Clinical guidance for maintaining oral hygiene in patients undergoing chemotherapy or radiation therapy: a scoping review

KEYWORDS
Dental care
Dental prophylaxis
Cancer
Mucositis
Stomatitis

SUMMARY
The aim of this scoping review was to identify clinical guidance for maintaining oral hygiene in patients undergoing chemotherapy, radiation therapy, or both. Electronic searches were conducted in PubMed, Embase, Cochrane Library, and Google Scholar for articles published between January 2000 and May 2020. Systematic reviews, meta-analyses, clinical trials, case series, and expert consensus reports were considered eligible for inclusion. The SIGN Guideline system was used to evaluate the level evidence and the grade of recommendations. A total of 53 studies met the eligibility criteria. The results showed the presence of recommendation for oral care in three domains: management of oral mucositis, prevention and control of radiation caries, and management of xerostomia. However, most of the included studies had low levels of evidence. The review provides recommendations for healthcare professionals caring for patients undergoing chemotherapy, radiation therapy, or both, but a standard oral care protocol could not be established owing to a paucity of evidence-based data.
Introduction
Patients undergoing chemotherapy, radiation therapy, or both for the treatment of head and neck cancers commonly experience oral side effects, including mucositis, thrush (candidiasis), xerostomia, radiation caries, trismus, tissue damage, and osteoradionecrosis. Implementing proactive management of oral problems during and after cancer treatment can decrease the severity of these side effects and enhance the patients’ oral health-related quality of life. It has been shown that poor oral hygiene is a significant risk factor for oral complications from chemotherapy and radiation therapy (Joshi 2010).

Oral mucositis (OM), a widespread side effect experienced by patients undergoing cancer treatment, can hinder proper oral health maintenance. Mucositis is an inflammatory condition that affects the submucosal connective tissues, potentially leading to symptoms in the oral cavity and throughout the digestive tract (Eilers et al. 2014). The severity of mucositis can vary greatly, from subtle changes in sensation to the development of painful, ulcerative, bleeding lesions, and infections (Eilers & Million 2011). The discomfort associated with mucositis can make maintaining oral hygiene difficult, making oral care protocols essential.

Given the importance of oral hygiene for patients undergoing chemotherapy, radiation therapy, or both, the objective of this scoping review was to collect information on evidence-based oral hygiene instructions, guidance, and tools to effectively manage oral hygiene in these patients. Additionally, the review sought to identify preventive programs and standardized protocols to promote oral hygiene in this patient population.

Material and methods
Four electronic databases, PubMed, Embase, Cochrane Library, and Google Scholar, were searched for studies published from January 2000 to March 2020 in English and German. The eligible sources included systematic reviews, meta-analyses, clinical studies, case series, expert opinions, and Delphi consensus reports that addressed aspects such as type of toothbrush, tooth brushing technique, frequency and duration of toothbrushing, type of toothpaste, mouthwash use, and interdental cleaning methods. Pamphlets, case reports, posters, and abstract-only reports were excluded.

For the electronic searches, the following keywords and Boolean operators were used:

- **Evidence level 3 or 4; or**
- **Evidence level 2; extrapolated evidence from studies rated as 2++**
- **At least one meta-analysis, systematic review, or RCT rated as 1++,** directly applicable to the target population, and demonstrating overall consistency of results
- **A body of evidence including studies rated as 2+, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+**

The electronic search, the removal of duplicates, the title and abstract screening, and the full text assessments were performed by a single investigator. Journals and author names were unblinded during the eligibility assessment. The level of evidence and the grade of recommendations of studies fulfilling the eligibility criteria were assessed according to the SIGN Methodology Checklist (Fiftieth guideline developer’s handbook, NHS Scottish Intercollegiate Guidelines Network sign. Revised edition November 2011). Figure 1 and Figure 2 provide detailed information on the levels of evidence and grades of recommendations, respectively.

Results
Of 176 articles included in the full text assessment, 53 fulfilled the eligibility criteria. One article was a meta-analysis, 10 articles were systematic reviews, 12 articles were clinical studies, and 30 articles were narrative reviews. Four of the 10 systematic
reviews were updates from guidelines of the Mucositis Study Group of the Multinational Association of Supportive Cancer in Cancer / International Society for Oral Oncology (MASCC/ISOO). The 12 clinical studies comprised one cohort study, a case series, and 10 clinical treatment trials (Fig. 3). The results of the assessment of the level of evidence and the grade of recommendations are reported in detail in Tables I–VI.

The findings revealed that three different guidelines exist for patients undergoing oncological treatment: for the management of oral mucositis, radiation caries (pre-, post and during...
cancer treatment), and xerostomia. The recommendations varied depending on the intended treatment outcome, certain advices were recommended or discouraged by the associations.

