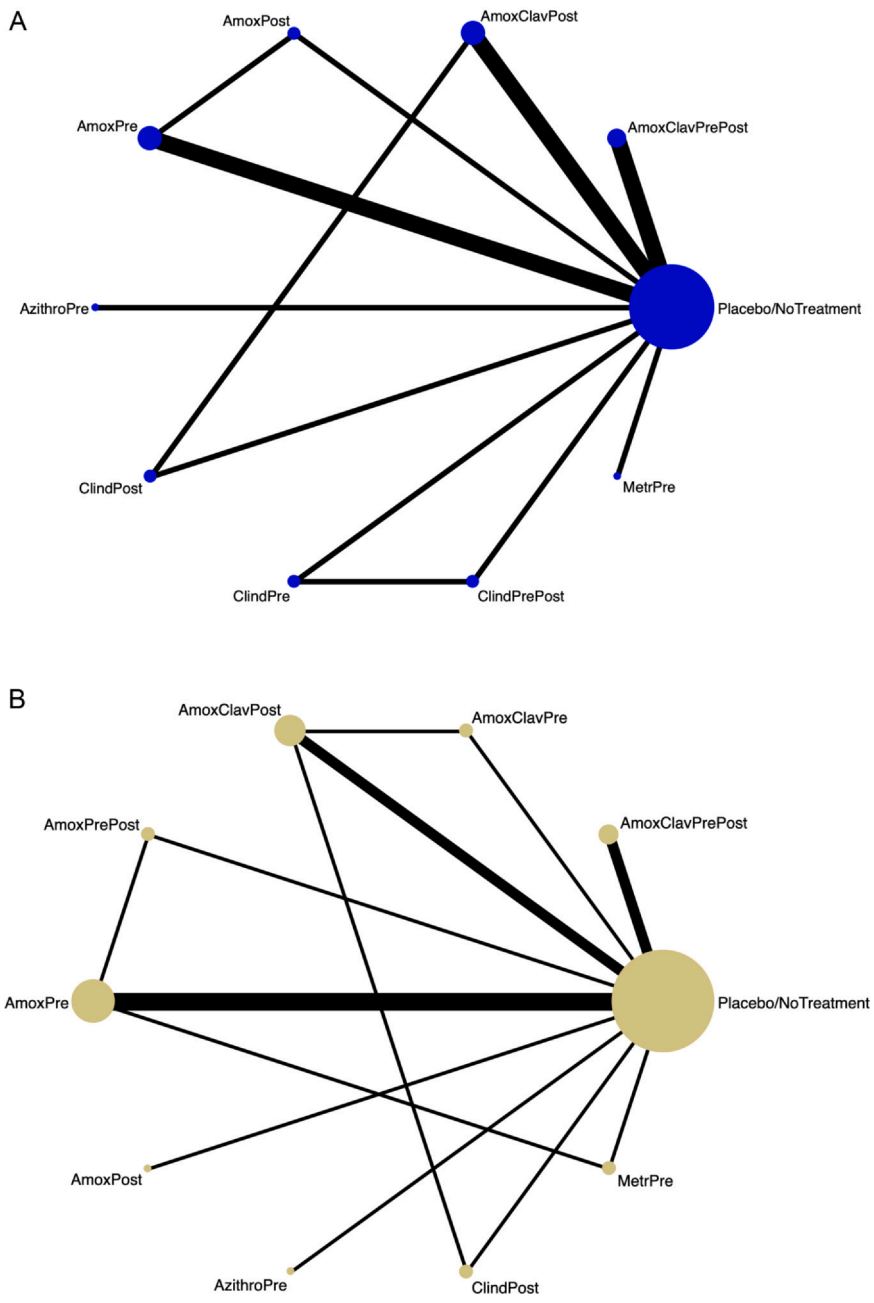

Fig. 3. Network meta-analysis graph (net diagram) of (A) dry socket and (B) surgical site infection. Abbreviations: AmoxClavPost, amoxicillin plus clavulanic acid postoperative administration; AmoxClavPre, amoxicillin plus clavulanic acid preoperative administration; AmoxClavPrePost, amoxicillin plus clavulanic acid pre- and postoperative administration; AmoxPost, amoxicillin postoperative administration; AmoxPre, amoxicillin preoperative administration; AmoxPrePost, amoxicillin pre- and postoperative administration; AzithroPre, azithromycin preoperative administration; ClindPost, clindamycin postoperative administration; ClindPre, clindamycin preoperative administration; ClindPrePost, clindamycin pre- and postoperative administration; MetrPre, metronidazole preoperative administration.

