

# Oral Hygiene Protocols and Basic Oral Care in Cancer Patients: A Systematic Review

Maria Cláudia Cuzzullin <sup>1</sup>, Marcelo Ivander Andrade Wanderley <sup>2</sup>, Maria Eduarda Pérez-de-Oliveira <sup>1</sup>, Ana Gabriela Costa Normando <sup>1</sup>, Anna Luíza Damaceno Araújo <sup>3</sup>, Joab Cabral Ramos <sup>4</sup>, Thaís Bianca Brandão <sup>4,5</sup>, Joel B. Epstein <sup>6,7</sup>, Alan Roger Santos-Silva <sup>1,\*</sup> and Ana Carolina Prado-Ribeiro <sup>1,2,5</sup>

- <sup>1</sup> Oral Diagnosis Department, Piracicaba Dental School, State University of Campinas (UNICAMP), Piracicaba 13414-903, SP, Brazil; mccuzzullin@gmail.com (M.C.C.); meduardaperezo@gmail.com (M.E.P.-d.-O.); gabinormando@gmail.com (A.G.C.N.); carol\_pr@yahoo.com.br (A.C.P.-R.)
- <sup>2</sup> Hospital Sírio-Libanês, São Paulo 01308-050, SP, Brazil; marcelo0andrade@gmail.com
- <sup>3</sup> Head and Neck Surgery Department, University of São Paulo Medical School, São Paulo 01246-903, SP, Brazil; anna\_luizaf5ph@hotmail.com
- <sup>4</sup> Dental Service, Hospital de Base, Fundação Faculdade de Medicina de São Jose do Rio Preto, São Paulo 15090-000, SP, Brazil; joab.cabral@hotmail.com (J.C.R.); thais.brandao@hc.fm.usp.br (T.B.B.)
- <sup>5</sup> Dental Oncology Service, Instituto do Câncer do Estado de São Paulo, Fundação da Faculdade de Medicina da Universidade de São Paulo (ICESP-FMUSP), São Paulo 01246-000, SP, Brazil
- <sup>6</sup> City of Hope National Medical Center, Duarte, CA 91010, USA; jepstein@coh.org
- <sup>7</sup> Cedars-Sinai Health System, Los Angeles, CA 90048, USA
- \* Correspondence: alan@unicamp.br

## Abstract

Oral hygiene protocols and basic oral care (BOC) are paramount for patients undergoing cancer treatment, although based upon limited evidence from clinical trials. There are a range of oral care guidelines proposed in the literature mainly focusing on oral mucositis prevention. This systematic review aimed to define the best procedures and practices in the scope of oral hygiene protocols and BOC interventions for the prevention and/or treatment of oral complications in patients under cancer treatment. This systematic review was conducted according to the PRISMA guidelines, and the methods were previously established and registered in PROSPERO (CRD42022319455). A systematic search was completed in six databases (PubMed, Scopus, Web of Science, LILACS, and the Cochrane Library, and gray literature). Eleven studies were included in the qualitative analysis including non-randomized (n = 1) and randomized clinical trials (n = 6), and cohort studies (n = 4). The included studies showed the effectiveness of soft brushes for daily oral hygiene with topical fluoride, and the use of mouthwashes with 0.12% chlorhexidine, doxepin, and benzydamine and saline solutions, as well as dental scaling/prophylaxis in decreasing the severity of oral toxicities. Although not well-explored by well-designed clinical studies, BOC protocols may be effective in prevention oral toxicities from cancer therapy and are supported in multiple guidelines. This review synthesized available evidence on BOC in head and neck cancer patients, focusing on the effectiveness of hospital-based dental protocols during cancer treatment.

**Keywords:** basic oral care; oral mucositis; patient education; dental care; guidelines; cancer



Academic Editor: Fernando Pérez-Rodríguez

Received: 2 June 2025

Revised: 31 August 2025

Accepted: 25 September 2025

Published: 1 October 2025

**Citation:** Cuzzullin, M.C.; Wanderley, M.I.A.; Pérez-de-Oliveira, M.E.; Normando, A.G.C.; Araújo, A.L.D.; Ramos, J.C.; Brandão, T.B.; Epstein, J.B.; Santos-Silva, A.R.; Prado-Ribeiro, A.C. Oral Hygiene Protocols and Basic Oral Care in Cancer Patients: A Systematic Review. *Hygiene* **2025**, *5*, 45. <https://doi.org/10.3390/hygiene5040045>

**Copyright:** © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Cancer is a significant public health problem worldwide, whose incidence and mortality have been increasing, due to aging, population growth, or changes in the distribution

and prevalence of cancer risk factors, both of which are associated with socioeconomic development [1]. The principle contemporary treatment modalities for cancer include solid tumors, surgical resection, radiation therapy (RT), chemotherapy (CT), targeted immunotherapy, and, for liquid tumors, chemotherapy and hematopoietic stem cell transplant [2].

RT, CT, and combined therapy for oral cancer treatment have a high potential to produce direct tissue damage of the oral cavity and some adverse effects on healthy tissues indirectly, which are often irreversible and may occur months to years after completing RT. These include xerostomia, oral mucositis (OM), dysphagia, lymphedema, radiation caries, periodontal disease, osteonecrosis of the jaw, dysgeusia, and oral pain [3–6]. The management of these toxicities and harmful side effects are essential in order to achieve a better quality of life.

Due to the significant impact upon quality of life, it is important to prevent both the acute and late oral toxicities of cancer treatment. A pretreatment dental assessment is critical and, in some cases, it is the only opportunity for the management of pre-existing dental conditions that could lead to significant and difficult-to-manage oral/dental toxicities and preventing complications during and following active cancer therapy [7]. Within the multidisciplinary team, the dentist is responsible for the prevention and management of such oral and dental toxicities. Treatment should be directed to the needs of each patient, which could lead to large variations in the dental care given because it is up to the individual and the dental treatment planning for the care of each patient. This may lead to inequalities in the care provided [8,9].

Basic oral care (BOC) is defined in this study as the routine set of procedures aimed at maintaining oral hygiene and preventing oral and systemic diseases, including mechanical plaque removal through toothbrushing, interdental and tongue cleaning, the appropriate use of antiseptic or fluoride mouth rinses, regular oral examinations, and biofilm control. Several reviews have proposed approaches to prevent and/or manage oral complications before, during, and after cancer therapy [10–12].

However, to the best of our knowledge, no systematic synthesis of the available evidence on BOC in patients with head and neck cancer has been conducted to date. Considering the critical role of dental professionals in the prevention and management of oral complications, particularly in light of the current lack of standardized protocols and the need for consistent strategies to manage treatment-related toxicities, this review aimed to identify, analyze, and synthesize the evidence on BOC protocols implemented by dentists in hospital settings, focusing on their effectiveness in managing oral toxicities during cancer therapy.

## 2. Material and Methods

### 2.1. Eligibility Criteria

The acronym PICOS was framed based on the guidance for defining review question (CHARMS Checklist) to guide the focused review question, to determine the best and most effective basic dental procedures within the concept of basic dental care in managing the effects resulting from cancer treatment and, also, to determine the inclusion criteria, of which are the following: P. head and neck cancer patients under RT and CT; I. dental procedures executed by dentists in a hospital environment, such as techniques for brushing teeth, including types of toothbrush, brushing time and frequency, and mouthwashes and its best components with high levels of antimicrobial efficiency and dental prophylaxis; C. comparison of the results found with previously published guides and studies; O. evaluation and synthesis of the most effective dental procedures in head and neck cancer

patients, based on current evidence; and S. randomized/non-randomized clinical trials and cohorts' studies.

