

Antibiotic prophylaxis for animal inflicted maxillofacial injuries: a systematic review and meta-analysis

Ricardo Grillo^{1,2^}, Mariana Aparecida Brozowski^{1^}, Sandro Bornelli Moreira^{1^}, Yuri Slusarenko da Silva^{3^}, Alexandre Meireles Borba^{4,5^}, Maria da Graça Naclério-Homem^{1^}

¹Department of Oral & Maxillofacial Surgery, Traumatology and Prosthesis, Faculty of Dentistry of the University of São Paulo, São Paulo, Brazil;

²Department of Oral & Maxillofacial Surgery, Faculty Patos de Minas, Brasília, Brazil; ³School of Dentistry, UniFG University Center, Guanambi, Brazil; ⁴Department of Oral and Maxillofacial Surgery, General Hospital of Cuiaba, Cuiaba, Brazil; ⁵Research Program on Integrated Dental Sciences, Faculty of Dentistry of the University of Cuiaba (UNIC), Cuiaba, Brazil

Contributions: (I) Conception and design: R Grillo; (II) Administrative support: None; (III) Provision of study materials or patients: R Grillo, MA Brozowski, SB Moreira, YS da Silva; (IV) Collection and assembly of data: R Grillo, MA Brozowski, SB Moreira, YS da Silva; (V) Data analysis and interpretation: R Grillo, MA Brozowski, YS da Silva, AM Borba, M da Graça Naclério-Homem; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ricardo Grillo, DDS, MBA, MSc. Department of Oral & Maxillofacial Surgery, Traumatology and Prosthesis, Faculty of Dentistry of the University of São Paulo, Av. Prof. Lineu Prestes, 2227 Cidade Universitária, São Paulo, SP 05508-000, Brazil; Department of Oral & Maxillofacial Surgery, Faculty Patos de Minas, Brasília, Brazil. Email: doutorgrillo@uol.com.br.

Background: Maxillofacial bite accidents are regular. This study review aims to assess the need for antibiotic prophylaxis in instances of bite injuries to maxillofacial area.

Methods: PubMed, Web of Science, Cochrane, Virtual Health Library, and Google Scholar had been searched up to October 2022; randomized and non-randomized controlled studies were included. This report followed the PRISMA guideline and PICOS criteria. This review has been registered at PROSPERO under the number CRD 42022327242. The risk of bias screening and data extraction was performed according to the guidelines by Cochrane. The quantitative analysis was performed using RevMan 5.4.

Results: A total of 11 studies were included in the systematic review and meta-analysis. Three articles were randomized whilst eight non-randomized clinical trials, both assessed according to Cochrane risk of bias tool. No article included has dealt with human bites. The evidence on literature is that antibiotic prophylaxis should be used only in cases of high-risk with a risk difference (RD) of 0.01 [95% confidence interval (CI): -0.02 to 0.05, P=0.40] when comparing antibiotic prophylaxis and control groups. A useful list of low- and high-risk maxillofacial bite injuries was created to aid maxillofacial surgeons in this decision.

Conclusions: Despite the limited evidence available, the use of antibiotic prophylaxis is not mandatory for all maxillofacial bite injuries. Bacterial resistance and risk of infection must be considered. Further research is needed to verify these findings. A challenge in this study is the complexity of conducting double-blind RCTs with statistically significant results while researching antibiotic prophylaxis for maxillofacial bite injuries.

Keywords: Antibiotic prophylaxis; systematic review; meta-analysis; maxillofacial injuries; animals, domestic

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[^] ORCID: Ricardo Grillo, 0000-0002-8096-738X; Mariana Aparecida Brozowski, 0000-0003-4669-4418; Sandro Bornelli Moreira, 0000-0002-3912-433X; Yuri Slusarenko da Silva, 0000-0002-8307-9134; Alexandre Meireles Borba, 0000-0001-5536-2285; Maria da Graça Naclério-Homem, 0000-0003-1329-1698.

