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Oncological treatments and oral health: integrative review

Carlos Nuno Pereira Matos [1] 0009-0001-9715-7279
Paulo Miguel Silva Pereira de Araújo [1] 0000-0002-0621-1744
Carla Guimarães Moutinho [1, 2, 3] 0000-0003-1310-4696

[1] Faculty of Health Sciences, Fernando Pessoa University, Porto, Portugal
[2] LAQV/REQUIMTE, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, Porto, Portugal
[3] RISE-Health, Faculty of Health Sciences, Fernando Pessoa University, Porto, Portugal

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Corresponding Author:
Carlos Nuno Pereira Matos;
Faculty of Health Sciences,
Fernando Pessoa University, Porto,
Portugal; 35434@ufp.edu.pt

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ABSTRACT

Introduction: Cancer therapies such as chemotherapy and radiotherapy, although effective, are frequently associated with oral complications that negatively impact patients' quality of life and treatment adherence. Oral mucositis and xerostomia are among the most prevalent adverse effects, requiring coordinated preventive and therapeutic strategies.
Objectives: This integrative review aims to evaluate the impact of oncological treatments on oral health, identify the most common complications, and analyze evidence-based interventions to mitigate these effects, highlighting the role of dental professionals in comprehensive cancer care.
Methodology: A systematic search was conducted across PubMed, SciELO, and the Cochrane Library, following the PICO(S) framework. Clinical between between February 2020 and February 2025, in English or Portuguese, assessing oral complications in cancer patients undergoing chemotherapy or radiotherapy were included. The risk of bias of the included studies was assessed using the Cochrane risk of bias tool 2.
Results: Seventeen studies were selected. Oral mucositis was the most frequently reported complication in chemotherapy, while xerostomia was predominant in radiotherapy. Interventions such as photobiomodulation, cryotherapy, zinc-based rinses, fluoride, and trehalose-based products demonstrated efficacy in reducing symptom severity and improving patient comfort. However, variability in protocols and limited access to dental care remain significant challenges.
Conclusion: Oral health must be integrated into multidisciplinary oncology care. Early preventive interventions and structured oral care protocols are essential to minimize complications and improve patient outcomes. Further high-quality studies are needed to standardize effective strategies and ensure equitable access to oral care in oncology settings.

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INFORMAÇÃO DO ARTIGO

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Autor correspondente:
Carlos Nuno Pereira Matos;
Faculdade de Ciências da Saúde, Universidade Fernando Pessoa, Porto, Portugal; 35434@ufp.edu.pt

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RESUMO

Introdução: Os tratamentos oncológicos, como a quimioterapia e a radioterapia, embora eficazes no tratamento do cancro, estão frequentemente associadas a complicações orais que comprometem a qualidade de vida e a adesão ao tratamento. A mucosite oral e a xerostomia são os efeitos adversos mais prevalentes, exigindo estratégias preventivas e terapêuticas coordenadas.
Objetivos: Esta revisão integrativa teve como objetivo avaliar o impacto dos tratamentos oncológicos na saúde oral, identificar as complicações mais comuns e analisar intervenções baseadas em evidência científica para a sua mitigação, destacando o papel dos profissionais de medicina dentária nos cuidados oncológicos integrados.
Metodologia: Uma pesquisa sistemática foi realizada nas bases de dados PubMed, SciELO e Cochrane Library, seguindo a estrutura PICO(S). Foram incluídos estudos clínicos publicados entre fevereiro de 2020 e fevereiro de 2025, em inglês ou português, que abordassem complicações orais em doentes oncológicos submetidos a quimioterapia ou radioterapia. O risco de viés dos estudos incluídos foi avaliado utilizando a ferramenta Cochrane Risk of Bias 2.
Resultados: Foram selecionados 17 estudos. A mucosite oral foi a complicação mais frequentemente reportada em doentes submetidos a quimioterapia, enquanto a xerostomia prevaleceu entre os doentes submetidos a radioterapia. Intervenções como a fotobiomodulação, crioterapia, soluções com zinco, aplicação de flúor e produtos à base de trealose demonstraram eficácia na redução da gravidade dos sintomas e na melhoria do conforto dos pacientes. No entanto, a heterogeneidade dos protocolos e o acesso limitado a cuidados dentários especializados permanecem desafios relevantes.
Conclusões: A saúde oral deve ser integrada nos cuidados oncológicos multidisciplinares. A implementação precoce de estratégias preventivas e de protocolos estruturados de cuidados orais é fundamental para minimizar complicações e melhorar os desfechos clínicos. São necessários estudos adicionais de elevada qualidade para padronizar intervenções eficazes e garantir o acesso equitativo a cuidados de saúde oral no contexto oncológico.

Introduction

In recent years, significant advances have been made in cancer treatment; however, adverse effects and complications associated with these therapies remain highly prevalent.[1] Cancer continues to be a major contributor to global morbidity, mortality, and disability. As cancer incidence increases, healthcare systems worldwide are placing greater emphasis on enhancing patient well-being and mitigating the impact of both the disease and its treatment, particularly chemotherapy (CTX) and radiotherapy (RT).[2,3]

Currently, cancer accounts for approximately 15% of all deaths globally each year, making it one of the leading causes of mortality.[2] Chemotherapy, a cornerstone of cancer therapy, is frequently associated with a wide range of short- and long-term adverse effects.[2] Although the development of modern oncological therapies has markedly improved survival rates, their side effects remain a significant concern for patients' quality of life.[3] Among these, oral mucositis (OM) is one of the most frequent and clinically significant complications, commonly associated with CTX, RT, or their combination.[3]

Oral mucositis refers to the development of erythematous and painful ulcerative lesions of the oral mucosa in patients undergoing cancer treatment. This condition affects up to 80% of patients receiving high-dose CTX, nearly all patients undergoing head and neck RT, and 20-40% of those on conventional CTX.[4,5] The importance of early dental assessment and the involvement of a multidisciplinary oral healthcare team cannot be overstated. This collaborative approach plays a pivotal role in reducing the severity of oral complications during cancer treatment.[1]

It is essential for oral health professionals to be familiar with the specific oncological therapies administered and to educate patients about potential oral side effects and strategies to minimize their impact.[5] Dental professionals, as integral members of the multidisciplinary oncology team, must ensure that cancer treatment is not delayed or interrupted due to oral complications. Clinicians should be able to recognize signs and symptoms affecting the oral cavity to perform appropriate assessments and initiate timely referrals.[5]

Early intervention, including preventive oral care and behavioral modifications initiated prior to the start of CTX or RT, can significantly improve clinical outcomes.[6] Continuous follow-up and comprehensive oral care throughout all phases of cancer treatment, including post-therapy support, are essential not only for physical health but also for the patient's psychological well-being.[5]

Despite the recognized importance of oral health in oncology patients, there remains a noticeable lack of cohesive and specific guidelines addressing this issue. Therefore, the aim of this study is to comprehensively analyze the effects of oncological treatments on oral health, identify the most prevalent complications, and discuss evidence-based preventive and therapeutic strategies, with the goal of contributing to more effective and integrated dental care.

