# A meta-analysis examining the impact of antibiotic prophylaxis on surgical site wound infection during third molar surgery

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**Abstract**

Backgrounds: The meta-analysis aims to estimate the effect of antibiotic prophylaxis (AP) on surgical site wound infection (SSWI) in third molar surgery (TMS).

Methods: Examinations comparing AP to placebo for TMS were utilized in the meta-analysis from various languages that met the inclusion criteria. Using dichotomous random or fixed effect models, the results of these investigations were examined, and the Odd Ratio (OR) with 95% confidence intervals was computed (CIs).

18 examinations from 2001 to 2023 were recruited for the current analysis including 4063 personals with TMS who were in the utilized examinations' starting point.

Results: AP had significantly lower SSWI (OR, 0.46; 95% CI, 0.33-0.65, p<0.001) with no heterogeneity ($I^2$ = 1%) compared to placebo in personals with TMS.

Conclusions: The examined data revealed that AP had significantly lower SSWI compared to placebo in personals with TMS. Nevertheless, caution should be exercised while interacting with its values since examinations were performed by different surgeons with different skills on different types of personals and the low sample size of numerous of the examinations selected for the meta-analysis.

**Keywords:** third molar surgery; placebo; antibiotic prophylaxis; surgical site wound infection; antimicrobial

**Introduction**

The procedure used most frequently in oral surgery and regular dental practices worldwide are the surgical extraction of compressed third molars (TMs). [1] The most frequent side effects following third molar surgery (TMS) are infection and inflammation linked to bacterial contamination because of the nature and setting of the procedure. [2] Postoperative infection affects 2% to 12% of personals. [3] After removal of the mandibular TM, around 1% of individuals may develop severe fascial space cellulitis that necessitates hospitalization. [4] Although such severe infections are uncommon, their effects can be costly and incapacitating. [5] The use of antibiotic prophylaxis (AP) after TMS has long been debatable in clinical settings. [6] Kay produced what appeared to be compelling data about the need for AP for TMS in his thorough examination of the pathophysiology of pericoronitis and problems after TM elimination in the 1960s. [7] He demonstrated that a higher rate of personals who had TMS without antibacterial prophylaxis experienced surgical site wound infections (SSWIs). In comparison, the incidence of SSWI decreased in personals who had a single dosage of penicillin before surgery. In individuals with pericoronitis, when a single dosage of penicillin decreased the occurrence of SSWI, the benefit of AP was even more striking. This study was the catalyst for the widespread prescribing of antibiotics for TMS. Even though the value of AP in TMS before or after the procedure was questioned. [8] Long-standing misunderstanding in clinical practice has resulted from the contradictory findings of randomized controlled clinical trials (RCTs), with proponents and detractors of AP each offering their supporting data. [6] Although the effectiveness, risk of allergic and anaphylactic responses, and potential for drug

resistance have led many to question the wisdom of routine AP, doctors continue to prescribe antibiotics to treat postoperative problems following TMS. [6] Several published RCTs have exacerbated the debate, with some arguing for and against the efficacy of AP. [9-11] Personals frequently endure a decreased quality of life and loss of productivity as a result of postoperative SSWI, which are supplemented by crippling pain and severe functional impairment. [12] Therefore, clinicians have been looking for a practical means of preventing postoperative problems following TMS for a very long time. The effectiveness of AP in reducing morbidity related to TMS has been the subject of numerous RCTs, but these studies all shared the same flaw: they lacked the statistical power to discern a significant difference between the examination groups. Rarely did a published clinical study have a sample size that allowed for a solid outcome analysis due to its much lower size. A synthetic quantitative analysis of RCTs on the efficiency of AP in TMS was conducted as part of this study. AP did not work to stop surgical problems, according to the null hypothesis. So, the meta-analysis aims to evaluate the effect of AP on SSWI in TMS.

**Method**

**Design of the examination**

The meta-analyses were a part of the epidemiological declaration and adhered to a predetermined examination procedure. For data collection and analysis, a wide number of databases, such as OVID, PubMed, the Cochrane Library, Embase, and Google Scholar, were accessed. These databases were used to collect examinations that focused on evaluating and comparing the effect of AP on SSWI in TMS.

**Data pooling**

Comparing AP and placebo techniques for the management of TMS resulted in SSWI as a main inclusion parameter. During the screening process and the selection of examinations to include, language restrictions were not taken into account. There were no restrictions imposed on the possible sample sizes of the examinations that were recruited. Reviews, editorials, and letters were not included in this synthesis that we have presented, because they do not include an intervention. The entirety of the process of examination identification is illustrated in Figure 1.