Introduction

An estimated 4.5 million dog bites occur across America each year (1). Bears, wild boars, snakes, leopards, crocodiles, and a variety of animals besides domestic ones have been reported to cause injuries. The number of attacks from wild animals is increasing and the main reason is human spread through wild areas (2). The social distancing measures during the pandemic have also significantly increased the number of attacks from domestic animals (3). Head and neck suffer more of these injuries because the maxillofacial region has a prominent anatomical position. It is estimated that 1% of all emergency room visits across the globe are due to animal bites (4). The overall range is hard to calculate due to the fact such a lot of attacks go unreported, however with this simple calculation it is possible to see the significance of animal attack management on the face. Human bites have to be additionally be a topic of research because the annual count is alarmingly growing (5,6).

Animal and human bites to the maxillofacial region are susceptible to contamination, making appropriate initial treatment crucial for preventing infections. The diverse range of bacteria found in these bites includes *Streptococcus*, *Escherichia coli* (*E. coli*), *Pasteurella*, *Prevotella*, *Bacteroides*, and others. While it is generally reasonable to use broad-spectrum antibiotic therapy to target both aerobic and anaerobic bacteria in most cases (7), there is no consensus within the literature regarding antibiotic prophylaxis, regardless of the animal species involved, type of wound, and other features (8-10). Although some authors contend that facial bite injuries exhibit a lower susceptibility to infection compared to injuries in other anatomical regions (6,10-12), it's crucial to acknowledge the

global apprehension regarding bacterial resistance and the overuse of antibiotics (13,14). This highlights the need for a balanced approach in determining the appropriateness of antibiotic prophylaxis in maxillofacial bite injuries, taking into consideration both the potential risks and benefits associated with their use.

The topic suffers from a dearth of recent articles, with a noticeable absence of a systematic review regarding animal bites. Therefore, the aim of this work is to systematically review the literature to answer whether antibiotic prophylaxis is obligatory in instances of animal and human maxillofacial bite injuries to prevent contamination of wounds. This query has to be discussed because of excessive bacterial resistance worldwide. In non-mandatory instances, antibiotic prophylaxis has to be avoided. We present this article in accordance with the PRISMA reporting checklist (15) (available at <https://fomm.amegroups.com/article/view/10.21037/fomm-23-18/rc>).

Methods

Search strategy

A systematic literature search was conducted for records of antibiotic prophylaxis and animal or human maxillofacial bite injuries. The search was conducted within the PubMed, Web of Science (WS), Cochrane, Virtual Health Library (BVS), and Google Scholar (GS) databases. Databases were searched from inception until August 31, 2023. The following strategy was used: ((bite OR (bites and stings) OR (bites, human)) AND (face OR head OR neck) AND (antibiotic OR prophylaxis) NOT hand) in PubMed, WS, Cochrane, and BVS. Because the search algorithm is different, an adaptation of the strategy using Boolean operators, quotation marks, or signals + and - was performed on GS: (+bite[title] +face +antibiotic -hand +trial -"case report" -"systematic review" -meta-analysis -letters -notes -editorials). A manual reference list search of the included records was performed to identify additional records relevant to the study.

The authors intended to answer the following focused question according to the PICO acronym: Should patients who have been victims of maxillofacial bite injuries (P) undergo antibiotic prophylaxis (I) or is it not mandatory (C) to reduce the occurrence of wound infection (O)? This review is registered on PROSPERO under the number CRD 42022327242.

Two researchers (R.G. and Y.S.S.) independently screened the titles and abstracts of all records for relevance.

Highlight box

Key findings

- The use of antibiotic prophylaxis is not mandatory for all maxillofacial bite injuries.

What is known and what is new?

- Maxillofacial injuries inflicted by animals are usual worldwide.
- Bacterial resistance and risk of infection must be carefully considered before prescribing antibiotic prophylaxis.

What is the implication, and what should change now?

- Some protocols must be updated and further research is needed to confirm these findings. Antibiotic prophylaxis should not be mandatory in all bites in head and neck region. Special attention must be provided notably due to antibiotic resistance.

