

# The Influence of Chlorhexidine Mouthwash Use on Post-Operative Infection Rate of Dental Implants- A Systematic Review

Faisal Abdullah AlShahrani<sup>1\*</sup>, Nawaf Sulaiman Alhussainan<sup>2</sup>, Saad Ahmed Al-Mofareh<sup>2</sup>, Nouf Zaid AlMeshari<sup>2</sup>, Sharifa Abdulwahab Amer<sup>3</sup>, Manal Faisal bin Sogaian<sup>4</sup>, Mohammed Saleh Alammash<sup>5</sup>, Mohammed Abdulkarim Alzahrani<sup>1</sup>

<sup>1</sup>Department of Prosthodontics, Prince Sultan Military Medical City, Riyadh, Saudi Arabia. <sup>2</sup>Department of Periodontics, Prince Sultan Military Medical City, Riyadh, Saudi Arabia. <sup>3</sup>Department of Periodontics, Assir Specialist Dental Center, Ministry of Health, Abha, Saudi Arabia. <sup>4</sup>Department of Restorative Dentistry, Prince Sultan Military Medical City, Riyadh, Saudi Arabia. <sup>5</sup>Department of Periodontics, Security Forces Hospital, Riyadh, Saudi Arabia.

## Abstract

Since its first introduction, the usage of chlorhexidine has increased. The same holds for dental implants. Implant failures can happen, even with the stated high survival rates of implants. This systematic review's objective. This systematic study aims to assess how often post-operative infections and early implant failures may be prevented by using a chlorhexidine peri-operative rinse. The materials and techniques included a manual search of significant journals and reference lists of relevant publications and an electronic search of the literature using predetermined search parameters at specific databases (CENTRAL, Medline, Embase, Web of Science, Scopus, ScienceDirect). After duplicates were eliminated, the 251 records found during the search were reduced to 108. Eleven full-text papers were acquired after titles and abstracts were screened. For this systematic review, one article met the eligibility requirements. There were 595 individuals in the population; 325 (the Treatment group) received a mouthwash containing 0.12% chlorhexidine prior to implant insertion surgery, whereas the Control group (325) received no peri-operative rinse. 5.8% of the treatment group and 9.3% of the control group had infectious problems. When chlorhexidine was utilized as a peri-operative rinse, the chance of infection problems after implant insertion was shown to be 36% lower, with a calculated relative risk of 0.63. In summary, very little evidence suggests that using a mouthwash containing chlorhexidine before surgery would lower the chance of infection after surgery. To enable the development of compelling recommendations based on evidence, further study in this area is required.

**Keywords:** Chlorhexidine mouthwash, Dental implant, Submerged healing, Post-operative infections

## INTRODUCTION

When researchers at Manchester's Imperial Chemical Industries were working to create anti-malarial medications in the 1940s, chlorhexidine was first created [1-3]. 1954 saw the confirmation of chlorhexidine's very wide antibacterial effects just before the drug's commercial launch in the UK as a topical antiseptic and disinfectant. Chlorhexidine was not originally brought to the US until the 1970s, which was a few years before its potential benefits for oral usage were first recognized in 1976 [4, 5]. According to research by Loe *et al.*, washing twice a day with a 0.2% chlorhexidine solution prevented gingivitis and plaque renewal in the absence of brushing. It has now evolved into the industry benchmark by which other antiplaque products are evaluated [6].

With a broad range of antibacterial action, little toxicity, and a high binding affinity to skin and mucous membranes, chlorhexidine is a cationic bisbiguanide antiseptic [7, 8]. It is effective against both gram-positive and gram-negative bacteria, certain viruses, and fungi, which has a membrane-

active antibacterial action [9, 10]. The substantivity of chlorhexidine has been linked to its antiplaque action [7, 9]. It can adhere to negatively charged bacterial walls and oral surfaces, including mucosa, saliva, teeth, and acquired pellicle. Saliva has been shown to have antibacterial action for up to 5 hours after intraoral chlorhexidine rinse 10 and to have salivary bacterial counts decreased for more than 12

**Address for correspondence:** Faisal Abdullah AlShahrani, Department of Prosthodontics, Prince Sultan Military Medical City, Riyadh, Saudi Arabia. F.AlShahrani@live.co.uk

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**How to cite this article:** AlShahrani FA, Alhussainan NS, Al-Mofareh SA, AlMeshari NZ, Amer SA, Sogaian MFB, et al. The Influence of Chlorhexidine Mouthwash Use on Post-Operative Infection Rate of Dental Implants- A Systematic Review. Arch Pharm Pract. 2023;14(3):112-24. <https://doi.org/10.51847/bcuSxILGy8>

hours [11].

Chlorhexidine has been recommended for usage in a number of clinical circumstances. It is used in general surgery to prevent post-operative sepsis in both the patient and the surgeon [12]. On the other hand, mouthwash containing chlorhexidine has been suggested in dentistry as a supportive measure for maintaining gingival health [13]. Numerous studies have shown that it is useful as a pre-or post-operative rinse to prevent alveolar osteitis after tooth extraction [13-18]. It has been shown that using mouthwash containing chlorhexidine is an efficient way to support dental health and lessen gingival irritation [19]. Its antiplaque qualities are relevant to this. Research has shown that the prevention of plaque development promotes quicker and less complicated healing of periodontal and peri-implant lesions [20-26]. Based on these rationales, several dentists recommend using chlorhexidine prior to implant implantation surgery.

Dental implants have been more popular as a means of replacing lost teeth ever since they were first introduced. Nowadays, implant placement is regarded as standard care in the restoration of both fully and partly dentured jaws [27]. Dental implants are predicted to have a high success rate; reports of survival rates range from 90% to 95% [28]. Failures can happen, however, and neither patients nor experts are usually particularly good at tolerating these setbacks and problems [29, 30]. Despite the many treatment options available, if an infection has formed around an implant, it is often necessary to remove the infected implant ultimately [29, 31]. A potential cause of infection and early failure associated with implants is bacterial contamination during insertion [32, 33] which is connected to the level of a sepsis during implant placement operations.

The main reason for doing this systematic review was the lack of agreement among experts about the use of mouthwash containing chlorhexidine during implant placement surgery to minimize post-operative problems and early implant failures. In order to provide evidence-based recommendations on existing practices and the peri-operative use of chlorhexidine mouthwash during implant placement surgery, analysis of the available data and evaluation of its quality is crucial.

### Objectives

This systematic review's objective The purpose of this systematic review is to evaluate the impact of using a mouthwash containing chlorhexidine prior to surgery on the incidence of infection problems after implant insertion and early implant failure. Failure of an implant to achieve osseointegration is known as early implant failure; this might occur before prosthesis loading or after a suitable amount of healing time after implant surgery [29].

In this research, the peri-operative phase lasts for two weeks, starting just before the implant placement procedure.

## MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) shall be adhered to in this systematic review [34, 35]. The PICO framework (Population, Intervention, Comparison, and Outcome) was used to develop the search approach [36, 37].

### Criteria for Selecting Studies for this Review

#### Types of Studies

All controlled clinical trials, randomized controlled trials, and comparative studies evaluating the impact of using a peri-operative Chlorhexidine mouthwash during implant placement surgery on the rates of i) Implant failure prior to prosthetic loading and ii) Infection related to implant placement comprise the target sample for this systematic review.

#### Participant Types

Patients under general anesthesia or local anesthesia with or without sedation who had dental implant installation surgery, regardless of age or gender. Included will be studies with submerged insertion using any root form implant method.