This review was guided by three main questions: (1) Which BOC interventions are effective in preventing or reducing oral toxicities (e.g., mucositis, xerostomia, or radiation caries) in head and neck cancer patients undergoing radiotherapy and/or chemotherapy?; (2) Which specific practices and agents (e.g., soft toothbrushes, fluoride application, chlorhexidine or benzydamine rinses, or dental prophylaxis) demonstrate measurable benefits in reducing the severity of oral complications?; and (3) What are the main methodological shortcomings of existing clinical studies evaluating BOC interventions in this population?

In this study, articles that did not explain in detail the dental procedures performed on cancer patients, at any time during treatment, performed by dentists in a hospital environment were excluded; studies in which dental procedures (described above) data were not available for data extraction due to grouping with other type of dental procedures, studies that did not clearly report the odds/risk ratio or for which this ratio could not be calculated, reviews, case reports, short communication, personal opinions, letters, conference abstracts, and laboratory research and articles whose full texts were not available were also all excluded. Table 1 describes a checklist used to select the articles used in this study.

**Table 1.** Standard checklist to report clinical trials and studies reporting basic oral procedures for oncological patients.

<b>Trial design and identification</b>	<ul style="list-style-type: none"> <li>- Identification as randomized clinical trial and description of the trial design;</li> <li>- Provide the medical center where the patients were treated.</li> </ul>
<b>Ethics and registration</b>	<ul style="list-style-type: none"> <li>- Provide center or city ethics committee;</li> <li>- Ensure that the trial is registered in a publicly accessible trials registration database.</li> </ul>
<b>Population</b>	<ul style="list-style-type: none"> <li>- Describe oncological treatment patients are being submitted (such as radiotherapy, chemotherapy, or stem cell transplant);</li> <li>- Detail the eligibility criteria and sample size;</li> <li>- Define the control group: placebo, different protocols, or another reference treatment;</li> <li>- Include procedures for randomization, patients' allocation, and patient-blinding.</li> </ul>
<b>Oral care intervention</b>	<ul style="list-style-type: none"> <li>- Specific description of the oral care procedure, such as toothbrush used, mouth rising used and concentration, prophylaxis, dental floss type, and fluor application;</li> <li>- The moment they performed said procedures, before, during, or after the oncological treatment;</li> <li>- Duration taken and technique to perform the procedures.</li> </ul>

## 2.2. Information Sources and Search Strategy

The literature search was conducted up to 12 April 2023, without an initial date restriction, and all articles published until then were considered eligible for screening. On that date, individualized strategies were applied across the following electronic databases: PubMed, Cochrane Library, Lilacs, Scopus, Web of Science, and gray literature sources (Google Academic and ProQuest). Gray literature was included in this review to ensure a more comprehensive and unbiased synthesis of the available evidence, enhances the scope of evidence considered, and may capture emerging or context-specific practices that are not yet published in indexed journals. The following descriptors included MeSH

(Medical Subject Headings): “Mouth neoplasms” combined with “or” and “oral cancer” an “and” “oral care”, “oral management”, “mouthrinse”, “tooth brushing”, “dental care”, “dental procedure”. The retrieved references were imported into the Endnote Web reference manager (Endnote Web, Clarivate Analytics, Philadelphia, PA), where duplicate references were removed. The search strategy is shown in Supplementary Material S1. Additional exclusion criteria comprised language (non-English publications), duplicates, studies without dental interventions, populations not undergoing head and neck radiotherapy, outcomes not related to oral toxicities, ineligible designs (reviews, case reports, letters, conference abstracts, and laboratory research), and articles whose full text was unavailable.

### 2.3. Selection Process

Study selection was independently and blindly performed in two phases by two authors (M.C.C. and A.L.D.A.), respecting the inclusion and exclusion criteria previously established. In the first phase, the titles and abstracts of the identified references were read on Rayyan<sup>®</sup> [13]. The studies which appeared to meet inclusion criteria went to the second phase of selection process, in which the full texts were read, and the eligibility criteria were confirmed. In addition, the reference lists of all included studies were read, and screened for potentially missing studies. Divergences in both phases were resolved by discussion and mutual agreement among the authors.

### 2.4. Data Collection Process and Data Items

The relevant data to be selected was discussed between all authors, extracted by M.C.C., and cross-checked by A.L.D.A. The extracted variables were author/year, number of patients, age, oncologic treatment, complication/toxicity/treated condition, alcohol and tobacco status, follow-up time, dental intervention, moment of the dental intervention (prior to, during, and after the oncologic treatment), instructions for the dental intervention usage, main and secondary results, and conclusion.

### 2.5. Risk of Bias Assessments

The quality of the information collected in article selected were assessed using the Joanna Briggs Institute Critical Appraisal Checklists for Randomized Clinical Trials, Non-randomized Clinical Trials and Cohort Studies [14]. One reviewer (M.C.C.) independently classified each study as “high” if the percentage of “yes” scores reached up to 49% score; “moderate” if the percentage of “yes” scores was between 50% to 69%; and “low” if the percentage of “yes” scores was more than 70%.

### 2.6. Effect Measures

The objective of this SR was to examine dental management recommended for patients who will undergo cancer treatment (radiotherapy and/or chemotherapy) to achieve best dental outcomes, including caries and periodontal disease during treatment, to reduce risk of fewer secondary infections in the mouth. Although the measure of effect considered was the odds ratio, due to the lack of homogeneity among the articles included, it was not possible to carry out the appropriate analysis to obtain such data, as the studies presented different designs, variables, and distinct outcomes.

A qualitative synthesis was performed, presenting a descriptive analysis of the available evidence. The primary results of the studies were reported, presenting the procedures performed on the patients and the specifications of each, associating them with the best statistically proven results, as described in the studies.