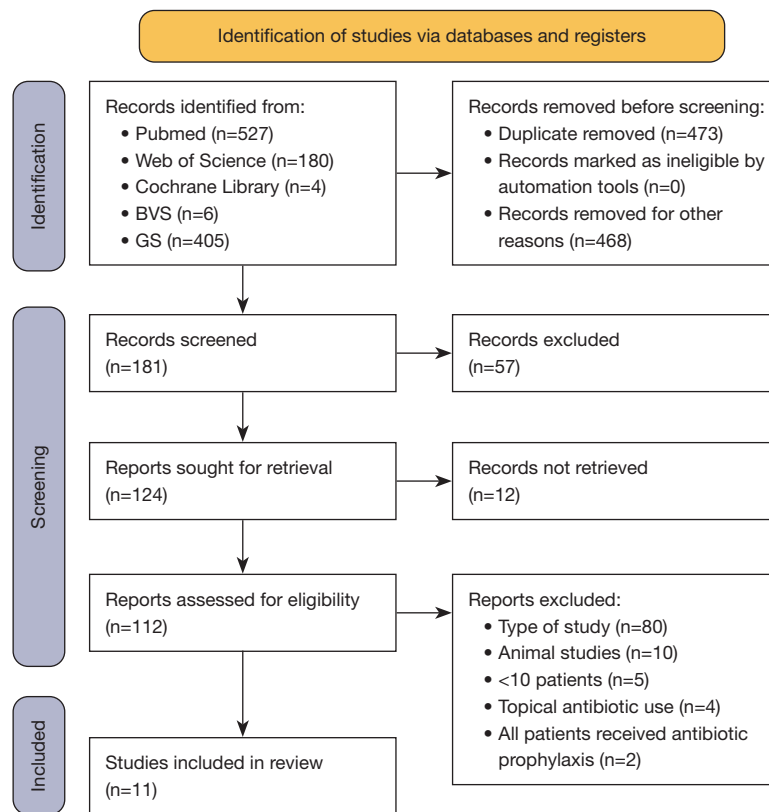


Figure 1 Flowchart of included articles. BVS, Virtual Health Library; GS, Google Scholar.

Disagreements were solved by a third author (M.A.B.). Records without an abstract underwent a full-text check. Irrelevant records were excluded. After an initial selection on title and abstract, the full texts of relevant data sets were retrieved. Full-text records were screened for eligibility based on predetermined inclusion and exclusion criteria. The inclusion criteria were (I) original research reporting maxillofacial bite injuries; (II) studies focusing on antibiotic prophylaxis; (III) written in any language; and (IV) year of publication. Exclusion criteria were (I) reviews, case reports, conference abstracts, letters, notes, and editorials; (II) animal studies; (III) studies including <10 patients; (IV) topical antibiotic use; and (V) studies in which all patients have received antibiotic prophylaxis. No restriction was considered based on patient age, comorbidities, or other health conditions.

Data extraction

The following data was extracted from the included records: type of study, number of included patients, gender, mean

age, types of attacks (animal or human), most commonly used antibiotic. The main outcome is the comparison of the number of wound infections in antibiotic and non-antibiotic prophylaxis for animal bites in the maxillofacial area.

Risk of bias across studies

Risk of bias across studies was assessed according Cochrane Risk of Bias Tool (RoB1). RStudio® (RStudio, GNU General Public License) was used to perform Egger's regression test and considered significant only with a 95% confidence interval (CI). The Review Manager Software [RevMan 5.4 (Computer Program), Copenhagen: The Nordic Cochrane Centre, 2014] was used to rate all studies for quality of evidence. The queries of the included studies are briefly explained in *Figure 1*.

Statistical analysis

The effect measure was assessed using risk difference (RD) via RevMan 5.4 and considered significant at $P < 0.05$.

Table 1 Characteristics of included articles

Reference	Origin	Type of study	N	Male/female	Mean age (years)	Animal/human	Most used antibiotic
Skurka <i>et al.</i> , 1986 (16)	USA	RCT	12	NC	NC	Dog	Penicillin
Dire <i>et al.</i> , 1992 (17)	USA	RCT	70	NC	9.1	Dog	Dicloxacillin
Quinn <i>et al.</i> , 2010 (18)	USA	RCT	94	55/39	32.53	Dog	Amoxi-Clav
Callaham, 1980 (19)	USA	nRCT	17	NC	NC	Dog	Penicillin
Javaid <i>et al.</i> , 1998 (20)	UK	nRCT	40	17/23	25	Dog	Amoxi-Clav
Wolff, 1998 (21)	Germany	nRCT	68	NC	NC	Mammalian	Penicillin
Kountakis <i>et al.</i> , 1998 (22)	USA	nRCT	29	18/11	12	Mammalian	Amoxi-Clav
Kesting <i>et al.</i> , 2006 (23)	Germany	nRCT	132	NC	NC	Animals	Amoxi-Clav
Zielińska-Kazmierska <i>et al.</i> , 2014 (24)	Poland	nRCT	26	9/17	39.43	Dog	Amoxi-Clav
Foster and Hudson, 2015 (25)	USA	nRCT	20	9/11	20	Dog	Ampicillin/sulbactam
Tabaka <i>et al.</i> , 2015 (26)	USA	nRCT	344	170/174	34.11	Dog	NC