Patients with diabetes, immunocompromised or immunosuppressed states, bacterial endocarditis risk, radiation treatment history with the implant site in the field, and rapid prosthetic loading on implants will not be included in this study.

#### Intervention Types

Studies that have assessed the effectiveness of using chlorhexidine mouthwash during the peri-operative period, regardless of the dosage, are necessary to avoid post-operative infections or dental implant failure after implant insertion surgery and before prosthesis loading. Studies must include a control group that receives no therapy at all or a placebo.

The term "peri-operative use" in this study refers to using chlorhexidine mouthwash at any concentration as part of a routine, either just before implant insertion surgery or for two weeks after implant surgery.

Studies that do not contain a no-treatment or placebo group will be eliminated from comparisons comparing the peri-operative usage of chlorhexidine mouthwash to other formulations of the drug, antiseptic mouthwashes, or antibiotics.

#### Different Kinds of Result Measurements

- Infections that occur post-operatively, such as osteomyelitis, infections of the soft tissue around the implant(s) and extra-orally, and any other subsequent systemic infections linked to implant placement. Reporting must occur during the healing phase after implant implantation surgery and before prosthesis

loading.

- Implant mobility or any implant that has to be removed because of discomfort, infection, or gradual marginal hard and soft tissue loss is referred to as implant failure prior to prosthetic loading.

Results measured at clinically significant intervals must be included in the studies taken into consideration for this evaluation. This would occur upon surgical exposure of implants after a minimum of three months of recovery and during post-operative follow-up within two weeks of implant placement.

### *Techniques for Finding Research Via Searches*

To find the papers that will be included in or taken into consideration for this review, comprehensive search procedures were created. The search phrases used were descriptive terms for every PICO element, which included implant placement, surgery, post-operative infection, loss of the implant, and failure of the implant. The following search parameters will be used to restrict results: controlled trials, randomized, randomized controlled trials, and humans.

Originally designed to search PubMed/Medline, the search method included phrases from regulated vocabulary and free text that Boolean operators linked [36]. It will be adjusted appropriately for every other database that is searched.

The Cochrane Handbook for Systematic Reviews of Interventions 5.1 describes how to modify and apply the Cochrane Highly Sensitive Search Strategy (CHSSS) for finding randomized, randomized controlled trials and controlled clinical trials where necessary [38].

### *Electronic Searches*

Up to June 30, 2023, the following electronic databases will be searched: PubMed/Medline; The Cochrane Central Register of Controlled Clinical Clinical (CENTRAL); Web of Science, ScienceDirect, EMBASE, and Scopus

The included research will not be restricted based on language, publication year, or status.

Furthermore, up to Jun 30, 2023, the following registries will be examined for any active studies:

- The National Library of Medicine and the US National Institutes of Health manage the Ongoing Trials Register (ClinicalTrials.gov).
- The World Health Organization International Clinical Trials Registry Platform (apps.who.int/trial search/); The EU Clinical Trials registration (clinical trials registration. eu/ctr-search); The International Prospective Register of Systematic Reviews (PROSPERO);

### *Other Resources*

This research will include hand-searching conducted as a component of the Cochrane Worldwide Hand-searching

Programme, which is accessible on CENTRAL. Furthermore, the following journals were found to be very relevant to this study; in cases where the Cochrane Oral Health Group has not yet hand-searched them, they will be done so until June 2023: Journal of Prosthetic Dentistry, International Journal of Prosthodontics, British Journal of Oral and Maxillofacial Surgery, Journal of Oral and Maxillofacial Surgery, International Journal of Oral and Maxillofacial Implants, International Journal of Oral and Maxillofacial Surgery, Journal of Oral Implantology, European Journal of Oral Implantology, Implant Dentistry, Journal of Clinical Periodontology, Journal of Periodontology, Clinical implant Dentistry and Related Research, Clinical Oral Implants Research, Journal of Dental Research, International Journal of Periodontics and Restorative Dentistry.

We will examine the reference lists of the publications we obtained and pertinent review articles to find any further trials that were not in the databases we searched. To find out about any current or unpublished studies, personal connections and the authors of the identified RCTs will be contacted. We will do more manual searches on Google Scholar.

### *Data Gathering and Analysis: Study Selection*

All recognized papers will have their titles and abstracts, where available, screened after duplicates have been removed. When the article is judged relevant or when the title and abstract do not provide enough information to verify that they meet the inclusion requirements, full-text copies will be acquired. My academic supervisor will be consulted if there is any doubt about whether any research may be included or not. Research that does not meet the criteria for inclusion in this review will be disregarded either now or in the future.

### *Extraction and Handling of Data*

The necessary data will be gathered from the selected articles using specially created data collection spreadsheet(**Table 4**). When more information is needed or clarification is needed, the authors will be notified.

The following information will be taken out for each trial:

1. Author(s), publishing year, nation of origin, and funding source
2. Trial procedures: (i) allocation strategy; (ii) participant and operator blinding; (iii) blinding outcome measures.
3. Participants: (i) age; (ii) sample size and calculation; (iii) nationality and ethnicity; (iv) inclusion and exclusion criteria.
4. Interventional details.
5. Outcomes: information on the stated results, such as the date and technique of assessment.

### *Evaluation of the Listed Studies' Bias Risk*

The Cochrane risk of bias tool, which is detailed in Chapter

8 of the Cochrane Handbook for Systematic Reviews of Interventions, will be used to evaluate the risk of bias in the studies that have been determined to be appropriate for inclusion in this review [37, 38].

A critical assessment instrument that has been specifically created will be used to evaluate each experiment [39]. The degree of bias risk for each of the following domains will be judged:

1. Bias in selection: (i) creation of sequences; (ii) allocation and concealment.
2. Performance bias: Participant and staff blinding.
3. Blinding result assessment: Detection bias.
4. Completeness of outcome data: Attrition bias.
5. Selective outcome reporting: A reporting bias.
6. Bias from other sources.

The whole risk of bias evaluation will be completed without hiding any information about the study's authors, organizations, or journal type from the assessor. When doing the risk assessment, I shall discuss any doubts with my academic supervisor. The evaluation's findings will classify the evaluated research in the following ways [37]:

- **Low Risk of Bias:** Every important domain was deemed to have a low risk of bias, meaning that a plausible bias was unlikely to change the findings materially.
- One or more domains are deemed to be at uncertain risk of bias (plausible bias that casts doubt on the findings).
- **High Risk of Bias:** one or more domains are deemed to be at high risk of bias (plausible bias that significantly reduces the confidence in the findings).

Furthermore, GRADE40—an acronym for Grading of Recommendations, Assessment, Development, and Evaluation—will be finished. Randomized controlled trials will be ranked highly using GRADE, whereas observational research will be ranked poorly. These ratings will then be improved or reduced based on further evaluation of certain characteristics [40-42]. The ultimate assessment of the evidence's quality will be as follows (**Table 1**).

**Table 1. Description of GRADE [40]**

Final Grade	Description
High ⊕⊕⊕⊕	It is very unlikely that further research will alter our level of confidence in the impact estimate.
Moderate ⊕⊕⊕○	Our level of confidence in the effect estimate is likely to be significantly impacted by further study, which might also alter the estimate.
Low ⊕⊕○○	Our confidence in the estimate of effect will likely be significantly impacted by further study, which will also modify the estimate.
Very Low ⊕○○○	Regarding the impact estimate, we have yet to learn.