### 3. Results

#### 3.1. Study Selection

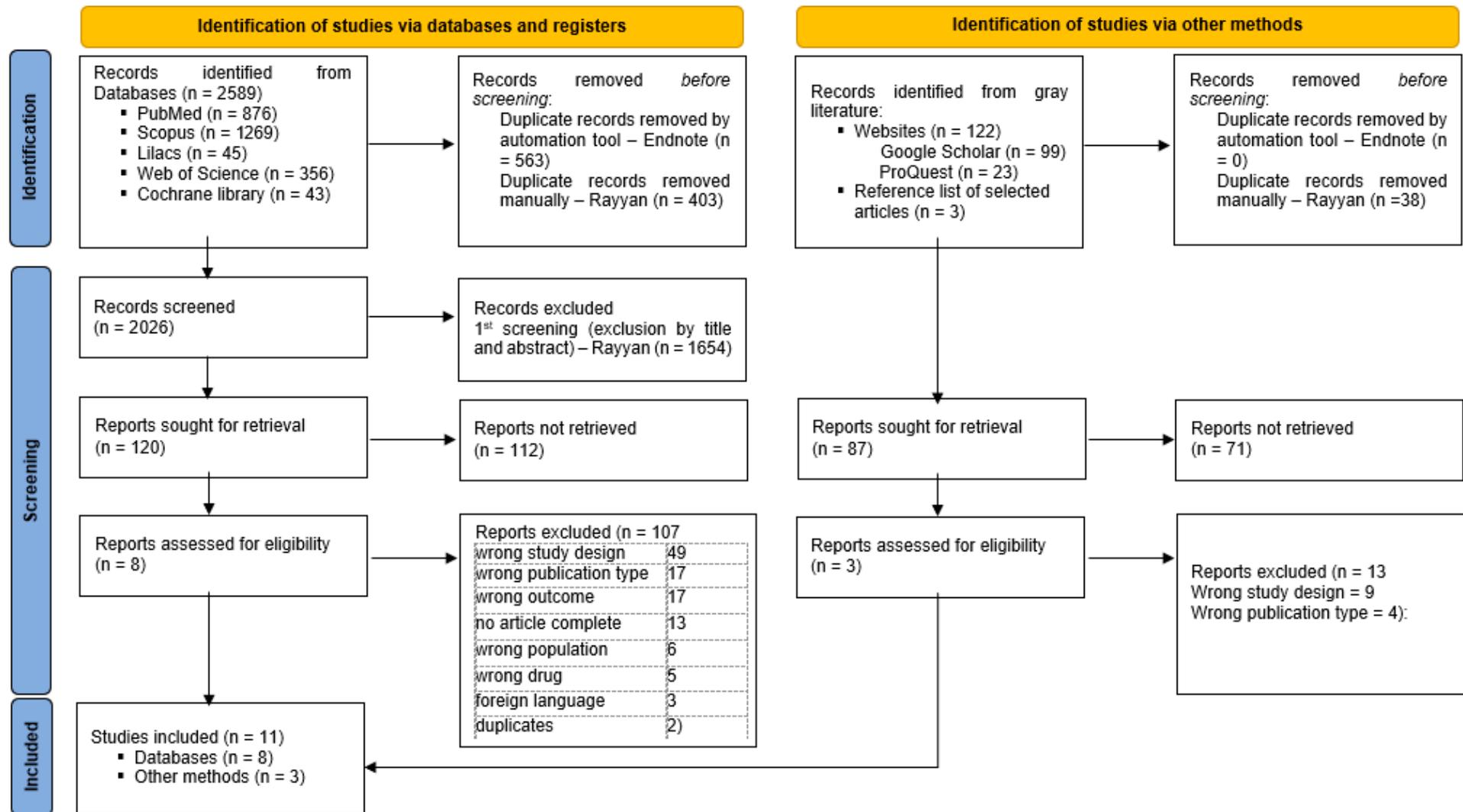
Among the total of 2589 articles identified through search strategy, 11 articles [12,15–24] were included in the quantitative synthesis. The selection process is summarized in the PRISMA flowchart (Figure 1) and the reasons for exclusion of each of the articles that were read in full are described in Supplementary Material S2.

#### 3.2. Study Characteristics

The data included 830 patients (607 males [73.13%]; 223 females [26.87%]; 176 not informed [37.93%]), with ages ranging from 7 to 82 years old, treated with diverse RT regimens (total dose ranging from 50 to 70 Gy), with or without concomitant CT. Mucositis was the condition more frequently treated (seven studies) [16–22], followed by periodontal health/biofilm control (two studies) [12,16], and osteoradionecrosis (two studies) [15,17]. Within the studies evaluating the grade of OM, two studies based their evaluation according to the RTOG (Radiation Therapy Oncology Group) grading system [15,19], while three were evaluated subjectively, using an Oral Mucositis Daily Questionnaire (OMDQ) [20,23,24]. One article applied the WHO score for OM and the OMDQ [18]. One study evaluated by the mean of mucositis which score was obtained by adding the single scores for each anatomic area at risk (defined as areas receiving a cumulative radiation dose of at least 4000 cGy) and dividing by the number of areas included in the RT field [22].

We found that 147 patients reported smoking and 140 alcohol use, but this information was only present in four articles [17–19]. In four studies, patients received interventions and were evaluated prior to, during, and after cancer treatment [12,15–17]. Oral hygiene habits before, during, and after cancer treatment were reported in three studies [12,16,17].

The patient's observation time ranged from 6 weeks to 10 years, with 36.3% of studies reporting a 6-month follow-up [16,17,20,21]. Table 2 presents the characteristics of the included articles.



**Figure 1.** PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers, and other sources. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit <http://www.prisma-statement.org/> (accessed on 20 May 2025) [25].

Table 2. Included studies.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
Epstein, 2001 [22]	Mucositis	Before, during, and after oncologic treatment	Benzydamine—to rinse 1.5 mg/mL benzydamine [15 mL] for 2 min, 4–8 times daily before and during RT, and for 2 weeks after completion of RT) and a Control group—placebo (excipients included 10% alcohol by volume, menthol, peppermint oil, clove oil, and other flavoring agents).	Benzydamine produced a 26.3% reduction in mean mucositis compared with placebo for the overall 0–5000 cGy interval. Moreover, benzydamine produced statistically significant reductions in mucositis in the highest two RT intervals compared with placebo: 36% in the 2500–3750-cGy interval and 25.3% in the 3750–5000-cGy interval. In addition, in a prophylactic use of benzydamine, mucositis scores in oropharyngeal areas at risk for ulceration in both treatment groups remained with no ulceration at cumulative RT exposures of 3750 and 5000 cGy.	The use of benzydamine 0.15% oral rinse is significant as a routine prophylactic in patients with head and neck carcinoma receiving a variety of RT regimens.
Kazemian, 2009 [19]	Mucositis	Before and during the oncologic treatment	Benzydamine—to rinse with 15 mL of 0.15% for 2 min, 4 times a day from the first day of RT to the end of the treatment	Benzydamine produced a statistically significant reduction in mucositis during RT. There was a statistically significant difference in the grade 3 mucositis in the two groups, which was 43.6% (n = 17) in the benzydamine group and 78.6% (n = 33) in the placebo group. Grade 3 mucositis was 2.6 times more frequent in the placebo group.	Benzydamine 0.15% oral rinse was safe and well-tolerated. It significantly reduced RT-induced mucositis, which also decreased the interruption of the treatment by the patients. The prophylactic usage may decrease the mucosal complications of RT.

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
			Control group—Placebo.		
Leenstra, 2014 [23]	Mucositis	During the oncologic treatment	Doxepin to rinse with a solution of doxepin 25 mg, diluted to 5 mL with 2.5 mL of sterile or distilled water.	The mean mouth and throat pain reduction was greater for doxepin (−9.1) compared with placebo. Crossover analysis of the two phases showed inpatient changes of 4.1 for the doxepin–placebo arm and −2.8 for the placebo–doxepin arm; the treatment difference of doxepin versus placebo was −3.5; there was an average mouth and throat pain score reduction of −2.0 (36.3%) from baseline for doxepin compared with −1.0 (18.9%) for placebo at 30 min after rinse.	Doxepin rinse is statistically significantly superior to a placebo in treating oral mucositis pain from head and neck radiotherapy with or without chemotherapy.
			Control group—placebo rinse prepared in a similar manner.		
Samarannayake, 1988 [21]	Mucositis	During the oncologic treatment	Chlorhexidine [to rinse with 15 mL of 0.2% aqueous chlorhexidine gluconate (Hibitane-ICI Pharmaceuticals) for 30 s twice daily]	The yeast carriage rate was significantly higher than the coliform carriage rate in both groups ( $p < 0.05$ ). The most common coliform found was <i>Klebsiella pneumoniae</i> . Patients using chlorhexidine presented less discomfort. The loss of weight in the control group was four times higher than the study group. The difference noted was highly significant ( $t = 3.73$ ; $df = 22$ ; $p < 0.01$ ).	Patients' acceptance of chlorhexidine is better than benzydamine, but there is little difference between the two mouthwashes both in controlling pain and mucositis or in the oral carriage of the microorganisms studied.