The management of oral mucositis

A meta-analysis assessed the impact of nine mouthwashes on the prevention of oral mucositis (Yu et al. 2020). Basic oral care and clinical guidelines for oral hygiene management were evaluated in a systematic review (Hong et al. 2019), a cohort study (Cheng et al. 2004), and three clinical treatment trials (Dodd et al. 2000; Kartin et al. 2014; Niikura et al. 2020). A clinical treatment trial assessed the effectiveness of three mouthwashes (Dodd et al. 2000). Another clinical treatment trial evaluated the effectiveness of a saline mouthwash and education program (Huang et al. 2018). One clinical treatment trial investigated the effect of improved dental care to prevent oral mucositis (Djuric et al. 2006). Four of these seven clinical treatment trials had a high risk of bias owing to poor randomization, deficiencies in group allocation concealment, shortcomings in blinding, and lack of a control group (Dodd et al. 2000; Cheng et al. 2004; Djuric et al. 2006; Kartin et al. 2014). These findings are summarized in Table I and Table II.

Guidelines for the prevention and treatment of oral mucositis

Oral care protocol

B/C A randomized controlled trial (RCT) assessed the impact of professional oral care on preventing everolimus-induced mucositis in 175 patients and was rated as level 1 (high level of evidence) with a grade B recommendation (Niikura et al. 2020). The latest update from the MASCC/ISOO association in 2019 showed that an oral care protocol including toothbrushing with a soft toothbrush, flossing, and using more than one mouthwash was effective in preventing oral mucositis. However, there was insufficient evidence to provide a universal oral care protocol recommendation for preventing oral mucositis, with a level of evidence 2+ (moderate) and a grade C recommendation (Hong et al. 2019). Despite this, evidence supports the use of a basic oral care protocol. Expert opinions were sought to provide guidance, as no clinical trials showed a clear superiority of one intervention over another (McGuire et al. 2013).

Mouthwash

A The effectiveness of different mouthwashes in preventing oral mucositis in patients undergoing chemotherapy and radiation therapy was assessed through a meta-analysis of randomized controlled trials. The results ranked the solutions based on their effectiveness, with curcumin and honey showing the greatest effectiveness, followed by benzydamine, chlorhexidine, allopurinol, sucralfat, granulocyte–macrophage colony-stimulating factor, povidone–iodine, aloe, and placebo in that order (Yu et al. 2020).

A The study by Huang et al. (2018) found that the combination of a 0.9% saline mouthwash and wet dressing gauze was effective in reducing symptoms of radiation-induced mucositis and improving oral comfort. This intervention was associated with improved physical and social–emotional function.

B The systematic review by MASCC/ISOO concluded that the use of chlorhexidine is not recommended for the prevention of oral mucositis in patients undergoing head and neck radiation therapy, owing to reported adverse effects such as increased discomfort, taste alteration, and teeth staining. There is limited or conflicting evidence regarding the use of chlorhexidine in cancer patients, hence a recommendation could not be made (Hong et al. 2019).

C No significant differences were found in the duration of the signs and symptoms of oral mucositis between chlorhexidine gluconate, magic mouthwash (consisting of Lidocain, Benadryl and Maalox), and a salt and sodium bicarbonate solution (Dodd et al. 2000).

D The MASCC/ISOO systematic review found limited data on the use of saline or sodium bicarbonate rinses in preventing oral mucositis, making it impossible to establish guidelines. Despite the paucity of data, these rinses were recognized as non-irritating and potentially helpful in maintaining oral hygiene and improving patient comfort (Hong et al. 2019).

D Experts recommended rinsing with bland solutions 4 to 6 times daily (Harris et al. 2008; Becker–Schiebe et al. 2012; Eilers et al. 2014; Peterson et al. 2015; De sanctis et al. 2016).

The management of radiation caries

Three systematic reviews established guidelines for oral care strategies, incorporating RCTs, cohort studies, and case control studies (Carvalho et al. 2018; Cohen et al. 2016; Hong et al. 2018). The systematic review by Cohen et al. (2016) only searched the PubMed database, a major methodological limitation. A randomized controlled trial by Papas et al. (2008) compared the effects of remineralizing and conventional toothpastes on caries prevention. Tables III and IV illustrate the evaluated studies.

Guidelines for prevention and treatment of radiation caries

Mechanical cleaning

A A systematic review that included only randomized controlled trials with a level 1+ or 1 evidence recommends brushing at least three times a day with an ultra-soft bristled toothbrush. In cases of open ulcerative lesions in the oral cavity or if the patient cannot tolerate a soft toothbrush or has a low neutrophil and platelet count (<500/mm³, <40,000/mm³, respectively) during oncological treatment, the oral cavity should be cleaned using gauzes moistened with 0.12% chlorhexidine or oral sponges (Carvalho et al. 2018).