Methodology

This integrative review followed a systematic approach, which involved establishing inclusion and exclusion criteria, developing a comprehensive research strategy, selecting relevant studies, and conducting data extraction and synthesis. The methodological framework, including the PICO strategy, database selection, and eligibility criteria, was defined a *priori* before the literature search was conducted. Although the review protocol was not registered in PROSPERO, the study followed predefined procedures, ensuring consistency and minimizing potential bias.

Inclusion and exclusion criteria

The inclusion criteria for article selection were as follows: studies written in English or Portuguese; publications from the past five years (February 2020 to February 2025); full text articles available in PDF format, randomized controlled studies, controlled studies, and clinical studies, including randomized clinical trials, prospective studies, or cohort studies, that analyzed oral complications in patients undergoing oncological treatments and included a follow-up period. Exclusion criteria included: systematic reviews, retrospective studies, narrative reviews, secondary studies with pediatric participants and studies whose titles or abstracts did not demonstrate relevance to the objectives of this review.

Search strategy

The research was conducted across three electronic databases: PubMed, SciELO, and the Cochrane Library. The search was restricted to the last five years (February 2020–February 2025) to capture the most recent clinical evidence and contemporary clinical practices in oncology-related oral care. Detailed search queries and database-specific filters are provided in Appendix Tables 3 and 4. The search terms included: “Oral Health”, “Cancer Patients”, “Chemotherapy”, “Oral Hygiene”, “Radiotherapy”, “Oral Mucositis”, “Prevention”, “Oral care protocols”, “Antineoplastic agents”, and “Dental care”.

The research strategy was guided by the PICO framework (Population, Intervention, Comparison, Outcome), which is commonly used to formulate clinical research questions and guide evidence-based practices. Based on this approach, two central research questions were developed: (1) What are the main effects of oncological treatments on oral health? was the primary outcome and (2) What are the best preventive and therapeutic strategies from a dental professional’s perspective? was the secondary outcome. In this framework, the population (P) consisted of patients undergoing CTX, RT, or targeted therapies for cancer.

The intervention (I) involved preventive and therapeutic dental care and interventions. The comparison (C) was defined as the absence of specific dental care. The outcome (O) focused on the impact of oncological treatments on oral health, particularly the occurrence of oral complications such as mucositis, xerostomia, osteonecrosis of the jaw, and opportunistic infections. Primary outcomes included the incidence and severity of oral mucositis (WHO or OMAS scales), xerostomia severity and salivary function parameters (e.g., salivary flow rate or validated xerostomia questionnaires). Secondary outcomes included oral health indicators such as plaque accumulation, gingival inflammation, and patient-reported quality-of-life measures.

Screening method

The selection process followed the predefined inclusion and exclusion criteria. The screening procedure began with the elimination of duplicate records, after which titles and abstracts were evaluated for relevance. Subsequently, full-text articles were examined to verify their eligibility and confirm whether they addressed the research question. The overall process is illustrated in the PRISMA 2020 flow diagram (Figure 1).[7]

The selection process was conducted by three independent investigators. Records retrieved from the selected databases were first exported into a reference management file to facilitate organization and screening. Duplicate references were identified and removed prior to the screening process by comparing titles, authors, publication years, and journal information across databases. When duplicate records were detected, only one instance of each study was retained.

After duplicate removal, titles and abstracts were screened according to the predefined inclusion and exclusion criteria. Potentially eligible studies were subsequently assessed through full-text evaluation to determine their eligibility.

Any disagreements regarding study eligibility or data extraction were resolved through face-to-face discussion among the investigators until consensus was reached.

The keyword combinations presented in Table 3 (appendix) represent exploratory search strategies used during the development and refinement of the final database search. These combinations were employed to identify relevant terminology and optimize article retrieval across the selected databases.

The total number of records reported in the PRISMA flow diagram corresponds to the final database searches conducted using the refined search strategy and database-specific filters.

Data extraction

Data were extracted from selected studies according to the following categories: authors and publication year; country of origin; participants' sample size; oncological treatment type; oral complications assessed; assessment methods; main findings; and preventive or therapeutic interventions. To ensure consistency in the presentation of results, each included study was assigned a numerical study identifier used consistently across tables and throughout the manuscript.

Risk of bias (RoB) assessment

The evaluation of risk of bias was performed using the ROB 2 tool for randomized clinical trials[8] (RCT) and the ROBINS-I tool for non-randomized clinical trials[9] (nRCT), both in accordance with the guidelines of the Cochrane Handbook for Systematic Reviews. According to Cochrane, non-randomized studies of interventions (NRSI) encompass cohort studies, case–control studies, controlled before-and-after studies, and interrupted time series.

Data synthesis

Due to the substantial clinical and methodological heterogeneity among the included studies, a quantitative synthesis (meta-analysis) was not performed. The studies differed considerably in terms of cancer types, oncological treatments, preventive and therapeutic interventions, outcome measures, and follow-up periods. These differences limited the possibility of pooling comparable datasets across studies. Therefore, the findings were synthesized using a structured narrative approach, which allowed the integration and interpretation of heterogeneous evidence within the context of an integrative review methodology.

Table 1: Risk of bias.