RCT, randomized clinical trial; NC, not clear or not stated; Amoxi-Clav, amoxicillin and clavulanic acid; nRCT, non-randomized clinical trial.

Relevant data from each included article, including the number of patients receiving antibiotic prophylaxis and in the control group, as well as the number of wound infections in each group, were input into the software. Different weights were assigned to each article based on the number of included patients. The choice between a random-effects model or fixed-effects model depends on the homogeneity of the articles. Apply a fixed-effects model when assuming homogeneity, suitable for small, similar studies. Use a random-effects model when expecting heterogeneity, suitable for diverse studies or unclear sources of variation.

The Egger's test is a statistical test used to assess the presence of publication bias in a meta-analysis. It helps determine whether there is a systematic relationship between the effect size of individual studies and their standard errors, which could indicate the presence of bias in the literature.

Results

Study selection

In total, 1,122 records were identified through the initial literature search and after the manual reference list search. After removing duplicates and irrelevant articles, 181 records were screened for relevance. After the initial screening and exclusions, 112 records were assessed for

full text assessment against the eligibility criteria. Finally, 11 records remained and were included after full-text assessment (*Figure 1*).

Study characteristics

Of the 11 records included, three were randomized clinical trials (RCT) (16-18) and eight were non-RCTs (nRCTs) (19-26). Eight studies evaluated dog bite data only (16-20,24-26), two evaluated mammals (21,22), and one evaluated animals in general (23). A total of 852 patients with facial attacks were analyzed in this literature review (*Table 1*). The vast majority of facial attacks were dog bites (90.49%) but there were two articles (22,23) which mentioned bites from cats (six cases), rodents (three cases), horses (two cases), donkey (one case), and bird (one case). No study on human bites was included. Despite searching, no human bite article was added to this work. In another article, the number of bites divided by animals was ambiguous, despite a significant number of dog bites (91%) (21). No articles featuring wild animals, venomous animals, insects, and human attacks met the inclusion criteria. No clear predominance between gender and age group was found between articles. Seven articles were from the USA (16-19,22,25,26) and four from the European continent (20,21,23,24).

Two articles concluded that maxillofacial bites should be treated with antibiotic prophylaxis (23,26). Two papers