were included for the analysis of adverse events (Supplementary Material Tables S2 and S3).[24,25,32–34,37,39]

There was no statistically significant difference between the antibiotic and control groups in the pairwise meta-analysis of direct comparisons (OR 1.08, 95% CI 0.60–1.94, $P = 0.79$, $I^2 = 63\%$) (Fig. 4C). A sensitivity analysis excluding both studies by Arteagoitia et al.[24,25] showed a decrease in heterogeneity, but there was still no statistically significant difference between the antibiotic and control groups (OR 0.73, 95% CI 0.51–1.03, $P = 0.07$, $I^2 = 0\%$).

There was statistical evidence of the violation of transitivity assumption, with a high inconsistency level ($\chi^2 = 12.59$; $P = 0.018$), which precluded NMA of the adverse events outcome.

As shown in Supplementary Material Fig. S2C, there was only one direct comparison with more than two studies, so it was not possible to assess the presence of publication bias for the adverse events outcome.

According to the GRADE tool, the level of evidence was very low because some of the included studies had a high risk of bias, the sample size was too small, and there was significant heterogeneity in the meta-analysis (Supplementary Material Table S4).

Discussion

The main goal of this NMA was to determine whether prophylactic administration of antibiotics has a positive effect in relation to the risk of developing DS and SSI after the removal of a L3M.

The results of the meta-analysis showed that the use of antibiotic prophylaxis after L3M extraction significantly reduced the number of DS and SSI events, but with a high NNT of 25 and 18, respectively. Similar meta-analyses have been published over past years, such as the one by Ren and Malmstrom,[1] which analysed 16 clinical trials and revealed that patients taking systemic antibiotics before third molar surgery were 1.8 times less likely to develop a SSI, with a NNT of 25, and were 2.2 times less likely to develop DS, with a NNT of 13. The meta-analysis published by Lodi et al.[3] in 2012 reported similar findings, indicating that antibiotic prophylaxis reduced the risk of SSI by 70%, with a NNT of 12, and also reduced the risk of DS by 38%, with a NNT of 38. Likewise, Ramos et al.[5] recorded a 60% reduction in infection risk (SSI and DS) in