Additional quality assessment will be carried out by verifying whether or not a sample size calculation was done, evaluating how clearly the inclusion and exclusion criteria were defined, evaluating the comparability of the treatment and control groups at enrolment, and determining whether or not the established study protocol has been followed.

### Metrics Evaluating the Impact of Therapy

The effectiveness of using mouthwash containing chlorhexidine before implant insertion surgery will be determined by comparing the rates of post-operative infections and implant early failures between the treatment and control groups.

When dealing with binary outcomes, the impact of the intervention will be estimated, represented as a Relative Risk, and the Reduction in Relative Risk (%) of the outcomes will be computed as a consequence of the intervention. In the case of continuous outcomes, mean differences and 95% confidence intervals will be utilized to summarize the data for each group based on the mean difference and standard deviations.

### The Subject of Analytic Problems

The patient and the implant will be the two units of analysis in this evaluation.

### Handling Incomplete Data

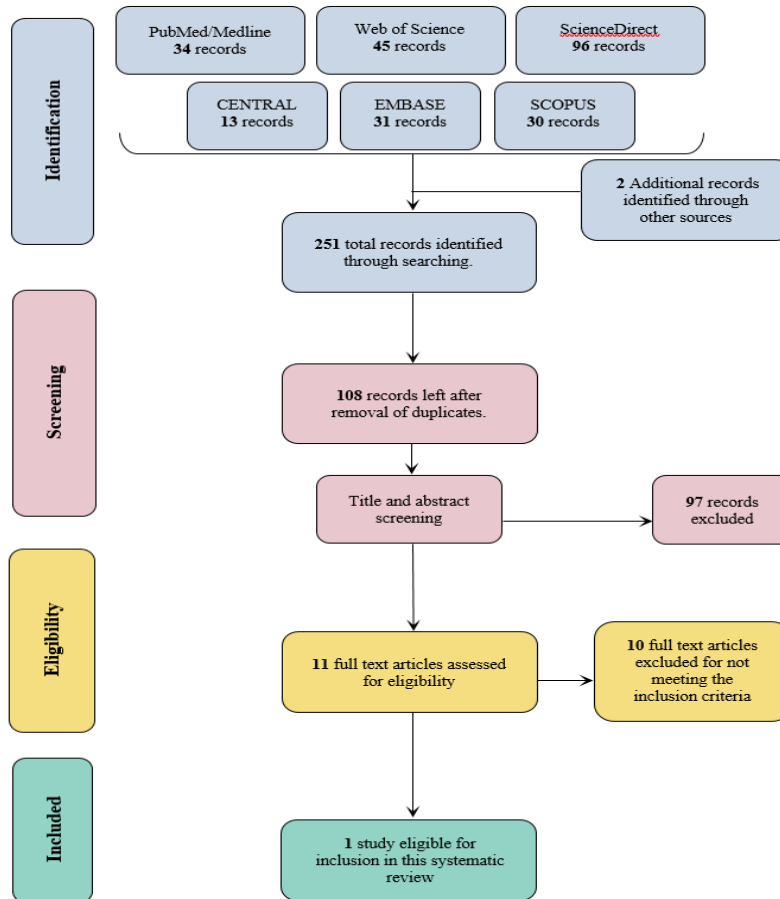
Any missing data from trials that are considered eligible or possibly eligible for inclusion in this research will be contacted by the authors.

### Evaluation of Heterogeneity

The assessment of clinical heterogeneity will be conducted by a comparative analysis of the attributes of the studies that meet the inclusion criteria for this review. We will compare PICO component similarities as stated in the included studies' criteria. Medical Both the methodological and clinical variety of the included research will be assessed. If enough papers are found that meet the criteria for inclusion and statistical analysis, and if the necessary expert assistance is available, further statistical analysis of heterogeneity and, if feasible, a meta-analysis will be carried out.

## RESULTS AND DISCUSSION

### Search Results



**Figure 1.** Study Flow Diagram

Two hundred fifty-one references to papers that fit the search parameters were found after the electronic search and further searches were finished. The diagram of the research flow is shown in **Figure 1**. After removing duplicate entries, 108 records were left.

After that, the remaining references were screened for titles and abstracts; publications that blatantly failed to satisfy the inclusion requirements were excluded. The 11 remaining papers that were judged obviously eligible or maybe eligible for inclusion in this study were acquired and subjected to further evaluation. Full-text copies of these publications were obtained [41-51].

To find any research that could be suitable for inclusion in this review, the bibliographical references of all possibly eligible studies and any linked papers were also looked through.

### Excluded Studies

Eleven potentially suitable studies were examined in their entirety but were not included in this evaluation for the following reasons:

- Absence of a placebo or "no treatment" group [42-44, 46].

- Inaccurate comparisons, interventions, or other inclusion requirements [45, 47-51].

### Included Research

There was just one research that qualified for this review's inclusion [42]. The sole research that met the requirements for this systematic review was this one, which assessed the impact of peri-operative chlorhexidine rinse on the frequency of post-operative problems and implant success. The following were the features of the included study:

#### Features of the trial environment and the investigators

0.12% Chlorhexidine Digluconate Rinses' Effect on Implant Success and Infectious Complication Rates 41 was a participant in a lengthy, prospective, multidisciplinary, randomized, multicenter trial that looked at how implant application, design, and insertion site affected crestal bone height and clinical outcome [51]. This research was one of the biggest of its type carried out in the United States of America and was carried out by the Dental Implant Clinical Research Group (DICRG) [51].

Conventional techniques were used to compute the sample size [52]. The calculation for a single percentage utilized a

one-tail test with  $\alpha = 5\%$  and a power of 90%, along with a predicted dropout of 10%. After this computation, a sample size of 300 cases was obtained, with 60 instances for each of the therapy groups mentioned in the participant characteristics section below.

The investigation was carried out in 32 geographically dispersed places under carefully monitored circumstances. These included two dentistry schools and thirty Department of Veterans Affairs (DVA) Medical Centers. Nearly 90% of the investigators had advanced specialist training, and all had expertise in clinical care and research. They included instructors from seven US dentistry schools (Temple University, University of Alabama at Birmingham, Indiana University, New York University, University of Michigan, University of Pittsburgh, Medical College of Virginia, and University of Michigan) as well as clinicians and researchers from the DVA.

An unbiased group of globally renowned scholars oversaw the examination. DICRG has published several publications since the start of this project in 1991 [41, 52-70].

### Characteristics of the Participants

The population was made up of 595 patients, the majority of whom were male Caucasians ranging in age from 20 to over 80.

**Groups:** 35 patients in the 20–29 age range, 36 patients in the 30-39 age range, 88 patients in the 40–49 age range, 74 patients in the 50–59 age range, 150 patients in the 60–69 age range, 94 patients in the 70–79 age range, and 3 patients in the 80+ age range.

**Ethnicity:** 378 White (Caucasians), 64 African American, 24 Hispanic, 8 Asian, and 3 Native American are among the ethnic groups represented. 244 individuals had a healthy American Society of Anesthesiology (ASA) rating, 226 had a moderate degree of systemic illness, and 9 had a severe type.

### Inclusion Criteria

- Patients are required to fall into one of five treatment categories: partial maxilla, partial mandible, partial posterior maxilla, partial anterior maxilla, and partial edentulous mandible.
- Tolerable at-home dental treatment.
- Qualified for care at any of the 1 million+ participating facilities around the country.