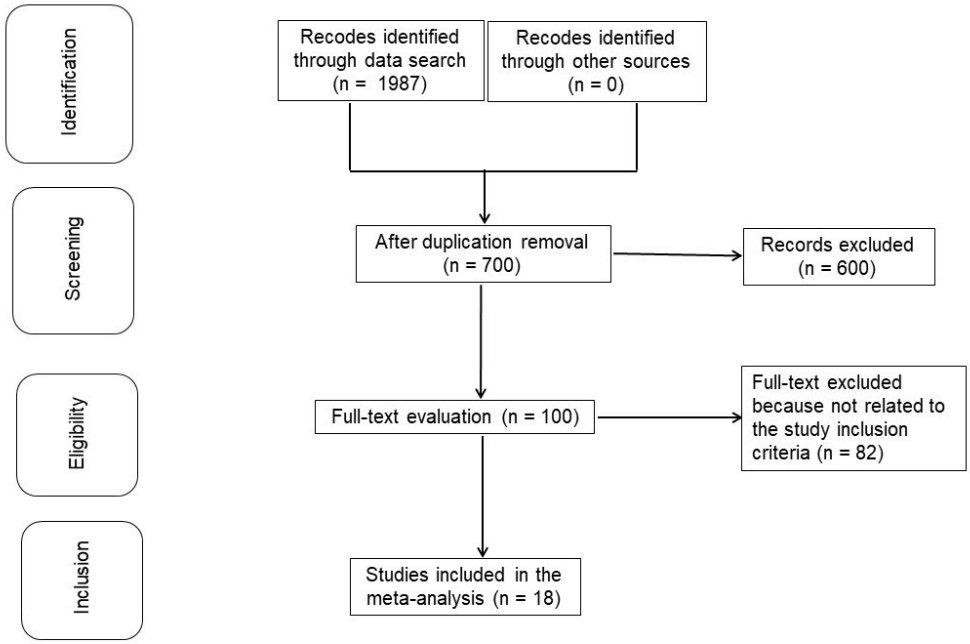


Figure 1. Schematic diagram of the examination procedure

**Eligibility of included examinations**

An investigation of the effects, both positive and negative, that AP and placebo methods have on the clinical outcome of TMS personals was conducted. Only publications that reported the influence of interventions on the occurrence of SSWI were included in the sensitivity analysis. To do sensitivity and subclass analyses, the interventional groups were compared to a wide variety of subtypes.

**Inclusion and exclusion criteria**

**Inclusion criteria:**

The criteria for inclusion in the meta-analysis were as follows: a comparison of the outcomes of AP compared to placebo on SSWI in personals with TMS. The expression of the outcome should be in the appropriate output to be included in statistical analysis.

**Exclusion criteria:**

Examinations that were not comparative in the design were excluded. In addition, letters, books, review articles, and book chapters were also excluded from the current examination.

**Identification of examinations**

A protocol of search strategies was devised and specified as follows by the PICOS principle, which states: P (population) personals with TMS; AP was the "intervention" or "exposure"; C (comparison): the comparative effectiveness of AP compared with placebo. O (outcome): SSWI; S (design of the examination): the planned examination had no boundaries.

We did a comprehensive search of the databases PubMed, Cochrane Library, Embase, OVID, and Google Scholar up until June 2023 using the keywords and associated phrases specified in Table 1 (Search techniques for different databases). A review was conducted on the titles and abstracts of all of the articles that had been compiled into a reference managing program, as well as any examination that did not correlate the type of treatments with clinical outcomes. Two authors also serve as reviewers to find appropriate examinations.

**Table 1.** Database Search Strategy for inclusion of examinations

| Database | Search strategy |
|---|---|
| **Google Scholar** | #1 "third molar surgery" OR "placebo" OR "antimicrobial"<br>#2 "antibiotic prophylaxis" OR "surgical site wound infection"<br>#3 #1 AND #2 |
| **Embase** | #1 'third molar surgery' /exp OR 'placebo' exp OR 'antimicrobial'<br>#2 'antibiotic prophylaxis'/exp OR 'surgical site wound infection'/<br>#3 #1 AND #2 |
| **Cochrane library** | #1 (third molar surgery):ti,ab,kw (placebo):ti,ab,kw (antimicrobial):ti,ab,kw (Word variations have been searched)<br>#2 (antibiotic prophylaxis):ti,ab,kw OR (surgical site wound infection):ti,ab,kw (Word variations have been searched)<br>#3 #1 AND #2 |
| **Pubmed** | #1 "third molar surgery"[MeSH Terms] OR "placebo" [MeSH] OR "antimicrobial"[All Fields]<br>#2 "antibiotic prophylaxis"[MeSH Terms] OR "surgical site wound infection "[All Fields]<br>#3 #1 AND #2 |
| **OVID** | #1 "third molar surgery"[All fields] OR "placebo"[All Fields] OR " antimicrobial" [All Fields]<br>#2 "antibiotic prophylaxis"[ All fields] OR "surgical site wound infection"[All Fields]<br>#3 #1 AND #2 |