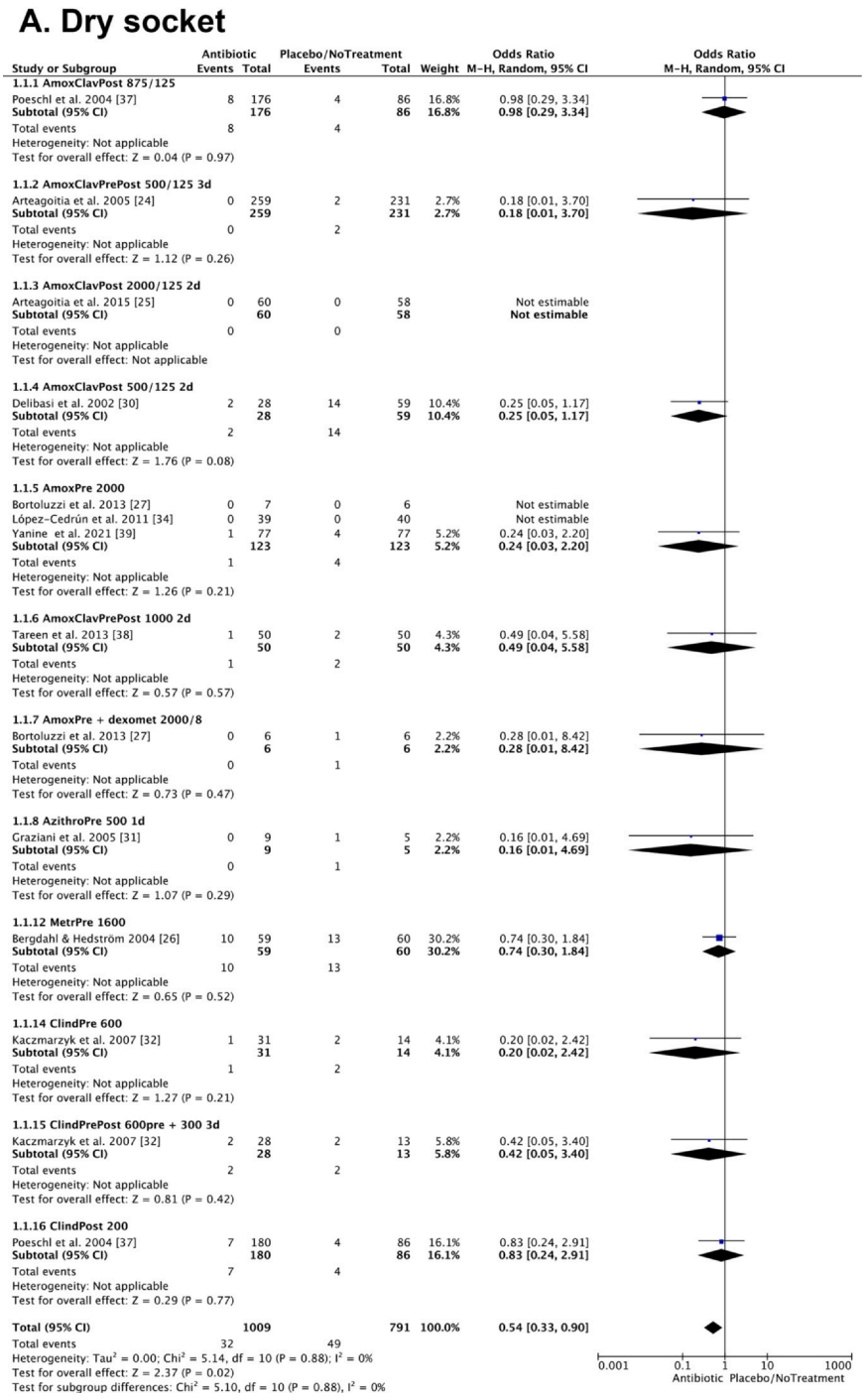

Fig. 4. Forest plots for (A) dry socket, (B) surgical site infection, and (C) adverse events. Abbreviations: AmoxClavPost, amoxicillin plus clavulanic acid postoperative administration; AmoxClavPre, amoxicillin plus clavulanic acid preoperative administration; AmoxClavPrePost, amoxicillin plus clavulanic acid pre- and postoperative administration; AmoxPost, amoxicillin postoperative administration; AmoxPre, amoxicillin preoperative administration; AmoxPrePost, amoxicillin pre- and postoperative administration; AmoxPre + dexamet, amoxicillin preoperative administration plus dexamethasone; AzithroPre, azithromycin preoperative administration; CI, confidence interval; ClindPost, clindamycin postoperative administration; ClindPre, clindamycin preoperative administration; ClindPrePost, clindamycin pre- and postoperative administration; d, days; MetrPre, metronidazole preoperative administration.,.

patients receiving antibiotics, with a NNT of 14. However, these three previous papers included both lower and upper third molar extractions,[2,3,5] while the current review focused exclusively on L3M extractions.

Most of the selected trials (13 out of 16) used amoxicillin alone[27,28,34–36,39] or combined with clavulanic acid[24,25,29,30,33,37,38] as antibiotic prophylaxis before and/or after L3M extractions. Amoxicillin is the most commonly prescribed antibiotic in dental practice, probably due to its safety and broad spectrum of activity.[2] In the present review, the SUCRA analysis indicated that postoperative administration of amoxicillin may be the most effective strategy for reducing SSI, followed by preoperative metronidazole and the combination of amoxicillin and clavulanic acid administrated both pre- and postoperatively. In contrast, the most effective antibiotic in reducing DS was preoperative clindamycin, followed by preoperative azithromycin, while preoperative amoxicillin ranked third and amoxicillin with clavulanic acid given both pre- and postoperatively ranked fourth. The efficacy of different antibiotic regimens in preventing DS and SSI after the removal of L3M remains uncertain. Preoperative antibiotics have been suggested as a measure to mitigate the risk of SSI and DS by modulating the oral microbiota.[1] While the results of the present study support these findings regarding the prevention of DS, in the case of SSI, the postoperative administration of amoxicillin seemed to be the most effective approach.