### Exclusion Criteria

Any of the following health issues or dental issues:

#### 1. Limiting Circumstances on Life Expectancy

- a. Acute illnesses
- b. Immunocompromised conditions
- c. Leukemia

- d. Disorders involving collagen (such as lupus erythematosus, scleroderma, etc.).
- e. A compromised state of health

#### 2. Medical Disorders That Could Make Demanding Dental Care Unsafe for the Individual Receiving Treatment or the Dentist

Insulin-dependent diabetes, long-term steroid treatment, radiation therapy to a possible implant site, anticoagulants, viral hepatitis, hemodialysis, severely mentally disturbed patients, heart surgery within the previous six months, and chronic nephritis are among the conditions that might be included.

#### 3. Health, Psychological, and Behavioral Traits That Reduce the Value of Therapy for the Patient or the Evaluation of Treatment Outcomes

The following conditions must be met

- a. extreme physical disability that impairs manual dexterity
- b. mental incompetence
- c. substance misuse
- d. excessive, unreasonable expectations of function and beauty
- e. poor motivation
- f. metabolic abnormalities
- g. severely being overweight or underweight.

#### 4. Dental Problems

- a. Inadequate oral hygiene
- b. Acute necrotizing ulcerative gingivitis
- c. Disorders of the temporomandibular joint
- d. Bruxism
- e. Jaw or facial pain
- f. Numbness or prickling feeling in the mouth
- g. Any infections in the mouth
- h. Background of facial or jaw fractures

#### Features that Make Up the Interventions

Pre-operative mouthwash with chlorhexidine as opposed to no pre-operative rinse.

- **Group Receiving Treatment:** Chlorhexidine digluconate 0.12% (Peridex, Proctor & Gamble, Cincinnati, OH) rinsed in the mouth both before and for two weeks after implant implantation.
- **Control Group:** Mouthwash was not used.
- **Qualities of the Result Measures**
- **Infection After Surgery:** The included research discussed "infectious complications." This group included the following conditions: "acute osteomyelitis," "chronic osteomyelitis," "persistent febrile condition," "peri-implant infection," "systematic infection secondary to implant," and "infection of soft tissue extra-orally."
- With the exception of one case that included

microbiological testing, all reports of infectious complications were based only on clinical judgment. The information was entered into standardized data-collecting forms on the day of implant placement, at the time of suture removal (5-7 days later), throughout the healing phase (4-6 months), and at implant exposure.

- **Implant Failure Prior to Prosthetic Loading:** While implant failure was reported in this trial, the data presented did not allow the evaluation of the intervention's impact on this outcome as required by the protocol for this review. The information supplied demonstrates how the existence of infectious complications impacts the frequency of implant failure to integrate. All patients with infectious problems from the "treatment" and "control" groups were included in this pooled data set; implant failure rates for each group were not examined or specified.

### Risk of Bias of the Included Study

Summary of risk of bias assessment: Lambert *et al.* 1997

- Random sequence generation (Selection bias)
- Allocation concealment (Selection bias)
- Blinding of participants and personnel (Performance bias)
- Blinding of outcome assessment (Detection bias)
- Incomplete outcome data (Attrition bias)
- Selective reporting (Reporting bias)
- Other bias

For research to be included in this category, all domains have to be judged to have a low risk of bias. The study's overall risk of bias will correspond with the degree of bias that was determined to be uncertain or high in any one of the evaluated areas.

The results of the included study were subjected to a risk of bias evaluation, and the overall risk of bias was determined to be High. The following are additional information for each of the evaluated domains:

**Allocations:** The purpose of the first study[53], which started the data gathering procedure, was to look into how implant application, design, and implantation site affected crestal bone height and clinical success. In order to randomly assign patients to each of the therapy groups, a computer-generated assignment was used in this research design. Additionally, there is proof of allocation concealment.

Nevertheless, there was no proof that patients had been randomly assigned to the designated "treatment" and "control" groups, as stated in the research that was part of this analysis [42]. The clinician's choice and practice pattern determined which patients were placed in which groups.

The patients in the "treatment" group were those seen by doctors who regularly administer peri-operative chlorhexidine rinse. In contrast, the patients in the "control" group were seen by doctors who do not usually provide chlorhexidine mouthwash. As a result, bias in allocation risk is deemed significant.

**Blinding:** Regarding the procedures detailed in the included trial, there was no indication that the patients or researchers were concealed. Nevertheless, this study's outcome assessment was blinded as, at the time of data collection, the researchers needed to be made aware of the treatments or study outcome measures that would be evaluated. There is proof that the risk of detection bias is minimal, and the danger of performance bias is significant.

**Incomplete Outcome Data:** The final analysis included all patients who started the trial and finished it. No significant adverse events, treatment withdrawals, trial group changes, or losses to follow-up occurred. Minimal chance of attrition bias.

**Selective Reporting:** There currently needs to be proven statistical techniques to identify selective reporting in research studies [37]. The findings presented in the results section were compared with the outcomes mentioned in the technique part of the included study. Furthermore, the published report was checked with the procedure that was retrieved. Despite this, there were no differences between the findings presented in the results section and the results given in the study's methodology. Not all of the results were included in the original protocol of the research.

Furthermore, the results for the outcome measure "implant failure" compared all patients with infectious complications to all other patients, irrespective of the allocation to a treatment group, rather than classifying the patients into "treatment" and "control" groups. It was not disclosed how many patients in the therapy or control groups eventually had an implant failure. For further information, we got in touch with the writers. It is uncertain whether reporting bias is a danger.

**Additional Possible Causes of Bias:** There is evidence that the original procedure needed to be followed in this research. The original protocol did not contain the interventions that are the subject of this research. Furthermore, it is said that the first guideline suggested that patients undergoing dental implants be given a prescription for Chlorhexidine mouthwash two weeks after the procedure and just before the implant installation procedure. According to the research, practitioners' individual "practice pattern" ultimately determines whether or not to administer chlorhexidine.

The protocols of this research contained a number of co-interventions, the effects of which were not explained by the

study's conclusions. Pre-operative antibiotic usage, which was given to a few of the patients included, is one instance of that. While the authors mentioned in passing how using peri-operative antibiotics affected the results in comparison to using chlorhexidine mouthwash, they did not go into detail about the precise number of patients or group assignment.

Core-Vent Bioengineering and the Department of Veterans Affairs contributed the majority of the funding for this research. Johnson & Johnson Professional Dental Care, Lactona Corporation, Oral-B Laboratories, Bio-Research/Siemens, Dentsply/Core-Vent Division, J.F. Jelenko & Company, Bausch & Lomb Oral Care Division, and Procter & Gamble Health and Personal Care Division also gave secondary assistance. Before the publishing, these sponsors were not subject to any data.

The quality of the evidence was deemed GRADE⓪OOO. (Table 1).

*Effects of Interventions*  
*Chlorhexidine Versus Placebo or No Treatment*

The included experiment contrasted using mouthwash containing 0.12% Chlorhexidine digluconate before implant implantation surgery (treatment group) with not using mouthwash before surgery (control group).

2,641 implants and 595 patients in total were involved in the research. There were 325 patients (1,387 implants) in the treatment group and 270 individuals (1254 implants) in the control group. By the time the research was over, every patient was registered.

**Table 2.** Patients with infection complications

	Infection (%)	No infection	Total
Treatment	19 (5.8)	306	325
Control	25 (9.3)	245	270
Total	44	551	595

**Table 3.** Implants with infection complications

	Infection (%)	No infection	Total
Treatment	57 (4.1)	1,330	1,387
Control	109 (8.7)	1,145	1,254
Total	166	2,475	2,641

*Post-Operative Infection (Implants)*

Infectious problems were documented in 166 implants overall after the implant insertion procedure. Out of these implants, 109 belonged to the control group, and 57 belonged to the treatment group. The study's findings revealed that the control group's 8.7% of implants had infectious problems more than twice as often as the treatment group's 4.1% (Table 3).

