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Effectiveness and safety of surgical antibiotic prophylaxis in dental procedures in patients without underlying cardiac conditions: an overview of systematic reviews

Eficácia e segurança da profilaxia antibiótica cirúrgica em procedimentos odontológicos em pacientes sem condições cardíacas subjacentes: uma visão geral de revisões sistemáticas

Efectividad y seguridad de la profilaxis antibiótica quirúrgica en procedimientos dentales en pacientes sin afecciones cardíacas subyacentes: una descripción general de las revisiones sistemáticas

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Abstract
Objective: This overview of systematic reviews aimed to assess the effectiveness and safety of surgical antibiotic prophylaxis for patients without underlying cardiac conditions undergoing dental surgical procedures. Methods: The searches were carried out at PubMed, Lilacs, Cochrane Library, Web of Science and Scopus databases. Systematic reviews of randomized controlled trials and non-randomized controlled trials that assessed the effectiveness and safety of surgical antibiotic prophylaxis in patients without underlying cardiac conditions undergoing dental surgical procedures were included in the study. A methodological quality assessment was carried out through AMSTAR-2. Results: The search resulted in 1910 studies and 15 systematic reviews were included in the overview. Three surgical procedures were identified: dental implant, dental extraction and endodontic surgery. Most systematic reviews (80%) did not present conclusive results on the effectiveness and safety of surgical antibiotic prophylaxis in procedures performed in patients without underlying cardiac conditions. Eleven studies showed low or critically low quality and four presented moderate methodological quality. Conclusion: The results are inconclusive to state that surgical antibiotic prophylaxis is more effective and safer for patients without underlying cardiac conditions undergoing dental implant, dental extraction and endodontic surgery compared to no intervention, as this overview of systematic review showed evidence that surgical antibiotic prophylaxis should be avoided in healthy patients to minimize the risk of antimicrobial resistance until studies with a lower risk of bias are available to support a favorable decision-making for use.
Keywords: Antibiotic prophylaxis; Evidence-based dentistry; Preventive dentistry; Practice patterns, dentists'.

Resumo
Objetivo: Esta visão geral de revisões sistemáticas teve como objetivo avaliar a eficácia e segurança da profilaxia antibiótica cirúrgica para pacientes sem condições cardíacas subjacentes submetidos a procedimentos cirúrgicos

odontológicos. Métodos: As buscas foram realizadas nas bases de dados PubMed, Lilacs, Cochrane Library, Web of Science e Scopus. Revisões sistemáticas de ensaios controlados randomizados e ensaios controlados não randomizados que avaliaram a eficácia e segurança da profilaxia antibiótica cirúrgica em pacientes sem condições cardíacas subjacentes submetidos a procedimentos cirúrgicos odontológicos foram incluídos no estudo. A avaliação da qualidade metodológica foi realizada por meio do AMSTAR-2. Resultados: A busca resultou em 1910 estudos e 15 revisões sistemáticas foram incluídas na visão geral. Foram identificados três procedimentos cirúrgicos: implante dentário, extração dentária e cirurgia endodôntica. A maioria das revisões sistemáticas (80%) não apresentou resultados conclusivos sobre a eficácia e segurança da antibioticoprofilaxia cirúrgica em procedimentos realizados em pacientes sem cardiopatias subjacentes. Onze estudos apresentaram qualidade baixa ou criticamente baixa e quatro apresentaram qualidade metodológica moderada. Conclusão: Os resultados são inconclusivos para afirmar que a profilaxia antibiótica cirúrgica é mais eficaz e segura para pacientes sem condições cardíacas subjacentes submetidos a implante dentário, extração dentária e cirurgia endodôntica em comparação com nenhuma intervenção, pois esta revisão sistemática mostrou evidências de que a profilaxia antibiótica cirúrgica deve ser evitada em pacientes saudáveis para minimizar o risco de resistência antimicrobiana até que estudos com menor risco de viés estejam disponíveis para apoiar uma tomada de decisão favorável ao uso.
Palavras-chave: Antibioticoprofilaxia; Odontologia baseada em evidências; Odontologia preventiva; Padrões de prática odontológica.

Resumen

Objetivo: Este resumen de revisiones sistemáticas tuvo como objetivo evaluar la efectividad y la seguridad de la profilaxis antibiótica quirúrgica para pacientes sin afecciones cardíacas subyacentes que se someten a procedimientos quirúrgicos dentales. Métodos: Las búsquedas se realizaron en las bases de datos PubMed, Lilacs, Cochrane Library, Web of Science y Scopus. Se incluyeron en el estudio revisiones sistemáticas de ensayos controlados aleatorios y ensayos controlados no aleatorios que evaluaron la efectividad y la seguridad de la profilaxis quirúrgica con antibióticos en pacientes sin afecciones cardíacas subyacentes que se sometieron a procedimientos quirúrgicos dentales. Se realizó una evaluación de la calidad metodológica a través de AMSTAR-2. Resultados: La búsqueda dio como resultado 1910 estudios y se incluyeron 15 revisiones sistemáticas en el resumen. Se identificaron tres procedimientos quirúrgicos: implante dental, extracción dental y cirugía endodóntica. La mayoría de las revisiones sistemáticas (80%) no presentaron resultados concluyentes sobre la efectividad y seguridad de la profilaxis antibiótica quirúrgica en procedimientos realizados en pacientes sin condiciones cardíacas subyacentes. Once estudios mostraron una calidad baja o críticamente baja y cuatro presentaron una calidad metodológica moderada. Conclusion: Los resultados no son concluyentes para afirmar que la profilaxis antibiótica quirúrgica es más efectiva y segura para los pacientes sin afecciones cardíacas subyacentes que se someten a implantes dentales, extracción dental y cirugía endodóntica en comparación con ninguna intervención, ya que este resumen de revisión sistemática mostró evidencia de que se debe evitar la profilaxis antibiótica quirúrgica en pacientes sanos para minimizar el riesgo de resistencia a los antimicrobianos hasta que se disponga de estudios con menor riesgo de sesgo que apoyen una toma de decisiones favorable para su uso.
Palabras clave: Profilaxis antibiótica; Odontología basada en la evidencia; Odontología preventiva; Pautas de la práctica en odontología.

1. Introduction

Surgical antibiotic prophylaxis (SAP) is a procedure realized with antibiotic use to avoid surgical site infection (SSI). However, not all surgical procedures need to have the SAP prescription. The SAP is required for all surgical procedures associated with high risk of infections, as clean-contaminated and contaminated surgeries, as well as those where there are severe consequences of infection, as cardiac surgeries, the SAP are required (Bratzler et al., 2013).

The restriction in SAP use is important to reduce the antibiotic consumption. One of the main public health concerns is the antimicrobial resistance, and the antibiotic use is associated with this growing problem (World Health Organization, 2014). It is estimated that by 2050, it will be among the most lethal health problems, in addition to generating an additional billion dollars in healthcare costs (O'Neill, 2016).

Invasive dental procedures include all dental treatments requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa and root canal procedures (Segura-Egea et al., 2018). This procedure is classified as a clean-contaminated surgery with an expected infection risk of 10 to 15%, but this risk can be reduced to 1% if proper technique is used (Khouly et al., 2019). Quirynen et al. (Quirynen et al., 2002) observed that when all techniques precautions to avoid postoperative infections were taken, the incidence of local infections after implant procedures was 2%, and these techniques did

not include surgical antibiotic prophylaxis. Despite this, SAP has been observed in about 90% of surgical procedures performed on healthy people (without underlying cardiac conditions), especially in procedures such as extraction of third molars and in dosage regimens that last up to seven days, which is considered by some researchers to be irrational (I. Arteagoitia et al., 2018; Mariscal-Cazalla et al., 2021; Suda et al., 2018; Yalcin-Ülker et al., 2020).

Although the risk of infection after invasive dental procedures is considered low when the proper techniques is used, there are some scientific evidences supporting the SAP use. A systematic review realized by Ata-Ali et al. (Ata-Ali et al., 2014) showed a reduction in postoperative infections after dental implant procedures when the SAP was used, as well as Moreno-Drada et al. (Moreno-Drada & García-Perdomo, 2016) observed in patients after dental extraction procedures. In contrast, Singh Gill et al. (Singh Gill et al., 2018) did not observe a reduction in the group of patients who used SAP after dental implant and dental extraction procedures. There is not an international consensus or guideline published recommending or not the use of SAP in dental procedures excepting from 2007 American Heart Association (Wilson et al., 2007) publication about the criteria for SAP utilization to avoid infective endocarditis in patients with risk factors for cardiac complications.

Since the gaps in the literature regarding the use of antibiotic prophylaxis in patients without risk factors for cardiac complications, the different behaviors of dental surgeons in clinical practice in relation to SAP use and the need to rationalize the antibiotic consumption, it is essential to study the effectiveness and safety of SAP in patients without underlying cardiac conditions undergoing dental procedures. This research summarizes systematic reviews of the available evidence on antibiotic prophylaxis in dental procedures. Therefore, the aim of this study was to evaluate the effectiveness and the safety of SAP in adult patients without underlying cardiac conditions undergoing dental procedures.

2. Methodology

This is an overview of systematic reviews registered in the International Prospective Register of Systematic Reviews (PROSPERO) under number CRD42020136407. The checklist "The Preferred Reporting Items for Overview of Systematic Reviews" (Bougioukas et al., 2018) was used in the study report. The study question was prepared according to the PICOS strategy (Table 1) (Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors)., 2021). The following question was addressed: Is the use of SAP in adult patients without underlying cardiac conditions undergoing dental procedures more effective and safer than the absence of this strategy?

Table 1. Study question according to the PICOS strategy.

