Cancer Care Ontario's Symptom Management Guide-to-Practice: Oral Care

July 2012

Preamble

Ontario Cancer Symptom Management Collaborative

An initiative of Cancer Care Ontario, the Ontario Cancer Symptom Management Collaborative (OCSMC) was undertaken as a joint initiative of the Palliative Care, Psychosocial Oncology and Nursing Oncology Programs. The overall goal of the OCSMC is to promote a model of care enabling earlier identification, communication and documentation of symptoms, optimal symptom management and coordinated palliative care.

The OCSMC employs common assessment and care management tools, including the Edmonton Symptom Assessment System (ESAS) screening tool, to allow patients to routinely report on any symptoms they are experiencing. Symptom Management Guides-to-Practice were developed to assist health care professionals in the assessment and appropriate management of a patient's cancer-related symptoms. In addition to the symptom specific Guides-to-Practice, quick-reference Pocket Guides and Algorithms were created. For a comprehensive management plan for patients with advanced disease, please refer to the Palliative Care Collaborative Care Plans.

Objective

The objective of this initiative was to produce Guides-to-Practice for the management of patients with cancer-related symptoms. These documents are clinical tools designed to assist health care practitioners in providing appropriate patient care and are not intended to serve as standards of care.

Scope

The scope is to produce Guides-to-Practice for the pharmacological and non-pharmacological management of cancer related oral complications, including dysgeusia, xerostomia, salivary gland hypofunction, mucositis and oral infections but excluding dysphagia. The scope of this Guide-to-Practice will also address the management of patients experiencing acute intra-oral adverse effects secondary to systemic and/or radiation therapy.

Target Population

The target population consists of adult patients who require symptom management related to cancer at any point in the disease trajectory.

Target Users

The Guides-to-Practice will be of interest to health professionals (family physicians, palliative care physicians, oncologists, nursing professionals, dietitians, general dentists, dental hygienists, speech language pathologists, pharmacists and radiation therapists) who provide care to patients with cancer-related symptom management needs at various stages of the disease pathway.

Methodology

The Guides-to-Practice were developed by the interdisciplinary Symptom Management Group (SMG), which included regional representation from across the province (refer to Post-amble for details). As an alternative to de novo development, the Guides-to-Practice were developed using the ADAPTE guideline adaptation approach that includes identifying existing guidelines, appraising their quality, selecting recommendations for inclusion and obtaining expert feedback (refer to Appendix A and B for details).

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Considerations

The following guidelines were used as the basis for the development of this Guide: *Best Practice Guidelines for the Management of Oral Complications from Cancer Therapy* from Cancer Care Nova Scotia (1); *Evidence-Based Interventions for the Management of Oral Mucositis* from the Oncology Nursing Society (2); *Oral Mucositis & Xerostomia* from the British Columbia Cancer Agency (3,4); *Oral cancer guideline* form HealthPartners Dental Group and Clinics (5); *Updated clinical practice guidelines for the prevention and treatment of mucositis* from Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (6). Recently published systematic reviews (7-11) were also used to supplement the evidence base.

Key recommendations are highlighted in shaded boxes. Source documents for each recommendation are denoted according to the symbols shown in Table 1. For example, if a recommendation is derived verbatim from the ONS guideline, it is indicated by the symbol ONS. Recommendations that are derived from the ONS guideline but have been modified are designated as ONS *Modified*. Recommendations that have been derived based on the expert opinion of the Oral Care SMG are designated as Oral Care SMG.

Table 1. Symbol Legend

Symbol	Definition
CCNS **ONS** **BCCA** **HPDG** **MASCC/ ISOO**	Verbatim extract from: ▪ Cancer Care Nova Scotia (CCNS) ▪ Oncology Nursing Society (ONS) ▪ British Columbia Cancer Agency (BCCA) ▪ Health Partners Dental Group (HPDG) ▪ Multinational Association of Supportive Care in Cancer/International ▪ Society of Oral Oncology (MASCC/ISOO)
CCNS ***Modified*** **ONS** ***Modified*** **BCCA** ***Modified*** **HPDG** ***Modified*** **MASCC/ ISOO** ***Modified***	Sections extracted from the guidelines which have been altered are indicated by the word *Modified*
Oral Care SMG	Sections written by the Oral Care Symptom Management Group

While some references to specific articles are provided, this Guide is not intended to be a comprehensive overview of the primary evidence, for a more in depth review the reader is encouraged to seek out the original guidelines. For a quick reference tool on oral care management, please refer to the Oral Care Pocket Guide and Algorithm. For a comprehensive management plan, for patients with advanced disease, please refer to the Cancer Care Ontario Collaborative Care Plans.

Definition of Terms

Dysgeusia: abnormal or impaired sense of taste; an unpleasant alteration of taste sensation; a distortion or perversion of the sense of taste; may be described as a bitter, metallic, salty, or unpleasant taste; linked to changes in olfaction and secondary loss of pleasure derived from eating (11).
Mucositis: mucosal injury of the gastrointestinal tract (mouth to anus) associated with cancer therapy. In this Guide, 'mucositis' refers only to oral mucositis (6).
Salivary gland hypofunction: diminished salivary flow (9).
Xerostomia: subjective sensation of a dry mouth (9).

Assessment

Oral Care SMG

- **Common symptoms to screen for include oral pain, dry mouth, taste changes and difficulty with opening/closing of the mouth.**
- **Common signs to screen for include cavities, bleeding, infections, ulcerations and abnormal lesions.**

BCCA *Modified*

Ongoing comprehensive assessment is the foundation of effective oral care management. Interdisciplinary team members are usually involved in the management of oral complications therefore it is important for the patient to have contact and general information from all health care professionals involved in their care (e.g., oncologist, family physician, dentist, dental hygienist, nurse, dietitian, radiation therapist, speech pathologist, pharmacist, etc). The OPQRSTUV Acronym (Table 2) suggests questions to guide oral care assessment; however, these may need to be individualized for each patient.

Table 2. Assessment using OPQRSTUV Acronym (*adapted from BCCA (3,4)*).

Onset	When did the symptoms begin? How often do they occur? How long do they last?
Provoking / **P**alliating	What makes it better? What makes it worse? What do you think may be causing the symptom? What are the aggravating or alleviating factors (e.g., medications, active treatment, dietary changes)?
Quality	Do you have a dry mouth? (e.g., decrease in amount or consistency of saliva). Do you have any redness, blisters, ulcers, cracks, or white patchy areas? If so, are they isolated, generalized, clustered or patchy?
Region/**R**adiation/ **R**elated Symptoms	Where are your symptoms? (e.g., on lips, tongue, mouth). Does your pain radiate anywhere? Do you have any other related or associated symptoms?
Severity	What is the intensity of this symptom (on a scale of 0 to 10 with 0 being none and 10 being worst possible)? Right Now? At Best? At Worst? On Average?
Treatment	*If dry mouth*: Fluid intake? Are you using any oral rinses? What type? Are they effective? Are you using any saliva substitutes or stimulants? What type? Are they effective? *If associated pain in mouth*: Are you using any pain medications? What type – topical/local, oral/injection? Are they effective? Are there any other treatments that you are using to help with pain? Alteration in diet texture? *If associated bleeding from mouth*: Does it occur spontaneously? Where is it located? What aggravates it? What treatments have been recommended and have been used? *What is your current oral care routine?* How effective is it? Have you had oral infections? What treatments have you used? How effective have they been? Do you have any side effects from the medications/treatments you have used for any of the above? What tests have you had for your oral symptoms, if any?
Understanding / Impact on **You**	How bothered are you by this symptom? Is your ability to eat or drink affected? By how much? Are you having difficulty swallowing or chewing? Is it for solids and/or liquids? Do you have any weight loss? How much? Over what time frame? Do you have taste changes (dysgeusia)? Do you have difficulty speaking? Are you able to wear dentures? Do any of your symptoms interfere with other normal daily activities? How does this symptom affect your day to day life?
Values	What is an acceptable level of severity for this symptom (0 – 10 scale)? What does this symptom mean to you? How has it affected you and your family and/or caregiver?