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
			Benzydamine [to rinse with 15 mL of 0.15% benzydamine hydrochloride ('Difflam', Carnegie Medical)]		
Satheeshkumar, 2010 [20]	Mucositis	During the oncologic treatment	Triclosan mouth rinse [to rinse with M/S Colgate Palmolive India Ltd. (Colgate Plax) containing triclosan 0.03%]	From grade 2–3, there was no statistical difference between the study and control groups. The effect of treatment in control of severity of mucositis found significant statistic difference at a very higher level ( $p < 0.001$ ). With regard to reversal of mucositis from grade 3 to grade 0, the study group had taken only a mean of 23.6 days in place of 36.5 days in the control group.	The calcium phosphate mouth rinse seems to have no influence on the frequency, duration, and severity of oral mucositis during CRT in patients with head and neck cancer.
			Control group—Sodium bicarbonate (2 g of sodium bicarbonate powder)		
Sio, 2019 [24]	Mucositis	During the oncologic treatment	Doxepin—(92 patients to rinse with doxepin mouthwash [25 mg/5 mL water]; 91 patients to diphenhydramine–lidocaine–antacid; and 92 patients to placebo).	Mucositis pain during the first 4 h decreased by 11.6 points in the doxepin mouthwash group, by 11.7 points in the diphenhydramine–lidocaine–antacid mouthwash group, and by 8.7 points in the placebo group. More drowsiness was reported with doxepin mouthwash vs. placebo (by 1.5 points), unpleasant taste (by 1.5 points), and stinging or burning (by 4.0 points).	The use of doxepin mouthwash or diphenhydramine–lidocaine–antacid mouthwash vs. placebo significantly reduced oral mucositis pain during the first 4 h after administration.

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
			Calcium phosphate (to rinse twice with 15 mL solution for 1 min, four times a day)		
Stokman, 2012 [18]	Mucositis	During the oncologic treatment	Calcium phosphate (to rinse twice with 15 mL solution for 1 min, four times a day)	The mean weight loss after 6 weeks of radiation was 4.0 kg (SD 3.7) in the CP mouth rinse group and 3.5 kg (SD 3.1) in the control group ( $p = 0.7$ ). Use of gastric tubes was necessary in 12 of the 25 patients in the CP mouth rinse group (55%) and in 6 of the 11 patients in the control group (48%) ( $p = 0.8$ ). No significant difference was found for oral pain between both groups.	The CP mouth rinse seems to have no influence on the frequency, duration, and severity of oral mucositis during (chemo) radiation in patients with head and neck cancer.
			Control group—salt/baking soda solution (1 tsp. of salt and 1 tsp. of baking soda in a liter of tap water) at least eight times a day to remove sticky saliva and debris.		

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
Bueno, 2013 [16]	Biofilm	Prior to the oncologic treatment	1.Oral hygiene instructions included instruction on brushing and interdental cleaning; 2. Coronal scaling (using an ultrasonic instrument), and polishing; 3. A kit containing a toothbrush and toothpaste; 4. The patients were prescribed 1% neutral fluoride solution to be used once daily, designed to prevent caries and postoperative sensitivity. The use of other mouthwashes was not allowed.	Reduction in PD (probing depth) between the T0/T1 and T0/T2; 2. Reduction in the frequency of PI (plaque index) and BOP (bleeding on probing) observed between the baseline assessment and 180 days after RT	Patients undergoing RT to the head and neck region with or without CT do not show aggravations of their clinical periodontal status for up to 6 months after cancer treatment if they also receive periodontal therapy and maintenance.
		During the oncologic treatment	1.Coronal polishing; 2. Topical application of 1% neutral fluoride gel; 3. Reinforcement of oral hygiene		
		After the oncologic treatment	1. Coronal polishing; 2. Topical application of 1% neutral fluoride gel; 3. Reinforcement of oral hygiene		

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
Nunez-Aguilar, 2018 [12]	Biofilm	Prior to, during, and after the oncologic treatment	<ol style="list-style-type: none"> <li>1. Teaching of oral hygiene, treatment of fluoride and chlorhexidine, scaling and polishing, scaling and root planning, selective carvings, prevention of bedsores in the oral mucosa teeth with sharp edges billed, prosthetic review, fillings, and dental extractions.</li> <li>2. Teaching of oral hygiene, and use of chlorhexidine and fluoride.</li> <li>3. Survey before the oncological treatment, after starting the treatment, and with 60% of the treatment complete.</li> </ol>	47.78% of the patients indicated that they had not had sore gums during CRT in the experimental group against 87.5% in the control group; in the experimental group, 17.07% patients had not had bleeding gums during CRT; in the control group, 35 patients had had bleeding gums; in the experimental group, 9.75% patients had ulcers during CRT; in the control group, it was 87.5% patients. In the experimental group, 17.07% of the patients had bleeding gums after CRT; in the control group, 87.80%.	Implementation of prevention protocols and the improvement in oral health among these patients is necessary.
Niewald, 2013 [15]	Osteoradionecrosis	Prior to the oncologic treatment	<ol style="list-style-type: none"> <li>1. Tooth extraction (followed up by an interval of at least 7–10 days using soft diet, valid antibiosis, and prosthodontic abstention) with primary tissue closure;</li> <li>2. Endodontic treatment;</li> <li>3. Removal of root remainders with primary tissue closure;</li> <li>4. Conserving treatment.</li> </ol>	12% of the patients were found to have developed infected osteoradionecrosis during follow-up. The one-year prevalence was 5%, the two- and three-year prevalence 15%— treated by conventionally fractionated RT applying doses of 50 Gy (1 pat.), 60 Gy (4 pats.), 64 Gy (3 pats.), and 70 Gy (3 pats.), respectively. We found 14% of the patients having been operated on had IORN compared to only 8% in the non-surgical patients.	Meticulous dental care resulted in an incidence of IORN of 12%; all of them had undergone conventionally fractionated radiotherapy; in the hyperfractionated group, no IORN occurred at all.
		During the oncologic treatment	Fluoridation was performed according to dental advice.		