These findings showed that using chlorhexidine mouthwash perioperatively significantly reduced the risk of infection problems surrounding implants (P=0.001). The computed relative risk was 0.49. When chlorhexidine is given perioperatively, there is a 51% decrease in the relative chance of an infectious complication developing in a submerged implant.

*Post-Operative Infection (Patients)*

Infectious problems were observed in 166 cases. There were 25 patients in the control group and 19 patients in the therapy group (Table 2). In the treatment group, the rate of infectious complications was 5.8%, but in the control group, it was 9.3% (P=0.397).

Further analysis of these findings revealed that there was no change in the incidence of infectious complications between the treatment and control groups (7.09% and 7.29%, respectively) when pre-operative antibiotics were taken. On the other hand, the incidence of infection complications was 14.62% in the control group and 8.29% in the treatment group when pre-operative antibiotics were not given. This showed that there was a significant difference (p=0.001) between the two groups.

When chlorhexidine is taken perioperatively, the likelihood of a patient experiencing an infectious complication associated with a submerged implant is reduced by 36%, with a relative risk of 0.63.

*Implant Failure Before Prosthetic Loading*

According to the review procedure, the included research failed to provide the data needed to analyze this outcome measure. The impact of infectious complications on implant integration failure was evaluated in this research, independent of the usage of mouthwash containing chlorhexidine. It was shown that there was a higher chance of the implant failing to osseointegrate when there was an infection problem after surgery.



**Table 4.** Data collection spreadsheet.

Authors	Year	Country	Funding	Allocation	Blinding Operators and Participants	Blinding Outcomes	Nationality/Ethnicity of participants	Samples size/ Calculation	Age	Criteria	Intervention	Outcomes
Lambert <i>et al.</i>	1997	United States	financed by both public and commercial entities, although data access is restricted before publication	Clinician's routine practices	No	Yes	Americans, mostly Caucasians	595 / sample size calculation done	20-80 years old	Patients with certain health problems and dental issues that might raise their risk of infection, etc., were excluded.	Mouthwash with 0.12% chlorhexidine (Treatment) compared to no mouthwash (Control)	- 4.1% of the treatment group and 8.7% of the control group had an infectious implant complication. - Patients with infectious complications: 9.3% under control and 5.8% undergoing treatment

It is thought that the main chemical agent for controlling plaque is chlorhexidine. There is no questioning its chemical effectiveness as an antiplaque agent—a large body of research supports its usage in this capacity [6]. Depending on when they start, implant failures are divided into two categories: early and late [71]. Failure to sustain osseointegration as a consequence of a process involving its breakdown (peri-implant illness) is the cause of late implant failure [71]. This category is beyond the purview of this evaluation; the medical community has reached an agreement about the use of chlorhexidine in treating implants that have peri-implant disease [72].

It is hypothesized that early implant failure stems from disruption of the healing process, leading to a failure to achieve osseointegration [71-78]. A certain percentage of early implant failures are thought to be caused by bacterial contamination during implant insertions [29, 31]. Preventing bacterial contamination of the surgical site is crucial for infection prevention and for fostering an environment that is conducive to post-operative recovery [19-23, 26-73, 79].

Furthermore, it has been shown that inflammation, which predominates in the early phases of post-operative wound healing, enhances the production of biofilms [74, 75]. While patient-performed mechanical plaque management is seen to be the best way to avoid periodontal and peri-implant infections, patients find it difficult to bear after surgery because of pain and sensitivity at the surgical site. Consequently, the only way that patient may accept controlling plaque in the early post-surgical time may be through pharmacological measures.

Recent systematic studies [30, 33] have examined preventive antibiotics and shown that taking them as a single dosage before surgery is beneficial. Antibiotic prophylaxis is outside the purview of this article. However, if using a mouthwash containing chlorhexidine right before implant

placement surgery can improve results, it could offer an alternative to prophylactic antibiotics, their side effects, and the worrying problem of bacterial resistance [80-82].

Because there is a dearth of scholarly literature on this subject, the protocol for this research has had to be updated and changed since it was first developed in order to be more comprehensive. Because randomized controlled trials provide high-quality data, it was originally determined that only these types of research would be included. Later on, however, comparative research and controlled trials were also included. Participants' types were not restricted to people with any medical disorders that would increase their risk of infection and post-operative complications, which might reduce the usefulness of extrapolating the treatments' effects over a larger population.

Studies that met the inclusion criteria had to assess the usage of chlorhexidine mouthwash during surgery. A drawback of this study is that it only looks at pre-operative and post-operative usage of Chlorhexidine mouthwash together in one group. The dearth of published trials necessitated accepting this. It was determined to exclude trials in which there was no treatment or placebo in order to assess the advantages of using chlorhexidine as opposed to not using it at all. It would not have answered the particular issue of this study to compare the usage of a mouthwash containing chlorhexidine to other mouthwashes [43, 83] or other types of chlorhexidine [42, 44, 46].

The inclusion criteria similarly restricted the implant design to root shape, submerged healing procedure, and no immediate loading. This was designed to promote uniformity and minimize the factors that would undermine the analysis's conclusions of confidence.

In order to assess the impact of chlorhexidine on the incidence of post-operative infections and problems that

might result in implant loss before prosthetic loading, the outcome measures outlined in the protocol for this study were chosen.

Only one article was deemed appropriate after a thorough search of the literature for trials that fit the inclusion criteria. The study's total risk of bias was found to be high, which significantly affects the value of the evidence it produced. Randomization of patients into treatment and control groups needed to be done correctly. This was based on the standard procedures followed by the professionals, which either included or did not entail the use of chlorhexidine during surgery. However, these medical professionals were unaware that the usage of chlorhexidine would be examined and assessed. It is difficult to hide the usage of chlorhexidine, whether the patient or the doctor is doing the hiding. Nonetheless, this may be used in well-thought-out studies.

The fact that the intervention was examined indirectly was the primary factor contributing to the high overall risk of bias in this research. It should have been covered in the first study's protocol [51]. After the bias risk was identified and the data were obtained indirectly, the study's initial preliminary GRADE of 2 was reduced to 1. This GRADE indicates that there is very little confidence in the impact of chlorhexidine on the results of dental implant surgery.

According to the study's findings, using a mouthwash containing chlorhexidine before surgery decreased the risk of infection problems throughout the healing process. It was also shown that there is a strong correlation between the probability of an infectious complication and implant failure during the submerged healing phase.

Chlorhexidine has been shown in several trials to be useful in lowering the bacterial load of microorganisms linked to periodontal disease. Numerous investigations have discovered these microbes in the peri-implant space [84-86]. Furthermore, studies have shown that chlorhexidine lowers the risk of problems from various intraoral surgical procedures as well as gingivitis [81, 84-90].

More recently, there have been concerning instances of an allergic response to chlorhexidine, resulting in anaphylaxis [91-93]. Serious side effects are uncommon, although they may occur while using chlorhexidine. A recent research paper found 65 published case reports of allergy linked to chlorhexidine that have been published since 1994 [79].

Hypersensitivity responses of Type I and Type IV may be brought on by chlorhexidine. A medical device warning and a medication safety update were published by the Medicines and Healthcare Products Regulatory Agency (MHRA) due to the underrecognition of chlorhexidine as a cause of anaphylaxis [94, 95]. These were intended to raise awareness of the possibility of allergic responses to chlorhexidine.