** For additional assessment resources refer to Appendix C.*

Physical Assessment

Vital Signs

BCCA *Modified*

- Measure and monitor temperature, pulse, respiratory rate, blood pressure and oxygen saturation. Monitor pain severity using the Visual Analogue Scale (VAS) or the Numerical Rating Scale (NRS).
- Measure weight and monitor weight change (Refer to Loss of Appetite Guide for more information).
- Monitor hydration status - daily oral intake and output, volume, frequency and characteristics of urine, assess mucous membranes, skin turgor, and capillary refill.

Oral Examination

HPDG/ BCCA *Modified*

An oral examination requires an adequate light source, tongue blade, non-sterile gloves, gauze squares, and a mouth mirror. The examination should focus on the following:

- Color – presence of pallor or erythema, abnormal white patches, discoloured areas.
- Moisture – note any accumulation of debris or coating, teeth discoloration, bad odour, altered texture, shininess, decrease in amount of saliva, increased thickness of saliva, pooling of saliva and blood.
- Oral hygiene – note accumulation of debris or coating, discoloration of teeth, bad odour.
- Mucosal integrity – note any presence of mucosal abnormalities (e.g., cracks, fissures, ulcers, blisters).
- Perception – note ability to swallow, changes in tone of voice and speech.

For additional assessment information refer to Table 3 below and the Oral Cancer Screening video courtesy of the American College of Prosthodontists http://www.gotoapro.org/videos/

Table 3. Eight Steps of Physical Assessment (*adapted from HPDG (5)*).

HPDG

1. Extraoral examination	▪ Inspect head and neck (anterior and posterior neck). ▪ Bimanually palpate lymph nodes and salivary glands. ▪ Inspect the face (including the external ears) for skin lesions, asymmetry and masses. ▪ Asses cranial nerve function.
2. Lips	▪ Inspect and palpate outer surfaces of lip, vermillion border and corners of the mouth. ▪ Inspect and bidigitally palpate inner labial mucosa (upper and lower).
3. Buccal mucosa	▪ Inspect and palpate inner cheek lining.
4. Alveolar ridge & gingiva	▪ Inspect maxillary/mandibular gingiva and alveolar ridges on both the buccal and lingual sides.
5. Tongue	▪ Have patient protrude tongue and inspect the dorsal surface. ▪ Have patient lift tongue and inspect ventral surface. ▪ Grasping tongue with a piece of gauze and gently pulling it out to each side, inspect the lateral borders of the tongue from its tip back to the lingual tonsil region posteriorly. ▪ Palpate tongue.
6. Floor of mouth	▪ Inspect and palpate floor of mouth bimanually.
7. Hard palate	▪ Inspect and palpate hard palate for any lumps.
8. Soft palate and oropharynx	▪ Gently depress the patient's tongue with a mouth mirror, inspect the soft palate, tonsillar pillars, and oropharynx.

Dental Assessment

CCNS *Modified*

Patients, who will be undergoing chemotherapy, head and neck radiotherapy, or hematopoietic stem cell transplant, must undergo a dental assessment by a qualified dentist prior to initiation of treatment or radiation treatment planning. It is important that all healthcare providers, involved in the care of patients receiving radiation treatment for head and neck cancer, be aware of this, because a missed dental assessment/procedure will delay treatment of the disease and possibly affect patient outcome. Other dental assessments may be done by the patient's community dentist in consultation with the oncology specialist(s). Dental examination **must be done as soon as possible after diagnosis**, to allow time for dental procedures and adequate healing prior to treatment. If dental work is indicated, it should be carried out **before** treatment is started. Dental follow-up and care can be provided during active therapy.

Etiology and Diagnosis

- **Significant risk factors for the development of oral complications include the type of cancer, type of cancer treatments, cumulative doses of chemotherapy or radiation treatment, method of delivery and duration of treatment (12).**
- **Predisposing medical, dental, and lifestyle factors may increase the severity of the complications (12).**
- **Oral complications can significantly affect the patient's morbidity, ability to tolerate treatment, and overall quality of life.**
- **Rigorous assessment, diagnosis and early intervention are important in preventing and decreasing oral complications (12)**.

Causes of oral complications

BCCA *Modified*

Identifying the underlying etiology is essential in determining the interventions required. The following are common causes of oral complications. (While the lists below offer a number of potential causes, they are not meant to be exhaustive).

Cancer Treatment Related Causes

BCCA *Modified*

1. Head and neck cancers (which encompasses radiation, +/- chemotherapy and surgery)
2. Systemic therapy (which encompasses chemotherapy, targeted therapy and bisphosphonates)
3. Hematopoietic Stem Cell Transplant (HSCT) +/- total body radiation.

Oral Care SMG

Neutropenia is a common adverse effect of systemic therapy, placing patients at an increased risk of oral mucositis and associated bacteraemia and sepsis.

Non-Pharmacologic Related Causes

BCCA *Modified*

1. Lifestyle factors (e.g., alcohol use, tobacco use, illicit drug use).
2. Medical conditions
   - Immune disorders (e.g., Sjogren's syndrome, HIV/AIDS)
   - Malignancies
   - Diabetes mellitus
   - Transplant patients
   - Poor baseline nutritional status based on screening
   - Poor performance status
   - Nutrient deficiencies (e.g., B12, folic acid)
   - Dehydration related to reduced fluid intake, diarrhea, vomiting, diaphoresis
   - Oxygen therapy
   - Immunosuppression
3. Pre-existing dental conditions
   - Caries, dental infections, periodontal disease, or salivary gland abnormalities
   - Poor oral hygiene, poor fitting dentures, fixed orthodontic appliances
4. Demographic
   - Age (older adults more susceptible to developing oral mucositis)
   - Females, due to hormonal factors
   - Low social economic status
   - Low dental health awareness

Pharmacologic Related Causes

Oral Care SMG

- **A large variety of medications may cause oral complications.**
- **These complications could be from an adverse drug effect, related to drug interactions, or a consequence of drug metabolism.**
- **Consultation with a pharmacist is strongly recommended for consideration of the interactions drugs might have with one another, with foods or with the specific issues of an individual patient.**

Pharmacologic agents used in cancer and non-cancer therapies may cause xerostomia and thus may predispose patients to developing oral mucositis. A comprehensive list of medications causing oral complications is beyond the scope of this document; Table 4 provides a list of potential agents.

Table 4. Examples of agents which may cause oral care problems *(adapted from CCNS).*

Oral Care Problem	Drug Classes	Medication Examples
Salivary Gland Hypofunction, Xerostomia (Dry Mouth)	Anticholinergics	Atropine, scopolamine, glycopyrrolate, ipratropium
	Antipsychotics	Chlorpromazine, olanzapine, prochlorperazine, risperidone
	Antihistamines	Diphenhydramine (Benadryl®), chlorpheniramine, dimenhydrinate (Gravol®)
	Anticonvulsants	Gabapentin, pregabalin
	Antihypertensives	Amlodipine
	Decongestants	Pseudoephedrine
	Diuretics	Furosemide, hydrochlorothiazide
	Muscle Relaxants	Cyclobenzaprine, baclofen, dicyclomine
	Opioids	Morphine, hydromorphone, fentanyl, methadone, oxycodone
	Tricyclic Antidepressants	Amitriptyline, nortriptyline, imipramine
	Selective serotonin reuptake inhibitors (SSRIs)	Citalopram, paroxetine
Gingival Hyperplasia	Antihypertensive	Nifedipine (calcium channel blockers)
	Anticonvulsant	Phenytoin
	Immunosuppressants	Cyclosporine
Oropharyngeal Candidiasis	Antibiotics	Erythromycin, clarithromycin, amoxicillin
	Immunosuppressants	Cyclosporine, steroids
Black Hairy Tongue	Antibiotics	Erythromyicn, clarithromycin
	Anticonvulsants	Phenytoin
	Antacids	Maalox®, Pepto-Bismol®, Kaopectate®
Mucositis	Chemotherapeutic Agents	Amsacrine, dactinomycin, doxorubicin, daunorubicin, epirubicin, idarubicin, mitomycin, mitoxantrone, busulfan (high dose), 5-fluorouracil (5-FU), capecitabine, methotrexate, pemetrexed, melphalan, etoposide, irinotecan, docetaxel.
Osteonecrosis of the Jaw	Bisphosphonate therapy	Zoledronic acid, clodronate, pamidronate, risedronate, alendronate
	RANK ligand inhibitor	Denosumab