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
		After the oncologic treatment	1. Patients were advised not to wear their dental prostheses up to 6–12 months after RT; 2. Tooth extraction with primary tissue closure; 3. Tooth extraction with primary tissue closure and conservative treatment; 4. Conservative treatment.		
Regezi, 1976 [17]	Osteonecrosis, mucositis, dysgeusia, and dysphagia	Prior to the oncologic treatment	1. Extraction of no salvageable teeth (teeth with gross dental caries, periapical pathology, advanced periodontal disease, and teeth supported by neoplasm); 2. Dental prophylaxis; 3. Restorative dental procedures as needed; 4. Initiation of oral hygiene regimen: a. Tooth brush instruction with soft brushes (patients were instructed to brush q.i.d. and to follow each brushing with oral lavage and fluoride rinse); b. Oral lavage instruction (1 L warm water with 1 teaspoon each of NaCl and NaHCO <sub>3</sub> ); c. Sodium fluoride rinse instruction (1 teaspoon 3yo NaF held in mouth 1 min, then expectorated). This rinse was discontinued during acute mucositis because of mucosal irritation.	Oral hygiene status went from fair/poor at initial examination to good/fair after radiation therapy; patients had normal healthy periodontium (25%), gingivitis (25%), and mild to moderate periodontitis (50%). Periodontal disease did not progress at a rate greater than we would expect in a non-irradiated population. Teeth decay increased 20% following irradiation. All patients had mucositis, which became evident after 2 to 4 weeks of therapy (dysgeusia, dysphagia, dysorhexia, and pain). Overgrowth of <i>Candida albicans</i> was demonstrated in these patients. These symptoms subsided in 3 to 4 weeks after therapy	It can be concluded from the data presented that the complications of osteoradionecrosis, dental caries, and periodontal disease associated with radiation therapy for oral cancer can be reasonably well-controlled using the regimen employed in this study.

Table 2. Cont.

Author, Year	Condition	Moment of the Dental Intervention	Dental Intervention	Main Results	Conclusion
		During the oncologic treatment	<ol style="list-style-type: none"> <li>1. Weekly prophylaxis with fluoridated polishing paste;</li> <li>2. Prescriptions for pain relievers, dietary supplements, and antifungal or antibiotic agents when needed.</li> </ol>		
		After the oncologic treatment	<ol style="list-style-type: none"> <li>1. Oral and neck examination for detection of recurrent or new neoplastic diseases;</li> <li>2. Dental prophylaxis;</li> <li>3. Restoration dental procedures as needed;</li> <li>4. Reinforcement of the previously instituted oral hygiene regimen.</li> </ol>		

CRT: chemoradiation therapy; RT: radiotherapy.

Of the included studies, six are randomized clinical trials, where four [19,22–24] are reported for blind patients regarding the proposed intervention; the other studies of the type [20,21] do not contain such information. The four papers discuss, before and during the cancer treatment, the effectiveness of mouthwashes on radiotherapy toxicities, with a main focus on OM. The non-randomized clinical study evaluates the effect of an oral hygiene protocol before, during, and after cancer treatment applied in the study group compared to a control group (simple oral hygiene instructions, without dental intervention) [12]. With the exception of Stokman, 2012 [18], where the effect of mouthwash during patient treatment is evaluated, the other three cohort studies [15–17] present the effects of oral care protocols at different stages of cancer treatment (before, during, and after).

#### Risk of bias in studies

Most of the included studies were classified as having a low risk of bias ( $n = 9$ ; 81.0%), two (18.1%) studies classified as having a moderate risk, and one was classified as having a high risk ( $n = 0.8\%$ ). A detailed description of the subjects and scenario, and the method used to evaluate the results were well-described in most studies ( $n = 9$ ; 81.0%), as well as the sample selection criteria. On the other hand, in three articles, the information about the follow-up was not clear in the details about the time ( $n = 27.2\%$ ). The risk of bias assessment is described in detail in Supplementary Material S3.

### 3.3. Results of Individual Studies

Seven studies investigated the impact of mouthwashes in the oral toxicities. Kazemian [19] demonstrated the effectiveness of benzydamine in reducing mucositis resulting from radiotherapy and its effects (such as pain), which consequently reduced the number of patients who had treatment interrupted due to complications. Samaranayake [21] also demonstrated the effectiveness of the mouthwash; however, the patients in the study reported greater comfort when using 0.12% chlorhexidine, whose antimicrobial and pain effectiveness was similar. Epstein [22] demonstrates the prophylactic effect of the benzydamine mouthwash in regimens up to cumulative doses of 5000 cGy of RT, where erythema and ulceration were reduced by approximately 30% compared with the placebo; 33% of benzydamine subjects remained ulcer-free compared with 18% of placebo subjects and the use of systemic analgesics was shown to be significantly delayed compared with the placebo. Satheeshkumar [20] evaluated the effectiveness of triclosan compared to the placebo (saline solution), but did not observe a statistically significant difference between them. Stokman [18] shows that concentrated solutions of calcium phosphates showed no significant difference compared to saline during cancer treatment. Leenstra [23] evaluated the effects of doxepin as a mouthwash compared to the placebo; the mouth and throat pain reduction was greater for doxepin; a crossover analysis of patients completing both phases confirmed that patients experienced greater mouth and throat pain reduction with doxepin; however, the mouthwash was associated with more stinging or burning, an unpleasant taste, and greater drowsiness than the placebo rinse. Sio [24] studied doxepin and found similar results as well; mucositis pain during the first 4 h was better decreased in the group, compared to the diphenhydramine–lidocaine–antacid mouthwash and placebo. More drowsiness was reported with the doxepin mouthwash than placebo, as well as an unpleasant taste and stinging or burning.

The use of brushes with soft bristles proved to be the most suitable for oral hygiene. Regezi [17] suggested that brushing at least twice a day had significant rates of biofilm clearance, thus preventing caries, as is well-known in the literature, but the study was focused on the importance of the softness of the bristles of the brushes so as not to traumatize the oral soft tissue during RT or CT.

Tooth surface scaling and root planning showed effectiveness in eliminating the foci of the bacteria; patients undergoing such procedures before cancer treatment had better periodontal results during and after treatment, with lower rates of the need for invasive treatments later [14]. Periodontal treatment before oncologic treatment and after showed a decreased measurement in probing depth and gingival bleeding. Complementing these findings, Nuñez-Aguilar [12] states that polishing rough edges or surfaces resulted in fewer complaints of discomfort and mucosal injuries during cancer treatment. Furthermore, the study demonstrated that restorations performed before oncological treatment presented significant rates of prevention and maintenance of oral health by preventing lesions in the oral mucosa due to poor adaptation between tooth-resin, cutting edges, and reducing the risk of periapical infection. Both of these studies used fluoride gels to prevent caries at all times during cancer treatment, with effective results, as was expected.

Niewald [15] states that dental treatment procedures should be performed within at least 7 to 10 days from the last procedure until the beginning of radiotherapy, ensuring minimal tissue healing (gum, bone, and periodontal ligament). Tooth extractions should mainly be performed aiming at suturing techniques with complete tissue closure and prophylactic antibiotic therapy starting one day before the procedure, extending up to 10 days after. Tooth extractions were performed according to a written protocol under “special care” (primary tissue closure, and perioperative antibiotics for 7–10 days starting one day before surgery). Patients were advised not to wear their dental prostheses up to 6–12 months after radiotherapy in order to preserve the gums. In the end, the rate of patients in the study who developed osteoradionecrosis was low, but the results show that the amount of radiation and whether there was hyperfractionation is a direct factor in the development of this toxicity.