Acronym PICOS	Dental procedures
Population	Adult population without underlying cardiac conditions undergoing any dental procedures.
Intervention	Use of antibiotic prophylaxis.
Comparator	No antibiotic/placebo
Outcomes	Effectiveness (postoperative infections) and safety (drug adverse effects)
Study design	Systematic review of randomized and non-randomized clinical trials.

Source: Authors.

Studies that met the following criteria were included: systematic reviews of randomized controlled trials (RCT) or non-randomized controlled trials performed with adults (≥ 18 years), without underlying cardiac conditions, in which the outcomes of antibiotic administration for prophylactic purposes in dental surgical procedures were analyzed. In turn, the following were excluded: studies with participants who had infections in the moment immediately before the dental surgical procedure; studies with immunocompromised people; studies that reported dental surgery performed outside the scope of primary health care; studies comparing different dosage of antibiotics in the intervention and control groups. In studies comparing antibiotic versus

placebo/no medication or antibiotic versus antibiotic in the intervention and control groups, only data referring to antibiotic versus placebo/no medication analysis were considered. The type of surgical procedure performed was not considered as an eligibility criterion.

Searches were conducted in PubMed, Lilacs, Cochrane Library, Web of Science, and Scopus databases from inception to January 27, 2021. MesH and DeCS descriptors were crossed using Boolean operators "AND" (intercategories) and "OR" (intracategories) (Table 2). The same strategy was used in all the databases, adapted to the peculiarities of each one of them. In addition, a manual search for other potentially eligible studies was performed in other sources, such as the reference list of included studies, a consultation with specialists and the grey literature (Open Grey and ProQuest) using the terms antibiotic prophylaxis and oral surgical procedure. Rayyan software (Ouzzani et al., 2016) was used in this phase of the study, as well as in the elimination of duplicates and selection of studies. No language or publication status restrictions were placed.

Table 2. Database search strategy.

Base (search date)	Crossing	Search strategy	N
Pubmed (January 27, 2021)	#69	(“oral surgical procedure”[MeSH Terms]) OR (“oral surgical procedure”) OR (“oral surgical procedures, preprosthetic”[MeSH Terms]) OR (“oral surgical procedures, preprosthetic”) OR (“dental care for children”[MeSH Terms]) OR (“dental care for children”) OR (“dental care for chronically ill”[MeSH Terms]) OR (“dental care for chronically ill”) OR (“dental care for aged”[MeSH Terms]) OR (“dental care for aged”) OR (“dental care for disabled”[MeSH Terms]) OR (“dental care for disabled”) OR (“dental care”[MeSH Terms]) OR (“dental care”) OR (“dental implantation”[MeSH Terms]) OR (“dental implantation”) OR (“surgery, oral”[MeSH Terms]) OR (“surgery, oral”) OR (“dental surgery”) OR (“dental extraction”) OR (“exodontics”[MeSH Terms]) OR (“exodontics”) OR (“dental implants”[MeSH Terms]) OR (“dental implants”) OR (“dental procedures”)	101,401
	#60	(“antibiotic prophylaxis”[MeSH Terms]) OR “antibiotic prophylaxis”) OR “infection control, dental”[MeSH Terms]) OR “infection control, dental”) OR “agents, antibacterial”[MeSH Terms]) OR “agents, antibacterial”)	21,270
	#69 AND #60	("oral surgical procedure"[All Fields] OR "oral surgical procedures, preprosthetic"[MeSH Terms] OR "oral surgical procedures, preprosthetic"[All Fields] OR "dental care for children"[MeSH Terms] OR "dental care for children"[All Fields] OR "dental care for chronically ill"[MeSH Terms] OR "dental care for chronically ill"[All Fields] OR "dental care for aged"[MeSH Terms] OR "dental care for aged"[All Fields] OR "dental care for disabled"[MeSH Terms] OR "dental care for disabled"[All Fields] OR "dental care"[MeSH Terms] OR "dental care"[All Fields] OR "dental implantation"[MeSH Terms] OR "dental implantation"[All Fields] OR "surgery, oral"[MeSH Terms] OR "surgery, oral"[All Fields] OR "dental surgery"[All Fields] OR "dental extraction"[All Fields] OR "exodontics"[All Fields] OR "dental implants"[MeSH Terms] OR "dental implants"[All Fields] OR "dental procedures"[All Fields]) AND ("antibiotic prophylaxis"[MeSH Terms] OR "antibiotic prophylaxis"[All Fields] OR "infection control, dental"[MeSH Terms] OR "infection control, dental"[All Fields] OR ("anti-bacterial agents"[Pharmacological Action] OR "anti-bacterial agents"[MeSH Terms] OR ("anti-bacterial"[All Fields] AND "agents"[All Fields]) OR "anti-bacterial agents"[All Fields] OR ("agents"[All Fields] AND "antibacterial"[All Fields])) OR "antimicrobial"[All Fields] OR "premedication"[All Fields]) AND Review[ptyp]	599
Lilacs (January 27, 2021)	#8	(Oral Surgical Procedures) OR (Procedimientos Quirúrgicos Orales) OR (Procedimentos Cirúrgicos Bucais) OR (Oral Surgical Procedures, Preprosthetic) OR (Procedimientos Quirúrgicos Preprotésicos Orales) OR (Procedimentos Cirúrgicos Pré-Protéticos Bucais) OR (Dental Care for Children) OR (Atención Dental para Niños) OR (Assistência Odontológica para Crianças) OR (Dental Care for Chronically Ill) OR (Atención Dental para Enfermos Crónicos) OR (Assistência Odontológica para Doentes Crônicos) OR (Dental Care for Aged) OR (Cuidado Dental para Ancianos) OR (Assistência Odontológica para Idosos) OR (Dental Care for Disabled) OR (Atención Dental para Personas con Discapacidades) OR (Assistência Odontológica para Pessoas com Deficiências) OR (Dental Care) OR (Atención Odontológica) OR (Assistência Odontológica) OR (Dental Implantation) OR (Implantación Dental) OR (Implantação Dentária) OR (Surgery, Oral) OR (Cirugía Bucal) OR (Cirurgia Bucal) OR (dental surgery) OR (cirugía dental) OR (cirurgia dentária) OR (cirurgia odontológica) OR (dental extraction) OR (extracción dental) OR (extração dentária) OR (exodontics) OR (exodoncia) OR (exodontia) OR (Dental Implants) OR (Implants Dentales) OR (Implants Dentários) OR (dental procedures) OR (procedimientos dentales) OR (procedimentos odontológicos)	30,423

	#10	(Antibiotic Prophylaxis) OR (Profilaxis Antibiótica) OR (Antibioticoprofilaxia) OR (Infection Control, Dental) OR (Control de Infección Dental) OR (Controle de Infecções Dentárias) OR (Anti-Bacterial Agents) OR (Antibacterianos) OR (Antibacterianos)	9,514
	#8 AND #10	(tw:((Oral Surgical Procedures) OR (Procedimientos Quirúrgicos Orales) OR (Procedimentos Cirúrgicos Bucais) OR (Oral Surgical Procedures, Preprosthetic) OR (Procedimientos Quirúrgicos Preprotésicos Orales) OR (Procedimentos Cirúrgicos Pré-Protéticos Bucais) OR (Dental Care for Children) OR (Atención Dental para Niños) OR (Assistência Odontológica para Crianças) OR (Dental Care for Chronically Ill) OR (Atención Dental para Enfermos Crónicos) OR (Assistência Odontológica para Doentes Crônicos) OR (Dental Care for Aged) OR (Cuidado Dental para Ancianos) OR (Assistência Odontológica para Idosos) OR (Dental Care for Disabled) OR (Atención Dental para Personas con Discapacidades) OR (Assistência Odontológica para Pessoas com Deficiências) OR (Dental Care) OR (Atención Odontológica) OR (Assistência Odontológica) OR (Dental Implantation) OR (Implantación Dental) OR (Implantação Dentária) OR (Surgery, Oral) OR (Cirugía Bucal) OR (Cirurgia Bucal) OR (dental surgery) OR (cirugía dental) OR (cirurgia dentária) OR (cirurgia odontológica) OR (dental extraction) OR (extracción dental) OR (extração dentária) OR (exodontics) OR (exodoncia) OR (exodontia) OR (Dental Implants) OR (Implants Dentales) OR (Implants Dentários) OR (dental procedures) OR (procedimientos dentales) OR (procedimentos odontológicos))) AND (tw:((Antibiotic Prophylaxis) OR (Profilaxis Antibiótica) OR (Antibioticoprofilaxia) OR (Infection Control, Dental) OR (Control de Infección Dental) OR (Controle de Infecções Dentárias) OR (Anti-Bacterial Agents) OR (Antibacterianos) OR (Antibacterianos)))	810
Cochrane Library (January 27, 2021)	#1	“oral surgical procedure” OR “oral surgical procedures, preprosthetic” OR “dental care for children” OR “dental care for chronically ill” OR “dental care for aged” OR “dental care for disabled” OR “dental care” OR “dental implantation” OR “surgery, oral” OR “dental surgery” OR “dental extraction” OR “exodontics” OR “dental implants” OR “dental procedures”	6,131
	#2	“antibiotic prophylaxis” OR “infection control, dental” OR “agents, antibacterial”	4,073
	#1 AND #2	“oral surgical procedure” OR “oral surgical procedures, preprosthetic” OR “dental care for children” OR “dental care for chronically ill” OR “dental care for aged” OR “dental care for disabled” OR “dental care” OR “dental implantation” OR “surgery, oral” OR “dental surgery” OR “dental extraction” OR “exodontics” OR “dental implants” OR “dental procedures” in Title Abstract Keyword AND “antibiotic prophylaxis” OR “infection control, dental” OR “agents, antibacterial” in Title Abstract Keyword - (Word variations have been searched)	72
Scopus (January 27, 2021)	#1	"oral surgical procedure" OR "oral surgical procedures, preprosthetic" OR "dental care for children" OR "dental care for chronically ill" OR "dental care for aged" OR "dental care for disabled" OR "dental care" OR "dental implantation" OR "surgery, oral" OR "dental surgery" OR "dental extraction" OR "exodontics" OR "dental implants" OR "dental procedures"	176,468
	#2	“antibiotic prophylaxis” OR “infection control, dental” OR “agents, antibacterial”	2,713
	#1 AND #2	"oral surgical procedure" OR "oral surgical procedures, preprosthetic" OR "dental care for children" OR "dental care for chronically ill" OR "dental care for aged" OR "dental care for disabled" OR "dental care" OR "dental implantation" OR "surgery, oral" OR "dental surgery" OR "dental extraction" OR "exodontics" OR "dental implants" OR "dental procedures" AND "antibiotic prophylaxis" OR "infection control, dental" OR "agents, antibacterial" AND (LIMIT-TO (DOCTYPE , "re"))	348
Web of Science (January 27, 2021)	#1	"oral surgical procedure" OR "oral surgical procedures, preprosthetic" OR "dental care for children" OR "dental care for chronically ill" OR "dental care for aged" OR "dental care for disabled" OR "dental care" OR "dental implantation" OR "surgery, oral" OR "dental surgery" OR "dental extraction" OR "exodontics" OR "dental implants" OR "dental procedures"	31,949
	#2	“antibiotic prophylaxis” OR “infection control, dental” OR “agents, antibacterial”	11,399
	#1 AND #2	TÓPICO: ("oral surgical procedure" OR "oral surgical procedures, preprosthetic" OR "dental care for children" OR "dental care for chronically ill" OR "dental care for aged" OR "dental care for disabled" OR "dental care" OR "dental implantation" OR "surgery, oral" OR "dental surgery" OR "dental extraction" OR "exodontics" OR "dental implants" OR "dental procedures") AND TÓPICO: (“antibiotic prophylaxis” OR “infection control, dental” OR “agents, antibacterial”). Refinado por: Tipos de documento: (REVIEW)	80