The primary risk associated with these allergic responses is that chlorhexidine was never considered a potential allergen by medical practitioners. Concerned organizations are addressing this problem, yet chlorhexidine usage in dentistry, medicine, cosmetics, and other non-healthcare industries is still growing [79, 96, 97].

The use of chlorhexidine during the peri-operative phase of implant insertion needs further investigation. The use of chlorhexidine as a topical antibacterial to guard against infectious problems may make more sense, given the growing danger of resistant strains of microorganisms emerging as a consequence of systematic antimicrobial overuse. However, only carefully planned studies will be able to establish this.

## CONCLUSION

Very little data suggests that using chlorhexidine as a peri-operative rinse lowers the likelihood of implant failure and post-operative infections during the submerged healing phase.

The suggestion for the peri-operative administration of chlorhexidine during implant insertion needs more solid data. Chlorhexidine has to be evaluated in more well-planned studies for that goal. Even in the unlikely event that no adverse effects are noted, these studies must be carefully monitored and report any that are.

**ACKNOWLEDGMENTS:** None

**CONFLICT OF INTEREST:** None

**FINANCIAL SUPPORT:** None

**ETHICS STATEMENT:** None

## REFERENCES

1. Payer M, Tan WC, Han J, Ivanovski S, Mattheos N, Pjetursson BE, et al. The effect of systemic antibiotics on clinical and patient-reported outcome measures of oral implant therapy with simultaneous guided bone regeneration. *Clin Oral Implants Res.* 2020;31(5):442-51.
2. Davies G, Francis J, Martin A, Rose F, Swain G. 1: 6-DI-4'-CHLOROPHENYLDIGUANIDOHXANE ("HIBITANE"). LABORATORY INVESTIGATION OF A NEW ANTIBACTERIAL AGENT OF HIGH POTENCY. *Br J Pharmacol Chemother.* 1954;9(2):192-6.
3. Puig-Silla M, Montiel-Company J, Almerich-Silla J. Use of chlorhexidine varnishes in preventing and treating periodontal disease. A review of the literature. *Med Oral Patol Oral Cir Bucal.* 2008;13(4):E257-60.
4. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Infect Control Hosp Epidemiol.* 2002;23(S12):S3-40. Available from: <https://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf>2002
5. Loe H, Schiött CR, Karring G, Karring T. Two years oral use of chlorhexidine in man. I. General design and clinical effects. *J Periodontol Res.* 1976;11(3):135-44.
6. Jones CG. Chlorhexidine: is it still the gold standard? *Periodontology* 2000. 1997;15(1):55-62.
7. Denton GW. Chlorhexidine. In: Block, S.S., Ed., *Disinfection, Sterilization, Preservations.* 4 ed. Philadelphia: Lea & Febiger; 1991.

8. Addy M. Chlorhexidine compared with other locally delivered antimicrobials: a short review. *J Clin Periodontol.* 1986;13(10):957-64.
9. Kornman KS. The role of supragingival plaque in the prevention and treatment of periodontal diseases: A review of current concepts. *J Periodontol Res.* 1986;21:5-22.
10. Rölla G, Løe H, Schiøtt CR. Retention of chlorhexidine in the human oral cavity. *Arch Oral Biol.* 1971;16(9):1109-16.
11. Rindom Schiøtt C. Effect of chlorhexidine on the microflora of the oral cavity. *Journal of Periodontal Research.* 1973;8:7-10.
12. Tanner J, Dumville JC, Norman G, Fortnam M. Surgical hand antisepsis to reduce surgical site infection. *Cochrane Database Syst Rev.* 2016;2016(1):CD004288.
13. James P, Parnell C, Harding M, Whelton H, Worthington HV, Beirne PV. Chlorhexidine mouth rinse as an adjunctive treatment for gingival health. *Cochrane Library.* 2010.
14. Tjernberg A. Influence of oral hygiene measures on the development of alveolitis sicca dolorosa after surgical removal of mandibular third molars. *Int J Oral Surg.* 1979;8(6):430-4.
15. Berwick MJE, Lessin CME. Effects of a chlorhexidine gluconate oral rinse on the incidence of alveolar osteitis in mandibular third molar surgery. *J Oral Maxillofac Surg.* 1990;48(5):444-8.
16. Larsen PE. The effect of chlorhexidine rinses on the incidence of alveolar osteitis following the surgical removal of impacted mandibular third molars. *J Oral Maxillofac Surg.* 1991;49(9):932-7.
17. Hermes C, Hilton T, Baker R, Biesbrock A, Hamlin J, McClanahan S, et al. Prophylactic use of Peridex (R) reduces the incidence of alveolar osteitis following third molar extraction. *InJournal of Dental Research* 1997 Jan 1 (Vol. 76, pp. 1835-1835). 1619 DUKE ST, ALEXANDRIA, VA 22314: AMER ASSOC DENTAL RESEARCH.
18. Hermes CB, Hilton TJ, Biesbrock AR, Baker RA, Cain-Hamlin J, McClanahan SF, et al. Peri-operative use of 0.12% chlorhexidine gluconate for the prevention of alveolar osteitis: efficacy and risk factor analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol.* 1998;85(4):381-7.
19. Corbet E, Tam J, Zee K, Wong M, Lo E, Mombelli A, et al. Therapeutic effects of supervised chlorhexidine mouthrinses on untreated gingivitis. *Oral Dis.* 1997;3(1):9-18.
20. Nyman S, Rosling B, Lindhe J. Effect of professional tooth cleaning on healing after periodontal surgery. *J Clin Periodontol.* 1975;2(2):80-6.
21. Lindhe J, Nyman S. The effect of plaque control and surgical pocket elimination on the establishment and maintenance of periodontal health. A longitudinal study of periodontal therapy in cases of advanced disease. *J Clin Periodontol.* 1975;2(2):67-79.
22. Rosling B, Nyman S, Lindhe J. The effect of systematic plaque control on bone regeneration in infrabony pockets. *J Clin Periodontol.* 1976;3(1):38-53.
23. Rosling B, Nyman S, Lindhe J, Jern B. The healing potential of the periodontal tissues following different techniques of periodontal surgery in plaque-free dentitions: A 2-year clinical study. *J Clin Periodontol.* 1976;3(4):233-50.
24. Nyman S, Lindhe J, Rosling B. Periodontal surgery in plaque-infected dentitions. *J Clin Periodontol.* 1977;4(4):240-9.
25. Westeelt E, Nyman S, Socransky S, Lindhe J. Significance of frequency of professional tooth cleaning for healing following periodontal surgery. *J Clin Periodontol.* 1983;10(2):148-56.
26. Wallkamm B, Ciocco M, Ettl D, Syfrig B, Abbott W, Listrom R, et al. Three-year outcomes of Straumann Bone Level SLActive dental implants in daily dental practice: a prospective non-interventional study. *Quintessence Int.* 2015;46(7):591-602.
27. American Academy of Implant Dentistry. Dental Implants Facts and Figures. Available from: [https://www.aaaid.com/about/press\\_room/dental\\_implants\\_faq.html](https://www.aaaid.com/about/press_room/dental_implants_faq.html) 2017
28. Needleman I, Almond N, Leow N, Phillips J. Outcomes of periodontal therapy: Strengthening the relevance of research to patients. A co-created review. *Periodontology* 2000. 2023.
29. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants, (I). Success criteria and epidemiology. *Copenhagen, DK;* 1998. p. 527-51.
30. Rodríguez Sánchez F, Rodríguez Andrés C, Arteagoitia I. Which antibiotic regimen prevents implant failure or infection after dental implant surgery? A systematic review and meta-analysis. *J Cranio-Maxillofac Surg.* 2018;46(4):722-36.
31. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants, (II). Etiopathogenesis. *Copenhagen, DK;* 1998. p. 721-64.
32. Pye A, Lockhart D, Dawson M, Murray C, Smith A. A review of dental implants and infection. *J Hosp Infect.* 2009;72(2):104-10.
33. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: antibiotics at dental implant placement to prevent complications. *Cochrane Library.* 2013.
34. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med.* 2009;151(4):264-9.
35. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med.* 2009;6(7):e1000100.
36. Schardt C, Adams MB, Owens T, Keitz S, Fontelo P. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak.* 2007;7(1):16.
37. Robinson KA, Dickersin K. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. *Int J Epidemiol.* 2002;31(1):150-3.
38. Higgins JP, Green S. *Cochrane handbook for systematic reviews of interventions* 5.1. 0. The Cochrane Collaboration. 2011:33-49.
39. Cabras M, Gambino A, Broccoletti R, Sciascia S, Arduino PG. Lack of evidence in reducing the risk of MRONJ after teeth extractions with systemic antibiotics. *J Oral Sci.* 2021;63(3):217-26.
40. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating the quality of evidence and strength of recommendations. (Grading of Recommendations Assessment, Development and Evaluation). *Br Med J.* 2008;336(7650):924.
41. Tan LW, Ng YE, Giok KC, Veetil SK, Menon RK. Comparative Efficacy of Different Amoxicillin Dosing Regimens in Preventing Early Implant Failure—A Systematic Review with Network Meta-Analysis. *Antibiotics.* 2023;12(3):512.
42. Genovesi A, Barone A, Toti P, Covani U. The efficacy of 0.12% chlorhexidine versus 0.12% chlorhexidine plus hyaluronic acid mouthwash on healing of submerged single implant insertion areas: a short-term randomized controlled clinical trial. *Int J Dent Hyg.* 2017;15(1):65-72.
43. Horwitz J, Machtei EE, Zuabi O, Peled M. Amine fluoride/stannous fluoride and chlorhexidine mouthwashes as adjuncts to single-stage dental implants: a comparative study. *J Periodontol.* 2005;76(3):334-40.
44. Francetti L, Fabbro MD, Basso M, Testori T, Taschieri S, Weinstein R. Chlorhexidine spray versus mouthwash in the control of dental plaque after implant surgery. *J Clin Periodontol.* 2004;31(10):857-62.
45. Young MP, Carter DH, Worthington HV, McCord JF, Korachi M, Drucker DB. The effects of an immediately pre-surgical chlorhexidine oral rinse on the bacterial contaminants of bone debris collected during dental implant surgery. *Clin Oral Implants Res.* 2002;13(1):20-9.
46. Laugisch O, Ramseier CA, Salvi GE, Hägi TT, Bürgin W, Eick S, et al. Effects of two different post-surgical protocols, including either 0.05% chlorhexidine herbal extract or 0.1% chlorhexidine, on post-surgical plaque control, early wound healing, and patient acceptance following standard periodontal surgery and implant placement. *Clin Oral Investig.* 2016;20(8):2175-83.
47. Kotha VS, Kanuri A, Mandelbaum M, Lakhiani C, Hung RW, Wang J, et al. Simultaneous Zygomatic Osteotomies With Reduction Mandibuloplasty—An Approach to Mid-and Lower-Facial Feminization in the Transfeminine Patient. *J Craniofac Surg.* 2022;33(5):1569-73.
48. Felo A, Shibly O, Ciancio S, Lauciello F, Ho A. Effects of subgingival chlorhexidine irrigation on peri-implant maintenance. *Am J Dent.* 1997;10(2):107-10.