A It is recommended to practice dental flossing regularly (Carvalho et al. 2018).

D Alternative methods to clean the oral cavity included using a gloved finger (Miller & Kearney 2001) or cotton Q-tip swabs (Joshi 2010).

D A single tufted toothbrush or a child’s toothbrush may be helpful for plaque control, as suggested by Eliyas et al. (2013; Kumar et al. 2013).

D It is recommended to brush for at least 90 s (Larson et al. 1998; Epstein & Schubert 1999; Rubenstein et al. 2004; Harris et al. 2008; Sieracki et al. 2009).

D It is recommended to replace the toothbrush every month (Peterson et al. 2015).

D Floss picks may be a useful aid for oral hygiene (Chai et al. 2006).
**D** Starting interdental cleaning during oncological treatment should be avoided, as it may cause gingival bleeding and damage the epithelial barrier, particularly if it has never been performed prior to therapy (Peterson 2015).

**Toothpaste**

**A** Two phases fluoride toothpastes (≥1100 ppm) with calcium and phosphate ions are recommended (Papas et al. 2008; Carvalho et al. 2018).

**D** Expert opinions recommended using toothpastes with an increased fluoride concentration of 5000 ppm (Kielbassa et al. 2006; Joshi 2010; Kumar et al. 2013; Ray–Chaudhuri et al. 2013; Jawad et al. 2015).

**D** For patients with ulcers and xerostomia, the preferred toothpastes are those without detergents (Moslemi et al. 2016), non–mint flavor (Turner et al. 2013; Elad et al. 2015) and free of sodium lauryl sulfate (Andrews & Griffiths 2001; Pilotte et al. 2011; Eliyas et al. 2013; Elad et al. 2016). In the absence of such toothpastes, a children’s toothpaste may serve as a suitable alternative (Pilotte et al. 2011; Pinna et al. 2015; Elad et al. 2016).

**D** Bicarbonate–based toothpastes (Andrews et al. 2001) were found to be effective in lowering the acidity of the mouth’s pH (Joshi 2010).

**D** Toothpastes containing casein phosphopeptide–amorphous calcium phosphate (CPP–ACP) have been suggested for the prevention of caries (Köstler et al. 2001; Chai et al. 2006; Rankin et al. 2008; Jawad et al. 2015; Palmer et al. 2020). In case of incipient carious lesions, the use of these toothpastes has been shown to aid in remineralizing the teeth (Joshi 2010).

**Mouthwash**

**A** It is strongly recommended to use a 0.05% fluoride mouthwash daily prior to undergoing oncological treatment and to continue using it after the treatment has been completed (Carvalho et al. 2018).

**A/B** Two systematic reviews support the use of 0.12% alcohol-free chlorhexidine for individuals with difficulty controlling bacterial biofilm (Carvalho et al. 2018; Hong et al. 2018). It is recommended to rinse the oral cavity with the solution once or twice daily for the reduction of plaque buildup and S. mutans counts (Hong et al. 2018).

**Toothbrushing techniques**

**D** The recommended toothbrushing techniques included the Bass and the modified Bass technique (Ray–Chaudhuri et al. 2013; Peterson et al. 2015).

**Fluoride application**

**A** It is essential to use fluoride daily at the start of oncological treatment in order to prevent caries in patients undergoing head and neck radiation therapy and to continue its use afterwards (Carvalho et al. 2018).

**A** An intraoral fluoride–releasing system (IFRS) that contains sodium fluoride was found to be as effective as a custom–made fluoride carrier with stannous fluoride gel in preventing caries (Chambers et al. 2006). IFRS is recommended as a viable alternative, especially for patients with low compliance.

**B** The choice of fluoride delivery system did not have a significant impact on the level of caries in post–head and neck radiation patients (Hong et al. 2018).

**D** The use of a custom–made carrier for 1% sodium fluoride gel application has been recommended by some experts (Vissink et al. 2003; Kielbassa et al. 2006; Rankin et al. 2008; Schwelyn et al. 2011; Cohen et al. 2016; Sheikh et al. 2020).

**D** It has been advised to use a brush–on technique to apply either 0.4% stannous fluoride or 1.1% sodium fluoride to the teeth (Toljanić & Saunders 1984; Keene & Fleming 1987; Chambers et al. 1995).

**Management of xerostomia**

A systematic review assessed topical treatments for reducing radiation–induced dry mouth (Furness et al. 2011). Two clinical treatment trials compared the efficacy of chewing gum to artificial saliva or standard care in reducing xerostomia, with both studies finding that chewing gum was more effective, though without statistically significant results (Davies 2000; Kaae et al. 2020). These studies were rated to have a high risk of bias owing to methodological limitations. Another RCT (Chambers et al. 2006) compared the use of intraoral fluoride–releasing systems and fluoride carriers, with no differences in caries rates between the two fluoride systems. The findings are summarized in Table V and Table VI.