Source: Authors.

After the search and duplicate elimination phase, two investigators read the title and abstract of the studies found independently. Systematic reviews that were both considered to meet the inclusion criteria were selected for further reading in their entirety. Disagreements were resolved in consensus meetings with a third researcher. The Kappa coefficient was calculated

to measure the level of agreement between researchers and a minimum value of 0.61 (substantial agreement) was considered acceptable (McHugh, 2012).

Two reviewers independently carried out data extraction in the included studies. The primary outcomes defined were effectiveness and safety. The parameters used to measure effectiveness and safety were postoperative infections and drug adverse effects, respectively, as defined by the authors of each systematic review. The variables of interest defined for data collection were authors; year; country; type of study; characteristics of the participants (sex, age and smoking); surgical procedure performed; antibiotic(s) used, concentration of the drug(s), dosage, route of administration, duration of treatment; observed outcomes (effectiveness and safety). The included studies were organized by type of dental procedure to ensure the homogeneity of analyzes. The information collected was compared among the investigators and disagreements were resolved by consensus with a third researcher.

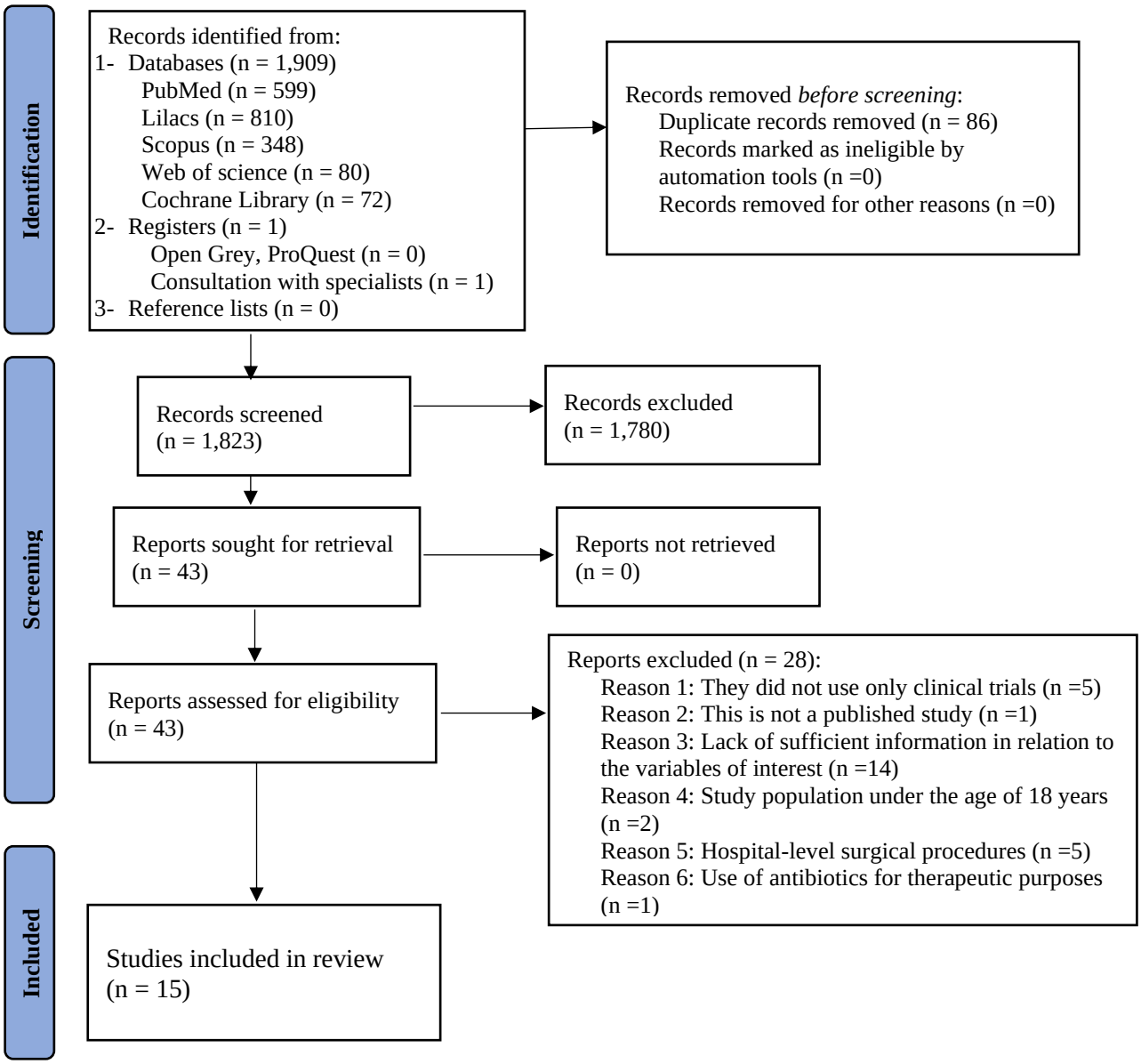
Two reviewers using AMSTAR-2 (Shea et al., 2017) independently assessed the methodological quality of the studies and the disagreements were resolved with a third researcher. The qualitative synthesis of the data was carried out, and the results were summarized considering the methodological quality and the outcomes observed in each study. Studies with a moderate or high level of methodological quality were considered acceptable or adequate for evidence synthesis. Studies with methodological quality classified as low or critically low and those that did not present enough statistical data to assess effectiveness and safety of SAP were considered inconclusive.

The overlapping of primary studies included in the systematic reviews was presented in table form (Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors)., 2021). Analysis of study overlapping in individual reviews was performed by calculating the corrected covered area overlap (CCA) measure (Pieper et al., 2014). The CCA was classified as mild (0-5%), moderate (6% -10%), high (11% -15%) and very high (more than 15%).

3. Results

One thousand nine hundred and ten studies were identified in the selected databases and fifteen systematic reviews were included (Figure 1). The Kappa coefficient resulted in almost perfect agreement between the researchers (agreement = 0.94; SE of Kappa = 0.04, 95% CI 0.87-1.00). The identification of the included studies and their characteristics are shown in Table 3. Twenty-eight studies were excluded for the reasons given in Table 4. Three surgical procedures were identified in the included studies: dental implant, dental extraction and endodontic surgery.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) fluxogram.



Source: Authors.

Table 3. General features of systematic reviews included in this overview (n=15).