Consequences of oral complications include:

BCCA *Modified*

- Altered nutrition, dehydration and cardiovascular compromise (e.g., hypotension, tachycardia).
- Increased rate of dental caries.
- Periodontal disease, osteoradionecrosis and bisphosphonate osteonecrosis.
- Possible delay, reductions, or discontinuation of cancer treatment.
- Decreased quality of life (e.g. psychological distress, difficulty eating, drinking and swallowing, altered speech and taste).
- Airway obstruction, respiratory distress.
- Systemic infection (sepsis).
- Local oral infections, which may be accompanied by systemic symptoms such as headache, fever, painful lymphadenopathy and malaise (See Appendix D for Presentation of Oral Infections).

Interventions

Interventions are classified into non-pharmacological and pharmacological entities for each symptom. The pharmacological section refers only to the use of drugs as part of management; all other treatment modalities are included in the non-pharmacological section.

1. General Oral Care

1.1 General Oral Care: Non-pharmacological Interventions

BCCA *Modified*

- **Good oral care is fundamental in preventing and decreasing oral complications and has the potential to modify the acute and long term sequelae of cancer therapy.**
- **The major purposes of oral care are to maintain normal function of the oral tissues, to maintain comfort and to reduce the risk of bleeding, local infection and systemic infection.**

Education

CCNS

Use of a uniform, systematic plan for oral care, along with standard educational approaches to help patients understand and cope with the symptoms of oral complications is recommended.

CCNS *Modified*

- Multidisciplinary team involvement is important to the development and evaluation of oral care protocols, before and during all phases of treatment.
- Comprehensive management plan(s) may reduce the severity of mucositis caused by chemotherapy or radiotherapy.

CCNS *Modified*

- Patients who are to receive chemotherapy or radiation therapy should start their education about possible oral complications and preventive mouth care practices prior to treatment.
- Patients should be encouraged to follow these practices during active treatment and recovery.
- Oral hygiene is particularly important for any patient who is immunocompromised.

- **An important component of oral care management is the assessment of nutritional status, including adequacy of oral solid and fluid intake.**

Nutritional Care

Oral Care SMG

There is limited research examining effective dietary modifications for managing oral complications during cancer treatment (7,13). Due to the lack of intervention studies, current best practice of oncology dietitians is based on experience, clinical judgment and an understanding of physiology.

General Nutritional Recommendations for Oral Hygiene

CCNS *Modified*

- Adequate nutrition and fluid intake, based on body weight, is important to maintain good oral tissue integrity.
- Alcohol and tobacco can be irritating to the oral tissues and contribute to salivary hypofunction.
- Therefore it is recommended to limit or stop the use of these substances.

Oral Care Plans

CCNS *Modified*

Vital factors in oral care are the frequency, thoroughness and consistency with which it is performed. To prevent complications, the frequency of care is more important than the agents employed. The following frequencies of oral care delivery, according to the patient's condition, are proposed:

- *World Health Organization (WHO) Grade 0*: Care every 4 to 6 hours may reduce the patient's potential for infection from microorganisms.
- *WHO Grade 1 and 2:* Care every 2 hours may reduce oral complications and may enhance patient comfort by keeping membranes moist.
- *WHO Grade 3 and 4:* Where possible, care every hour (or more frequently) is appropriate for patients requiring oxygen therapy, patients who breathe through their mouths, patients with oral infections, unconscious patients, and patients with severe mucositis.
  Refer to Appendix C for Grading Scales.

General Principles of Oral Care:

CCNS *Modified*

- Keep oral mucosa and lips clean, soft, moist and intact to prevent infection.
- Remove food debris/dental plaques from teeth and gums without damaging the gingival tissue/periodontium.
- Optimize oral hygiene.
- Prior to commencing cancer therapy remove all fixed orthodontic appliances.
- Repair ill-fitting dentures or discontinue use.
- Repair, replace or recontour broken restorations on teeth to avoid injury to the tissues.
- Alleviate any other pain/discomfort to enhance oral intake.
- Treat acute and chronic infections of the oral cavity.
- Assess for trismus (the patient's ability to open/close the mouth).

Oral Care SMG

  - Assess for infection or potential cancer recurrence as etiology
  - Consider using Therabyte ™ as directed, using the 7-7-7 protocol (7 Stretches performed 7 times a day, each stretch held for 7 seconds).

Oral Care SMG

- **The recommended rinsing solution is a bland rinse (1 teaspoon salt, 1 teaspoon baking soda in 1 liter/ 4 cups of water). The rinse should be prepared at least once daily and should not be refrigerated.**
- **Following emesis, patients should be instructed to rinse mouth with the bland rinse to neutralize the mouth immediately, minimizing tooth enamel demineralization**.
- **Patients may chew xylitol gum or suck on xylitol lozenges up to 6 grams a day (14).**
- **While there is no evidence to recommend either for or against the use of club soda, the Oral Care SMG suggests it should be avoided due the acidic pH, a result of the carbonic acid content found in carbonated soft drinks.**

CCNS *Modified*

Oral Care Plans (Table 5) can be divided into three categories based on past and current treatments for oral complications.

Basic Oral Care Plan

CCNS *Modified*

A basic regimen of oral care, intended for all cancer patients without oral complications, is considered a prevention strategy and is essential to minimize the risk of developing future complications. This plan should be initiated before treatment begins and continued until the risk of side effects or oral complications is over. These practices are for the patient with Grade 0 to 1 mucositis using RTOG or WHO mucositis rating scales.

Intensified Oral Care Plan

CCNS *Modified*

Intensified oral care practices are intended for the patients who have been graded on the RTOG or WHO mucositis rating scales as 2 or greater. These practices build on those of basic oral care practices and may be considered as treatment interventions.

End of Life Oral Care Plan

Oral Care SMG

Patients approaching end of life will experience oral complications that may contribute to pain, communication difficulties, malnutrition, and a decreased quality of life. This population of patients has many risk factors, and nearly all of these patients will experience oral complications (15).

- **Discussions with patients and their families should be done early and as often as necessary along the illness trajectory to explain the etiology of mouth complications, to determine the patient's goals of care, to clarify their declining health status and to determine desired levels of care pertaining to nutrition, hydration and interventions (15).**

Oral complications affect the individual at a holistic level, in terms of comfort, nutrition and communication. In particular, contact with loved ones may be affected, and the patient may become isolated if adequate oral care is not provided. The goals are to keep the teeth, oral mucosa, tongue, lips and nose clean and moist and to maintain airway patency. The patient's condition, preference and ability to tolerate oral hygiene will determine the frequency, intensity and agents used (15).

- **As patients approach the end of life, the primary objective of oral care is to avoid complications, treat potentially reversible conditions rapidly and/or provide relief of symptoms caused by the offending oral complication (15).**

- **Oral candidiasis is common in this patient population and therefore the oral cavity should be evaluated daily (15).**

How to use this table: Start with the basic oral care plan first, proceed to intensified oral care plan as needed, then continue to end of life oral care plan as needed.