Despite being different studies in methodological design, they were the ones with the best design. Nunez-Aguilar evaluated the effects of oral hygiene guidance, restorative procedures, and periodontic and surgical procedures on the patient’s quality of life at each stage of treatment, by evaluating the mucositis severity, gingival bleeding, pain, weight loss, and trauma to the mucous, similar to Bueno, who evaluated, before and after cancer treatment (180 days after), the effects of basic periodontal treatment on patients, finding the depth of periodontal probing to be decreasing, also resulting in an improvement in the quality of the patient’s health. Samarannayake showed the effectiveness of the rinse with 0.12% chlorhexidine in improving oral mucositis, with antimicrobial activity.

#### 4. Discussion

This SR evaluated protocols in the literature that address the issue of basic oral health care for patients undergoing cancer treatment. The importance of the toothbrush choice for daily brushing, the brushing technique, the choice of alcohol-free rinses, the preference for saline or chlorhexidine, and the timing of these procedures are essential in order to guarantee success and comfort for the patient, from the dental and oncological point of view.

The mechanical cleaning of teeth is a prerequisite for good oral health, especially among cancer patients [19,26,27], and attention to maintaining good daily oral hygiene practices, including cleaning the interdental spaces with dental floss [28]. Meurman [29] showed that tooth brushing combined with chlorhexidine rinses prevented bacteremia in immunosuppressed patients due to oncologic treatment, which supports the findings in the study of Nunez-Aguilar [12]. The administration of antibacterial agents to control oral biofilms is a recommended strategy for patients with oral cancer, considering that rinses improve the removal of oral biofilms and oral debris, promote oral hygiene, and improve patient comfort during cancer therapy.

Chlorhexidine is the gold standard for chemical plaque control, but its effectiveness in preventing caries is still uncertain [30,31]. Hancock [32] recommended that patients start prophylactic chlorhexidine mouthwashes to prevent the onset of microbial infection, gingival inflammation, and bleeding, and to reduce the risk of caries pre-cancer treatment. Foote [33] report that an oral rinse with chlorhexidine has potential effects on OM, as with Samarannayake [21], even though it has not shown a significant effect on oral pain or in the oral carriage of the microorganisms. The benzydamine rinse showed significant action against pain with a topical analgesic effect, bringing a more comfortable experience to the patient. Epstein [22] also points out that throat pain was also reduced with benzydamine compared with placebo. Laine [34] compared the use of saline-based mouthwashes with sodium bicarbonate and showed that the use of alcohol-based mouthwashes and hydrogen peroxide mouthwashes should be discontinued due to their drying and irritating effects on the oral mucosa. Stokman [18] adds to the list that calcium phosphate does not have an effective action against OM, in addition to presenting discomfort in the study group. Furthermore, the rinse with doxepin showed interesting results in controlling pain; patients showed interest in continuing the treatment even with adverse effects [35]. Doxepin has effects on both the central and peripheral nervous systems, making it an option that can be used for the treatment of radiotherapy-induced oral mucositis pain.

Fluoride prophylaxis is one of the methods of choice for combatting caries, especially in patients with oral cancer due to the ease of access to the procedure [36]. Fluoride strengthens the acid resistance of dental hard tissues and can inhibit the cariogenic oral microbiota. Meyerowitz found that the different application methods used are not critical as long as the patient receives daily fluoride and understands his daily need [37].

Although the management of xerostomia is a critical component of supportive care in head and neck cancer patients—given its significant impact on oral function, comfort, and overall quality of life—studies focusing on xerostomia were not included in this review, mostly based on the predefined inclusion criteria, which required interventions to be performed within hospital settings and by qualified dental professionals specifically addressing radiotherapy-related complications as part of a broader oral care protocol.

The various problems that an oral cancer patient may face in maintaining oral health require prophylactic protocols and personalized treatment modes. Basic oral care performed by trained professionals is a necessity, in addition to the patient's daily self-care. The adherence to dental treatment recommendations can be an obstacle to the prevention of complications. General principles for prevention and the treatment of patients with reduced salivary flow, dental caries, and oral candidiasis are also valid for oral cancer patients. These at-risk patients need intensified prophylaxis and procedures to prevent even life-threatening systemic infections from the mouth. Good oral health care is also directly related to patients' quality of life.

The prevention of oral complications, and the early recognition, diagnosis, and management of oral complications generally unite the experience in medical and dental care within a multidisciplinary team [38]. It is important to remember that the planning of any dental treatment begins with a thorough oral examination and radiographic examinations. It is recommended that the patient continue weekly follow-ups with the oral care professional during cancer therapy [9].

## 5. Limitations

In evaluating the studies, some limitations were found. An important point was the lack of clarity in detailing the design of the studies carried out. Some report results and conclusions that cannot be affirmed by the way the research was conducted.

Another relevant limitation is that control groups in periodontal studies received minimal or no dental procedures, and this may bias the interpretation of periodontal results.

During the research, we found many works with complex interventions or with a lack of details about the basic procedures. There is a need to detail the stages of adaptation of patients, and which steps were taken and products used; many works only mention that this step in the treatment of the patient was carried out. Only with this information will it be possible to determine a basic oral care protocol supported by consistent and logical evidence.

## 6. Conclusions

Limited data is available on the impact of dental care prior to cancer therapy, and oral care during active cancer care. There is, however, general consensus supporting oral evaluation and treatment prior to cancer treatment and continuing oral care during and after therapy [35,36]. The findings of this review show us that preventive dental action has an impact on the quality of life of patients, in terms of controlling toxicities resulting from cancer treatment. The use of mouthwash with 0.12% chlorhexidine, soft brushes, and topical fluoride applications at all stages of treatment and follow-up are essential. It is still necessary to develop a basic care protocol, and basic prevention procedures in a more specific way in order to guarantee better results and more comfort for patients.

In this systematic review, some questions could not be conclusively answered due to insufficient and heterogeneous data, particularly regarding the following: (i) the comparative effectiveness of individual BOC components versus standard care; (ii) the optimal timing, frequency, and dosing (e.g., concentrations and duration) of key agents such as topical fluoride, chlorhexidine, and benzydamine; and (iii) the long-term outcomes and patient-reported measures.

Recommendations for future primary studies

After evaluating the articles in this review, we suggest the following guidelines for future studies: randomized blinded clinical trials, details of the stages of oral preparation of cancer patients, details of the cancer (type/stage), and details of the cancer therapy and patient demographics. Studies with a good methodological design with controlled trials are the goal. Publications presenting details of the procedures performed, including details of the oral care provided, compliance with oral care recommendations, the product delivery of the products used, including the format of the product (e.g., rinse, cream, gel concentrations, amounts, and time), directions for product use, and a description of the hygiene instructions for the patient, and frequency and duration of products used.

## 7. Other Information

**Protocol and registration:** The methods of this SR were established before starting the review, and the resulting protocol was based on PRISMA-P [39,40] which was registered at the International Prospective Register of SRs (PROSPERO) database under registration number CRD42022319455 [41]. Additionally, the present SR was reported according to the Preferred Reporting Items for SRs and Meta-Analyses (PRISMA) checklist [42].