Study ID	ROB Tool	Design	D1	D2	D3	D4	D5	D6	D7	Overall
Elsaadany, 2024	ROB2	RCT	!	+	+	+	+	⊘	⊘	!
Umeda, 2021	ROB2	RCT	!	+	+	!	!	⊘	⊘	!
Khalil, 2025	ROB2	RCT	!	+	+	+	+	⊘	⊘	!
Walladbegi, 2022	ROB2	RCT	+	+	+	+	+	⊘	⊘	+
Lam-ubol A, 2021	ROB2	RCT	+	+	+	+	+	⊘	⊘	+
Piboonratanakit, 20	ROB2	RCT	+	+	+	-	+	⊘	⊘	!
Jiang N,2024	ROB2	RCT	+	+	+	-	+	⊘	⊘	!
Morsy BM, 2023	ROB2	RCT	+	+	+	+	+	⊘	⊘	+
Jiang, 2022	ROB2	RCT	+	+	+	-	+	⊘	⊘	!
Vesty, 2020	ROB2	RCT	+	+	+	+	+	⊘	⊘	+
Mohammadi, 2022	ROB2	RCT	+	+	+	-	+	⊘	⊘	-
Rodrigues, 2020	ROB2	RCT	+	+	+	-	+	⊘	⊘	-
Nielsen, 2021	ROB2	RCT	+	+	+	+	+	⊘	⊘	+
Sahebnasagh, 2023	ROB2	RCT	+	+	+	+	+	⊘	⊘	+
Lee et al., 2021	ROBINS-I	nRCT	-	+	+	!	+	!	+	-
Elsehrawy et al., 20	ROBINS-I	nRCT	-	+	+	!	+	!	+	-
Rogers SN, 2021	ROB2	RCT	-	+	+	!	+	⊘	⊘	-

Caption: + Low risk; ! Some concerns; - High risk; ⊘ the domains are not part of ROB2. ROB2 domains- D1, Randomization; D2, deviations from intended intervention; D3, missing data; D4, outcome measurement; D5, selection of reported result; ROBINS-I domains- D1, confounding; D2, selection of participants; D3, classification of interventions; D4, deviations from intended interventions; D5, missing data; D6, measurement of outcomes; D7, selection of the reported result.

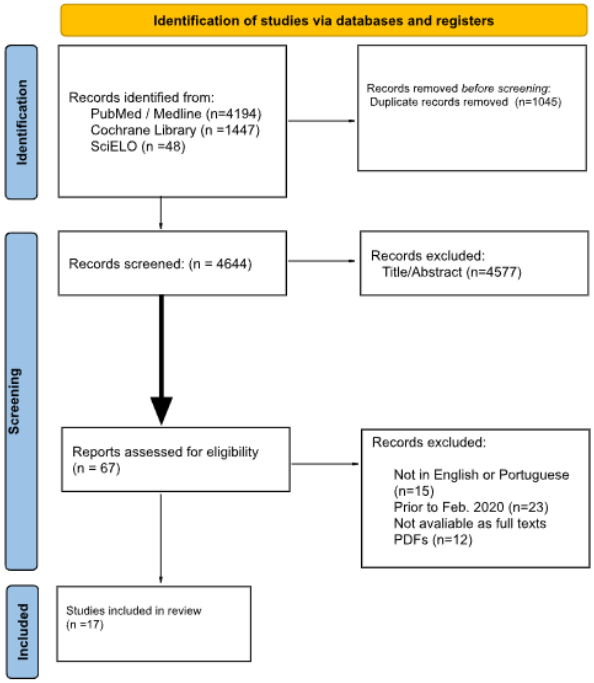

Figure 1. Flowchart of the article selection process.

Results

Study selection and characteristics of included studies

During the title and abstract screening phase, 4577 articles were excluded for not meeting the inclusion criteria, retrospective studies, narrative reviews, secondary studies, articles without full-text availability, and those whose titles or abstracts are not relevant to the topic were excluded, leaving 67 articles for full-text review.

In the full-text review stage, 50 additional articles were excluded due to failure to meet the inclusion criteria. Consequently, 17 studies were selected for data extraction and analysis. Figure 1 provides a flowchart illustrating the article selection process.

Analysis of the results of the selected studies

To ensure clarity in presenting the findings, the results are organized according to the type of oncological treatment: chemotherapy and radiotherapy, the two most commonly used. This structure aligns with the objective of understanding the specific oral health impacts of each therapy, while avoiding redundancy among the included studies. Table 2 summarizes the primary information extracted, comprising study design, population, cancer type, treatment modality, clinical setting, oral condition assessed, diagnostic criteria, presence of control/placebo group, and duration of follow-up.

Chemotherapy

Oral mucositis

Oral mucositis was the most frequently reported complication associated with chemotherapy. Several randomized controlled trials demonstrated that professional oral healthcare protocols significantly reduced the severity of mucositis and improved overall oral health, particularly in patients with breast cancer.[10]

Photobiomodulation (PBM) therapy, when used preventively, showed efficacy in lowering the incidence of OM and improving patient-reported quality of life.[6]

A randomized clinical trial by Walladbegi et al.[11] assessed the efficacy of a novel intraoral cryotherapy device in patients undergoing high-dose CTX followed by autologous hematopoietic stem cell transplantation. Results showed a marked reduction in both the incidence and severity of mucositis compared to conventional ice chips.

In patients receiving targeted therapies (e.g., everolimus and exemestane), professional oral care, including mechanical cleaning and topical dexamethasone, also led to lower incidence and severity of OM.[10] This aligns with findings from studies emphasizing the role of structured oral hygiene guidance in mitigating mucositis severity and enhancing functional outcomes.[5,10]

Xerostomia (XER) and other complications

The Patient Concerns Inventory demonstrated value in addressing xerostomia, a frequently underreported side effect, by improving communication between patients and clinicians and guiding supportive care.[12]

In addition to OM, xerostomia was commonly reported, with studies exploring management strategies such as saliva substitutes[13] and trehalose-based sprays[14], both of which improved salivary pH, buffering capacity, and oral comfort.

Other complications, such as dental caries and periodontal disease, were common, particularly among patients with insufficient oral hygiene support[15]. The combination of reduced salivary flow and microbial imbalance further promoted enamel demineralization and increased the risk of opportunistic infections.[13]

Prophylactic and supportive interventions

Several studies emphasized the effectiveness of preventive interventions implemented before or during chemotherapy, including individualized oral care protocols, fluoride treatments, and antimicrobial rinses such as chlorhexidine or zinc-based formulations, all of which helped reduce the incidence and severity of oral lesions.[5,15]

Educational strategies also played a significant role, especially in developing countries where oral health literacy remains limited.[15]

Follow-up durations varied significantly across studies, from as little as 1–2 weeks to full treatment cycles, influencing the ability to assess both the onset and resolution of complications and their broader impact on nutrition, adherence, and quality of life.