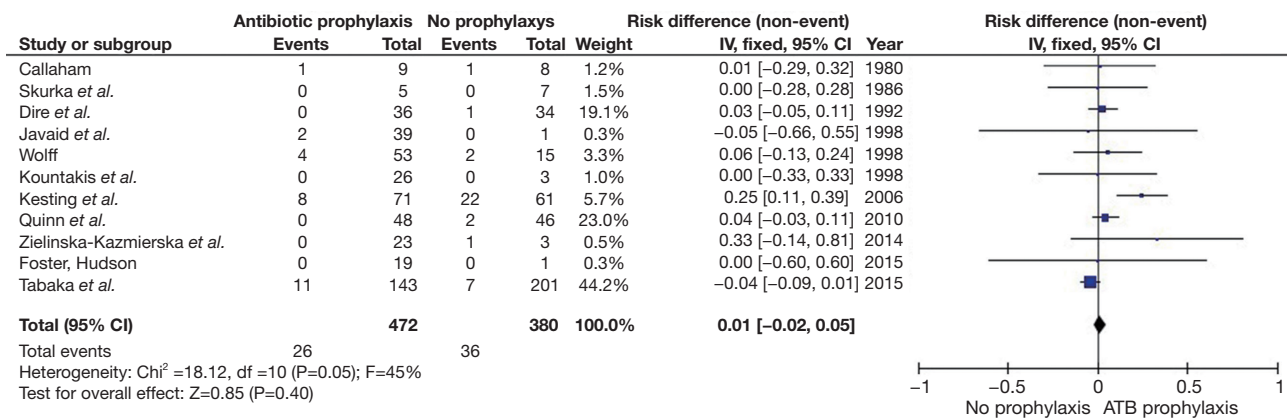


Figure 2 Forest plot showing evidence of nonmandatory use of antibiotic prophylaxis in all cases of maxillofacial bites. IV, inverse variance; CI, confidence interval; ATB, antibiotic.

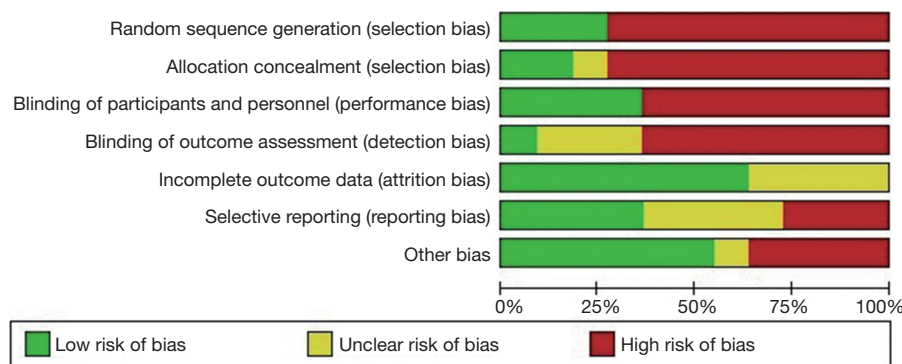


Figure 3 Risk of bias graph of included articles.

claimed that prophylaxis is only used in high-risk situations (18,19) while one contraindicated its use in low-risk wound infections (17). Three articles attested no benefit of using antibiotic prophylaxis in all cases given that the incidence of wound infections was similar in both groups (16,21,22). Amoxicillin + clavulanic acid (Amoxi-Clav) was the most commonly prescribed antibiotic prophylaxis in five articles (18,20,22-24).

Attacks on the face were less susceptible to wound infection than other anatomical regions, particularly the hands (16,19). Primary care seemed to be essential to prevent wound infection and for aesthetic and functional reasons (23). Five studies reported that this care was more important than the antibiotic prophylaxis (16,19-22).

Meta-analysis

A forest plot was created using RevMan 5.4 to evaluate the

risk ratio of the included articles concerning the association between wound infection and antibiotic prophylaxis (Figure 2). The analysis indicated that the risk of wound infection was similar in both the antibiotic prophylaxis group and the control group, with a slightly higher but not statistically significant RD of 0.01 (95% CI: -0.02 to 0.05, P=0.40). The assessment of heterogeneity revealed moderate evidence of variability among the studies (P=0.05, I²=45%). To perform the meta-analysis, the fixed-effects model was employed.

The risk of bias of the included articles was rated as high due to the lack of randomization (19-26) and blindness within the studies (Figure 3). Reporting bias was found in three articles (20,22,26). Some studies were at a high-risk of other biases due to non-use of most recommended antibiotics according to the literature (16,17,19,21).

A funnel plot was constructed to visualize the studies comparing antibiotic prophylaxis (Figure 4). It was observed

that two studies (23,26) fell outside the boundaries of the funnel plot. This deviation can be attributed to the larger sample sizes in these studies compared to others. In order to further investigate the potential publication bias, Egger's test was conducted, yielding a value of 5.2875 (95% CI: -10.6200 to 21.3276) with a significant P value of less than 0.0001. This significant asymmetry between studies indicates a high risk of bias in the publication of these studies. Egger's test is a statistical analysis used to assess the presence of publication bias in research studies.

A list of excluded articles and their reasons was created (Table 2). These excluded articles were used for discussion but not for meta-analysis.