49. Wortmann DE, Boven CG, Schortinghuis J, Vissink A, Raghoobar GM. Patients' appreciation of pre-implant augmentation of the severely resorbed maxilla with calvarial or anterior iliac crest bone: a randomized controlled trial. *Int J Implant Dent*. 2019;5(1):1-9.
50. Yohannan LM. Incidence and Outcome of Pulmonary Complications after Cardiac Surgery. Lietuvos sveikatos mokslų universiteto Leidybos namai; 2019. pp.91-3.
51. Cheung J. On the Role of Sub-Anesthetic Ketamine For Post-Operative Analgesia Following Third Molar Surgery (Doctoral dissertation). 2019.
52. Livie V, Livie J, Hilton-Christie S. Improving the use of the 'COUGH' bundle in surgical high dependency unit, Ninewells Hospital, Dundee. *BMJ Open Qual*. 2020;9(2):e000851.
53. Gillam DG, Chatzopoulou D. Post-operative pain following non-surgical and surgical periodontal procedures. *Periodontology and Dental Implantology*. IntechOpen. 2019:163-78.
54. Hsieh TY, Funamura JL, Dedhia R, Durbin-Johnson B, Dunbar C, Tollefson TT. Risk factors associated with complications after treatment of mandible fractures. *JAMA Facial Plast Surg*. 2019;21(3):213-20.
55. El Azrak M, Polyzois I. Prescription of antibiotics for the prevention of failures and post-operative infections in oral implantology: a literature review. *J Ir Dent Assoc*. 2021;67(4, August/September).
56. Khoully I, Braun RS, Chambrone L. Antibiotic prophylaxis may not be indicated for the prevention of dental implant infections in healthy patients. A systematic review and meta-analysis. *Clin Oral Investig*. 2019;23:1525-53.
57. Zhao AH, Kwok CH, Jansen SJ. How to Prevent Surgical Site Infection in Vascular Surgery: A Review of the Evidence. *Ann Vasc Sur*. 2022;78:336-61.
58. Chaudhari S, Jangale AG, Dhande S, Jangale SA. Breakthrough in Surgeries during Covid-19 Pandemic Era: An Orthopedic Perspective. *J Rhem Ortho Sports Sci*. 2022;2(1):1-7.
59. Goswami A, Ghorui T, Bandyopadhyay R, Sarkar A, Ray A. A general overview of post-extraction complications-prevention, management, and importance of post-extraction advices. *Fortune J Health Sci*. 2020;3(3):135-47.
60. Fee L. BA BDS MJDF (Word count: 2,999).
61. Sartelli M. Healthcare-associated infections in the surgical setting: How to prevent and treat them. *Adv Human Biol*. 2022;12(2):127-37.
62. Berton F, Constantinides F, Rizzo R, Franco A, Contarin J, Stacchi C, et al. Should we fear direct oral anticoagulants more than vitamin K antagonists in a simple single-tooth extraction? A prospective comparative study. *Clin Oral Investig*. 2019;23(8):3183-92.
63. Nathwani S. Management of patients on oral anticoagulants in dental practice. *Dent Update*. 2020;47(11):912-22.
64. Ishaq M, Noor B, Ahad A, Muhammad N, Bibi R. Chlorhexidine for the Prevention of Omphalitis in neonates with a single dose. *Pak J Med Health Sci*. 2023;17(04):141.
65. Mauceri R, Panzarella V, Pizzo G, Oteri G, Cervino G, Mazzola G, et al. Platelet-Rich Plasma (PRP) in dental extraction of patients at risk of bisphosphonate-related osteonecrosis of the jaws: A two-year longitudinal study. *Appl Sci*. 2020;10(13):4487.
66. Manz MC. Radiographic assessment of peri-implant vertical bone loss: DICRG Interim Report No. 9. *J Oral Maxillofac Surg*. 1997;55(12):62-71.
67. Bedeloğlu E, Yalçın M, Koyuncuoğlu CZ. Is Peri-operative Antibiotic Necessary in Straightforward Implant Placement Procedures? *J Oral Implantol*. 2021;47(2):135-9.
68. Grisar K, Smeets M, Ezeldeen M, Shaheen E, De Kock L, Politis C, et al. Survival and success of autotransplanted impacted maxillary canines during short-term follow-up: A prospective case-control study. *Orthod Craniofac Res*. 2021;24(2):222-32.
69. Cheung J, Alashi A, Koto P, Brady J, Davis B. Does Sub-Anesthetic Ketamine Provide Post-operative Analgesia for Third Molar Surgery?. *J Oral Maxillofac Surg*. 2019;77(12):2452-64.
70. Shriki M, Almoussli A, Abdul Z, Hausien O, Al-Ghazal SK. Management of Muslim Patients Undergoing Local Anaesthetic Procedures During Ramadan. *J Br Islam Med Assoc*. 2021;7(3):1-11.
71. Sykara M, Maniatakos P, Tentolouris A, Karoussis IK, Tentolouris N. The necessity of administering antibiotic prophylaxis to patients with diabetes mellitus prior to oral surgical procedures systematic review. *Diabetes Metab Syndr Clin Res Rev*. 2022;16(10):102621.
72. Darnell LH. The Effect of a Chitosan-based Mouthwash on Oral Pathogens During Initial Wound Healing—An In-Vitro Study. Part I: Antimicrobial Properties (Doctoral dissertation, Saint Louis University). 2020.
73. Schwarz F, Obreja K, Mayer S, Ramanauskaite A, Sader R, Parvini P. Efficacy of autogenous tooth roots for a combined vertical and horizontal alveolar ridge augmentation and staged implant placement. A prospective controlled clinical study. *J Clin Periodontol*. 2022;49(5):496-505.
74. White A, van de Lande LS, O'Hara J, Hartley J, Hayward R, James G, et al. Fronto-facial surgery: reducing infection with the development and 6-year outcome of a fronto-facial protocol. *Plast Reconstr Surg*. 2023;152(4):833-40.
75. Castagna V, Pardo A, Lanaro L, Signoriello A, Albanese M. Periodontal healing after lower third molars extraction: a clinical evaluation of different flap designs. *InHealthcare 2022 Aug 21 (Vol. 10, No. 8, p. 1587)*. MDPI.
76. Caggiano M, D'Ambrosio F, Giordano F, Acerra A, Sammartino P, Iandolo A. The "Sling" Technique for Horizontal Guided Bone Regeneration: A Retrospective Case Series. *Appl Sci*. 2022;12(12):5889.
77. Jordan K, Carter E, Devine CP, Tsihklaki A, Jones J. Osteogenesis imperfecta: minimizing complications in oral surgery/orthodontic treatment. *Dent Update*. 2021;48(9):726-30.
78. Stiesch M, Grischke J, Schaefer P, Heitz-Mayfield LJ. Supportive care for the prevention of disease recurrence/progression following peri-implantitis treatment: A systematic review. *J Clin Periodontol*. 2023;50(s26):113-34.
79. Roca-Millan E, Estrugo-Devesa A, Merlos A, Jané-Salas E, Vinuesa T, López-López J. Systemic antibiotic prophylaxis to reduce early implant failure: a systematic review and meta-analysis. *Antibiotics*. 2021;10(6):698.
80. Herrera D, Berglundh T, Schwarz F, Chapple I, Jepsen S, Sculean A, et al. Prevention and treatment of peri-implant diseases—The EFP S3 level clinical practice guideline. *J Clin Periodontol*. 2023;50(s26):4-76.
81. Sargent RE, Jacobsen J, Cole K, Olson R, Gibbs DM, Amaya R, et al. Association of Pre-Operative Full-Body Surgical Preparation with Reduced Incidence of Surgical Site Infection at a Large, Urban Safety-Net Medical Center. *Surg Infect*. 2022;23(1):1-4.
82. Radhika B. To Evaluate the Role of Antibiotics in Periodontal Flap Surgery-A Comparative Clinical Study (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
83. Praveen AA, Venkadassalopathy S, Victor DJ, Prakash PS, Umesh SG, Ali Baeshen H, et al. Efficacy of Two Different Hydrodynamic Sinus Lift Systems for Atraumatic Elevation in Immediate Implant Placement. *Patient Prefer Adher*. 2023;17:1197-207.
84. Alassy H, Pizarek JA, Kormas I, Pedercini A, Wolff LF. Antimicrobial adjuncts in the management of periodontal and peri-implant diseases and conditions: a narrative review. *Front Oral Maxillofac Med*. 2021;3:16.
85. Quinton K, Guy-Frank CJ, Syed S, Klugh JM, Dhanani NH, Adibi SS, et al. Poor Oral Health in Trauma Intensive Care Unit Patients: Application of a Novel Oral Health Score. *Surg Infect*. 2023;24(7):657-62.
86. Brookes ZL, Bescos R, Belfield LA, Ali K, Roberts A. Current uses of chlorhexidine for management of oral disease: a narrative review. *J Dent*. 2020;103:103497.
87. Duyan HA, Evlice BU. Evaluation of Mandibular Condyle of Patients with Cleft Lip/Palate. 2021.
88. Kij-artorn MP, Buranawat B, Suwanprateeb J. Clinical evaluation of 3D printed nano-bioengineered bone graft for alveolar ridge preservation: a randomized controlled trial (Doctoral dissertation, Thammasat University). 2019.
89. Mekcha MP. Custom 3d printed hydroxyapatite bone block graft for alveolar ridge reconstruction: a pilot clinical study (Doctoral dissertation, thammasat university). 2021.
90. Wongpaironpanich J, Buranawat B, Suwanprateeb J. Clinical efficacy of porous polyethylene membrane for alveolar ridge preservation: a pilot study (Doctoral dissertation, Thammasat University). 2020.