Over the last few years, several studies have analysed the effectiveness of antibiotic therapy in the prevention of DS, even though its pathogenesis and aetiology remain unclear. Despite this lack of evidence, antibiotics have continued to be commonly prescribed for this purpose.

In the present review, a NMA for the adverse events outcome could not be performed due to high heterogeneity among the studies and a lack of data. Only seven studies evaluated the occurrence of adverse events.[24,25,32–34,37,39] These complications were generally mild and of

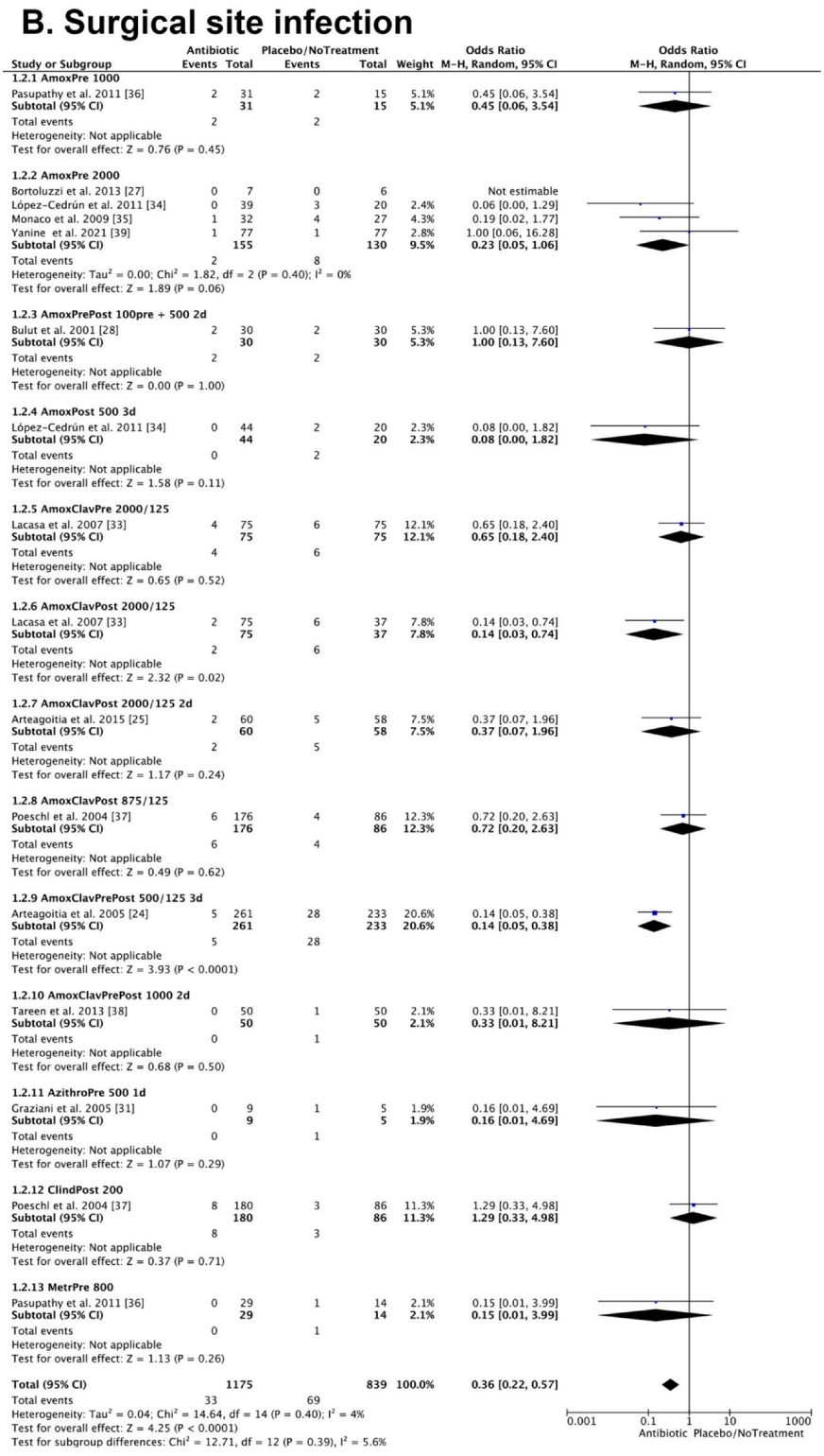

Fig. 4. (*continued*)

short duration (nausea, vomiting, gastric pain, diarrhoea, headache, and mycosis).[24,25,32–34,37] The fact that most of the studies failed to report the occurrence or absence of adverse events constitutes a reporting bias, which might have led to an underestimation of the real incidence of these complications. In fact, studies examining drug-related adverse events have shown that antibiotics continue to be a common cause of these complications. Indeed, these agents are frequently related to adverse events in elderly patients[40] and after hospital discharge.[41] Systemic antibiotics have also been associated with approximately one fifth of all emergency department visits for drug-related adverse events. The most common adverse events are allergic-type reactions, followed by gastrointestinal disorders.[42]

Therefore, even though the results of this meta-analysis showed a significant reduction of SSI and DS after L3M extraction with the use of antibiotic prophylaxis, the systematic use of antibiotics in this surgical procedure is still debatable. It is broadly accepted that antibiotics should be prescribed routinely for a specific patient profile, i.e. elderly individuals, patients with significant systemic diseases, and patients with immune depression, among others. However, in young healthy patients, the indication for their use is not as clear. In the present review, the NNT for both complications was high, meaning that several people need to receive prophylactic therapy in order for one person to benefit. Furthermore, aside from adverse events, when evaluating the need for antibiotic prophylaxis, other public health variables should be considered. The routine administration of antibiotics after L3M extractions could represent an important financial burden for public health systems. Furthermore, over the past decades, there has been a dramatic worldwide increase in antimicrobial-resistant bacteria. Thus, new strategies against the development of antibiotic resistance are clearly needed, and dentists should be involved in this major global public health challenge.[43]

The effect of systemic antibiotic prophylaxis in patients undergoing L3M extractions upon the microbiome of these patients was outside the scope of this study. Future research on this relevant topic is needed