Table 5. Oral Care Plans *(Adapted from CCNS (1), BCCA (3,4) and Su et al (14))*.

Intervention	Basic Oral Care Plan	Intensified Oral Care Plan	End of Life Oral Care Plan
Flossing	• Floss at least once daily. • Waxed floss may be easier to use and minimize trauma to the gingivae. • If flossing causes bleeding of the gums, which does not stop after 2 minutes, it should be discontinued. • Flossing may be restarted when the platelet count is > $20x10^9$cells/L or as instructed by cancer care team. • Patients who have not flossed routinely before cancer treatment should not begin flossing at this time. • Patients with mouth cancers may not be able to floss.	• Continue until discomfort becomes too great. • Discontinue flossing if gums bleed for longer than 2 minutes. • Advise patient to try to begin flossing again when platelet count rises >$20x10^9$cells/L.	• Discontinue flossing if patient chooses.
Brushing	• Use a small, ultra soft-headed, rounded-end, bristle toothbrush (an ultrasonic toothbrush such as sonicare, may be acceptable). • Use a prescription strength fluoride toothpaste (e.g., prevident, flouridex, XPur). Spit out the foam but do not rinse mouth. • Use remineralizing pastes (e.g., MIpaste, Oral Science) and chewing gum containing recaldent to replenish calcium and phosphate ions. • Brush within 30 minutes after eating and before bed. Ensure the gingival portion of the tooth and periodontal sulcus are included. • Rinse toothbrush in hot water to soften the brush before using. • Brush tongue gently from back to front. • Rinse brush after use in hot water and allow to air dry. • Change toothbrush when bristles are not standing up straight. • If gingival tissue bleeds for more than 2 minutes, brushing may be stopped and teeth cleaned with clean, moist gauze or foam swab (personal preference may guide practice). Once platelets are >$20x10^9$cells/L then brushing may be resumed. <u>Patients with Head & Neck Cancers</u> • Brushing may not be appropriate in the area of tumor involvement. • Patients should be assessed for the use of daily Fluoride tray. • Consult with a dentist. <u>Dentures</u> • Remove dentures, plates and prostheses before brushing. • Brush and rinse dentures after meals and at bedtime. • Remove from mouth for long periods (at least 8 hours per 24 hours) and soak in rinsing solution.	• Use ultra soft toothbrush or soften brush bristles under hot water. • Encourage patient to continue brushing through treatment phase even when it causes discomfort. • If unable to tolerate brushing, seek assistance from nursing or dental staff. • To remove debris and mucus consider using moist gauze or a foam swab soaked in rinsing solution. • Discontinue use of toothpaste if it is too astringent and dip toothbrush in bland rinse (1 teaspoon salt, 1 teaspoon baking soda in 4 cups of water). • If bleeding occurs, encourage gentler brushing. • If there has been an oral infection, use a new toothbrush after infection has resolved. <u>Dentures</u> • Keep dentures out of mouth as much as possible, especially if painful.	• Continue with basic and intensified mouth care plan. • Instead of moist gauze may use a warm, moist face-cloth, dipped in bland rinse to loosen thickened secretions and plaque.

Rinsing	• Rinsing the oral cavity vigorously helps maintain the moisture in the mouth, removes the remaining debris and toothpaste, and reduces the accumulation of plaque and infection. • Patients should rinse, swish and spit with a bland rinse (1 teaspoon salt, 1 teaspoon baking soda in 4 cups of water) several times after each brushing or flossing and as needed. • Club soda should be avoided, due to the presence of carbonic acids. • Commercial mouthwashes with hydroalcoholic base or astringent properties are not recommended for patients with oral complications. • Debriding should only be done if absolutely necessary, if tissue is loose causing gagging or choking. <u>Dentures</u> • After removing dentures rinse mouth thoroughly with rinse solution. • Brush and rinse dentures after meals and at bedtime. • Rinse with rinsing solution before placing in mouth. • Remove from mouth for long periods (at least 8 hours per 24 hours) and soak in rinsing solution.	• Perform in place of brushing if patient is absolutely unable to brush. • Seek dental care where possible for removing plaque. • In addition to rinsing after meals, encourage rinsing every 1-2 hours while awake and every 4 hours through the night if awake (to minimize complications of decreased saliva). • If unable to clean using toothette, gauze or swishing (or tilting head), syringe rinsing solution into different areas of mouth if platelet level is not too low.	• Continue with basic and intensified mouth care plan.
Moisturizing the Oral Cavity	• Moisturize the mouth with water or artificial saliva products (e.g., Moi-Stir Spray, Biotene products) or other water soluble lubricants for use inside the mouth. Mouth kote not recommended as pH is acidic, don't need to state that but is should be removed. • Avoid glycerin or lemon-glycerin swabs as they dry the mouth and do not moisturize. • Apply lubricant after each cleaning, at bedtime, and as needed. • Water-based lubricant needs to be applied more frequently. • Frequent rinsing as needed with basic mouth rinse.	• Continue with basic mouth care plan with increased frequency and intensity.	• Continue with basic mouth care plan with increased frequency and intensity, as needed. • May use a cool mist humidifier at night.
Lip Care	• To keep lips moist and to avoid chapping and cracking use water soluble lubricants, lanolin (wax-based), or oil based (mineral oil, coco butter) lubricants. • Water soluble lubricants should be used inside and outside the mouth, and may also be used with oxygen, e.g., products compounded with Glaxal base or Derma base (K-Y Jelly, Dermabase). • Apply lubricant after each cleaning, at bedtime, and as needed. • Water-based lubricants need to be applied more frequently. • Avoid oil based lubricants on the inside of the mouth. • Petroleum based products should be avoided. • Patients should be encouraged not to touch any lip lesions.	• Continue with basic mouth care plan with increased frequency and intensity.	• Continue with basic mouth care plan, with increased frequency and intensity, as needed.

1.2 General Oral Care: Pharmacological Interventions

Pharmacological interventions for general oral care include topical anesthetics before brushing to minimize pain and the use of a non-flavoured, non-alcoholic chlorhexidine gluconate rinse to aid in plaque control and decreasing oral streptococcus mutans scores (16). Other pharmacologic agents used in general oral care can be divided into analgesics and agents commonly used for management of excessive secretions. The following recommendations are based on additional resources (15) and the expert opinion of the Oral Care SMG.

Analgesics

- When continuous pain is present (example moderate to severe oral mucositis) an oral analgesic prescribed **regularly** may be considered to allow for more thorough tooth brushing. Consult specialists in pain and palliative care as needed. Refer to the Pain Guide-to-Practice for more information regarding opioid prescribing.
- When appropriate, oral opioid analgesics are preferably given 60 minutes before brushing.
- Topical anesthetics (e.g., viscous lidocaine 2% or viscous xylocaine 2%, 2-5 ml) may be applied 10 minutes before eating to provide enough comfort for the person to be able to eat or drink. An alternative would be to take an oral analgesic 1 hour prior to eating.
- For cognitively intact head and neck cancer patients receiving radiation therapy, 2 to 5 ml of viscous lidocaine 2% may be swallowed, up to a maximum of 6 times per day, to allow for adequate hydration, nutrition and oral care. This advisement would be at the discretion and recommendation of the patient's most responsible physician.
- If topical anesthetics are used only for rinsing of the oral cavity, without swallowing, then the recommended maximum dose of viscous lidocaine 2% is 60 ml per day.
- If patient is allergic to lidocaine, dyclonine 0.5 to 1% may be used (5 ml q6-8 hours, swish and swallow as needed for pain).