**Guidelines for saliva substitutes and stimulants**

**A** Artificial saliva should be used to lubricate the oral mucosa in cases of xerostomia. It should be applied before meals, before sleeping, and whenever necessary to promote lubrication of the oral cavity (Carvalho et al. 2018).

**A** A systematic review evaluated saliva stimulants and substitutes and found that the oxygenated glycerol triester saliva substitute spray was more effective than an electrolyte spray. Additionally, chewing gum was equally effective in increasing saliva production for individuals with xerostomia compared to saliva substitutes (Furness et al. 2011). This conclusion was confirmed by a recent randomized controlled trial (Kaae et al. 2020).

**A** A case series by Warde et al. (2000) found that using a combination of Biotene mouthwash, toothpaste, chewing gum, and Oralbalance gel could alleviate many symptoms of xerostomia caused by radiation therapy.

**A** A mixture of baking soda, salt, and water was found to effectively alleviate symptoms of xerostomia (Cohen et al. 2016).

**Discussion**

The aim of this scoping review was to assess the recommendations for maintaining oral health in patients undergoing chemotherapy, radiation therapy, or both. A total of 53 articles were evaluated and categorized into three groups based on their treatment objective: oral mucositis management, radiation caries prevention, and xerostomia management. The recommendations varied depending on the intended treatment outcome. Chlorhexidine was not advised for preventing oral mucositis in patients receiving head and neck radiation therapy, however, it was effective in preventing caries.

Most of the articles included in this scoping review were based on expert opinions with low levels of evidence, but the review also included ten systematic reviews and one meta–analysis with high levels of evidence. This demonstrates the availability of robust evidence for oral care in these patients.

The studies included in this review are found to entail risks of bias, such as ascertainment bias, comparison bias, and performance bias, leading to a lower rating of the level
of evidence and grade of recommendation according to the SIGN Guidelines. Furthermore, the use of different mucositis severity gradings, such as the WHO Oral Toxicity Scale and Eiler’s Oral Assessment Guide, made it difficult to compare the studies. In some cases, recommendations could not be made owing to a dearth of data. The MASSC/ISOO study group was unable to provide guidelines for the use of saline or sodium bicarbonate mouthwashes in preventing oral mucositis, but suggested that their use might be beneficial for oral hygiene. A systematic review by (Furness et al. 2011) found that an oxygenated glycerol triester saliva substitute was more effective for treating xerostomia than an electrolyte spray, but there was not enough evidence to strongly recommend its use.

This scoping review incorporated a broad range of articles, including both high- and low-evidence-based sources, but was limited by the fact that the eligibility assessment was conducted by only one investigator. It was unable to establish a standardized oral care protocol. Instead, it provided recommendations that should be considered as potential management approaches based on the current evidence base. However, it is crucial to consider that further research in the form of randomized controlled clinical trials, systematic reviews, and meta-analyses are needed to establish more robust evidence-based recommendations.

Conclusions
This scoping review analyzed guidelines for oral health management in patients undergoing oncological treatments, including the management of oral mucositis, radiation caries, and xerostomia. The following recommendations were based on high-quality evidence:

- Oral mucositis management: Oral care protocols and professional oral care are effective in alleviating symptoms of oral mucositis. Honey and curcumin were found to be helpful in the management of oral mucositis.
- Radiation caries management: Daily use of a fluoride toothpaste with ≥1100 ppm, a 0.05% fluoride mouthwash, topical fluoride application, and a fluoride-releasing system are recommended for reducing the burden of radiation caries.
- Xerostomia management: Saliva stimulants and substitutes may lubricate the oral cavity, and chewing gum was found to be as effective as saliva substitutes in increasing saliva production.

### Table 1: Overview of the evidence derived from systematic reviews and meta-analyses on the management of oral mucositis