Radiotherapy

Radiotherapy, particularly in the head and neck region, was linked to a wide range of oral complications including xerostomia, mucositis, candidiasis, dental caries, periodontal disease, and in severe cases, osteoradionecrosis (ORN). [5,13]

Xerostomia

Xerostomia emerged as the most consistent long-term side effect, caused by irreversible damage to salivary glands and subsequent alterations in salivary flow and composition.[13,15-17] This condition increases the risk of plaque accumulation, enamel demineralization, and secondary infections.[13,18]

Symptom management strategies included saliva substitutes, trehalose sprays, and moisturizing oral gels[14], which provided partial relief and improved salivary parameters.

Oral hygiene and supportive interventions

Structured oral hygiene protocols, including fluoride use, chlorhexidine rinses, and dental cleanings, reduced the incidence of dental caries and gingival inflammation.[5,15] The role of oral probiotics was also explored in specific *Streptococcus salivarius* M18.[18]

Table 2. Included studies

Ref	Study design	Country /Sample	Oral conditions	Diagnostic criteria	Clinical setting	Cancer type/ Stage	Treatment modality	Follow-up	Placebo /Control group
[1]	Phase III RCT	Egypt / 100 patients	OM	WHO	Hospital	HNC	RT, CTX	Weekly for 6-7 weeks	Benzydamine hydrochloride control
[5]	QES	South Korea / 61 patients	Caries, plaque, BOP, hyposalivati-on	WHO, O'Leary Index, BOP, SSF	Oncology Hospital	HNC	RT	Baseline, post-RT, 3 mos, 6 mos	Yes, control group received only oral health education
[6]	Double-blind RCT	Syria / 45 patients	OM, XER	OMAS, scale, OHIP-14	Oncology Hospital	Digestive tract cancers	CTX	7- and 14-days post-CTX	Yes, Group 1 received only basic oral care instructions
[10]	Phase III RCT	Japan / 169 patients	OM	OAG	Cancer Centers	Breast cancer	Everolimus, Exemestane	Weekly for 8 weeks	Yes, Control group received oral hygiene instruction and gargling only
[11]	Phase III RCT	Sweden and Norway / 182 patients	OM	OMAS, NPRS	University Hospitals	Multiple myeloma, lymphoma	CTX	From baseline to 28 days post transplan-tation	Yes, Control group received conventional ice chips
[12]	Cluster RCT	United Kingdom / 288 patients	Qol, XER	UW-QOLv4, EQ-5D-5L	Outpatient Oncology Clinics	HNC	RT	Baseline, 6 mos, and 12 mos	Yes, Control group completed same questionnaires
[13]	Single- blind RCT	Thailand / 56 patients	XER	SSF, pH, buffering, CFU	Oncology Hospital	HNC	RT	Baseline, 1 mo, and 2 mos	Yes, GC dry mouth gel
[14]	Double-blind RCT	Thailand / 70 patients	XER	USF, pH, XeQoLS, VAS	Oncology Hospital	HNC	RT	Baseline and 14 days post-interventi-on	Yes, Control group received carboxymethylcellulose based oral spray
[15]	RCT	China / 92 patients	Caries, plaque, gingival inflammation	PI, GI, DMFT	Tertiary Hospital	HNC	RT, CTX	Baseline, end of RT, 3 mos, 12 mos	Yes, control group received only usual oral care
[16]	RCT	Egypt / 34 patients	RT-OM	WHO, VAS, MDASI-HN	Oncology Hospital University	HNC	RT	Baseline, 3 weeks, and 6 weeks after treatment start	Yes, Control group received conventional treatment
[17]	RCT	China / 92 patients	XER, salivary hypofunction	XQ. CTCAE, salivary flow rate	Hospital	HNC	RT	Baseline, end of RT, 3 mos, and 12 mos	Yes, Control group received usual care
[18]	Pilot RCT, double-blind	New Zealand / 13 patients	XER, Periodontitis, Plaque	CPITN, O'Leary Index, 16S rRNA	Oncology Hospital	HNC	RT, CTX	4-week interventi-on with pre- and post- treatment assessment	Yes, Placebo lozenges (identical in appearance, without *Streptococcus salivarius* M18
[19]	QES	Egypt / 108 patients	OM	WHO	Oncology Hospital	Hematologic & other malignancies	CTX	Baseline / 1 /3 m	Yes, Control group received routine care only
[20]	RCT double-blind, parallel	Iran / 144 adult patients	OM	WHO, QLQ-C30	Oncology Hospital	Various cancers	CTX	Weekly ×3	Yes, Placebo group received mouthwash with sterile water
[21]	Multi- center RCT	Brazil / 60 patients	OM	WHO	Oncology Hospital	Solid tumors	CTX	Baseline, Day 7, Day 14 post-CTX	Yes, Control group performed mouthwash
[22]	Double-blind RCT	Denmark Sweden/ 60 patients	OM	WHO; VAS	Oncology Hospital	Hematologic malignancies and HSCT patients	CTX	24h post-interventi-on + pain assessed every 3h	Yes, Placebo group received both placebo oromucosal solution and placebo intravenous infusion
[23]	Double-blind RCT	Iran / 67 patients	OM	WHO, OMAS, VAS	University Hospital	HNC	RT	Weekly, for 7 weeks	Yes, there was a placebo group without active ingredients

Abbreviations: RCT – Randomized Controlled Trial, **QES** – Quasi-experimental studies, **OM** – Oral Mucositis, **WHO** – World Health Organization, **HNC** – Head and Neck Cancer, **RT** – Radiotherapy, **CTX** – Chemotherapy, **mos** – Month(s), **OMAS** – Oral Mucositis Assessment Scale, **BOP** – Bleeding on Probing, **SSF** – Subjective Salivary Flow, **QLQ-C30** – Quality of Life Questionnaire – Core 30, **XER** – Xerostomia, **OHIP-14** – Oral Health Impact Profile – 14, **VAS** – Visual Analogue Scale, **XeQoLS** – Xerostomia-related Quality of Life Scale, **pH** – Potential of Hydrogen, **USF** – Unstimulated Salivary Flow, **CPITN** – Community Periodontal Index of Treatment Needs, **16S rRNA** – 16S Ribosomal Ribonucleic Acid, **CFU** – Colony-Forming Unit, **PI** – Plaque Index, **GI** – Gingival Index, **DMFT** - Decayed,-missing-filled teeth index, **MDASI-HN** – MD Anderson Symptom Inventory – Head and Neck Module, **XQ** – Xerostomia Questionnaire, **UW-QOLv4** – University of Washington Quality of Life Questionnaire – Version 4, **EQ-5D-5L** – EuroQol 5 Dimensions – 5 Levels, **NPRS** – Numeric Pain Rating Scale, **OAG** – Oral Assessment Guide, **CTCAE** – Common Terminology Criteria for Adverse Events