Discussion

The increasing bacterial resistance observed in bacteria

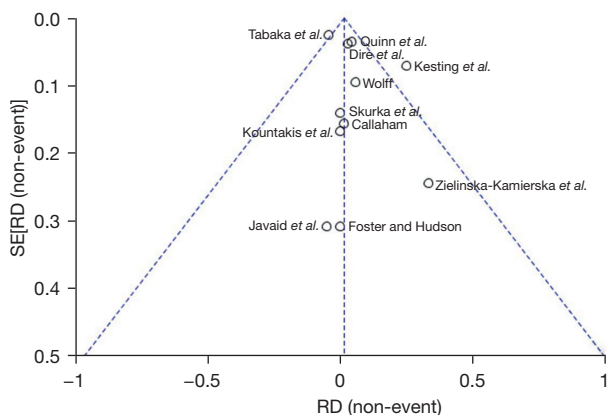


Figure 4 Funnel plot assessing potential publication bias. SE, standard error; RD, risk difference.

such as *Streptococcus*, *E. coli*, *Pasteurella*, *Prevotella*, and *Bacteroides* emphasizes the critical importance of avoiding the overuse of antibiotic prophylaxis (10,27). Overuse and misuse of antibiotics can lead to the emergence of resistant strains, rendering these medications ineffective in combating infections. Antibiotic resistance is a global public health concern that threatens our ability to effectively treat bacterial infections. By practicing appropriate antibiotic stewardship, healthcare professionals can help preserve the efficacy of antibiotics for future generations. This entails using antibiotics judiciously, only when necessary, and adhering to evidence-based guidelines for antibiotic prophylaxis. It is vital to weigh the potential benefits against the risks of antibiotic use, considering the individual patient's condition and the specific circumstances of the procedure or injury. By adopting a multidisciplinary approach and working collaboratively, healthcare providers, researchers, policymakers, and the public can collectively address the challenge of antibiotic resistance and safeguard the effectiveness of these life-saving medications.

A preceding systematic review (4) concluded that antibiotic prophylaxis reduces the chance of contamination after human bites but not cat and dog bites. The same study confirmed that hand bite wound infections may be decreased while antibiotic prophylaxis is used, however solely two researches associated with the maxillofacial region were included (15,16). A richer blood supply to the head and neck might justify the decreased chance of wound contamination than in other anatomical regions (11,20,24,28).

Primary care for animal bite wounds is the cornerstone of preventing infection (29,30), superior to antibiotic prophylaxis (16,20). Wound irrigation with concerning

Table 2 Excluded articles after full assessment and their reasons

Reason for refusal	Reference
(I) Animal studies	da Costa <i>et al.</i> (27)
(II) Antibiotic prophylaxis in all patients	Olaitan <i>et al.</i> (5), Paschos <i>et al.</i> (28), Kuvat <i>et al.</i> (29), Zangari <i>et al.</i> (30), Vitomir and Dragana (31), Donkor and Bankas (32), Gelvez <i>et al.</i> (33)
(III) Type of study	Chhabra <i>et al.</i> (34)
(IV) Not clear how many patients received antibiotic prophylaxis	Aloua <i>et al.</i> (8), Nkomo <i>et al.</i> (40), Reuter Muñoz <i>et al.</i> (41), Sribnick <i>et al.</i> (42)
(V) Unclear about the affected anatomical region	Lang and Klassen (43), Brakenbury and Muwanga (44), Akhtar <i>et al.</i> (45), Changratanakorn <i>et al.</i> (46), Jones and Stanbridge (47)
(VI) Not found	Dahl (48), Seijo <i>et al.</i> (50), Tomasetti <i>et al.</i> (51)

Table 3 Summary of wound infections risk due to attacks on the face

Features	Low risk (antibiotic prophylaxis no indicated)	High risk (antibiotic prophylaxis indicated)
Anatomical region	Face	Hand
	Scalp	Foot
	Neck	
Animal type	Dog	Cat
	Birds	Monkey and other primates
	Rodents	Human
	Insects' stings	Wild animals Unknown animal
Time of initial treatment	Right after trauma	Delayed
Wound type	Widest lesions	Puncture
	Lacerations	Deep bites
	Abrasions	Contaminated bites Closed wounds
Health factors	–	Immunosuppressed Diabetics Advanced age Alcoholism

150–250 ml of saline with pressure is highly suggested (8,16,19-21,23-25). Punctures and deeper injuries are extra tough to irrigate (19,23). This explains why these types of wounds have a higher prevalence of infections. Cat bites additionally succeed a higher prevalence of infections for this reason, since cat teeth are thinner than other animal teeth (34). An antiseptic rinse after saline irrigation is considered crucial to lessen wound infections. A range of antiseptics may be used, including iodine-povidine (16,20) and hydrogen peroxide (23). Flushing with antibiotic solution has no evidenced benefit (25).