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Evidence level</th>
<th>Objective</th>
<th>Methodology</th>
<th>Study quality</th>
<th>Type of studies</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yu YY et al. 2020: Effects of 9 oral care solutions on the prevention of OM: a network meta-analysis of randomized controlled trials</td>
<td>1++</td>
<td>Effect of different oral care solutions on the prevention of OM in patients that had chemotherapy or radiation therapy</td>
<td>PubMed, Embase, Scopus, Cochrane Library, Google Scholar</td>
<td>Cochrane Handbook, risk ratios (RR) with 95% confidence intervals (CIs), inconsistency test, network meta-analysis</td>
<td>RCT (n = 28)</td>
<td>Chlorhexidine, benzylamine, honey and curcumin were more effective than placebo (p &lt; 0.05); honey and curcumin were more effective than povidone-iodine (p &lt; 0.05). Probability ranking according to the Surface Under the Cumulative Ranking curve showed the following treatments: curcumin &gt; honey &gt; benzylamine &gt; chlorhexidine &gt; allopurinol &gt; sucralfate &gt; granulocyte-macrophage colony-stimulating factor &gt; povidone-iodine &gt; aloe &gt; placebo.</td>
</tr>
<tr>
<td>Hong CHL et al. 2019: Systematic review of basic oral care for the management of OM in cancer patients and clinical practice guidelines</td>
<td>1+</td>
<td>Update clinical practice guidelines for the use of basic oral care interventions for the prevention and treatment of OM</td>
<td>PubMed, Web of Science</td>
<td>Levels of evidence by Somerfield criteria, flaws by Hadorn criteria</td>
<td>RCT (n = 8), comparative studies (n = 7), non-comparative studies (n = 2)</td>
<td>Oral care protocol is beneficial (level of evidence III). Chlorhexidine should not be used to prevent OM in patients that are undergoing head and neck radiation therapy (level of evidence III). No guideline was possible for professional oral care, patient education, saline, sodium bicarbonate.</td>
</tr>
</tbody>
</table>
**Tab. II  Overview of the evidence derived from clinical treatment trials on the management of oral mucositis**

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Study type</th>
<th>Evidence level</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow-up</th>
<th>Outcome measure</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheng KKF et al. 2001: Evaluation of an oral care protocol intervention in the prevention of chemotherapy-induced oral mucositis in paediatric cancer patients</td>
<td>cohort study</td>
<td>2+</td>
<td>n = 42: intervention (n = 21), control (n = 21)</td>
<td>Children (6–17 years), had high–dose or combination chemotherapy for haematological malignancies or solid tumors, were capable to brush or rinse</td>
<td>Intervention group: toothbrush: soft bristles for 90 s mouth rinse: 60 ml of 0.9% sodium chloride for 30 s, 10 ml of 0.2% chx for 30 s technique: Bass Sulcular</td>
<td>Effect of oral care protocol</td>
<td>8 months</td>
<td>Severity of mucositis (Eilers’ Oral Assessment Guide), oral mucositis–related pain (Faces Scale)</td>
<td>Interaction group: significant reduction of severity of oral mucositis (p = 0.000002) and related pain (p = 0.0001)</td>
</tr>
<tr>
<td>Cheng KKF et al. 2004: Prevention of oral mucositis in paediatric patients treated with chemotherapy: a randomised crossover trial comparing two protocols of oral care</td>
<td>RCT</td>
<td>2-</td>
<td>n = 40: 1st group: chx (n = 20), 2nd group: benzydamine (n = 20)</td>
<td>Children (6–17 years), had high–dose or combination chemotherapy for haematological malignancies or solid tumors, were capable to brush or rinse</td>
<td>Mouth rinse: saline, 0.2% chx gluc or 0.15% benzydamine hydrochloride Technique: Bass</td>
<td>chx vs benzydamine</td>
<td>6 weeks</td>
<td>Severity of mucositis (Eilers’ Oral Assessment Guide), occurrence of ulcerative lesions</td>
<td>chx group: significant reduction in ulcerative lesions (p &lt; 0.05) and severity of mucositis (p &lt; 0.05)</td>
</tr>
<tr>
<td>Dodd MJ et al. 2000: Randomized clinical trial of the effectiveness of 3 commonly used mouthwashes to treat chemotherapy-induced mucositis</td>
<td>RCT</td>
<td>2+</td>
<td>n = 200: 1st group: chx (n = 51), 2nd group: magic (n = 42), 3rd group: salt and soda (n = 49)</td>
<td>Adults (&gt;18 years), are receiving stomatoxic chemotherapy, presence of mucositis</td>
<td>toothbrush: 90 s mouth rinse: 0.12% chx gluc or magic mouthwash (lidocaine, benadryl and maalox) or salt and soda mouthwash 4 t/d/20 s</td>
<td>chx gluc vs magic mouthwash vs salt and soda</td>
<td>Until cessation of signs and symptoms of OM, or 12 days</td>
<td>Severity of mucositis (Eiler’s Oral Assessment Guide), time of cessation, pain score</td>
<td>Non-significant differences between these three mouth rinses</td>
</tr>
<tr>
<td>Djuric M et al. 2006: Mucositis prevention by improved dental care in acute leukemia patients</td>
<td>RCT</td>
<td>1-</td>
<td>n = 34: intervention (n = 15), control (n = 19)</td>
<td>adults (&gt;19 years), had acute leukemia, are receiving induction remission therapy, at least 10 teeth</td>
<td>Intervention group: prechemotherapy: scaling and polishing, restorative measurements toothbrush: round–ended soft nylon bristles or cotton buds, 21/d mouth rinse: 0.12% chx gluc mixed with 3% H2O2 and nystatin, 31/d technique: Stillman Control group: mouth rinse: 0.12% chx gluc mixed with 3% H2O2 and nystatin, 31/d</td>
<td>Effect of dental care program</td>
<td>28 days</td>
<td>OHI, GI, WHO Oral Toxicity Scale</td>
<td>Intervention group: lower mean values of GI, OHI and mucositis score, but not statistically significant on most of the examination days</td>
</tr>
</tbody>
</table>