**Screening of examinations**

The following criteria were used to reduce the amount of data: examination and subject features presented in a standardized format; the surname of the examination's first author; the period and year of the examination; the country in which the examination was conducted; and the gender; the population type that was recruited for the examinations; the total number of subjects; qualitative and quantitative evaluation methods; demographic data; clinical and treatment characteristics; information sources; outcome evaluations. Two anonymous reviewers looked at the possibility of bias in each examination as well as the quality of the methods used in the examinations that were chosen for further investigation. The methodology of each examination was evaluated separately by two different reviewers.

**Statistical analysis**

In the current meta-analysis, the Odds Ratio (OR) with a 95% confidence interval (CI) was determined using dichotomous random- or fixed-effect models. The $I^2$ index, a numeric value between 0 and 100, was computed (percent). $I^2 = 0$ indicates that there is no heterogeneity, whereas higher $I^2$ values suggest greater heterogeneity. The random effect was used when I2 was 50% or greater; if I2 was less than 50%, the choice to use the fixed effect increased.[13] As indicated previously, subcategory analysis was performed by stratifying the first evaluation into result categories. Publication bias was analyzed quantitatively using Begg's and Egger's tests, and it was deemed present if $p>0.05$. The p-values were determined using a test with two tails. Using Jamovi 2.3, statistical analyses and graphs were produced.

**Results**

18 examinations published between 1974 and 2014 were included in the meta-analysis because they fit the inclusion criteria following a review of 2035 relevant examinations. [9-11, 14-28] Table 2 summarizes the findings of these investigations. 4063 personals with TMS were in the utilized examinations' starting point, 1792 of them were utilizing AP, and 2271 were utilizing placebo. The sample size was 24 to 1222 personals.

AP had significantly lower SSWI (OR, 0.46; 95% CI, 0.33-0.65, p<0.001) with no heterogeneity ($I^2$ = 1%) compared to placebo in personals with TMS, as revealed in Figure 2.
The quantitative Egger regression test and the visual clarification of the funnel plot did not reveal any evidence of examination bias (p = 0.86) as shown in Figure 3. However, most of the involved examinations were found to have poor practical quality and no bias in selective reporting.

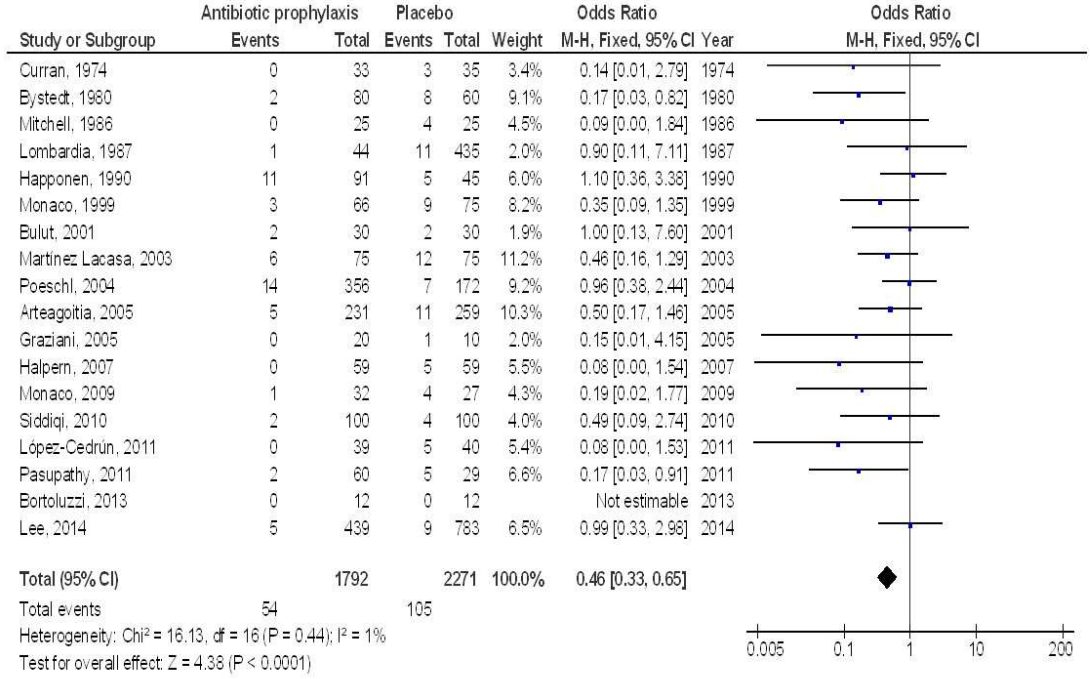


Figure 2. The effect's forest plot of the AP compared to placebo on SSWI in personals with TMS