Author Year (Country)	Included studies	Characteristics of the participants				Characteristics of the intervention and control groups					
						Intervention (Drug / Concentration / Posology / Duration / Administration route)			Control (Drug / Concentration / Posology / Duration / Administration route)		
	N (type of study)	N participants	Sex	Age (years)	Smoking habit	Preoperative	Postoperative	T	Preoperative	Postoperative	T
						Dental Implant					
(Ata-Ali et al., 2014) (Spain)	4 (RCT)	475	M,F	NR	NR	Amoxicillin / 2g / 1h before / single dose / OR	-	NR	Placebo	-	NR
						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 2g / 12h-12h / 2 days / OR	NR	-	-	NR
						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 2g / 24h-24h / 7 days / OR	NR	Placebo	-	NR
						-	Amoxicillin / 2g / 24h-24h / 7 days / OR	NR	-	-	NR
(Braun et al., 2019) (USA)	8 (RCT)	2869**	M,F	18 - 86	NRS	Amoxicillin / 2g / 1h before / single dose / OR	-	3	-	-	3
						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 2g / 12h-12h / 7 days / OR	3	NR	NR	3
						-	Amoxicillin / 1g / 12h-12h / 7 days / OR	3	NR	NR	3
						Amoxicillin / 1g / single dose / OR	Amoxicillin / 500mg / 12h-12h / 3 days / OR	3	NR	NR	3
						Amoxicillin / 1g / night before + 2g 1h before / two doses / OR	Amoxicillin / 1g / 12h-12h / 2 days / OR	3	NR	NR	3
						Amoxicillin / 3g / 1h before / single dose / OR	-	3	NR	NR	3
						Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	3	NR	NR	3
(Canullo et al., 2020) (Italy)	9 (RCT)	1984	M,F	NR	NRS	Amoxicillin / 3g / before / single dose / NR	-	1	Placebo	NR	1
						Amoxicillin / 2g / 1h before / single dose / NR or Clindamycin / 600 mg / before / single dose / NR	-	4	Placebo	NR	4
						Amoxicillin / 2g / 1h before / single dose / NR or Clindamycin / 600 mg / before / single dose / NR	Amoxicillin / 2g / after / single dose / NR Amoxicillin / 2g / 12h-12h / 7 days / OR	3	Placebo	NR	3
						Amoxicillin / 2g / 1h before / single dose / NR Clindamycin / 600 mg / before / single dose / NR	-	4	Placebo	Placebo	4
						Amoxicillin / 2g / 1h before / single dose / NR or Clindamycin / 600 mg / before / single dose / NR	-	4	Placebo	NR	4
						Amoxicillin / 2g / 1h before / single dose / NR or Clindamycin / 600 mg / before / single dose / NR	Amoxicillin / 2g / after / single dose / NR	2	Placebo	NR	2
						Amoxicillin / 2g / 1h before / single dose / NR or Clindamycin / 600 mg / before / single dose / NR	-	3	Placebo	NR	3
						NR	-	5	NR	NR	5

						NR	-	6	NR	NR	6
(Chen et al., 2017) (China)	9 (RCT)	1851	M,F	18 - 88	NR	Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	2	-	-	2
						Amoxicillin / 2g / 1h before / single dose / OR	-	2	Placebo	-	2
						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 1g / 12h-12h / 7 days / OR	2	-	-	2
						-	Amoxicillin / 1g / 12h-12h / 7 days / OR	2	Placebo	-	2
						-	Amoxicillin / 2g / immediately after / OR	2	Placebo	-	2
(Esposito et al., 2008) (UK)	2 (RCT)	NR	M,F	NR	NR	Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	3	Placebo / -	NR	NR
						Amoxicillin / 1g / 1h before / single dose / OR	-	3	Placebo / -	NR	NR
						Amoxicillin / 2g / 1h before / single dose / OR	-	3	Placebo / -	NR	NR
(Esposito et al., 2010) (Sweden)	4 (RCT)	~462	M,F	NR	NR	Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	5	Placebo	NR	NR
						NR	NR	3	Placebo	-	
						Amoxicillin / 2g / 1h before / single dose / OR	-	4	Placebo	-	
(Khouly et al., 2019) (Germany)	10 (RCT)	NR	M,F	NR	NR	Amoxicillin / 2g / 1h before / single dose / OR	-	3	-	NR	NR
						Amoxicillin / 2g /1g the night before + 1h before / OR	Amoxicillin / 1g / 12h-12h / 2 days / OR	3	-	NR	NR
						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 1g / 12h-12h / 7 days / OR	3	-	NR	NR
						-	Amoxicillin / 1g / 12h-12h / 7 days / OR	3	-	NR	NR
						Amoxicillin / 1g / 1h before / single dose / OR	-	3	-	NR	NR
						Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / 3 days / OR	3	Placebo	NR	NR
						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / on the 2nd and 3rd day after / OR	3	Placebo	NR	NR
						Amoxicillin / 2g / immediately before / single dose / OR	-	3	Placebo	NR	NR
						Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	3	Placebo	NR	NR
						-	Amoxicillin / 500mg / 8h-8h / 2 days / OR	3	Placebo	NR	NR
(Marín Escobar	5 (RCT)	1091	M,F	NR	NR	Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	3	Placebo	NR	NR
						Amoxicillin / 2g / 1h before / single dose / OR	-	3	Placebo	NR	NR

et al., 2013) (Chile)						Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / 5 days / OR	3	Placebo	NR	NR
						-	Amoxicillin + Clavulanic Acid / 625mg / 12h-12h / 5 days / OR	3	Placebo	NR	NR
(Romandini et al., 2019) (Italy)	9 (RCT)	NR	NR	NR	NR	Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 6h-6h / 2 days / OR	3	-	-	3
						Amoxicillin / 2g / 1h before / single dose / OR	-	3	Placebo	-	3
						Amoxicillin / 500mg / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h/ 7 days/ OR	3	Placebo	-	3
						Amoxicillin / 3g / 1h before / single dose / OR	-	3	Placebo	-	3
						Dental extraction					
(M.-I. Arteagoitia et al., 2016) (Spain) Continued	10 (RCT)	NR	M,F	NR	NRS	Amoxicillin + Clavulanic Acid / 2000 + 125mg / 2h before / single dose / OR	Amoxicillin + Clavulanic Acid / 2000 + 125mg / 12h-12h / 4 days / OR	NR	Placebo	Placebo	NR
						-	Amoxicillin + Clavulanic Acid / 500 + 125mg / 8h-8h / 4 days / OR	NR	-	Placebo	NR
						Amoxicillin / 1g / 1h before / single dose / OR	-	NR	Placebo	-	NR
						Amoxicillin / 2g / 60 a 90 minutes before / single dose / OR	-	NR	Placebo	-	NR
						Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / 4 days / OR	NR	Placebo	-	NR
						-	Amoxicillin + Clavulanic Acid / 2000mg + 125mg / 24h-24h / 5 days / OR	NR	Placebo	Placebo	NR
(M.-I. Arteagoitia et al., 2016) (Spain) Continued	10 (RCT)	NR	M,F	NR	NRS	Amoxicillin / 2g / 2h before / single dose / OR	Amoxicillin / 500mg / 24h-24h / 5 days / OR	NR	Placebo	Placebo	NR
						Metronidazole / 800 mg / 1h before / single dose / OR	-	NR	Placebo	-	NR
						Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / 2 days / OR	NR	Placebo	Placebo	NR
						Amoxicillin / 500mg / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / 3 days / OR (Clindamycin / 300mg / NR / NR / OR for allergy to Amoxicillin)	NR	Placebo	Placebo	NR
(Cervino et al., 2019) (Italy)	12 (RCT)	NR	M,F	NR	NR	Amoxicillin / 2g / 2h before / single dose / NR	Amoxicillin / 500mg / 8h-8h / 7 days / NR	NR	Placebo	-	NR
						Amoxicillin + Clavulanic Acid / 875 + 125mg / single dose / 2 days / NR	Amoxicillin + Clavulanic Acid / 500 + 125mg / 12h-12h / 4 days / OR	NR	Placebo	-	NR
						Amoxicillin + Clavulanic Acid / 875+125mg / single dose / 2 days / NR	Amoxicillin + Clavulanic Acid / 875+125mg / 12h-12h / 4 days / OR	NR	Placebo	-	NR

(Lodi et al., 2012) (Italy) Continued	18 (RCT)	2456	M,F	NR	NR	Benzylpenicillin / 300 mg + procaine penicillin 300mg / IM / 30 minutes before	-	NR	Placebo IM 30 min before	-	NR
						Azidocillin / 750mg / 1h before / NR / NR	Azidocillin / 750mg / 12h-12h / 7 days / NR	NR	Placebo	Placebo	NR
						Erythromycin / 500mg / 90 minutes before / NR or Clindamycin / 300mg / 90 minutes before / NR	Erythromycin / 250mg / 6h-6h / 7 days / NR or Clindamycin / 150mg / 6h-6h / 7 days / NR	NR	Placebo	Placebo	NR
						Doxycycline / 200mg / 180 minutes before / NR	Doxycycline / 100mg / 180 minutes before / once daily / 7 days / NR	NR	Placebo	Placebo	NR
						Phenoxmethylpenicillin / 800mg / 1h before / NR	Phenoxmethylpenicillin / 800 mg / 12h-12h / 7 days / NR	NR	Placebo 1h before	Placebo / 12h-12h / 7 days	NR
(Lodi et al., 2012) (Italy) Continued	18 (RCT)	2456	M,F	NR	NR	Azidocillin / 750mg / 1h before / NR	Azidocillin / 750mg / 12h-12h/ 7 days / NR	NR	Placebo 1h before	Placebo / 12h-12h / 7 days	NR
						-	Metronidazole / 400mg / 12h-12h / 3 days / NR	NR	-	Placebo / 12h-12h / 3 days / NR	NR
						-	Arnica 200 / 12h-12h / 3 days / NR	NR	-	Placebo / 12h-12h / 3 days / NR	NR
						Tinidazole / 500mg / 12h before / OR	-	NR	Placebo / 12h before / OR	-	NR
						Metronidazole / 400mg / 1h before / OR	Metronidazole / 400 mg / 8h-8h / 3 days / NR	NR	Placebo / 1h before / NR	Placebo / 8h-8h / NR	NR
						Phenoxmethylpenicillin / 660mg / 1h before / NR	Phenoxmethylpenicillin / 660mg / 8h-8h / 5 days / NR	NR	Placebo / 1h before / NR	Placebo / 8h-8h / 5 days / NR	NR
						Tinidazole / 500mg / 1h before / NR	Tinidazole / 500 mg / 8h-8h / 5 days / NR	NR	Placebo / 1h before / NR	Placebo / 8h-8h / 5 days / NR	NR
						Metronidazole / 1000mg / 30 minutes before / NR	-	NR	Placebo / 2 tablets / 30 minutes before	-	NR
						Amoxicillin / 1g / 1h before / OR	Amoxicillin / 1g / 6h after / NR / OR	NR	Placebo / 1h before / NR	Placebo / 6h after / NR	NR
						Metronidazole / 1 g / 1h before / OR	-	NR	Placebo	-	NR
						-	Metronidazole / 400mg / 8h-8h / 5 days	NR	-	Placebo	NR
						Metronidazole / 1600mg / single dose / 45 minutes before	-	NR	Placebo / single dose / 45 minutes before	-	NR
						-	Amoxicillin/clavulanic acid / 500/125mg / 8h-8h / 4 days / OR	NR	-	Placebo / 8h-8h / 4 days / OR	NR
(Lodi et al., 2012) (Italy)	18 (RCT)	2456	M,F	NR	NR	Solution of penicillin (15,000 units/kg) or, penicillin-allergic, clindamycin /600mg / 1h before / IVR	-	NR	Placebo (10cc saline 0.9%) / 1h before / IVR	-	NR