*General note: Risk of bias: no blinding of subjects and investigators.*

*General note: Risk of bias: this study did not include a control group; poor description of randomization.*

*General note: Risk of bias: this study did not include a control group; poor description of randomization.*

*General note: Risk of bias: no blinding of subjects and investigators; groups were not treated equally at baseline; intervention group became dental treatment before chemotherapy consisting of scaling, polishing and restorative measurements, whereas control group did not receive any.*

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Study type</th>
<th>Evidence level</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow-up</th>
<th>Outcome measure</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huang B et al. 2017: The effectiveness of a saline mouth rinse regimen and education programme on radiation-induced oral mucositis and a quality of life in oral cavity cancer patients: A randomised controlled trial</td>
<td>RCT</td>
<td>1++</td>
<td>n = 96: intervention (n = 5), control (n = 45)</td>
<td>Adults (&gt;20 years), diagnosed with oral cavity cancer and undergoing postoperative adjuvant radiation therapy and concurrent chemotherapy</td>
<td>Interventions group: mouth rinse: 0.9% saline with wet dressing gauze 4 t/d/8 w Control group: mouth rinse: boiled water</td>
<td>Saline mouth rinse and education program vs standard care</td>
<td>8 weeks</td>
<td>WHO Oral Toxicity Scale, MSS–moo, UW–QOL</td>
<td>Intervention group: significant better physical and social–emotional QOL (p &lt; 0.05), WHO Oral Toxicity Scale and MSS–moo no significant difference</td>
</tr>
<tr>
<td>Kartin PT et al. 2014: Effect of an oral mucositis protocol on quality of life of patients with head and neck cancer treated with radiation therapy</td>
<td>RCT</td>
<td>1-</td>
<td>n = 50: intervention (n = 20), control (n = 30)</td>
<td>Adults (&gt;18 years), nasopharyngeal, laryngeal, gingival, hypopharyngeal, tongue and salivary gland head neck cancers, absence of oral mucositis</td>
<td>Interventions group: toothbrush: soft-bristled, after every meal and before bed mouth rinse: sodium bicarbonate 4 t/d, water or oral care solution after meals, before bed and during night technique: Stillman other aids: dental floss, sugar-free chewing gum, ice chips, tongue cleaner</td>
<td>Effect of oral care and nutrition protocol</td>
<td>20 months</td>
<td>WHO Oral Toxicity Scale, VAS, SGA, EORTC QLQ–C30</td>
<td>Intervention group: significant decrease of VAS (p = 0.014), mucositis degree (p &lt; 0.001) and malnutrition (p &lt; 0.05)</td>
</tr>
<tr>
<td>Nikura N et al. 2020: Oral care evaluation to prevent oral mucositis in estrogen receptor–positive metastatic breast cancer patients treated with everolimus (Oral Care–BC): A randomized controlled phase III trial</td>
<td>RCT</td>
<td>1+</td>
<td>n = 175: intervention (n = 82), control (n = 87)</td>
<td>Women aged 20 years or older, postmenopausal, metastatic hormone receptor–positive, HER1–negative breast cancer, adequate renal function, newly prescribed everolimus 10 mg and exemestane 25 mg</td>
<td>Intervention group: periodontal treatment: scaling, crown polishing brushing; tongue cleaning mouth rinse: 0.2% Neostatin Green other aids: dexamethin ointment control group: mouth rinse: saline</td>
<td>Professional oral care before everolimus treatment</td>
<td>8 weeks</td>
<td>Incidence of oral mucositis</td>
<td>Significant decrease of incidence of grade 1 and 2 oral mucositis in the intervention group (p = 0.34, p = 0.15, respectively)</td>
</tr>
</tbody>
</table>


General notes: Risk of bias: poor description of randomization; no concealment method; no blinding of subjects and investigators, SGA: Subjective Global Assessment.