91. Bhargava V, Renton T. Routine exodontia: preventing failed extractions. *Dent Update*. 2019;46(9):866-79.
92. Solderer A, Schmidlin PR. Regenerative surgical therapy of peri-implantitis: an umbrella review of answered/unanswered questions and future perspectives. *Front Dent Med*. 2020;1:614240.
93. Ockerman A. The influence of anticoagulants on bleeding and healing after dental extraction (PhD thesis). 2021.
94. Garner SJ. Development of a Chlorhexidine-Hexametaphosphate Coating for Titanium to Combat Early Implant Failure (Doctoral dissertation, University of Bristol). 2020.
95. Payer M, Tan WC, Han J, Ivanovski S, Mattheos N, Pjetursson BE, et al. The effect of systemic antibiotics on clinical and patient-reported outcome measures of oral implant therapy with simultaneous guided bone regeneration. *Clin Oral Implants Res*. 2020;31(5):442-51.
96. Khan AM, Gangoo IK, Ali NA, Khan M, Javed MQ, AlAttas MH, et al. The effect of calcium hydroxide, triple antibiotic paste and chlorhexidine on pain in teeth with symptomatic apical periodontitis: a randomised controlled trial. *Int J Environ Res Public Health*. 2023;20(4):3091.
97. Camenzuli C. Development of a scarless and gasless trans-oral video-assisted thyroidectomy (Doctoral dissertation). 2021.