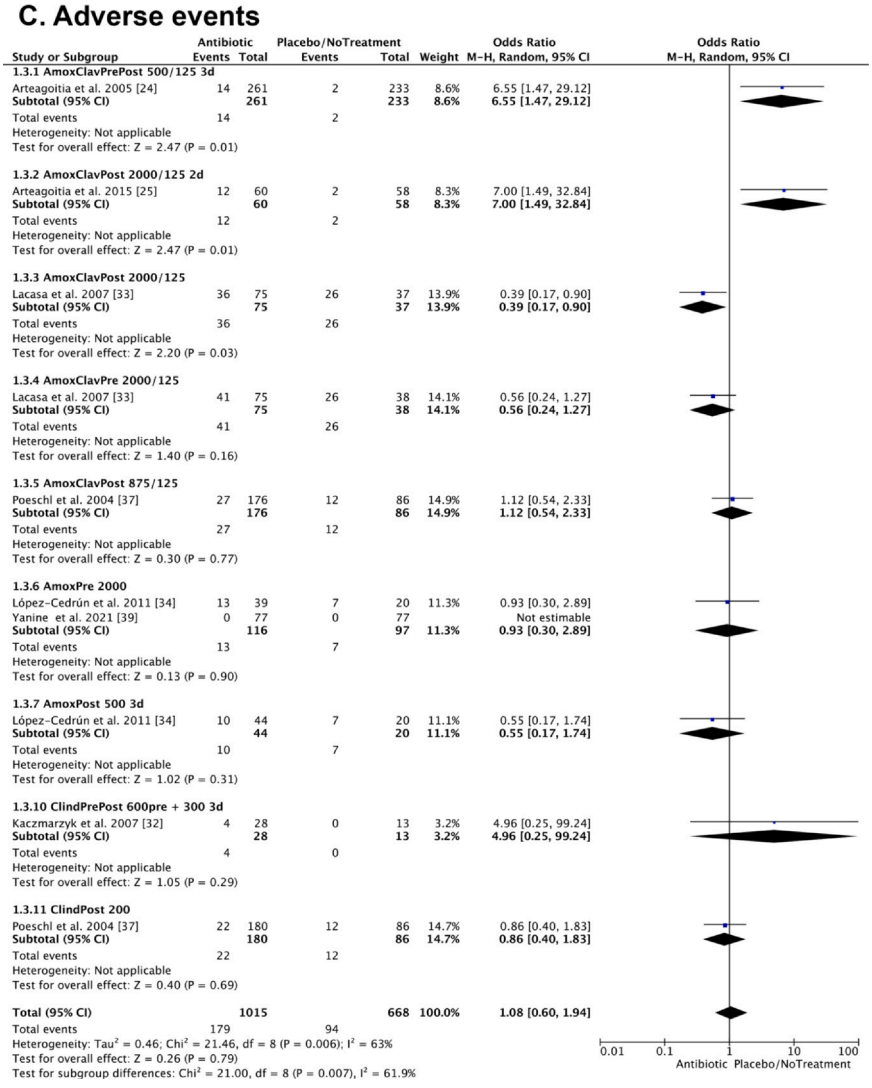

Fig. 4. (*continued*)

since clinicians require additional data to adequately decide whether antibiotic prophylaxis in L3M extractions is truly indicated.

This review has some limitations. Firstly, some risk factors for infectious complications such as surgical difficulty, surgeon experience, presence of pre-existing infections, or smoking habit were not considered in this review. Secondly, there were differences among the included studies regarding the patient population and postoperative instructions. These factors are likely to have increased the heterogeneity between studies. Finally, the included studies had a high or unclear risk of bias, which underlines the need to interpret the results with caution.

Although antibiotic prophylaxis was observed to significantly reduce the risk of dry socket and surgical site infections in healthy patients undergoing lower third molar extraction in the present review, the number of patients needed to treat was high. The preoperative administration of clindamycin was found to be the most effective treatment to prevent dry socket, while the postoperative administration of amoxicillin was found to be the most effective treatment to prevent surgical site infections. Since antimicrobial resistance is considered an important threat to global health, dentists should evaluate the need to prescribe antibiotics for each individual patient, taking into consideration the presence of systemic conditions and the case-specific risk of developing postoperative infections and/or dry socket after lower third molar removal.