**Supplementary Materials:** The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/hygiene5040045/s1>.

**Author Contributions:** All authors made substantial contributions to the conception (M.C.C., A.R.S.-S., and A.C.P.-R.); draft and material preparation, data collection, and analysis: (M.C.C., M.I.A.W., M.E.P.-d.-O., A.G.C.N., and A.L.D.A.); and review (J.C.R., T.B.B., J.B.E., A.R.S.-S., and A.C.P.-R.) of the data for the work. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Brazil) process number 8887.640785/2021-00. None of the authors received research support from companies or similar organizations that may gain or lose financially through the publication of this manuscript. A.L.D.A. is a Post-Doctoral researcher who holds a fellowship funded by The São Paulo Research Foundation (FAPESP: 2021/14585-7). A.R.S-S (grant number 307604/2023-3) and A.C.P-R (grant number 304397/2025-3) are research grantees of the National Council for Scientific and Technological Development (CNPq).

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Acknowledgments:** The authors would like to gratefully acknowledge the Coordination for the Improvement of Higher Education Personnel (CAPES/PROEX, Brazil) process number 001, the National Council for Scientific and Technological Development (CNPq, Brazil), and the grants from São Paulo Research Foundation (FAPESP, Brazil).

**Conflicts of Interest:** The authors have no relevant financial or non-financial interests to disclose.

## References

1. Bray, F.; Ferlay, J.; Soerjomataram, I.; Siegel, R.L.; Torre, L.A.; Jemal, A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **2018**, *68*, 394–424, Erratum in *CA Cancer J. Clin.* **2020**, *70*, 313. [[CrossRef](#)]
2. Caribé-Gomes, F.; Chimenos-Küstner, E.; López-López, J.; Finestres-Zubeldia, F.; Guix-Melcior, B. Dental management of the complications of radio and chemotherapy in oral cancer. *Med. Oral.* **2003**, *8*, 178–187. [[PubMed](#)]
3. Mosel, D.D.; Bauer, R.L.; Lynch, D.P.; Hwang, S.T. Oral complications in the treatment of cancer patients. *Oral Dis.* **2011**, *17*, 550–559. [[CrossRef](#)] [[PubMed](#)]
4. Epstein, J.B.; Hong, C.; Logan, R.M.; Barasch, A.; Gordon, S.M.; Oberlee-Edwards, L. A systematic review of orofacial pain in patients receiving cancer therapy. *Support Care Cancer* **2012**, *18*, 1023–1031.
5. Burlage, F.R.; Coppes, R.P.; Meertens, H.; Stokman, M.A.; Vissink, A. Parotid and submandibular/sublingual salivary flow during high dose radiotherapy. *Radiat. Oncol.* **2001**, *61*, 271–274. [[CrossRef](#)]
6. Almståhl, A.; Finizia, C.; Carlén, A.; Fagerberg-Mohlin, B.; Alstad, T. Explorative study on mucosal and major salivary secretion rates, caries and plaque microflora in head and neck cancer patients. *Int. J. Dent. Hyg.* **2018**, *16*, 450–458. [[CrossRef](#)]
7. Jensen, S.B.; Jarvis, V.; Zadik, Y.; Barasch, A.; Ariyawardana, A.; Hovan, A. Systematic review of miscellaneous agents for the management of oral mucositis in cancer patients. *Support Care Cancer* **2013**, *21*, 3223–3232. [[CrossRef](#)]
8. Lanzós, I.; Herrera, D.; Lanzós, E.; Sanz, M. A critical assessment of oral care protocols for patients under radiation therapy in the regional University Hospital Network of Madrid. *J. Clin. Exp. Dent. Spain* **2015**, *27*, 613–621. [[CrossRef](#)]
9. De Sanctis, V.; Bossi, P.; Sanguineti, G.; Trippa, F.; Ferrari, D.; Bacigalupo, A. Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements. *Crit. Rev. Oncol./Hematol.* **2016**, *100*, 147–166. [[CrossRef](#)]
10. Moon, D.H.; Moon, S.H.; Wang, K.; Weissler, M.C.; Hackman, T.G.; Zanation, A.M. Incidence of, and risk factors for, mandibular osteoradionecrosis in patients with oral cavity and oropharynx cancers. *Oral Oncol.* **2017**, *72*, 98–103. [[CrossRef](#)]
11. Pauli, N.; Johnson, J.; Finizia, C.; Andréll, P. The incidence of trismus and long-term impact on health-related quality of life in patients with head and neck cancer. *Acta Oncol.* **2013**, *52*, 1137–1145. [[CrossRef](#)]
12. Nuñez-Aguilar, J.; Fernández-Olavarría, A.; Oliveros-López, L.G.; Torres-Lagares, D.; Serrera-Figallo, M.A.; Gutiérrez-Corrales, A.; Gutiérrez-Pérez, J.L. Evolution of oral health in oral cancer patients with and without dental treatment in place: Before, during and after cancer treatment. *J. Clin. Exp. Dent.* **2018**, *10*, 158–165. [[CrossRef](#)]
13. Ouzzani, M.; Hammady, H.; Fedorowicz, Z.; Elmagarmid, A. Rayyan—A web and mobile app for systematic reviews. *Syst. Rev.* **2016**, *5*, 210. [[CrossRef](#)]
14. Moola, S.; Munn, Z.; Tufanaru, C.; Aromataris, E.; Sears, K.; Sfetcu, R.; Currie, M.; Lisy, K.; Qureshi, R.; Mattis, P.; et al. Chapter 7: Systematic Reviews of Etiology and Risk. In *JBI Manual for Evidence Synthesis*; Aromataris, E., Munn, Z., Eds.; JBI: Kingston, Jamaica, 2020. [[CrossRef](#)]
15. Niewald, M.; Fleckenstein, J.; Mang, K.; Holtmann, H.; Spitzer, W.J.; Rube, C. Dental status, dental rehabilitation procedures, demographic and oncological data as potential risk factors for infected osteoradionecrosis of the lower jaw after radiotherapy for oral neoplasms: A retrospective evaluation. *Radiat. Oncol.* **2013**, *8*, 227. [[CrossRef](#)] [[PubMed](#)]