Table 2. Characteristics of examinations

| Study | Country | Total | AP | Placebo |
|---|---|---|---|---|
| Curran, 1974 [14] | Canada | 68 | 33 | 35 |
| Bystedt, 1980 [15] | Sweden | 140 | 80 | 60 |
| Mitchell, 1986 [16] | Germany | 50 | 25 | 25 |
| Lombardia, 1987 [17] | Spain | 479 | 44 | 435 |
| Happonen, 1990 [18] | Finland | 136 | 91 | 45 |
| Monaco, 1999 [19] | Italy | 141 | 66 | 75 |
| Bulut, 2001 [20] | Turkey | 60 | 30 | 30 |
| Martínez Lacasa, 2003 [9] | Spain | 150 | 75 | 75 |
| Poeschl, 2004 [21] | Austria | 528 | 356 | 172 |
| Arteagoitia, 2005 [10] | Spain | 490 | 231 | 259 |
| Graziani, 2005 [11] | Italy | 30 | 20 | 10 |
| Halpern, 2007 [22] | USA | 118 | 59 | 59 |
| Monaco, 2009 [23] | Italy | 59 | 32 | 27 |
| Siddiqi, 2010 [24] | New Zealand | 200 | 100 | 100 |
| López-Cedrún, 2011 [25] | Spain | 79 | 39 | 40 |
| Pasupathy, 2011 [26] | India | 89 | 60 | 29 |
| Bortoluzzi, 2013 [27] | Brazil | 24 | 12 | 12 |
| Lee, 2014 [28] | Korea | 1222 | 439 | 783 |
| | **Total** | **4063** | **1792** | **2271** |

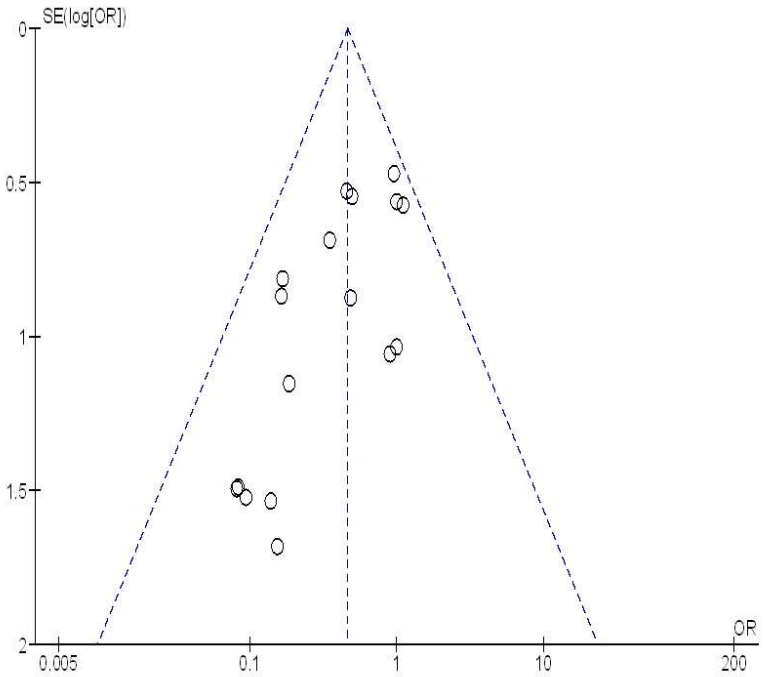


Figure 3. The funnel plot of the AP compared to placebo on SSWI in personals with TMS

**Discussion**

18 examinations from 1974 to 2014 were recruited for the current analysis including 4063 personals with TMS in the utilized examinations' starting point, 1792 of them were utilizing AP, and 2271 were utilizing the placebo. [9-11, 14-28] The examined data revealed that AP had significantly lower SSWI compared to placebo in personals with TMS. Nevertheless, caution should be exercised while interacting with its values since examinations were performed by different surgeons with different skills on different types of personals and the low sample size of numerous of the examinations selected for the meta-analysis (8 out of 18 ≤100 personals).