Table 1. Network meta-analysis results for dry socket. A netleague table is a square matrix showing both direct and indirect comparisons. The values represent the odds ratios and 95% confidence intervals.

MetrPre									
1.67 (0.19, 14.62)	ClindPrePost								
3.85 (0.29, 50.38)	2.31 (0.18, 28.83)	ClindPre							
1.14 (0.24, 5.41)	0.68 (0.08, 6.09)	0.30 (0.02, 3.93)	ClindPost						
4.78 (0.14, 160.50)	2.86 (0.06, 132.57)	1.24 (0.02, 73.05)	4.18 (0.12, 141.69)	AzithroPre					
2.62 (0.36, 19.37)	1.57 (0.13, 19.55)	0.68 (0.04, 12.05)	2.30 (0.31, 17.20)	0.55 (0.01, 23.13)	AmoxPre				
1.55 (0.04, 63.49)	0.93 (0.02, 51.61)	0.40 (0.01, 28.15)	1.35 (0.03, 56.02)	0.32 (0.00, 42.54)	0.59 (0.02, 20.59)	AmoxPost			
1.25 (0.32, 4.82)	0.75 (0.10, 5.78)	0.32 (0.03, 3.82)	1.09 (0.36, 3.32)	0.26 (0.01, 8.13)	0.48 (0.07, 3.06)	0.81 (0.02, 30.76)	AmoxClavPost		
1.83 (0.23, 14.38)	1.10 (0.08, 14.33)	0.47 (0.03, 8.78)	1.60 (0.20, 12.77)	0.38 (0.01, 16.68)	0.70 (0.06, 7.90)	1.18 (0.02, 62.04)	1.47 (0.21, 10.10)	AmoxClavPrePost	
0.74 (0.25, 2.18)	0.44 (0.07, 2.90)	0.19 (0.02, 1.97)	0.65 (0.21, 1.97)	0.15 (0.01, 4.37)	0.28 (0.05, 1.51)	0.48 (0.01, 16.63)	0.59 (0.26, 1.33)	0.40 (0.07, 2.33)	Placebo/ No Treatment