Medications for Excessive Secretions

- For individuals with excessive salivary secretions, tricyclic antidepressants (e.g., nortriptyline) are a consideration, starting at a low dose and titrating to effect.
- Another possibility is scopolamine transdermal 1.5 mg patch changed every 72 hours.
- As persons approach the end of life, decreased cognitive ability, extreme fatigue and weakness may contribute to the patient's inability to clear secretions from their nose, mouth or throat.
  - Anticholinergic medications are often useful for managing excessive secretions at end of life.
  - Atropine 1% ophthalmic solution administered sublingually 1-2 drops (1 drop ~0.5 mg) q4h prn
  - Ipratropium 0.03% Nasal Spray administered intranasally or sublingually, 2 sprays at bedtime.
  - Scopolamine 0.2 to 0.8 mg subcut q2-4h prn
  - Glycopyrrolate 0.2 to 0.6 mg subcut q2-4h prn
  - Buscopan (hyoscine butylbromide) 10 mg subcut q4h prn
  - Glycopyrrolate is less sedating than scopolamine
- Thickened secretions are best managed by increasing the frequency and intensity of moisturizing the oral cavity. It is also possible to use nebulized saline. It is important to review the patient's medications to identify those that may be contributing to this problem.

2. Oral Mucositis

2.1 Prevention of Oral Mucositis: Non-pharmacological Interventions

For patients at high risk of developing oral mucositis prevention is the most effective strategy.

- **There is some evidence for the use of ice chips for the prevention of oral mucositis (7).**

Ice Chips (for patients receiving bolus 5-fluorouracil (5-FU))

- Ice chips were found to be beneficial in the prevention of all outcome categories of mucositis (7).

CCNS *Modified*

- Patients receiving bolus 5-FU chemotherapy are instructed to swish ice chips in their mouth, if possible, starting 5 minutes prior to the bolus and for 30 minutes duration.
- Cold packs or frozen ice bags may be used alternatively to relieve 5-FU related side effects.
- These instructions are not practical for continuous infusions of 5-FU.
- Do NOT use ice chips for regimens containing both 5-FU and oxaliplatin as cold-induced dysesthesia from oxaliplatin is a common and preventable toxicity of this agent.

Ice Chips (for patients receiving melphalan)

MASCC/ ISOO *Modified*

- Patients receiving high-dose melphalan as part of a conditioning regimen for stem cell transplant should be treated with ice chips to prevent oral mucositis.

Intensity Modulated Radiation Therapy (IMRT)

MASCC/ ISOO *Modified*

- IMRT is currently the treatment of choice for head and neck patients. IMRT allows for the delivery of high-doses of radiation while sparing healthy tissues in close proximity.
- If IMRT is not available, three-dimensional radiation treatment to the oral cavity may be used.

Low Level Laser Therapy (LLLT)

ONS *Modified*

- There is some evidence that LLLT may reduce the incidence of oral mucositis and its associated pain in patients receiving high-dose chemotherapy or chemo-radiotherapy before Hematopoietic Stem Cell Transplant (HSCT).
- Laser therapy requires specialized equipment and training, which is not widely available.

Multivitamin

Oral Care SMG

- To prevent nutritional deficiencies a multivitamin may be considered for inclusion.

2.2 Prevention of Oral Mucositis: Pharmacological Interventions

CCNS *Modified*

- **A systematic approach to oral care should be followed to reduce the amount of microbial flora, reduce pain and bleeding, prevent infection and reduce the risk of dental complications.**

- **There is no evidence of benefit for the use of chlorhexidine for the prevention of oral mucositis when compared with placebo or no treatment (7).**

Human Keratinocyte Growth Factors (KGF)

- KGF (palifermin) was found to be beneficial for the prevention of all outcome categories of mucositis (ranging from mild to severe) (7).

CCNS
- In patients with hematological malignancies receiving high dose chemotherapy and total body radiation with stem cell transplant, KGF (palifermin) in a dose of 60 mcg/kg/day for 3 days prior to treatment and for 3 days post-transplant is recommended for the prevention of oral mucositis.

- KGF (palifermin) is not commonly used in Ontario due to high costs and limited availability.

ONS *Modified*
- Where available, it should be used for patients most likely to develop severe mucositis.
- The most common side effects of KGF (palifermin) include mild rash and taste changes.

2.3 Management of Oral Mucositis: Non-Pharmacological Interventions

Nutritional Care

General Nutritional Recommendations for Patients Experiencing Symptoms

CCNS *Modified*
- Individual tolerance may vary from patient to patient.
- Consult a dietitian for nutritional advice on managing individual oral care symptoms.

Mild and Moderate Oral Mucositis

CCNS *Modified*
- Choose texture as tolerated and modify as required.
- May need to start with soft, moist, smooth foods; if not tolerated try extra soft/pureed foods.
- Choose foods high in calories and protein, 6-8 small meals/snacks daily.
- Cook solid foods until tender, use moist sauces, choose soft, bland foods (13).
- Avoid foods that irritate the mouth or throat (13).

Oral Care SMG
- Avoid eating foods which are abrasive, rough, tart, salty, spicy, acidic, very hot or very cold.
- Oral commercial nutritional supplements may be necessary.
- There is insufficient evidence to support the use of vitamin B12, beta-carotene calcium, multivitamin, chamomile, glutamine, or curcumin in the treatment of oral mucositis (7,17,18).
- If oral intake is inadequate for a prolonged period consider using a regular strength multivitamin.

Severe Oral Mucositis

- Choose texture, as tolerated, and modify as required.

Oral Care SMG
- May need to start with extra soft/pureed diet.
- If only liquids are tolerated, choose high calorie, high protein fluids every 2 hours.
- Oral commercial nutrition supplements are recommended.
- A liquid regular strength multivitamin may be recommended.
- Severe oral mucositis during cancer treatment (grade 3 or 4) may be managed with an appropriately placed feeding tube or total parenteral nutrition (TPN) depending on the patient's goals of care (19).
- The type of tube (i.e., gastrostomy or jejunostomy) and the method of placement (i.e., surgical or radiological) should be determined by the degree and extent of mucositis and the potential worsening of symptom due to planned cancer treatment (19).
- Consult dietitian if possible.

For specific food and recipe suggestions refer to the BCCA's "Food ideas to try with a sore mouth", the Canadian Cancer Society's "Eating Well When You Have Cancer" booklet or the Princess Margaret Hospital's "Goes Down Easy" cookbook.

2.4 Management of Oral Mucositis: Pharmacological Interventions

Opioids

- **Systemic analgesia with morphine (or other strong opioid) is the recommended treatment of choice for oral mucositis pain in patients undergoing HSCT (6).**

Systemic Analgesia with Opioids

- Regular oral pain assessment using validated self-reporting instruments is essential (6).
- There is some evidence of benefit for the use of patient-controlled analgesia (PCA) with opioids for oral mucositis pain in patients undergoing HSCT (6).
- There is no evidence to suggest that there is a difference in pain control between continuous morphine infusion and PCA. However, the PCA group required less morphine than the continuous infusion group and the pain lasted for 2 days less (8).
- For pain management, please refer to Pharmacological Interventions under General Oral Care, for additional information on opioids please refer to the Pain Guide-to-Practice .

Other Agents

Table 6 lists agents with insufficient evidence due to lack of clinical trials, inadequate sample size or methodological flaws. Until additional high quality trials become available it is difficult to make recommendations for, or against, the use of these interventions.