In the probiotic trial with *Streptococcus salivarius* M18, the taxa most affected were periodontopathogenic genera, specifically *Campylobacter*, *Fretibacterium*, *Selenomonas*, and *Treponema*.[18] These anaerobic organisms are well established contributors to periodontal disease, driving biofilm maturation and eliciting a host inflammatory response through cytokines such as interleukin-1 beta (IL-1β), IL-6, and tumor necrosis factor-alpha (TNF-α).[18] While overall microbial diversity remained unchanged, negative interactions between *S. salivarius* M18 and these pathogens suggest a suppressive effect on their relative abundance.[18] This finding is clinically relevant, as these genera are implicated in periodontal tissue destruction and chronic inflammation, and it supports the potential of oral probiotics as adjuncts to standard oral care in mitigating post-radiotherapy periodontal deterioration.[18]

One study developed a predictive model for radiation-induced xerostomia, linking radiation dose to the salivary glands with symptom severity. Patient-specific factors, such as age and hypertension, were identified as modifiers of risk.[15]

Additional interventions

Benzydamine hydrochloride is a topical non-steroidal anti-inflammatory drug with analgesic and antimicrobial properties, used to reduce pain and inflammation of the oral mucosa.[1] On the other hand, rebamipide, a quinolinone derivative classified as a mucosal-protective agent, exhibits antioxidant and cytoprotective properties that promote epithelial repair and enhances mucosal defense.[1] In a randomized clinical trial, rebamipide was more effective than benzydamine hydrochloride in reducing mucositis severity among patients undergoing RT with or without CTX.[1] Although the overall incidence did not differ significantly, rebamipide led to a higher proportion of mild cases (Grade 1) and fewer severe cases (Grade 3).[24]

Another study assessed an integrated supportive program (including oral hygiene education, facial exercises, and salivary gland massage) in patients receiving low-dose RT.[17] This approach significantly improved xerostomia symptoms and salivary function at both 3- and 12-months post-treatment.[17]

Zinc supplementation, shown to be effective in CTX settings, was also beneficial in patients undergoing RT, further supporting its role in reducing OM.[20]

The use of the Patient Concerns Inventory (PCI) in patients with head and neck cancer undergoing CTX was associated with improved quality of life, particularly regarding symptoms such as oral pain and dryness.[12]

Lastly, structured post-treatment follow-up was emphasized as essential in managing long-term effects of RT. Unlike chemotherapy-induced OM, which usually resolves post-treatment, RT-related complications such as xerostomia and fibrosis may persist for years and require long-term dental support.[15,17]

Methodological quality of the included studies

The risk of bias appraisal, conducted with ROB2 for RCTs and ROBINS-I for non-randomized studies, showed that most randomized trials had a low to moderate risk of bias, with occasional concerns regarding the randomization process and outcome measurement.

In contrast, the two non-randomized studies presented a serious risk of bias, mainly due to confounding, participant selection, and outcome assessment.[5,19]

Discussion

Comparative analysis: Chemotherapy vs. Radiotherapy

This integrative review demonstrated that oral mucositis, xerostomia, and osteonecrosis are the most prevalent oral complications associated with chemotherapy and radiotherapy, significantly affecting patients' quality of life and continuity of cancer treatment.[13,15,19]

The evidence consolidated in this review reaffirms that both therapies significantly impair oral health, albeit in different ways, with OM, xerostomia, and osteonecrosis emerging as the most prevalent complications.[13,15]

Although both CTX and RT are associated with oral complications, their mechanisms, clinical presentations and implications for oral management differ substantially. CTX induces systemic and often acute toxicity, with OM typically appearing early and resolving shortly after treatment discontinuation.[6,19] In contrast, RT is linked to chronic, localized damage, such as xerostomia, opportunistic infections, dental caries and osteoradionecrosis, often persisting long after treatment ends.[5] Notably, OM manifests in both modalities but with distinct clinical profiles: CTX related OM is generally diffuse and transient, whereas RT induced OM is localized and tends to worsen progressively.[25] These differences justify distinct clinical approaches. Patients receiving CTX, especially those undergoing hematopoietic stem cell transplantation, benefit from rigorous monitoring and supportive oral care.[19] RT patients, on the other hand, require preventive strategies such as pre-irradiation dental extractions and salivary gland shielding.[15] The combination of CTX and RT exacerbates toxicity, with OM incidence approaching 90% in head and neck cancer patients.[19] The literature also reveals a discrepancy in research focus: CTX studies typically examine acute outcomes, whereas RT studies emphasize chronic toxicity and long-term complications.[26] This dichotomy underscores the need for modality specific protocols. Importantly, these effects can disrupt treatment continuity and degrade quality of life.[26] For instance, a reported case of delayed dental care led to an abscess requiring CTX interruption.[24] Such findings reinforce the importance of timely oral interventions within multidisciplinary cancer care.

Comparative analysis: Results vs. Current Clinical Recommendations (MASCC/ISOO)[36]

The findings of this integrative review broadly corroborate the current clinical recommendations issued by the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO) for the management of OM and xerostomia.[26] While interventions such as Photobiomodulation (PBM),[8] phytotherapeutic agents[23] and structured oral care programs[5] are consistently supported in the literature, their incorporation into clinical practice remains uneven, particularly in resource limited settings or outside academic centers, limiting widespread implementation.[27-30] Among all strategies, PBM emerges as the most consistently validated, demonstrating significant reductions in both incidence and severity of OM, especially in patients undergoing head and neck RT or high-dose CTX.[31] For photobiomodulation therapy, the protocols reported in the included studies typically employed red or near-infrared wavelengths ranging between approximately 630 and 980 nm, with energy densities commonly between 2 and 6 J/cm² applied to the oral mucosa at multiple intraoral sites before or during oncological therapy sessions. PBM was generally delivered in repeated sessions throughout chemotherapy or radiotherapy cycles, targeting areas most prone to mucositis development, and was most often applied preventively, starting prior to or at the initiation of oncological treatment and continuing throughout the treatment course.[6,31] However, variability was observed across studies in terms of device type, exact wavelength, power output, exposure time per point, and total number of sessions, which may influence clinical outcomes. This highlights the gap between the potential of

emerging therapies and the strict requirements of evidence-based clinical validation. Zinc based mouthwashes, particularly those containing zinc chloride, illustrate the growing gap between emerging evidence and guideline adoption.[29] While preliminary studies[20,23] report improvements in mucosal healing and patient reported outcomes, these formulations have yet to be formally recommended.