Delay in first attendance may be unfavorable (28,31-35). No delay pattern was found. Every study has established a unique lag time to suggest antibiotic prophylaxis, from 3 (21), 6 (22,23), 8 (24) to 24 hours (16,19).

The present study did not find evidence to indicate antibiotic prophylaxis in all instances of maxillofacial animal bites (95% CI: 0.01). Some studies indicate antibiotic prophylaxis in high-risk wound infections however not on low-risk conditions (16-19,21,26). Even for high-risk injuries, a few authors do not essentially advocate antibiotic prophylaxis, however instead conduct close follow-up (26).

The extent appears not as crucial as the depth of the damage (17,21). Despite Lackmann's (52) beneficial classification of bite wounds to the face and head by the severity, wound type was defined due to the fact few authors have used it (21,23). A summary of low- and high-risk of wound infections was provided (Table 3).

Due to the huge variety of animals microorganisms, there may be no particular antibiotic for all conditions (16). As the substantial majority of animal attacks are due to dog bites, approximately 80% to 90% (28,30,43), the foremost commonly prescribed antibiotic prophylaxis is Amoxi-Clav (18,20,22-24,37). The earlier use of penicillin has been replaced by Amoxi-Clav over the years. Useful towards a range of microorganisms typically found on bites, consisting of *Streptococcus*, *E. coli*, *Pasteurella*, *Prevotella*, and *Bacteroides*, in addition to *Staphylococcus aureus* (*S. aureus*) and *Staphylococcus epidermidis* (*S. epidermidis*) on the patient's facial skin. There appear to be a disagreement concerning the number of days of antibiotic intake. Some authors required prophylaxis of wound infection for 3 days (16,18) and for others 5 to 7 days (19,23). Some authors advocate adding metronidazole to Amoxi-Clav for injuries caused by

wildlife, humans and delayed initial treatment to manage anaerobic microorganisms (20,21). Patients with penicillin allergy ought to receive doxycycline (7) or azithromycin (23) as a second option.

Any person who has suffered an animal attack should have a history of tetanus vaccination. Animal bites, mainly wild and unknown are suspected to be related to tetanus and rabies (7). The equal applies to rabies prophylaxis particularly for cat, dog and wild animal bites. Contrary to the view of a few authors that antibiotic prophylaxis is much less vital for facial bites, rabies prophylaxis is more urgent because of the proximity to the central nervous system (43). Several alternative infectious diseases may be transmitted through bites such as Ebola, herpes, monkeypox, yellow fever, hepatitis B, human immunodeficiency virus (HIV), and tuberculosis (53).

One limitation of this study is the great difficulty of performing double-blind RCTs with statistical significance when investigating antibiotic prophylaxis in maxillofacial bite injuries (19). The included studies were not completely homogeneous ($P=0.05$, $I^2=45\%$), thus additional comparative studies with larger patient populations are desired to assess experimental and control groups and to achieve more evidence-based data and ideal doses. Secondly, relevant patient factors such as comorbidities, patient age, and wound factors (depth, tissue layers, size) were not assessed as they are not available in most of the included articles. And finally, due to a lack of protocol in antibiotic prophylaxis, it was not possible to evaluate the appropriate dose, route of administration, and duration of treatment in each situation. The authors suggest that multicenter studies worldwide ought to assist on this situation. Internet use and worldwide collaboration should be beneficial.

Conclusions

According to the available literature this systematic review has demonstrated no definitive conclusion on whether or not antibiotic prophylaxis should be given or not to patients with animal bites (RD: 0.01). Antibiotic prophylaxis should be earned in high-risk cases. The cost-benefit of growing bacterial resistance needs to be appraised. Studies with a lower risk of bias are required on this topic.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <https://fomm.amegroups.com/article/view/10.21037/fomm-23-18/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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