### Tab. III  Overview of the evidence derived from systematic reviews and meta-analyses on the management of radiation caries

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Evidence level</th>
<th>Objective</th>
<th>Methodology</th>
<th>Study quality</th>
<th>Type of studies</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvalho CG et al. 2018: Guide for health professionals addressing oral care for individuals in oncological treatment based on scientific evidence</td>
<td>1++</td>
<td>Guide for oral care of oncological patients</td>
<td>PubMed, Cochrane, EBSCOHost</td>
<td>SIGN, PICO, AMSTAR, MERGE</td>
<td>n = 54: RCT, systematic review of RCT</td>
<td>Oral assessment and professional and home care before, during and after oncological treatment Treatment of xerostomia with saliva substitute and hydration</td>
</tr>
<tr>
<td>Cohen EEW et al. 2016: American Cancer Society Head and Neck Cancer Survivorship Care Guideline</td>
<td>2+</td>
<td>Guideline that provides recommendations on best practices in the management of adults after head and neck cancer treatment</td>
<td>PubMed</td>
<td>Level of evidence, expert panel was convened to develop guideline based on this systematic review</td>
<td>RCT, cohort studies, case-control</td>
<td>Most evidence is not sufficient to provide a strong recommendation. Brushing with remineralizing dentifrice, use of dental floss and fluoride use (1.1% sodium fluoride as dentifrice or incustomized delivery trays)</td>
</tr>
<tr>
<td>Hong CHL et al. 2018: A systematic review of dental disease management in cancer patients</td>
<td>1+</td>
<td>Update efficiency of dental strategies in preventing dental-related complications in cancer patients</td>
<td>PubMed, Embase</td>
<td>Electronic collection form customized for reviewing dental disease data, level of evidence by Somerfield criteria, flaws by Hadorn criteria</td>
<td>n = 59: RCT, cohort studies, case series, cross-sectional studies</td>
<td>Use of fluoride products to prevent dental caries. Type of fluoride delivery system does not significantly influence caries activity (level of evidence II, grade of recommendation B). Use of chx mouth rinse 0.12–0.2% once or twice daily (level of evidence II, grade of recommendation B)</td>
</tr>
</tbody>
</table>

**General notes:** AMSTAR: Assessing the Methodological Quality of Systematic Reviews. MERGE: Method for Evaluating Research and Guideline Evidence.

### Tab. IV  Overview of the evidence derived from clinical treatment trials on the management of radiation caries

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Study type</th>
<th>Evidence level</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow-up</th>
<th>Outcome measure</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papas A et al. 2008: Caries clinical trial of a remineralising toothpaste in radiation patients</td>
<td>RCT</td>
<td>1++</td>
<td>n = 57: Enamelon (n = 28), conventional (n = 29)</td>
<td>Adults (&gt;18 years), had radiation to the head and neck, reduction of unstimulated salivary flow to below 0.2 ml/min, at least 10 teeth</td>
<td>Enamelon toothpaste 1100 ppm with additional calcium phosphate (intervention group), conventional fluoride toothpaste 1100 ppm (control group); mouthrinse: 0.05% sodium fluoride 1 t/d Other aids: topical fluoride varnish, dental floss, pilocarpine</td>
<td>Enamelon toothpaste with 1100 ppm and additional calcium phosphate vs conventional toothpaste 1100 ppm</td>
<td>12 months</td>
<td>root caries, coronal cavities, salivary flow rate, PI, GI, level of S. mutans and lactobacillus</td>
<td>toothpaste: significant lower root caries (p = 0.03), no significant difference for coronal caries</td>
</tr>
</tbody>
</table>

### Tab. V  Overview of the evidence derived from a systematic review on the management of xerostomia

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Evidence level</th>
<th>Objective</th>
<th>Methodology</th>
<th>Study quality</th>
<th>Type of studies</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furness S et al. 2011: Interventions for the management of dry mouth: topical therapies</td>
<td>1++</td>
<td>Topical treatments that are effective in reducing xerostomia</td>
<td>Cochrane, Medline, Embase, Cinahl, Amed, Cancerlit</td>
<td>Data extraction form, RR with 95% CIs, risk of bias using two-part tool by Cochrane reviews, sensitivity analysis</td>
<td>RCT (n = 36)</td>
<td>No strong evidence that any topical therapy is effective for relieving the symptom of dry mouth. Oxygenated glycerol triester saliva substitute spray is more effective than an aqueous electrolyte spray. Chewing gum increases saliva production, but there is no evidence that gum is better or worse than saliva substitution.</td>
</tr>
</tbody>
</table>
Tab. VI  Overview of the evidence derived from clinical treatment trials on the management of xerostomia