Since oral surgery is always performed in a clean, contaminated environment with a high concentration of bacteria, and since postoperative problems are frequently brought on by bacterial contamination and infections, it would seem reasonable to prescribe antibiotics to prevent and reduce the frequency of postoperative problems. On the other hand, there is no agreement on how antibiotics should be administered in TMS since the occurrence of postoperative problems is comparatively low and typically not life-threatening, and multiple underpowered RCTs have yielded contentious findings. The objective of this quantitative assessment of RCTs is to compile all relevant data and offer recommendations for AP in TMS. These clinical relevance findings are possibly not as obvious as their statistical significance in terms of odds ratios. The quality of life and productivity of those who experience TM surgical issues are frequently reduced since they are so painful and incapacitating. [29] These problems have financial costs that are unquestionably above those of widely administered antibiotics like amoxicillin. From a cost-effectiveness standpoint, it might be reasonable to recommend preventive antibiotic medication for TMS, but the hazards of probable antimicrobial resistance and severe adverse effects are problematic to assess and cannot be completely dismissed in clinical decision-making. [30] The surgeon is ultimately in charge of deciding whether or not to provide AP before TMS. He must assess all probable causes of postoperative problems to determine if the advantages of antibiotic therapy exceed the hazards. As a result of the disappearance of the blood clot in the extraction socket, the site of surgery is not seen as bacterial infection-related.

Age, gender, and surgical trauma are all known risk factors for developing postoperative problems. [31] Using AP solely in individuals thought to have higher risks of postoperative problems may be beneficial. The timing of the antibiotic treatment is crucial for its ability to reduce surgical problems. To have an impact on bacteria that taint surgical incisions and blood clots, the antibiotic must be present at a therapeutic level at the time of the initial incision and before the operation. This necessitates giving the antibiotic around an hour before surgery. [32] The present study's findings supported the preoperative administration of antibiotics as being effective for preventing postoperative problems and the uselessness of postoperative dosing. The most reliable dosage strategy for the prevention of SSWIs was an antibiotic given 30 to 90 minutes before the initial incision and continued for 3 to 5 days after the procedure. Antibiotics given as a single dosage before surgery's impact on postoperative SSWIs was less predictable. An antibiotic dose given one hour before surgery may be the most cost-effective method for removing a TM because the incidence of SSWI was lower (6%) in personals who did not take APs than it was in personals who did. A wide-spectrum antibiotic, which is effective against both aerobic and anaerobic bacteria, and a

narrow-spectrum antibiotic, which is exclusively effective against anaerobic bacteria, were utilized in the majority of the clinical studies that were examined. Although the importance of anaerobic bacteria in postoperative problems has been highlighted, [33] both types of bacteria are found in the oral cavity and in proximity to TMs. [34] Numerous aerobic and anaerobic bacteria are extremely susceptible to amoxicillin and other penicillin derivatives in the oral cavity. In TMS, they might be the initial option for AP. [34]

Despite our efforts to utilize a random effect model to increase the rigor of the statistical analysis and to use subgroup analysis to separate the higher quality studies from the lower quality studies, the results of this study cannot be used as a strict guideline in clinical practice regarding AP in TMS. Although the results of this investigation might be the strongest evidence currently available, a well-planned multicenter RCT is required to draw a firm conclusion. Such a conclusive clinical trial should take into account well-known risk variables like age, gender, and smoking, as well as include a well-defined case inclusion or exclusion criterion, a standard operating procedure for surgical and antimicrobial interventions, and a reliable methodology for outcome assessments. [35-41]

Limitations of the meta-analysis were as next; there can be an assortment bias because some of the tests that were chosen for the meta-analysis were excluded. Despite this, the omitted study did not meet the requirements for inclusion in the meta-analysis. We also required the information to control if factors like age, gender, and ethnicity affected the outcomes. Reviewing the impact of AP on SSWI in TMS was the examination's main objective. The use of inaccurate or incomplete data from a previous analysis could have increased bias. The individual's nutritional status, together with their race, gender, and age, were probably the root reasons for discrimination. Due to incomplete data and some unpublished studies, values may inadvertently be affected.

**Conclusions**

The examined data revealed that AP had significantly lower SSWI compared to placebo in personals with TMS. Nevertheless, caution should be exercised while interacting with its values since examinations were performed by different surgeons with different skills on different types of personals and the low sample size of many of the examinations selected for the meta-analysis (8 out of 18 ≤100 personals).

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