Table 6. Agents Which Have **Insufficient Evidence** for Prevention or Treatment of Mucositis

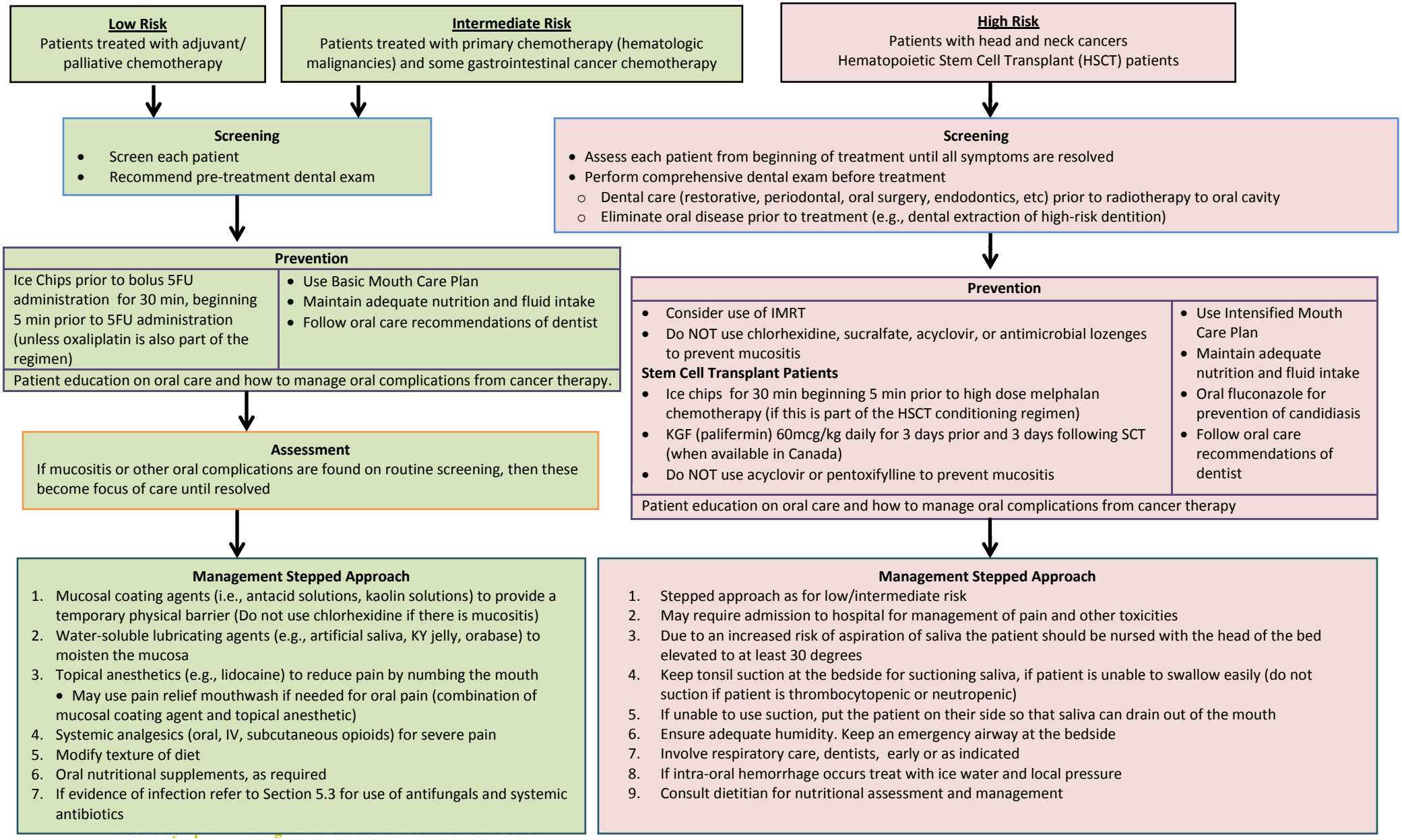
Intervention	Insufficient Evidence Prevention	Insufficient Evidence Treatment
Aloe Vera	☑ (7)	
Allopurinol, Vitamin E	☑ (7)	☑ (1,8).
Amifostine (Not available for treatment in Canada).	☑ (7)	☑ (2)
Antimicrobial Lozenges	☑ (2,7)	
Anti-inflammatory Rinses	☑ (2,7)	☑ (1)
Benzydamine	☑ (7)	☑ (8)
Filgrastim	☑ (1,7)	
Flurbiprofen	☑ (2)	
Glutamine (Systemic)	☑ (7)	☑ (2)
Glutamine (topical or oral suspension)	☑ (7)	
Granulocyte–macrophage-colony stimulating factor (GM-CSF) Mouthwash	☑ (6,7)	☑ (1,2,8)
Histamine Gel	☑ (7)	
Honey	☑ (7)	
Hydrolytic enzymes	☑ (7)	
Multiagent ("Magic" or "Miracle") Rinses		☑ (2,8)
N-acetylcysteine (oral rinse)	☑ (1)	
Sucralfate	☑ (2,7)	☑ (8)
Systemic Anti-inflammatory	☑ (7)	
Pentoxifylline	☑ (7)	
Pilocarpine	☑ (7)	
Povidone-iodine (oral rinse)	☑ (2,7)	
Zinc Sulphate		☑ (7)

CCNS *Modified*

When patients develop oral mucositis, they require appropriate therapeutic intervention to manage symptoms and prevent symptom progression. Once mucositis has developed, its severity and the degree of myelosuppression govern appropriate oral management. It is suggested to use the "stepped" approach (Figure 1) for mucositis management, adding agents as symptoms present.

Cancer Care Ontario
Action Cancer Ontario

Figure 1. Prevention and management of oral mucositis based on patient risk stratification. *(adapted from CCNS).*



3. Xerostomia

3.1 Prevention of Xerostomia: Non-Pharmacological Interventions

- **The use of parotid sparing IMRT is recommended for prevention of salivary gland hypofunction and xerostomia in head and neck cancer patients (9).**

Intensity Modulated Radiation Therapy (IMRT)

- IMRT can reduce the dose to parotid, submandibular/sublingual, and minor salivary glands while helping maintain adequate whole saliva flow rates and reducing xerostomia (9, 20).

3.2 Management of Xerostomia: Non-Pharmacological Interventions

Nutritional Care

The following section offers recommendations based on additional resources (21-24) and the expert opinion of the Oral Care SMG:

- Add extra moisture to foods, increase fluid consumption.
- Oral rinses may improve swallowing and taste problems.
- Soft, mild tasting food is often better tolerated.
- Moisten food by adding sauces, gravy, butter, dressings, broth or another liquid.
- Food and drinks should be cold or tepid.
- Plain ice cubes, sugar-free popsicles, sugar-free gum, frequent sips of cold water, or mouth sprays may increase fluid consumption and help to cool and moisten the mouth.
- Any foods, fluids and other items which may further dry or irritate mouth and teeth should be avoided including highly acidic foods and fluids, foods high in sugar, caffeine and alcohol.
- To stimulate residual salivary secretion and to ameliorate the condition of the mucosa, regular use of fresh, lightly acidic fruits, slices of cold cucumber and tomato or thin slices of cold apples are recommended as long as patient is not experiencing mucositis.
- The use of milk, jello, sherbet, applesauce and ice cream is also suggested.

Other modalities

Acupuncture

- Acupuncture treatment is a possible intervention for the treatment of radiation-induced xerostomia in patients with a residual functional capacity of the salivary glands and is a treatment modality without serious adverse effects (9).

Artificial saliva

CCNS
- Artificial saliva products may also be considered for a brief course to determine effectiveness and patient acceptability, followed by continuing therapy when warranted.

Table 7 offers a brief overview of agents with insufficient evidence due to lack of clinical trials, inadequate sample size or methodological flaws. Until additional high quality trials become available it is difficult to make recommendations for, or against, the use of these interventions in the treatment of xerostomia.

Table 7. Non-pharmacological Interventions with **Insufficient Evidence** for the Management of Xerostomia.

Gustatory and masticatory stimulation	• Sugar-free lozenges, acidic candies, or chewing gum may potentially produce transitory relief from xerostomia by stimulating residual capacity of salivary gland tissue (9). • However this has been sparsely addressed within the field of salivary gland hypofunction and xerostomia as sequelae of cancer therapies (9).
Surgical transfer of submandibular gland	• Early results suggest that surgical transfer of one submandibular gland to the submental space potentially may be of relevance to preserve salivary gland function and reduce xerostomia in strictly selected oropharyngeal and hypopharyngeal cancer patients to be irradiated (9). • The obtained level of sparing by submandibular salivary gland transfer might be of clinical significance (9).
Hyperbaric oxygen treatment	• There is insufficient data available to make a recommendation regarding hyperbaric oxygen treatment (9).