<table>
<thead>
<tr>
<th>Author and title</th>
<th>Study type</th>
<th>Evidence level</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow-up</th>
<th>Outcome measure</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chambers MS 2005: Clinical evaluation of the intraoral fluoride releasing system in radiation-induced xerostomic subjects. Part 2: Phase I study</td>
<td>RCT</td>
<td>1++</td>
<td>n = 22; intervention group (n = 10), control group (n = 12)</td>
<td>Adults (&gt;18 years), undergone radiation therapy min 40 Gy at least 3 months prior to study, unstimulated salivary flow less than 0.3 g/min</td>
<td>Toothbrush: Colgate-Palmolive Toothpaste: 1100 ppm fluoride 2t/d Intervention group: intraoral fluoride-releasing system Control group: custom-made fluoride carriers with 0.4% stannous fluoride gel, 1t/d/10 min</td>
<td>Intraoral fluoride-releasing system vs fluoride carriers</td>
<td>48 weeks</td>
<td>Caries, hematologic and renal parameters</td>
<td>No significant differences in caries rate, hematologic or renal complications</td>
</tr>
<tr>
<td>Davies AN 2000: A comparison of artificial saliva and chewing gum in the management of xerostomia in patients with advanced cancer</td>
<td>RCT</td>
<td>2-</td>
<td>n = 43, crossover design</td>
<td>Xerostomia, malignant disease, estimated prognosis of 2 weeks</td>
<td>Artificial saliva: mucin-based Saliva Orthana in spray form 4 t/d Chewing gum: sugar-free Freedent 4 t/d/10 min, 2 pieces at a time</td>
<td>Chewing gum vs artificial saliva</td>
<td>12 days</td>
<td>VAS, questionnaire</td>
<td>No statistically significant difference in VAS Questionnaire: relief of xerostomia, but side effect</td>
</tr>
<tr>
<td>Kaae JK et al. 2020: A randomized phase III trial for alleviating radiation-induced xerostomia with chewing gum</td>
<td>RCT</td>
<td>1+</td>
<td>n = 109: 1st group: chewing gum (n = 68), 2nd group: standard care (n = 41)</td>
<td>Adults (&gt;18 years), physician–assessed xerostomia, &gt;6 months after radiation therapy, disease-free and able to chew gum</td>
<td>1st group: chewing gum tasteless and sugar-free, 5 t/d/5 min 2nd group: saliva substitutes or stimulants</td>
<td>Chewing gum vs standard care</td>
<td>1 month</td>
<td>EORTC QLQ-H&amp;N35, GRIX questionnaire, salivary flow and viscosity</td>
<td>Both groups: reduction of dry mouth scores, salivary flow increase and viscosity decrease, but no significant differences between these two groups</td>
</tr>
<tr>
<td>Warde P et al. 2000: A phase II study of Biotene in the treatment of postirradiation xerostomia in patients with head and neck cancer</td>
<td>Case series</td>
<td>3</td>
<td>n = 28</td>
<td>Post–irradiation xerostomia, more than 75% of both parotid glands included in the primary radiation field</td>
<td>Toothbrush: soft Toothpaste: Biotene (fluoridated and lactoperoxidase) Mouthrinse: Biotene 3 t/d Other aids: Biotene chewing gum, Oralbalance gel</td>
<td>Effect of Biotene dentifrice, mouthwash, chewing gum and Oralbalance gel</td>
<td>2 months</td>
<td>VAS, xerostomia questionnaire</td>
<td>Significant improvement of VAS, subjective improvement of oral dryness, ability to eat, oral discomfort</td>
</tr>
</tbody>
</table>

General notes: Risk of bias: this study did not include a control group, poor description of randomization, no blinding of subjects and investigators, no concealment method, high drop-out rate of 36%.

General notes: Risk of bias: no blinding of subjects and investigators, no concealment method. EORTC QLQ-H&N35: scoring of dry mouth. GRIX questionnaire: Groningen Radiotherapy-Induced Xerostomia.

VAS: Visual Analogue Scale
Zusammenfassung
Einleitung
Ziel dieses Scoping Review war, eine klinische Leitlinie für das Management der Mundgesundheit von Patienten nach Chemo- und/oder Radiotherapie zu erstellen.

Materialien und Methoden

Ergebnisse

Diskussion
Dieses Review umfasst Leitlinien für medizinisches Fachpersonal, das Patienten betreut, die eine Chemo- und/oder Strahlentherapie erhalten haben. Eine einzige Standardempfehlung konnte aufgrund mangelnder hochevidenzbasierter Daten nicht erstellt werden.

References
**Résumé**

Introduction

L’objectif de cette revue de littérature exploratoire était d’établir une ligne directrice clinique pour la gestion de la santé bucco-dentaire des patients après une chimiothérapie et/ou une radiothérapie.

Matériaux et méthodes


Discussion

Cette revue de littérature exploratoire contient des lignes directrices pour les professionnels de la santé qui s’occupent de patients ayant reçu une chimiothérapie et/ou une radiothérapie. Il n’a pas été possible d’établir une recommandation standard en raison du manque de données à haut niveau de preuve.

Résultats

S3 études ont rempli les critères de sélection. Les résultats ont indiqué l’existence de recommandations pour les patients suivant une radiothérapie et/ou une chimiothérapie : le traitement de la muqueuse buccale, la prévention et le contrôle des lésions radiaives et le traitement de la xérostomie. La majorité des études incluses étaient basées sur un niveau de preuve faible.