Continued						Clindamycin / 600mg / 1h before / OR	Clindamycin / 300mg / 8h-8h / 5 days / OR	NR	Placebo / 600mg / 1h before / OR	Placebo / 300mg / 8h-8h / 5 days / OR	NR
						Amoxicillin/clavulanate / 1000/62.5mg / 2 tablets / single dose / before / NR	Amoxicillin/clavulanate / 1000/62.5mg / 2 tablets / 12h-12h / 5 days / NR	NR	Placebo / 2000/125mg / 2 tablets / single dose / before / NR	Placebo / 2000/125mg / 12h-12h / 5 days / NR	NR
						-	Amoxicillin/clavulanate / 1000/62.5mg / 2 tablets / 12-12h / 5 days / NR	NR	Placebo / 2000/125mg / single dose / before / NR	Placebo / 2000/125mg / 12h-12h / 5 days / NR	NR
						Amoxicillin / 500mg / 2 tablets / 1h before / OR	-	NR	Placebo / 2 tablets / 1h before	-	NR
						Amoxicillin / 500mg / 4 tablets / 2h before / NR	-	NR	-	Placebo / 15 tablets / 8h-8h / 5 days / NR	NR
						-	-	NR	Placebo / 4 tablets / 2h before	Placebo / 15 tablets / 8h-8h / 5 days / NR	NR
						-	Amoxicillin / 500mg / 15 tablets / 8h-8h / 5 days / NR	NR	Placebo / 4 tablets / 2h before	-	NR
						Amoxicillin / 1g / 1h before / OR	-	NR	Placebo	-	NR
						Metronidazole / 800mg / 1 h before / OR	-	NR	Placebo	-	NR
(Menon et al., 2019) (China)	8 (RCT)	1242	M,F	NR	NR	Amoxicillin + Clavulanic Acid / 1g + 62.2mg / single dose / immediately before / NR	NR	1	Placebo	NR	1
						Amoxicillin / 1g / 1h before / single dose / OR	NR	1	Placebo	NR	1
						Amoxicillin / 1g / 1h before / single dose / OR	Amoxicillin / 500mg / 8h-8h / 2 days / OR	1	Placebo	Placebo	1
						Amoxicillin / 1g / 1h before / single dose / NR	NR	1	Placebo	NR	1
						Amoxicillin / 2g / 1h before / single dose / NR	NR	1	Placebo	NR	1
						NR	Amoxicillin / 500mg / 8h-8h / 5 days / NR	1	Placebo	Placebo	1
						Amoxicillin / 1g / 1h before / single dose / NR	NR	1	Placebo	NR	1
						Metronidazole / 800mg / 1h before / single dose / NR	NR	1	Placebo	NR	1
						NR	Amoxicillin / 500mg / 8h-8h / 7 days / OR	1	-	-	1
						NR	Clindamycin / 300mg / 6h-6h / 7 days / OR	1	-	-	1

						Amoxicillin + Clavulanic Acid / 2g + 125mg / 2h before / NR	Amoxicillin + Clavulanic Acid / 2g + 125mg / 12-12h / 4 days / NR	2	Placebo	Placebo		2
Mixed procedures: Dental implant, dental extraction, endodontic surgery												
(Moreno-Drada & García-Perdomo, 2016) (USA)	14 (RCT)	2063	M,F	NR	NR	Amoxicillin / NR / NR / NR / OR	-	NR	Placebo	-		NR
						Penicillin / NR / NR / NR / IVR Clindamycin / NR / NR / NR / IVR	-	NR	Placebo	-		NR
						Amoxicillin / NR / NR / NR /OR Clindamycin /NR / NR / NR /OR Moxifloxacin / NR / NR / NR /OR	-	NR	Placebo	-		NR
						Amoxicillin / NR / NR / NR / OR Clindamycin / NR / NR / NR / OR	-	NR	-	-		NR
						Amoxicillin / NR / NR / NR / OR Clindamycin / NR / NR / NR / Topic	-	NR	-	-		NR
						Penicillin V / NR / NR / NR / OR Erythromycin / NR / NR / NR / OR	-	NR	-	-		NR
						Teicoplanin / NR / NR / NR / IVR Amoxicillin / NR / NR / NR / IM	-	NR	-	-		NR
						Clindamycin / NR / NR / NR / OR	-	NR	Placebo	-		NR
Mixed procedures: Dental implant, dental extraction												
(Singh Gill et al., 2018) (UK)	7 (RCT)	1368	M,F	Adults	NRS	Amoxicillin / 2g / 1h before / single dose / OR	Amoxicillin / 2g / 24h-24h / 7 days / OR	3	Placebo	NR		NR
						Amoxicillin / 2g / 1h before / single dose / OR	-	4	Placebo	NR		NR
						Metronidazole / 1g / 1 hour before / single dose / OR	Metronidazole / 400mg / 6h-6h / 5 days / OR	NR	Placebo	NR		NR
						Amoxicillin + Moxifloxacin + Clindamycin / 2g + 400mg + 400mg / Preoperative / NR / NR	-	NR	Placebo	NR		NR
						Clindamycin / 600mg / NR / NR / NR	-	NR	Placebo	NR		NR
						Amoxicillin + Ac. Clavulanic / 2g + 0.125g / single dose / OR	Amoxicillin + Acid. Clavulanic / 2g + 0.125g / for 7 days / OR	NR	Placebo	NR		NR

M: male. F: female. NR: Not reported. NRS: No restriction on smoking. OR: oral route; IVR: intravenous route; IMR: intramuscular route; t: minimum follow-up time (in months); RCT: Randomized controlled trial. Source: Authors.

Table 4. Studies excluded during the full reading stage (n=28).

Author, year	Title	Reason for exclusion
Kim et al. 2020	Antibiotic prophylaxis for implant placement: systematic review of effects on reduction of implant failure.	1
Castro-Rodriguez et al. 2020	Eficacia de la profilaxis antibiótica en la prevención de infecciones posquirúrgicas la cirugía del tercer molar impactado.	4
Salgado-Peralvo et al. 2021	Preventive antibiotic therapy in bone augmentation procedures in oral implantology: A systematic review.	1
Li et al. 2019	Prophylactic antibiotics can prevent early implant failure, but postoperative antibiotics may not be beneficial for dental implant placement.	2
Abdallah MN 2017	Inconclusive evidence on using antibiotic prophylaxis before dental procedures to prevent infective endocarditis.	3
Blatt et al. 2019	A systematic review of latest evidence for antibiotic prophylaxis and therapy in oral and maxillofacial surgery.	1
Cahill et al. 2017	Antibiotic prophylaxis for infective endocarditis: a systematic review and meta-analysis.	4
Arteagoitia et al. 2002	Antibioterapia sistémica preventiva de la alveolitis seca en la exodoncia del tercer molar inferior: revisión sistemática.	3
Dayer et al. 2018.	Antibiotic prophylaxis for infective endocarditis: a systematic review and meta-analysis.	3
Ellervall et al. 2010	Antibiotic prophylaxis in oral healthcare - the agreement between Swedish recommendations and evidence.	3
Fernándes et al. 2018	Antimicrobial prophylaxis for transient bacteremia during dental procedures.	3
Hedström et al. 2007	Effect estimates and methodological quality of randomized controlled trials about prevention of alveolar osteitis following tooth extraction: a systematic review.	3
Hong et al. 2010	A systematic review of dental disease in patients undergoing cancer therapy.	3
Kreutzer et al. 2014.	Current evidence regarding prophylactic antibiotics in head and neck and maxillofacial surgery.	5
Löffler et al. 2017.	The effect of interventions aiming to optimise the prescription of antibiotics in dental care-A systematic review.	6
Marchionni et al. 2017	The effectiveness of systemic antibiotic prophylaxis in preventing local complications after tooth extraction. A systematic review.	3
Menon et al. 2019	Does the use of amoxicillin/amoxicillin–clavulanic acid in third molar surgery reduce the risk of postoperative infection? A systematic review with metaanalysis.	3
Mingot-Castellano et al. 2015.	Spanish consensus guidelines on prophylaxis with bypassing agents for surgery in patients with haemophilia and inhibitors.	3
Naimi-Akbar et al. 2018	Antibiotic prophylaxis in orthognathic surgery: A complex systematic review.	5
Oomens et al. 2014	Prescribing antibiotic prophylaxis in orthognathic surgery: A systematic review.	5
Park et al. 2018	Is there a consensus on antibiotic usage for dental implant placement in healthy patients?	1
Rademacher et al. 2017.	Antibiotic prophylaxis is not indicated prior to dental procedures for prevention of periprosthetic joint infections.	3
Arteagoitia et al. 2016	Efficacy of amoxicillin and amoxicillin/clavulanic acid in the prevention of infection and dry socket after third molar extraction. A systematic review and meta-analysis.	3
Robinson et al. 2017	Infective endocarditis - An update for dental surgeons.	3
Shridharani et al. 2013	The role of postoperative antibiotics in mandible fractures: A systematic review of the literature.	5
Tan et al. 2011	Perioperative antibiotic prophylaxis in orthognathic surgery: A systematic review and meta-analysis of clinical trials.	5
Tong et al. 2004	Antibiotic prophylaxis in dialysis patients undergoing invasive dental treatment.	3
Asenjo-Lobos et al 2015	Use of Antibiotics in Dental Implant Surgery: A Decision Based on Evidence from Systematic Review.	1

1- They did not use only clinical trials; 2- This is not a published study; 3- Lack of sufficient information in relation to the variables of interest; 4- Study population under the age of 18 years; 5- Hospital-level surgical procedures; 6- Use of antibiotics for therapeutic purposes. Source: Authors.