For zinc-based interventions, the available trials suggest clinically relevant reductions in oral mucositis severity. In the chemotherapy study by Mohammadi et al., 77.1% of patients in the zinc chloride group were free of oral mucositis at week 3, compared with 41.7% in the placebo group, while grade 3 mucositis occurred in 2.1% *versus* 10.4%, respectively. Quality-of-life scores also improved substantially in the zinc group (40.89 to 70.61), whereas no meaningful improvement was observed in the placebo group.[20] In the radiotherapy setting, zinc sulfate mouthwash significantly reduced mucositis severity and pain from weeks 2 to 7, with 47.1% of patients remaining symptom-free at week 7.[20,23] In short, despite the promising results[20,23], it is not yet considered a valid option supported by a substantial number of comprehensive and specific studies demonstrating undeniable benefits.

Among low-cost interventions, cryotherapy has emerged as particularly promising. In the reviewed studies, cryotherapy protocols involved either conventional ice chips or dedicated intraoral cooling devices. Standard protocols required patients to hold ice chips in the mouth beginning approximately 5 minutes before chemotherapy infusion and continuing for about 30 minutes during drug administration. This approach induces local vasoconstriction, thereby reducing the exposure of the oral mucosa to cytotoxic agents. Device-based systems are designed to achieve comparable mucosal cooling through controlled intraoral temperature reduction and have demonstrated similar reductions in oral mucositis severity.[11,21,32] These systems may also improve patient comfort and compliance by providing more uniform and controlled cooling conditions. Recent phase III trials[11] comparing conventional ice chips with intraoral cooling devices confirm significant reductions in OM severity and onset, nevertheless cryotherapy shows great potential to become one of the most widely used therapies, provided its benefits are solidly demonstrated, due to its ease of application, minimal cost and the local vasoconstrictive effect of ice.[32-34] While effective, their applicability in hematological vs. solid tumors remains unevenly explored, suggesting the need for stratified protocols. The role of professional oral care protocols, including dental prophylaxis, hygiene reinforcement and regular monitoring remains central.[35] A novel and promising intervention is the omega-3 nanoemulgel, which not only decreased OM severity but also demonstrated potential to modulate the oral microbiome by reducing dysbiosis.[16] While still in early phases of validation, this dual action suggests a therapeutic innovation that warrants further investigation and rigorous evaluation before approval. Regarding xerostomia, the evidence increasingly supports a multimodal management strategy.[36] Oral moisturizing jelly outperformed traditional saliva substitutes by improving salivary pH, reducing *Candida* colonization, and offering better mucosal adhesion, although the results are superior to those of traditional saliva substitutes, further studies are still needed to confirm these results. Similarly, trehalose-based formulations have demonstrated measurable benefits. In a randomized clinical trial, a 10% trehalose spray significantly improved salivary pH and unstimulated salivary flow rate after 14 days, reaching 7.16 ± 0.56 and 0.20 ± 0.24 mL/min, respectively. Although XeQoLs scores were not significantly different from those observed with carboxymethylcellulose, both groups improved and patient satisfaction was higher in the trehalose group.[14] Functional rehabilitation techniques, such as salivary gland massage and targeted exercises, showed particular benefit in patients with residual gland function mainly those exposed to lower doses of RT.[37,38] Furthermore, it is still the main cornerstone for this condition.[39] Laser therapy targeting salivary glands, especially when based on PBM, also yielded measurable improvements in salivary flow.[6] This aligns with MASCC/ISOO's dual endorsement of PBM for both OM and radiation induced xerostomia. Pilocarpine remains the best-established pharmacologic sialogogue for cancer therapy-induced xerostomia, particularly in guideline-based management. However, the clinical trials included in the present review mainly evaluated non-pharmacologic supportive approaches, such as oral moisturizing gels, trehalose-based sprays, and integrated supportive programmes. These interventions should therefore be interpreted as complementary or alternative supportive strategies, particularly in patients with residual salivary gland function, intolerance to systemic sialogogues, or limited access to pharmacologic treatment. Thus, rather than replacing pilocarpine, these modalities may occupy an adjunctive role within multimodal xerostomia management.[13,14,17,40] Lastly, across multiple studies, these interventions consistently reduced OM incidence and improved mucosal outcomes. However, their success is often contingent on access to trained dental personnel and institutional support. These logistical factors, rarely addressed in clinical research, may hinder real world effectiveness, particularly in settings without integrated oral oncology services.[41] In short, it is quite evident that professional oral care protocols are essential, however, not all oncology patients have access to these services. In addition to experiencing physical symptoms, cancer patients often face significant financial hardships, which in many cases limits their ability to seek such care.[42]