AmoxClavPost, amoxicillin plus clavulanic acid postoperative administration; AmoxClavPrePost, amoxicillin plus clavulanic acid pre- and postoperative administration; AmoxPre, amoxicillin preoperative administration; AmoxPost, amoxicillin postoperative administration; AzithroPre, azithromycin preoperative administration; ClindPost, clindamycin postoperative administration; ClindPre, clindamycin preoperative administration; ClindPrePost, clindamycin pre- and postoperative administration; MetrPre, metronidazole preoperative administration.

Table 2. Network meta-analysis results for surgical site infection. A netleague table is a square matrix showing both direct and indirect comparisons. The values represent the odds ratios and 95% confidence intervals.

MetrPre									
0.12 (0.00, 2.82)	ClindPost								
0.83 (0.01, 71.85)	7.10 (0.23, 223.82)	AzithroPre							
0.10 (0.00, 4.60)	0.78 (0.06, 10.01)	0.15 (0.00, 9.00)	AmoxPrePost						
1.57 (0.02, 104.47)	13.42 (0.6, 300.34)	1.89 (0.02, 155.09)	12.24 (0.35, 432.14)	AmoxPre					
1.17 (0.03, 117.84)	15.12 (0.68, 337.77)	2.13 (0.03, 174.51)	13.79 (0.39, 486.09)	1.13 (0.02, 58.12)	AmoxPost				
0.89 (0.03, 26.15)	7.62 (1.20, 48.56)	1.07 (0.03, 40.58)	6.95 (0.55, 88.48)	0.57 (0.02, 15.52)	0.50 (0.02, 13.75)	AmoxClavPost			
0.43 (0.02, 11.00)	3.71 (0.77, 17.85)	0.52 (0.02, 17.25)	3.38 (0.32, 35.37)	0.28 (0.01, 6.51)	0.25 (0.01, 5.77)	0.49 (0.09, 2.74)	AmoxClavPre		
0.76 (0.03, 17.64)	6.51 (1.64, 25.76)	0.92 (0.03, 27.86)	5.94 (0.64, 54.72)	0.49 (0.49, 13.19)	0.43 (0.02, 9.23)	0.85 (0.14, 5.07)	1.76 (0.40, 7.77)	AmoxClavPrePost	
0.08 (0.00, 1.53)	7.85 (0.26, 233.12)	7.07 (0.26, 193.92)	0.07 (0.00, 1.36)	0.14 (0.03, 0.67)	5.78 (0.87, 38.46)	2.54 (0.26, 24.76)	0.30 (0.09, 0.96)	0.17 (0.07, 0.42)*	Placebo/ No Treatment

AmoxClavPost, amoxicillin plus clavulanic acid postoperative administration; AmoxClavPre, amoxicillin plus clavulanic acid preoperative administration; AmoxClavPrePost, amoxicillin plus clavulanic acid pre- and postoperative administration; AmoxPost, amoxicillin postoperative administration; AmoxPre, amoxicillin preoperative administration; AmoxPrePost, amoxicillin pre- and postoperative administration; AzithroPre, azithromycin preoperative administration; ClindPost, clindamycin postoperative administration; MetrPre, metronidazole preoperative administration. *Significantly associated ($P < 0.05$).

Ethical approval

Not applicable.

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Competing interests

The authors Octavi Camps-Font, Rui Figueiredo, and Eduard Valmaseda-Castellón have declared their conflicts of interest outside of the scope of this review (Supplementary Material File S1).

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Patient consent

Not required.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijom.2023.08.001.

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