Most systematic reviews (80%) did not present conclusive results on the effectiveness and safety of SAP in the procedures performed in this population (Table 5). Eleven studies (M.-I. Arteagoitia et al., 2016; Ata-Ali et al., 2014; Braun et al., 2019; Canullo et al., 2020; Cervino et al., 2019; Chen et al., 2017; Esposito et al., 2008, 2010; Marín Escobar et al., 2013; Menon et al., 2019; Moreno-Drada & García-Perdomo, 2016; Singh Gill et al., 2018) presented low or critically low quality and four (Braun et al., 2019; Khouly et al., 2019; Lodi et al., 2012; Romandini et al., 2019) presented moderate methodological quality. According to the AMSTAR-2 tool in the item referred to the analysis of risk of bias, fourteen systematic review (M.-I. Arteagoitia et al., 2016; Ata-Ali et al., 2014; Braun et al., 2019; Canullo et al., 2020; Cervino et al., 2019; Chen et al., 2017; Esposito et al., 2008, 2010; Khouly et al., 2019; Lodi et al., 2012; Menon et al., 2019; Moreno-Drada & García-Perdomo, 2016; Romandini et al., 2019; Singh Gill et al., 2018) used the recommendations of the Cochrane Collaboration and one systematic review (Marín Escobar et al., 2013) did not report/did not carry out this analysis (Table 6).

Regarding the three studies with conclusive results, one (Lodi et al., 2012) showed a reduction in postoperative infections after dental extraction when the SAP was used, while the other study (Khouly et al., 2019) showed no differences in the incidence of postoperative infections after dental implant between the groups who used SAP and the other who did not use. The third study (Braun et al., 2019) did not assess the effectiveness of SAP use. These three studies assessed the safety of SAP use, and the first (Lodi et al., 2012) found evidence of a significant increase in the risk of adverse drug in the group using SAP. However, the other two studies (Braun et al., 2019; Khouly et al., 2019) found no differences in the safety of SAP use (Table 5). There was one study (Romandini et al., 2019) classified as moderate methodological quality, but did not present results about effectiveness and safety.

Table 5. Effectiveness and safety of prophylactic antibiotic after dental procedures in patients without underlying cardiac conditions (n = 15).

Author Year	Intervention	Control	Effectiveness RR (95% CI); p-value	Safety RR (95% IC); p-value	Methodological quality	Conclusion
Dental Implant						
(Ata-Ali et al., 2014)	Amoxicillin	-	1.091 (0.629-1.893); 0.754*	NR	Critically low	**Inconclusive** The quality of the study is not adequate for conclusions
(Braun et al., 2019)	Amoxicillin	Placebo	NR	1.00 (0.06-15.85); >0.99[#] 1.00 (0.06-15.85); 1.00	Moderate	**Inconclusive** There is not enough statistical data to certify effectiveness. **No evidence of safety** There was no significant difference between the intervention and control groups
(Canullo et al., 2020)	Amoxicillin	Placebo Antibiotic free	NR	NR	Low	**Inconclusive** There is insufficient statistical data to assess effectiveness and safety
(Chen et al., 2017)	Amoxicillin	Placebo	0.73 (0.39-1.35); 0.31	NR	Low	**Inconclusive** The quality of the study is not adequate for conclusions
(Esposito et al., 2008)	Amoxicillin	Placebo Antibiotic free	0.68 (0.12-3.92); NR	1.00 (0.06-15.85); NR	Low	**Inconclusive** The quality of the study is not adequate for conclusions
(Esposito et al., 2010)	Amoxicillin	Placebo	0.74 (0.37-1.47); 0.39	1.00 (0.06-15.85); 1.00	Low	**Inconclusive** The quality of the study is not adequate for conclusions
(Khouly et al., 2019)	Amoxicillin	Placebo	0.94 (0.54-1.62); 0.82[**] 1.05 (0.59-1.84); 0.88[**] 0.88 (0.05-15.28); 0.93[**] 0.60 (0.07-5.16); 0.64[**] 0.82 (0.41-1.62); 0.57[##] 1.49 (0.24-9.11); 0.66[##]	0.15 (0.01-2.93); 0.21	Moderate	**Not effective** There was no significant difference between the intervention and control groups
(Marín Escobar et al., 2013)	Amoxicillin, Amoxicillin + Clavulanic	Placebo	NR	NR	Low	**Inconclusive** There is not enough statistical data to certify effectiveness and safety

(Romandini et al., 2019)	Amoxicillin	Placebo Antibiotic free	NR	NR	Moderate	**Inconclusive** There is insufficient statistical data to assess effectiveness and safety
Dental extraction						
(M.-I. Arteagoitia et al., 2016)	Amoxicillin + Clavulanic Amoxicillin Metronidazole Clindamycin	Placebo Antibiotic free	0.350 (0.21-0.57); <0.001	1.188 (0.66-2.15); 0.567	Low	**Inconclusive** The quality of the study is not adequate for conclusions
(Cervino et al., 2019)	Amoxicillin + Clavulanic	Placebo	NR (NR); >0.05	NR (NR); >0.05	Low	**Inconclusive** The quality of the study is not adequate for conclusions
(Lodi et al., 2012)	Amoxicillin Amoxicillin + Clavulanic Azidocillin Clindamycin Doxycycline Erythromycin Metronidazole Penicillin Phenoxymethylpenicillin Tinidazole	Placebo	0.29 (0.16-0.50); <0.0001	1.98 (1.10-3.59); 0.02	Moderate	**Effective** Prevents postoperative infections **Not safe** Increases the risk of drug adverse effects
(Menon et al., 2019)	Amoxicillin Amoxicillin + Clavulanic	Placebo Antibiotic free	0.25(0.15-0.42); 0.001	Amoxicillin: 1.57(0.55-4.50); 0.405 Amoxicillin + Clavulanic: 4.12(1.16-7.50); 0.023	Low	**Inconclusive** The quality of the study is not adequate for conclusions
Mixed procedures: Dental implant, dental extraction and endodontic surgery						
(Moreno-Drada & García-Perdomo, 2016)	Amoxicillin Penicillin Clindamycin Moxifloxacin Penicillin V Erythromycin	Placebo Antibiotic free	0.49 (0.24-0.99); NR	NR	Low	**Inconclusive** The quality of the study is not adequate for conclusions
Mixed procedures: Dental implant, dental extraction						
(Singh Gill et al., 2018)	Amoxicillin Metronidazole Moxifloxacin Clindamycin	Placebo	NR	1.84 (0.59-5.77); 0.30	Low	**Inconclusive** The quality of the study is not adequate for conclusions

*: The measure of effect used was the odds ratio. **: The outcome was assessed in four intervention groups: All antibiotics vs Antibiotic free or placebo; Preoperative antibiotic vs Antibiotic free; pre- and postoperative antibiotics vs Antibiotic free; pre- and post-operative or post-operative antibiotic vs Antibiotic free. #: The outcome was evaluated in two intervention groups: All antibiotics vs Antibiotic free or placebo; preoperative antibiotic vs Antibiotic free or placebo. ##: The authors also divided into 2 groups according to the time of development of postoperative infection: Postoperative infection (one or two weeks) with all regimens of Antibiotics vs Antibiotic free or placebo; Postoperative infection (three or four months) with all regimens of Antibiotics vs Antibiotic free or placebo. NA: Not applicable NR: Not reported. Source: Authors.

Table 6. Methodological quality assessment by AMSTAR-2.