Critical insights and emerging challenges

Oral mucositis remains the most common oral toxicity associated with CTX, particularly in HSCT and high-dose regimens.[11,19] Baseline poor oral health, prevalent in many oncology patients, increases susceptibility to complications.[43] Delays in initiating dental evaluation are linked to acute infections and treatment disruptions.[44] The integration of dental care into oncology teams is therefore not optional but essential. Dentists play a critical role in identifying infectious foci, tailoring preventive strategies, and maintaining oral health throughout treatment, however, integration is often limited to head and neck cancer units.[45] In terms of therapeutic strategies, natural agents such as zinc have demonstrated anti-inflammatory and healing properties, particularly in hematological malignancies.[46] Nonetheless, zinc it is not yet included in formal guidelines, due in part to methodological heterogeneity and the limited scale of existing studies. More robust data is needed to support their routine use.[29] On the other hand, PBM is increasingly recognized for its efficacy: a 2023 meta-analysis[47] involving 869 RT patients found a consistent reduction in OM incidence from the second week of treatment onward. Despite this, an umbrella review[36] has highlighted that the overall quality of PBM related evidence remains low, owing to variation in protocols and study designs. Topical opioid rinses, such as morphine, have shown variable results and remain controversial due to insufficient high-quality data and a lack of significant evidence.[22] Xerostomia, especially following RT, is a debilitating and long-lasting condition. It results from irreversible salivary gland damage, contributing to dental decay, dysgeusia, and candidiasis.[13] These approaches may represent viable long-term strategies, although more longitudinal data is needed to confirm their sustained benefits. Other oral complications, such as caries, periodontal disease, and osteoradionecrosis, are particularly common in patients exposed to combined CTX and RT.[46,48] ORN, exclusive to RT, arises from chronic tissue hypoxia and impaired bone remodeling, posing major challenges for oral rehabilitation.[46] In contrast, osteonecrosis of the jaw associated with CTX is rare and typically linked to adjunct therapies such as bisphosphonates or denosumab.[49] Nurses remain underutilized in oral care delivery despite their central role in patient monitoring. Many lack the training and confidence to detect or manage oral complications. Additionally, general dentists in community settings often lack oncology specific training, undermining post discharge care.[46] Furthermore, although international recommendations support the integration of dental services into oncology care, many cancer centers, particularly those not focused on head and neck cancers, still lack embedded dental teams.[50] This underscores the need for targeted education and clearer referral pathways, ensuring that oral health is maintained across all phases of cancer treatment. Taken together, these findings highlight the urgent need for standardized oral care protocols that are tailored to the specific toxicities of each oncological modality. Bridging the gap between evidence and implementation will require investment in training, interprofessional collaboration, and policy reform.

In the Portuguese healthcare context, the integration of dental professionals in oncology should be regarded as a matter of high priority.

Based on the evidence synthesized in this review, a structured oral care pathway can be proposed to improve the prevention and management of treatment-related oral complications in oncology patients. This framework should ideally be integrated into multidisciplinary cancer care and adapted according to institutional resources.

The first stage involves pre-treatment screening and risk assessment. Before initiating chemotherapy or radiotherapy, patients should undergo a comprehensive oral examination to identify potential sources of infection, untreated caries, periodontal disease, or mucosal lesions, enabling early preventive measures.

The second stage focuses on prophylactic interventions during oncological therapy. Preventive oral care protocols, including oral hygiene instructions, fluoride application, antimicrobial mouth rinses, photobiomodulation therapy, and cryotherapy, may reduce the incidence and severity of oral mucositis.

The third stage concerns the management of acute complications. When oral mucositis or xerostomia occurs, supportive approaches such as saliva substitutes, trehalose-based sprays, zinc-containing mouthwashes, and topical anti-inflammatory or analgesic agents may help alleviate symptoms and improve patient comfort.

Finally, long-term follow-up is essential, particularly for patients receiving head and neck radiotherapy, who frequently develop chronic complications such as xerostomia, dental caries, and periodontal disease. Continuous dental monitoring and reinforcement of oral hygiene practices are therefore necessary to maintain oral health and quality of life.

Implementation of these strategies should also consider resource availability, with basic preventive measures applied in low-resource settings and more specialized therapies implemented in centers with appropriate infrastructure

Efforts to align national practice with international recommendations, such as those from MASCC/ISOO, are urgently needed, especially considering growing evidence that early oral intervention improves patient outcomes and reduces treatment interruptions.

Limitations and future directions

This integrative review has several limitations that should be considered when interpreting its findings. One limitation of this review is the restriction of the search to studies published within the last five years (2020-2025). Although

this approach allowed the identification of the most recent clinical evidence, it may have excluded earlier landmark trials evaluating interventions such as photobiomodulation or cryotherapy. Nevertheless, these foundational studies and existing clinical guidelines were considered in the discussion to contextualize the findings of the included studies. The included studies varied in design, sample size, cancer type, treatment protocols, and outcome measures, which may limit the generalizability of findings. Furthermore, some promising approaches, such as the use of phytotherapeutic agents, are supported by limited or low-quality evidence emphasizing the need for cautious interpretation and further validation.[15] These factors should be considered when interpreting the results and making clinical recommendations. This review acknowledges variability in follow-up durations across studies, which limits assessment of chronic toxicity. Another important methodological consideration concerns the absence of a quantitative synthesis. Although a meta-analysis was initially considered, the marked heterogeneity among the included studies prevented meaningful statistical pooling. Consequently, a narrative synthesis was considered the most appropriate approach to summarize the available evidence while preserving the clinical context of each intervention. This approach is consistent with the objectives of integrative reviews, which aim to combine diverse types of clinical evidence to provide a broader understanding of complex healthcare interventions. Publication bias may also skew results toward positive outcomes, particularly for interventions like PBM and zinc. Additionally, grey literature and real-world data were not included.[15,20,23] Future research should prioritize well designed randomized controlled trials with standardized protocols to assess long term efficacy of interventions such as PBM, probiotics and trehalose-based agents. Combined therapies (e.g., PBM plus zinc, or cryotherapy plus chlorhexidine) also warrant investigation. Beyond clinical outcomes, implementation studies should examine operational aspects like interprofessional collaboration, referral efficiency, patient adherence, and cost effectiveness. Moreover, one component that has not been thoroughly explored is the financial aspect. Several treatments are costly and difficult to access[1,6,16], which becomes a significant barrier for oncology patients, who are often financially impacted by their condition, limiting their ability to benefit from these therapies. Qualitative studies exploring patient experiences and self-care strategies may further inform people centered oral oncology care. Oral health must no longer be seen as a peripheral concern in oncology. Its central role in patient well-being, treatment continuity and quality of life demands structural changes in how cancer care is delivered. Multidisciplinary collaboration, professional training, and equitable access to dental services should be viewed not as optional enhancements, but as essential components of comprehensive oncological care.

Conclusion and implications for clinical practice and research

This integrative review reaffirms the critical role of oral health in the comprehensive care of patients undergoing chemotherapy and radiotherapy. Both treatment modalities are associated with a high incidence of oral complications, albeit with distinct pathophysiological mechanisms, clinical manifestations, and temporal profiles. While chemotherapy is primarily linked to acute mucosal damage, most notably oral mucositis, radiotherapy tends to produce long-lasting, localized effects such as xerostomia and osteoradionecrosis. These complications not only impair oral function and nutritional status but also significantly affect patient comfort, quality of life, and treatment adherence, with potential repercussions on oncologic outcomes.