3.3 Management of Xerostomia: Pharmacological Interventions

Pilocarpine (During Radiotherapy)

- The use of oral pilocarpine during radiotherapy in head and neck cancer patients for improvement of xerostomia cannot be recommended as results of various randomized clinical trials were not unequivocal. The improvement of salivary gland hypofunction was shown to be limited (9).
- The dissimilar results on sparing of salivary gland function are thought to be highly dependent on the wide range of cumulative doses applied (9).

- **Oral pilocarpine (sialogogue) <u>following</u> radiation therapy is recommended in head and neck cancer patients for improvement of xerostomia (9).**
- **Results for the use of pilocarpine HCl concomitantly with radiation therapy to reduce xerostomia and salivary gland hypofunction are inconsistent, however in some patients a beneficial effect has been shown on xerostomia (9).**

Pilocarpine (Following Radiotherapy)

- Administration of pilocarpine HCl following radiation therapy has shown reduced prevalence of xerostomia and improved salivary gland function to some extent. However, the effect is temporary and of relatively short duration, thus treatment needs to be lifelong (9).
- Pilocarpine is generally well tolerated but may induce mild to moderate systemic anticholinergic adverse effects. Patients with cardiovascular and pulmonary diseases should be monitored (9).
- The dosage of pilocarpine HCl tablets varies in dose titration studies, ranging from 5 mg single dose up to 30 mg daily. However, a fixed dose of 5 mg three times daily was mostly used (9).
- Pilocarpine is available as tablets, and in Canada the ocular formulation (1%, 2%, and 4% solutions) is available for off label use.

Amifostine

- No consensus could be reached regarding a recommendation as most clinical studies do not have the statistical power to evaluate the influence of amifostine on the therapeutic index (9).

4. Dysgeusia

4.1 Prevention of Dysgeusia: Non-Pharmacological Interventions

Other modalities

Radiation Therapy (not including the tip of tongue)

- One randomized controlled trail containing 118 patients with head and neck cancer, treated with radiotherapy +/− chemotherapy, reported no patients' complaints of dysgeusia when the tongue tip was excluded from the radiotherapy field. By contrast, for patients who had the tip of the tongue included in the radiation treatment field, there were marked increases in mean threshold values to the four taste qualities being tested (salt, sweet, sour, and bitter) (11).

4.2 Prevention of Dysgeusia: Pharmacological Interventions

- **Zinc gluconate is not recommended for the prevention of dysgeusia in head and neck cancer patients (11).**

Zinc gluconate

- Studies that specifically examined prevention and/or management strategies for dysgeusia using zinc provided variable results (11).
- The specific role of zinc in relation to taste perception is unknown, but it is a recognized cofactor of alkaline phosphatase, which is the most abundant enzyme within the taste bud membrane (11).
- In addition, zinc may play a role in the conformation of proteins involved in regulation of the pores of taste bud microvilli (11).

Amifostine

- **Amifostine is not recommended solely for the prevention of dysgeusia in head and neck cancer patients (11).**

- The two studies that looked at the use of amifostine in preventing dysgeusia showed that while amifostine reduced the incidence and severity of acute and late toxicities in general, the effects of amifostine on dysgeusia specifically were not as impressive (11).
- Amifostine is a thiol compound which protects normal organs and tissues from oxidative damages induced by cancer therapy by the scavenging of free radicals produced by either chemotherapy or radiotherapy (11).

4.3 Management of Dysgeusia: Non-Pharmacological Interventions

Nutritional Care

The following section offers recommendations based on additional resources (11, 25-27) and the expert opinion of the Oral Care SMG.

- As taste changes are unique to each person and can vary over time, an individualized approach needs to be taken to identify tolerable foods. Ongoing follow up is recommended.
- To prevent compromised food intake, patients may need encouragement and support to try foods again that may have resulted in food aversions secondary to taste changes.

- Encourage patients to:
  - Enjoy foods that taste good.
  - Experiment with food flavours to enhance taste.
  - Drink plenty of fluids.
  - Avoid strong smells.
- Nutritional counseling is recommended.
- Refer to BCCA's "Food ideas to cope with taste and smell changes" for additional information.

5. Intra-Oral Infections

Intra-oral infections can be classified as fungal, bacterial and viral.

5.1 Prevention of Intra-Oral Infections: Non-Pharmacological Interventions

Oral Care SMG

- **The best prevention for any intra-oral infections is non-pharmacological in nature.**
- **It is necessary to follow meticulous oral care plans as discussed previously.**

5.2 Prevention of Intra-Oral Infections: Pharmacological Interventions

No recommendations were found in the literature for the pharmacological prevention of intra-oral bacterial or viral infections. However the following recommendations were found for the pharmacological prevention of intra-oral fungal infections.

- **Fluconazole is found to be very effective in the prevention of clinical oral fungal infections and in reducing oral fungal colonization in patients receiving cancer therapy (10).**

CCNS

- Prophylactic fluconazole 100 mg po daily (400 mg po daily for HSCT patients) may be considered for prevention of oral candidiasis in cancer patients.
- Other systemic agents such as the lipid formulations of amphotericin B, and the echinocandins (caspofungin, anidulafungin, and micafungin) as prophylaxis agents in certain oncology settings (e.g., patients receiving head and neck radiation therapy over 6−7 weeks) can be problematic. The emergence of resistant species is one important concern with such prophylactic use (10).

5.3 Management of Intra-Oral Infections: Pharmacological Interventions

Fungal infections

Considering the high prevalence of clinical oral fungal infection in patients receiving cancer therapy, identification of more effective topical antifungal agents to avoid the potential side effects of systemic agents would be beneficial.

- **In general, topical agents are considered preferable to systemic agents for the management of mild intra-oral fungal infection due to the lower risk of side effects and drug interactions (e.g., sugarless nystatin rinse) (10).**
- **If topical agents are not well tolerated or the response rate is poor, then it is advised to proceed with the use of systemic agents.**

Topical Agents

- Clotrimazole lozenges or sugarless nystatin suspension may be used as first-line therapy for the management of mild oropharyngeal candidiasis. However, the available studies present an inconsistent picture of the efficacy of topical agents in patients receiving cancer therapy (10).
- Sugarless nystatin suspension 100,000 units/ml may be used as follows:
  - Swish around and hold in the mouth for at least one minute, then swallow; use 5 ml qid 4 times daily for 7-14 days (works by direct contact).

CCNS ***Modified***

- Soak dentures overnight in sugarless nystatin 100,000 units/ml solution or use sugarless nystatin 100,000 units/ml cream to treat dentures.
- Use sugarless nystatin popsicles (for cooling relief).
- Clotrimazole oral suspension (1mg/ml) may be used as follows:
  - Swish around mouth for 1 minute and then swallow; use 10 ml qid 4 times daily for 7-14 days.

Systemic Agents

- The use of systemic fluconazole as first-line therapy may be used for the management of moderate to severe oropharyngeal candidiasiss (10).
- Fluconazole 100 mg daily is equal or more effective against oropharyngeal candidiasis in cancer patients than nystatin or clotrimazole (10).
- To prevent relapse after initial treatment, maintenance therapy using fluconazole 50 mg (up to 400 mg) daily may be considered (10).
- For fluconazole refractory disease, itraconazole or posaconazole are recommended, with voriconazole and amphotericin B reserved for refractory cases (10).
- Patients who cannot tolerate fluconazole (or other antifungals) may use sugarless nystatin suspension. Additional systemic agents include the lipid formulations of amphotericin B, and the echinocandins (caspofungin, anidulafungin, and micafungin) (10).
- Use of these systemic agents may be limited by their side effects, especially for amphotericin B.
- These agents are optimally used for short durations of treatment.