Items	Studies														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
1.Did the research questions and inclusion criteria for the review include the components of PICO? For Yes: - population - intervention - comparator group - outcome Optional (recommended): Timeframe for follow up	Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes	No	No	No	No	No	Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes
2.Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? For Partial Yes: - review question (s) - a search strategy - inclusion/exclusion criteria - a risk of bias assessment For Yes: As for partial yes, plus the protocol should be registered and should also have specified: - a meta-analysis/synthesis plan, if appropriate, and - a plan for investigating causes of heterogeneity - a plan for investigating causes of heterogeneity	Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes	No	No Yes Yes Yes Yes	No	No	Partial Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	No	Partial Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes
3.Did the review authors explain their selection of the study designs for inclusion in the review? For Yes, the review should satisfy ONE of the following: - Explanation for including only RCTs - OR Explanation for including only NRSI - OR Explanation for including both RCTs and NRSI	Yes Yes	No	Yes Yes	No	No	Yes Yes	No	Yes Yes	No	No	No	No	Yes Yes	No	No
4.Did the review authors use a comprehensive literature search strategy? For Partial Yes (all the following): - searched at least 2 databases (relevant to research question) - provided key word and/or search strategy - justified publication restrictions (e.g. language). For Yes, should also have (all the following): -searched the reference lists/ bibliographies of included studies searched trial/study registries - included/consulted content experts in the field - where relevant, searched for grey literature - conducted search within 24 months of completion of the review.	Partial yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes	Partial Yes Yes Yes	Partial Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes	No	Partial Yes Yes Yes Yes Yes	Partial Yes Yes Yes	Partial Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes	Partial Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes

Items	Studies														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
5. Did the review authors perform study selection in duplicate? For Yes, either ONE of the following: - at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include - OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.	Yes Yes	Yes Yes	Yes Yes	Yes Yes	Yes Yes	Yes	-	Yes Yes	Yes Yes	Yes Yes	Yes Yes	Yes Yes	-	Yes Yes	Yes Yes
6. Did the review authors perform data extraction in duplicate? For Yes, either ONE of the following: - at least two reviewers achieved consensus on which data to extract from included studies - OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.	Yes Yes	Yes Yes	Yes Yes	-	Yes Yes	Yes Yes	.	Yes Yes	Yes Yes	Yes Yes	Yes Yes	-	-	Yes Yes	Yes Yes
7. Did the review authors provide a list of excluded studies and justify the exclusions? For Partial Yes: provided a list of all potentially relevant studies that were read in full-text form but excluded from the review. For Yes, must also have: Justified the exclusion from the review of each potentially relevant study.	Yes Yes	Yes Yes Yes	Yes Yes Yes	Partial Yes Yes	No	No	No	Yes Yes	No	Yes Yes	Yes Yes	No	No	No	Yes Yes Yes
8. Did the review authors describe the included studies in adequate detail? For Partial Yes (ALL the following): - described populations - described interventions - described comparators - described outcomes - described research designs For Yes, should also have ALL the following: - described population in detail - described intervention in detail (including doses where relevant) - described comparator in detail (including doses where relevant) - described study's setting - timeframe for follow-up	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	No	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	Partial yes Yes Yes Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes Yes Yes Yes Yes	Partial Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes

Items	Studies														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? RCTs For Partial Yes, must have assessed RoB from -unconcealed allocation, and -lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality). For Yes, must also have assessed RoB from: - allocation sequence that was not truly random, and - selection of the reported result from among multiple measurements or analyses of a specified outcome. NRSI For Partial Yes, must have assessed RoB: - from confounding, and - from selection bias. For Yes, must also have assessed RoB: - methods used to ascertain exposures and outcomes, and - selection of the reported result from among multiple measurements or analyses of a specified outcome	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RCT- NRSI-	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Partial Yes Yes Yes NRSI -	RCT Partial Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RC Yes Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Partial Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes Yes NRSI 0
10. Did the review authors report on the sources of funding for the studies included in the review? For Yes: Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies.	Yes Yes	Yes Yes	Yes Yes	Yes Yes	No	Yes Yes	No	No	No	No	No	No	No	No	Yes Yes

Items	Studies														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? RCTs, For Yes: - The authors justified combining the data in a meta-analysis - AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present - AND investigated the causes of any heterogeneity. For NRSI, For Yes: - The authors justified combining the data in a meta-analysis - AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present - AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available - AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review.	RCT Yes Yes Yes Yes NRSI 0	RCT Yes NRSI Yes	RCT Yes Yes Yes NRSI 0	RCT Yes Yes Yes NRSI 0	RCT Yes Yes Yes NRSI 0	RCT Yes Yes Yes NRSI 0	RCT 0 NRSI -	RCT Yes Yes NRSI 0	RCT Yes Yes Yes Yes NRSI 0	RCT No NRSI -	RCT Yes Yes Yes Yes NRSI 0	RCT 0 NRSI -	RCT Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes NRSI 0	RCT Yes Yes Yes Yes NRSI 0
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? For Yes: - included only low risk of bias RCTs - OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.	Yes	No	Yes	No	No	No	0	No	No	No	No	0	No	No	No
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review? For Yes: - included only low risk of bias RCTs - OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results.	Yes Yes	Yes	Yes Yes	No	No	No	No	No	No	Yes Yes	No	No	No	No	Yes Yes

Items	Studies														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? For Yes: - There was no significant heterogeneity in the results - OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	Yes Yes	-	No	Yes Yes	No	Yes Yes	-	Yes Yes	Yes Yes	Yes Yes	Yes Yes	-	-	No	Yes Yes
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? For Yes: -performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	No	No	No	Yes Yes	No	No	0	No	No	No	Yes Yes	0	No	No	Yes Yes
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? For Yes: - The authors reported no competing interests OR - The authors described their funding sources and how they managed potential conflicts of interest.	No	Yes Yes	Yes	Yes Yes	Yes Yes	No	No	Yes Yes	No	Yes Yes	Yes Yes	Yes Yes	Yes Yes	Yes Yes Yes	Yes Yes Yes
Quality Review	Moderate	Moderate	Moderate	Low	Low	Low	Low	Critically low	Low	Low	Low	Low	Low	Low	Moderate

1: (Braun et al., 2019); 2: (Romandini et al., 2019); 3: (Khouly et al., 2019); 4: (Menon et al., 2019); 5: (Chen et al., 2017); 6: (Esposito et al., 2010); 7: (Marín Escobar et al., 2013); 8: (Ata-Ali et al., 2014); 9: (Moreno-Drada & García-Perdomo, 2016); 10: (Canullo et al., 2020); 11: (M.-I. Arteagoitia et al., 2016); 12: (Cervino et al., 2019); 13: (Singh Gill et al., 2018); 14: (Esposito et al., 2008); 15: (Lodi et al., 2012). Source: Authors.

The drugs used by these three studies were different: two of them (Braun et al., 2019; Khouly et al., 2019) assessed only amoxicillin; Lodi et al. (Lodi et al., 2012) assessed amoxicillin, amoxicillin/clavulanate, azidocillin, clindamycin, doxycycline, erythromycin, metronidazole, penicillin, Phenoxymethylpenicillin and tinidazole.

Among the 11 studies which presented inconclusive results due to low and critical low methodological quality, six (Ata-Ali et al., 2014; Cervino et al., 2019; Chen et al., 2017; Esposito et al., 2008, 2010; Moreno-Drada & García-Perdomo, 2016) showed no difference of postoperative infection and two (M.-I. Arteagoitia et al., 2016; Menon et al., 2019) presented a reduction in postoperative infection when the SAP was used. The other three studies (Canullo et al., 2020; Marín Escobar et al., 2013; Singh Gill et al., 2018) did not present reduction of postoperative infection as effectiveness outcome. Regarding the safety outcome, only one study (Menon et al., 2019) presented more adverse drug reactions in the group who used SAP (the antibiotic used was the amoxicillin + clavulanate). Five studies (Ata-Ali et al., 2014; Canullo et al., 2020; Chen et al., 2017; Marín Escobar et al., 2013; Moreno-Drada & García-Perdomo, 2016) did not present safety assessment of SAP use and five studies (M.-I. Arteagoitia et al., 2016; Cervino et al., 2019; Esposito et al., 2008, 2010; Singh Gill et al., 2018) showed differences that were not statistically significant.

The overlapping between studies was moderate (10.92%) (Table 7).

Table 7. Overlapping identified in the included studies (n=43).

	Systematic Reviews included														
Authors	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Abu-Ta ‘a et al. (2008)	X	X	X		X	X	X			X		X	X		
Anitua et al. (2009)	X	X	X		X		X	X			X	X	X		
Arduino et al. (2015)	X	X	X									X			
Caiazzo et al. (2011)	X	X	X			X					X	X	X		
El-Kholey et al. (2014)	X	X	X									X			
Esposito et al. (2008)	X	X	X		X	X	X			X		X	X		
Esposito et al. (2010)	X	X	X		X	X	X	X			X	X	X		
Moslemi et al. (2015)	X		X										X		
Nolan et al. (2014)	X	X	X					X				X	X		
Tan et al. (2014)		X	X										X		
Monaco et al. (2009)				X											
Luaces-Rey et al. (2010)				X											
Sidiqqi et al. (2010)				X					X					X	
Bezerra et al. (2011)				X				X	X					X	X
Adde et al. (2012)				X										X	
Sisalli et al. (2012)				X											
Duvall et al. (2013)				X				X							
Crincoli et al. (2014)				X											

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Arteogoitia et al. (2015)	X			X			X	
Milani et al. (2015)	X							
Xue et al. (2015)	X			X				
Braimah et al. (2017)	X							
Karakay et al. (2011)		X						
Halpern et al. (2007)			X					X
Diz Dios et al. (2006)			X		X			
Maharaj et al. (2012)			X					
Vergis et al. (2001)			X					
Josefsson et al. (1985)			X					
Hall et al. (1996)			X					
Lockhart et al. (2008)			X					
Shanson et al. (1987)			X					
Lindeboom et al. (2005)			X					
Arteogoitia et al. (2005)				X			X	X
Bortoluzzi et al. (2013)				X				
Bulut et al. (2001)				X				
Lacasa et al. (2007)				X	X		X	X
López-Cedrún et al. (2011)				X			X	X
Pasupathy et al. (2011)				X			X	X
Sekhar et al (2001)					X			X
Kaczmarzyk et al (2007)					X			X
Kashaini et al (2019)						X		
Barclay JK (1987)								X
Bergdahl et al (2004)								X
Bystedt et al (1980)								X
Bystedt et al (1981)								X
Happonen et al (1990)								X
Kaziro GS (1984)								X
Leon Arcila et al (2001)								X
MacGregor et al (1980)								X
Mitchell DA (1986)								X
Ritzau et al (1992)								X

1: (Romandini et al., 2019); 2: (Chen et al., 2017); 3: (Khouly et al., 2019); 4: (Cervino et al., 2019); 5: (Marín Escobar et al., 2013); 6: (Ata-Ali et al., 2014); 7: (Esposito et al., 2010); 8: (Moreno-Drada & García-Perdomo, 2016); 9: (M.-I. Arteagoitia et al., 2016); 10: (Esposito et al., 2008); 11: (Singh Gill et al., 2018); 12: (Braun et al., 2019); 13: (Canullo et al., 2020); 14: (Menon et al., 2019); 15: (Lodi et al., 2012). Source: Authors.