16. Bueno, A.C.; Ferreira, R.C.; Barbosa, F.I.; Jham, B.C.; Magalhães, C.S.; Moreira, A.N. Periodontal care in patients undergoing radiotherapy for head and neck cancer. *Support Care Cancer* **2013**, *21*, 969–975. [[CrossRef](#)] [[PubMed](#)]
17. Regezi, J.A.; Courtney, R.M.; Kerr, D.A. Dental management of patients irradiated for oral cancer. *Cancer* **1976**, *38*, 994–1000. [[CrossRef](#)] [[PubMed](#)]
18. Stokman, M.A.; Burlage, F.R.; Spijkervet, F.K. The effect of a calcium phosphate mouth rinse on (chemo) radiation induced oral mucositis in head and neck cancer patients: A prospective study. *Int. J. Dent. Hyg.* **2012**, *10*, 175–180. [[CrossRef](#)]
19. Kazemian, A.; Kamian, S.; Aghili, M.; Hashemi, F.A.; Haddad, P. Benzylamine for prophylaxis of radiation-induced oral mucositis in head and neck cancers: A double-blind placebo-controlled randomized clinical trial. *Eur. J. Cancer Care* **2009**, *18*, 174–178. [[CrossRef](#)]
20. Satheeshkumar, P.S.; Chamba, M.S.; Balan, A.; Sreelatha, K.T.; Bhatathiri, V.N.; Bose, T. Effectiveness of triclosan in the management of radiation-induced oral mucositis: A randomized clinical trial. *J. Cancer Res. Ther.* **2010**, *6*, 466–472. [[CrossRef](#)]
21. Samaranyake, L.P.; Robertson, A.G.; MacFarlane, T.W.; Hunter, I.P.; MacFarlane, G.; Soutar, D.S.; Ferguson, M.M. The effect of chlorhexidine and benzylamine mouthwashes on mucositis induced by therapeutic irradiation. *Clin. Radiol.* **1988**, *39*, 291–294. [[CrossRef](#)]
22. Epstein, J.B.; Silverman, S., Jr.; Paggiarino, D.A.; Crockett, S.; Schubert, M.M.; Senzer, N.N.; Lockhart, P.B.; Gallagher, M.J.; Peterson, D.E.; Leveque, F.G. Benzylamine HCl for prophylaxis of radiation-induced oral mucositis: Results from a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Cancer* **2001**, *92*, 875–885. [[CrossRef](#)] [[PubMed](#)]
23. Leenstra, J.L.; Miller, R.C.; Qin, R.; Martenson, J.A.; Dornfeld, K.J.; Bearden, J.D.; Puri, D.R.; Stella, P.J.; Mazurczak, M.A.; Klish, M.D.; et al. Doxepin rinse versus placebo in the treatment of acute oral mucositis pain in patients receiving head and neck radiotherapy with or without chemotherapy: A phase III, randomized, double-blind trial (NCCTG-N09C6 [Alliance]). *J. Clin. Oncol.* **2014**, *32*, 1571–1577. [[CrossRef](#)] [[PubMed](#)]
24. Sio, T.T.; Le-Rademacher, J.G.; Leenstra, J.L.; Loprinzi, C.L.; Rine, G.; Curtis, A.; Singh, A.K.; Martenson, J.A., Jr.; Novotny, P.J.; Tan, A.D.; et al. Effect of Doxepin Mouthwash or Diphenhydramine-Lidocaine-Antacid Mouthwash vs. Placebo on Radiotherapy-Related Oral Mucositis Pain: The Alliance A221304 Randomized Clinical Trial. *JAMA* **2019**, *321*, 1481–1490. [[CrossRef](#)] [[PubMed](#)]
25. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Moher, D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* **2021**, *372*, n71. [[CrossRef](#)]
26. Epstein, J.B.; Güneri, P.; Barasch, A. Appropriate and necessary oral care for people with cancer: Guidance to obtain the right oral and dental care at the right time. *Support Care Cancer* **2014**, *22*, 1981–1988. [[CrossRef](#)]
27. Huang, B.S.; Wu, S.C.; Lin, C.Y.; Fan, K.H.; Chang, J.T.; Chen, S.C. The effectiveness of a saline mouth rinse regimen and education programme on radiation-induced oral mucositis and quality of life in oral cavity cancer patients: A randomised controlled trial. *Eur. J. Cancer Care* **2018**, *27*, e12819. [[CrossRef](#)]
28. Bonnaure-Mallet, M.; Bunetel, L.; Tricot-Doleux, S.; Guérin, J.; Bergeron, C.; LeGall, E. Oral complications during treatment of malignant diseases in childhood: Effects of tooth brushing. *Eur. J. Cancer* **1998**, *34*, 1588–1591. [[CrossRef](#)]
29. Meurman, J.H.; Grönroos, L. Oral and dental health care of oral cancer patients: Hyposalivation, caries and infections. *Oral Oncol.* **2010**, *46*, 464–467. [[CrossRef](#)]
30. Antunes, H.; Ferreira, E.; Faria, L.; Schirmer, M.; Rodrigues, P.C.; Small, I.; Colares, M.; Bouzas, L.-F.-d.S.; Ferreira, C.-G. Streptococcal bacteraemia in patients submitted to hematopoietic stem cell transplantation: The role of tooth brushing and use of chlorhexidine. *Med. Oral Patol. Oral Cir. Bucal* **2010**, *15*, 303–309. [[CrossRef](#)]
31. Autio-Gold, J. The role of chlorhexidine in caries prevention. *Oper. Dent.* **2008**, *33*, 710–716. [[CrossRef](#)]
32. Hancock, P.J.; Epstein, J.B.; Sadler, G.R. Oral and dental management related to radiation therapy for head and neck cancer. *J. Can. Dent. Assoc.* **2003**, *69*, 585–590.
33. Foote, R.L.; Loprinzi, C.L.; Frank, A.R.; O’Fallon, J.R.; Gulavita, S.; Twefik, H.H.; Novotny, P. Randomized trial of a chlorhexidine mouthwash for alleviation of radiation-induced mucositis. *J. Clin. Oncol.* **1994**, *12*, 2630–2633. [[CrossRef](#)]
34. Laine, P.; Meurman, J.H.; Murtomaa, H.; Lindqvist, C.; Torkko, H.; Pyrhönen, S.; Teerenhovi, L. One-year trial of the effect of rinsing with an amine fluoride–stannous– fluoride-containing mouthwash on gingival index scores and salivary microbial counts in lymphoma patients receiving cytostatic drugs. *J. Clin. Periodontol.* **1993**, *20*, 628–634. [[CrossRef](#)] [[PubMed](#)]
35. Sudoh, Y.; Cahoon, E.E.; Gerner, P.; Wang, G.K. Tricyclic antidepressants as long-acting local anesthetics. *Pain* **2003**, *103*, 49–55. [[CrossRef](#)] [[PubMed](#)]
36. Epstein, J.B.; Chin, E.A.; Jacobson, J.J.; Rishiraj, B.; Le, N. The relationships among fluoride, cariogenic oral flora, and salivary flow rate during radiation therapy. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **1998**, *86*, 286–292. [[CrossRef](#)] [[PubMed](#)]
37. Meyerowitz, C.; Watson, G.E., 2nd. The efficacy of an intraoral fluoride-releasing system in irradiated head and neck cancer patients: A preliminary study. *J. Am. Dent. Assoc.* **1998**, *129*, 1252–1259. [[CrossRef](#)]

38. Epstein, J.B.; van der Meij, E.H.; Lunn, R.; Stevenson-Moore, P. Effects of compliance with fluoride gel application on caries and caries risk in patients after radiation therapy for head and neck cancer. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **1996**, *82*, 268–275. [CrossRef]
39. National Comprehensive Cancer Network. Head and Neck Cancers (Version3.2021). 2021. Available online: [https://www.nccn.org/professionals/physician\\_gls/pdf/head-and-neck.pdf](https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf) (accessed on 18 August 2021).
40. Shamseer, L.; Moher, D.; Clarke, M.; Ghersi, D.; Liberati, A.; Petticrew, M.; Shekelle, P.; Stewart, L.A.; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: Elaboration and explanation. *BMJ* **2015**, *349*, g7647. [CrossRef]
41. Cuzzullin, M.C.; Pérez-de-Oliveira, M.E.; Normando, A.G.C.; Santos-Silva, A.R.; Prado-Ribeiro, A.C. Basic oral care in cancer patients: A systematic review. *PROSPERO CRD42022319455*. Available online: [https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42022319455](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022319455) (accessed on 5 March 2022).
42. Page, M.J.; Moher, D.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. *BMJ* **2021**, *372*, n160. [CrossRef]

**Disclaimer/Publisher’s Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.