The findings underscore the efficacy of early and individualized preventive oral care interventions in reducing the incidence and severity of these adverse effects. Strategies such as fluoride application, antimicrobial rinses, PBM, trehalose-based products, and zinc supplementation have demonstrated meaningful clinical benefits when applied appropriately according to the patient's treatment phase and immunological status. However, evidence remains inconsistent for some approaches, particularly opioid-based mouth rinses, highlighting the need for further research to establish safe and effective protocols.

Despite growing recognition of the relevance of oral health in oncology, significant gaps remain. The absence of standardized clinical protocols, heterogeneity across studies, and limited long-term data continue to hinder the generalizability and implementation of evidence-based interventions. Furthermore, disparities in access to dental care and fragmented communication between medical and dental professionals present real-world barriers to the integration of oral health into oncology care.

To address these challenges, it is imperative to embed oral assessments and preventive strategies into multidisciplinary cancer care frameworks. Dental professionals must be actively involved from diagnosis through survivorship, working collaboratively with oncologists, nurses, dietitians, and other health professionals. Educational initiatives should be expanded to ensure that dental teams are equipped to detect, manage, and prevent treatment-related oral toxicities.

Future research should prioritize high-quality, multicenter clinical trials to evaluate both established and emerging interventions, including natural compounds, new salivary stimulants, and regenerative therapies. The development of predictive biomarkers and risk stratification tools would further enable targeted prevention and early management of complications in high-risk patients. Long-term follow-up studies are also needed to assess the lasting impact of

oral toxicities on survivors' functionality, well-being, and quality of life.

Ultimately, this review supports the view that oral health is not ancillary but integral to the success of cancer treatment. Ensuring the incorporation of evidence-based dental care into oncology practice represents a necessary step toward improving treatment outcomes while enhancing both the overall experience and the dignity of cancer patients.

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Informed Consent Statement

Not applicable.

Data Availability Statement

Data were extracted from the original studies included in this integrative review.

Conflicts of Interest

The authors declare no conflict of interest

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Appendix

Table 4 (database-specific filters) appears to be missing from the current version of the manuscript. Additionally, the note and abbreviations associated with Table 3 are not currently displayed. We would appreciate confirmation as to whether these elements were intentionally removed during formatting or omitted following editorial or reviewer recommendations.

Database	Search query (keywords and Boolean operators) (01/02/2020 to 01/02/2025)	Nº of articles after applying filters	Nº of articles remaining after inclusion and exclusion criteria
CL	("Chemotherapy" OR "Radiotherapy" OR "Targeted therapy") AND ("Prevention" OR "Oral care protocols") AND ("Cancer treatment" OR "Antineoplastic agents") AND ("Oral Health" OR "Oral Hygiene")	10	2
CL	("Oral health" OR "Dental care") AND ("Cancer treatment" OR "Antineoplastic agents")	7	1
CL	("Oral Health" OR "Oral Hygiene") AND ("Cancer Patients" OR "Oncology Patients") AND ("Quality of Life")	26	2
CL	("Cancer Patients" OR "Oncology Patients") AND ("Chemotherapy" OR "Immunotherapy") AND ("Oral Mucositis" OR "Candidiasis" OR "Periodontitis")	196	7
CL	("Oral Mucositis" OR "Candidiasis" OR "Periodontitis") AND ("Cancer patients" OR "Oncology patients") AND ("Early Intervention" OR "Multidisciplinary Care") NOT "Pediatric"	364	10
CL	("Cancer patients" OR "Oncology patients") AND ("Oral health" OR "Dental care") AND ("Prevention" OR "Oral care protocols")	16	3
PM	("Cancer treatment" OR "Antineoplastic agents") AND ("Prevention" OR "Oral care protocols") AND "Oral Health"	8	1
PM	("Cancer patients" OR "Oncology patients") AND ("Oral health" OR "Dental care") AND ("Prevention" OR "Oral care protocols")	8	3
PM	("Chemotherapy" OR "Radiotherapy" OR "Targeted therapy") AND ("Prevention" OR "Oral care protocols") AND ("Cancer treatment" OR "Antineoplastic agents") AND ("Oral Health" OR "Oral Hygiene")	8	2
PM	("Oral health" OR "Dental care") AND "Prevention" AND ("Cancer treatment" OR "Antineoplastic agents")	8	1
PM	("Oral Health" OR "Oral Hygiene") AND ("Cancer Patients" OR "Oncology Patients") AND ("Quality of Life")	8	2
PM	("Oral health" OR "Dental care") AND ("Treatment discontinuation" OR "Therapeutic failure" OR "Cancer Treatment")	9	3
PM	("Cancer Patients" OR "Oncology Patients") AND ("Chemotherapy" OR "Radiotherapy") AND ("Oral Health" OR "Oral Hygiene")	17	8
PM	("Cancer Patients" OR "Oncology Patients") AND ("Chemotherapy" OR "Immunotherapy") AND ("Oral Mucositis" OR "Candidiasis" OR "Periodontitis")	24	5
PM	("Cancer patients" OR "Oncology patients") AND "Oral Health"	22	7
PM	("Oral Health"[MeSH] OR "oral health" OR "oral hygiene" OR "dental care") AND ("Neoplasms"[MeSH] OR "cancer patients" OR "oncologic patients") AND ("Antineoplastic Agents"[MeSH] OR "chemotherapy" OR "radiotherapy") AND ("Oral Mucositis"[MeSH] OR "xerostomia" OR "oral complications") AND ("prevention" OR "management" OR "oral care protocols")	44	11
PM	("Oral health" OR "Dental care") AND ("Cancer treatment" OR "Antineoplastic agents")	14	1
PM	"Supportive Care"[MeSH] AND "Oral Health"[MeSH]	2	1
SC	("Cancer patients" OR "Oncology patients") AND ("Oral health" OR "Dental care") AND ("Prevention" OR "Oral care protocols")	1	0
SC	("Oral health" OR "Dental care") AND ("Cancer treatment" OR "Antineoplastic agents")	3	0
SC	("Cancer Patients" OR "Oncology Patients") AND ("Chemotherapy" OR "Immunotherapy") AND ("Oral Mucositis" OR "Candidiasis" OR "Periodontitis")	2	0
SC	("Chemotherapy" OR "Radiotherapy" OR "Targeted therapy") AND ("Oral health" OR "Oral hygiene") AND ("Oral mucositis" OR "Xerostomia" OR "Dysgeusia" OR "Osteonecrosis" OR "Oral infections")	1	0