4. Discussion

Based on what has been verified in the literature, this is the first study that sought to collect evidence from different systematic reviews to prove whether there is effectiveness and safety in the use of SAP in patients without underlying cardiac conditions undergoing dental surgical procedures. The results could provide new perspectives for the clinical practice of dental surgeons and for the training of new professionals. However, the results obtained were not conclusive.

Among the 15 systematic reviews included in the study, in four (Braun et al., 2019; Khouly et al., 2019; Lodi et al., 2012; Romandini et al., 2019) the methodological quality was acceptable to warrant evidence regarding the effectiveness and safety of SAP. Studies of low and critically low methodological quality presented biases such as the lack of PICOS to structurer the question and organize the search strategy (Ata-Ali et al., 2014; Chen et al., 2017; Esposito et al., 2010; Marín Escobar et al., 2013; Moreno-Drada & García-Perdomo, 2016). It is noteworthy that these systematic reviews were published after 2010, when organizations like Cochrane began to recommend the use of this acronym to plan the search for information for evidence-based practice (Bernardo et al., 2004; Santos da Costa et al., 2007).

In four of the systematic reviews included (Canullo et al., 2020; Esposito et al., 2010; Marín Escobar et al., 2013; Menon et al., 2019), there was no mention of the elaboration of a study protocol prior to the beginning of the study. In four other reviews (M.-I. Arteagoitia et al., 2016; Ata-Ali et al., 2014; Cervino et al., 2019; Chen et al., 2017) superficially described the methodological protocol, which is fundamental in the development of a systematic review (Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors)., 2021).

Another fact that compromised the quality of the included studies was the lack of a comprehensive search in the selection stage. The search must be sensitive, transparent, and reproducible and performed in at least three databases, with the use of appropriately defined descriptors and keywords (de Luca Canto, 2020; Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors)., 2021). In addition to this main search, it is also necessary to have a manual search in the gray literature, in the reference list of the included studies and a consultation with specialists on the subject (de Luca Canto, 2020). Only four systematic reviews (Braun et al., 2019; Khouly et al., 2019; Lodi et al., 2012; Romandini et al., 2019) met these criteria. In addition, there were studies in which the data selection stage (Marín Escobar et al., 2013; Singh Gill et al., 2018) and data extraction (Cervino et al., 2019; Marín Escobar et al., 2013; Menon et al., 2019; Singh Gill et al., 2018) was not performed in duplicate.

The impact of the risk of bias was not considered in the result of the meta-analysis in 80% of the eleven studies that performed this analysis (M.-I. Arteagoitia et al., 2016; Ata-Ali et al., 2014; Canullo et al., 2020; Chen et al., 2017; Esposito et al., 2008, 2010; Lodi et al., 2012; Menon et al., 2019; Moreno-Drada & García-Perdomo, 2016; Romandini et al., 2019; Singh Gill et al., 2018). In addition, some authors did not explain the heterogeneity observed in the results of the review (Cervino et al., 2019; Chen et al., 2017; Esposito et al., 2008; Khouly et al., 2019; Marín Escobar et al., 2013; Romandini et al., 2019; Singh Gill et al., 2018). In addition to these questions, none of the included studies found information intrinsic to the surgical procedure, which could influence the analysis of effectiveness and safety. The experience and technical skills of the dental surgeon, although not always subject to control in an RCT, are examples of information missing in systematic reviews. Likewise, in none of them presented enough data on the strategies for controlling or analyzing possible biases resulting from the duration of the procedure, the type of procedure performed, the degree of tissue invasion and the compliance to the aseptic chain (Andrade, 2014; Cervino et al., 2019). The absence of this information and the methodological deficiencies found directly impact on the certainty of the evidence.

In specific surgical procedures, some late events may indirectly indicate problems in the effectiveness of SAP. In dental implant, for example, implant failures may be signs that the use of antibiotic prophylaxis was not satisfactory for the prevention of postoperative infections. In this sense, the researchers tried to verify whether it would be possible to estimate the effectiveness of SAP in implant reviews based on the failure report. However, in this process, another important factor makes it difficult to strengthen the evidence regarding the effectiveness in the use of antibiotics: the wide variation in the definition of implant failures found in the studies. Definitions of implant failure related to postoperative infections were found, such as the presence of signs of infection at the implant site (Canullo et al., 2020; Marín Escobar et al., 2013; Menon et al., 2019), radiolucencies perimplant radiographs that did not respond to a course of antibiotics (Ata-Ali et al., 2014; Braun et al., 2019; Chen et al., 2017). There were also definitions of implant failures that could be caused by other factors, such as periodontist judgment after flap surgery (Chen et al., 2017), evaluation by Osstell (Braun et al., 2019; Chen et al., 2017), removal of the implant after osseointegration failure (Ata-Ali et al., 2014; Braun et al., 2019; Chen et al., 2017), implant mobility measured manually (Ata-Ali et al., 2014; Braun et al., 2019; Chen et al., 2017). In addition, there were studies that did not even mention which parameter was used in the evaluation of implant failure (Esposito et al., 2008; Marín Escobar et al., 2013; Moreno-Drada & García-Perdomo, 2016; Romandini et al., 2019; Singh Gill et al., 2018).

In this sense, it is also worth noting the absence of information in systematic reviews on the strategies used in RCTs to control the oral hygiene variable. It is known that adequate oral hygiene before and after the procedure is essential to prevent postoperative infection. Experts recommend brushing your teeth and using mouthwashes with chlorhexidine 0.2% vigorously for one minute before the procedure and gently three times a day for seven days or until you remove the suture (Bryce et al., 2014; Palma et al., 2017). However, six systematic reviews (Ata-Ali et al., 2014; Chen et al., 2017; Marín Escobar et al., 2013; Moreno-Drada & García-Perdomo, 2016; Romandini et al., 2019; Singh Gill et al., 2018) did not mention whether there was this control or described the oral hygiene procedures adopted in the primary studies. Braun and colleagues (Braun et al., 2019), Esposito and colleagues (Esposito et al., 2008), Esposito and colleagues (Esposito et al., 2010) and Arteagoitia and colleagues (M.-I. Arteagoitia et al., 2016) described all oral hygiene measures; however, the procedures were different between the RCTs included.

The characteristics of the sample included in the RCTs, such as the presence of comorbidities (diabetes mellitus, immunosuppressive diseases), use of immunosuppressive medication, diagnosis of bruxism, smoking or age can also influence the outcomes under analysis (Do et al., 2020; Smeets et al., 2014). Therefore, it is important that these variables be controlled in RCTs, which in general was not observed in the studies. Chen and colleagues (Chen et al., 2017), Marín-Escobar and colleagues (Marín Escobar et al., 2013) and Ata-Ali and colleagues (Ata-Ali et al., 2014) did not present the characteristics of the population included in the RCTs. Singh Gill and colleagues (Singh Gill et al., 2018) reported that no RCT included immunosuppressed patients, children and the elderly. Braun and colleagues (Braun et al., 2019) described the characteristics of the patients included in the primary studies, but discussed the lack of information about the control of the smoking variable in the primary studies, assuming possible interference of the variable in the results found.

It should also be noted that the use of different drugs did not change the outcome of interest. Healthy patients generally have a low risk of postoperative infection when they obey the criteria of oral hygiene and adequate surgical technique. In addition, unnecessary or indiscriminate exposure to any medication increases the risk of adverse effects and the costs of the procedure or treatment (Mota et al., 2010).

Finally, it is important to highlight that overview of systematic reviews are robust instruments for health decision-making because they gather the best available evidence on a given subject. However, the overlap of primary studies in the included reviews may leave the result biased. In the present overview, the moderate classification of overlapping would be a suggestive factor of reanalysis of the data from reviews that did not have overlapping studies, thus minimizing bias. However,

as a way of just presenting and describing the current body of evidence on the topic, there would be no problem in maintaining the analysis considering the overlaps. As there were not a greater number of studies with results that pointed to the effectiveness or safety of SAP (or even the absence of these outcomes), the overlapping identified did not interfere with the result (Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors)., 2021; Pieper et al., 2014).

As limitations of the study, it is recognized that the heterogeneity of the data collected, especially in relation to the type of dental surgical procedure and the characteristics of the patients, may have hindered the analysis of effectiveness and safety. However, the overview of systematic reviews has intrinsic limitations such as the lack of access to the database of primary studies and the unavailability of information collection that is not included in the included systematic reviews. Even knowing this, it was decided to carry out this type of study because it represents the best level in the hierarchy of scientific evidence. In addition, it is worth mentioning that the evidence obtained in the included systematic reviews came from 51 RCTs.

5. Conclusion

The results are inconclusive to state that SAP is effective and safe for patients without underlying cardiac conditions undergoing dental surgical procedures. Most of the included studies did not present adequate methodology for the synthesis of evidence. Among those with moderate quality, important information was lacking for the analysis of defined outcomes. This coupled with the need to optimize the use of antibiotics due to resistance to antimicrobials suggests not using antibiotics as prophylaxis in patients without underlying cardiac conditions, at least in procedures like dental extraction, dental implant and endodontic surgery. Studies with better methodological quality in which the variables that increase the risk of implant failure (surgical technique, smoking, bruxism, use of immunomodulatory drugs and the presence of uncontrolled diabetes mellitus) are controlled are necessary for a subsequent measurement of the real effectiveness and safety of SAP. Therefore, we encourage researchers to carry out more studies in this area to improve the level of evidence of the accessible information to favor decision-making in health.

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