Bacterial Infections

For management of periodontal and odontogenic infections, the following is recommended:

Oral Care SMG

- First line: amoxicillin 500 mg po q8h for 7-10 days
- Alternative: penicillin V 300-600 mg po q6h for 7-10 days
- Alternative: clindamycin 300-450 mg po q6h for 7-10 days
- Amoxicillin/ clavulanic acid (Clavulin®): 500 mg tablet (contains amoxicillin 500 mg and clavulanic acid 125 mg) po q8h OR the 875 mg tablet (contains amoxicillin 875 mg and clavulanic acid 125 mg) po q12h for 7-10 days
- If one is certain that the infection is periodontal in origin then the recommendation for first line therapy is metronidazole 500 mg po q8h for 7-10 days.

Viral infections

Herpes simplex

CCNS *Modified*

- Topical acyclovir (ointment/cream): Apply to affected area q3-4h, for a total of 6 times/day for 7 days (apply a sufficient quantity to adequately cover all lesions use a finger cot or rubber glove to avoid transmission to other parts of the body).
- Systemic acyclovir for larger lesions:
  - Primary HSV: Acyclovir 200 mg po q4h, 5 times/day for 10 days or 400 mg po tid (3 times daily for 7-10 days (in immunocompromised patients, consider 400 mg po q4h, 5 times/day for 10 days).
  - Recurrent HSV: Acyclovir 200 mg po q4h, 5 times/day for 5 days
- Valacyclovir 500 mg po bid (twice daily) or q12h for 3 days.

Varicella-zoster

- Acyclovir 400 mg po 5 times/day for 7-10 days.

CCNS *Modified*

- For severe infection, acyclovir 5 mg (base) per kg body weight IV q8h for 5-7 days (administer over at least 1 hour).
- For immunocompetent: Acylcovir oral 800 mg every 4 hours (5 times daily) for 7 -10 days ; IV acyclovir 10mg/kg/dose every 8 hours for 7 days.
- Patients with acute or chronic renal impairment may require dose reduction (e.g., acyclovir 200 mg po q12 hours when CrCl is 0-10 ml/min).
- Valacyclovir 1000 mg po tid for 7 days (superior to acyclovir for post-herpetic infections). Adjust for renal dysfunction.

Cytomegalovirus

- Ganciclovir: *induction:* 5mg/kg IV over 1 hour q12h, *maintenance:* 5 mg/kg IV over one hour once per day (28).
- Dose reductions are recommended for renal impairment.
- Ganciclovir should not be administered in patients with severe neutropenia (ANC less than 500/μL) or severe thrombocytopenia (platelets less than 25,000/μL) or severe anemia (hemoglobin less than 80 g/L) (28).

Appendices

Appendix A: Methodology

The Standards, Guidelines and Indicators Sub-group of the Re-Balance Focus Action Group, established under the Canadian Cancer Control Strategy, performed a literature review and environmental scan.[i] This review was used by the SMG as a source from which to identify existing guidelines relative to the symptoms of interest. Additionally, SMG members reached out to regional cancer programs in Ontario, searched the Cancer Care Ontario Program in Evidence-based Care website and their own personal sources for any relevant guidelines.

The Re-Balanced Focus Action Group used the following search criteria in their review:

Inclusion Criteria

1. Standards focused on care delivered by cancer organizations; and/or processes of care; and/or professional practice standards specific to cancer.
2. Guidelines focused on clinical practice of practitioners relevant to psychosocial, supportive or palliative care provision to cancer patient populations.
3. Guidelines that were more generic in focus but relevant to supportive care aspects of cancer populations in areas such as prevention and screening were also included.

Exclusion Criteria

1. Guidelines that did not base the development of substantive statements/recommendations on a review of evidence from the literature and/or were not based on a source that used evidence to support the guideline development process.
2. Guidelines that were focused on providing direction to patients and families for which it was not clear that the guideline statements or recommendations were based on a review of evidence from the literature and/or were not based on a source that used evidence to support the guideline development process.

Databases Searched

Health Sciences literature databases used in this scan include HealthStar, Medline, CINAHL, Embase and PsycINFO. The internet search engine Google Scholar was utilized for the grey literature search for scientific and non-scientific sources. Databases for the following organizations were also reviewed:

a) All oncology professional associations and organizations for psychosocial oncology and palliative care inclusive of oncology social workers, clinical oncology;
b) All Canadian provincial cancer care organizations;
c) International organizations or agencies or associations whose mandate is focused on systematic reviews or guideline development.

The literature search and environmental scan was updated in December 2008, 2009 and again in 2011.

[i] Re-Balance Focus Action Group. Literature Review and Environmental Scan: Psychosocial, Supportive and Palliative Care Standards and Guidelines. Updated 2009.

Results

Based on the literature review and environmental scan described above, the Oral Care SMG identified seventeen oral care related guidelines for inclusion in this Guide-to-Practice. Eleven guidelines (29-39) were rejected at the onset by the group because they fell outside of the scope of this Guide-to-Practice. The remaining six guidelines (1-6) were screened and assessed for quality, currency, content, consistency, and acceptability/applicability, using the Appraisal of Guidelines Research and Evaluation (AGREE) instrument (www.agreetrust.com). Taking into consideration the AGREE scores and expert consensus, the working groups chose the most applicable and relevant guidelines to be included in the Guide-to-Practice (Table 8).

Table 8. AGREE Scores

AGREE Scores	CCNS	ONS	BCCA*	HealthPartners Dental	MASCC/ ISOO
Scope & Purpose	87%	81%	89%	76%	65%
Stakeholder Involvement	72%	76%	61%	48%	65%
Rigour of Development	84%	76%	61%	26%	74%
Clarity & Presentation	96%	85%	93%	65%	89%
Acceptability	56%	67%	42%	24%	65%
Editorial Independence	92%	81%	100%	17%	92%
Overall Quality Assessment	Recommend with Provisos.	Recommend with Provisos.	Recommend with Provisos.	Recommend with Provisos.	Recommend with Provisos

**scores were identical for the xerostomia and oral mucositis BCCA guidelines; hence they are combined in the table.*

The ADAPTE II process (http://www.adapte.org/) was then used to systematically endorse or modify applicable components of the six guidelines (1-6). The guideline development process, utilizing ADAPTE, proceeds under the assumption that the original recommendations are reasonable and supported by the evidence. Confidence in this assumption is fostered by satisfactory AGREE scores. In situations where evidence was not available or not applicable to specific clinical situations, systems and contexts recommendations were modified based on the expert consensus of the working group. It is beyond the scope of the Guide-to-Practice development process and this document to make the connection between the recommendations and the original key evidence. For those who wish to do so, please refer to the CCNS (1), ONS (2), BCCA (3,4), HealthPartners Dental (5) and MASCC/ISOO (6) documents.

Appendix B: Peer Review Summary

Expert feedback was obtained through an internal and external review.

Internal Review

The internal review consisted of an anonymous appraisal of the Guides by members from each of the three working groups (Oral Care, Bowel Care and Loss of Appetite). The intent of this review was to ensure that the Guide development process was methodologically rigorous; the recommendations are supported by the evidence in a transparent way; and that the Guides are clinically relevant and applicable to practice. A total of 39 online surveys were collected during the internal review. Ten participants completed the Oral Care Guide-to-Practice survey (Table 9). The survey feedback was thoroughly reviewed by each of the corresponding working groups and, where appropriate, changes were made to the Guides.

Table 9. Responses to 16 key questions on the Oral Care Internal Review survey (10 respondents)

Question	**Strongly Agree** (Response count)	**Agree** (Response count)	**Disagree** (Response count)	**Strongly Disagree** (Response count)
The methodology used to search for evidence is clearly described.	60% (6)	40 % (4)	0%	0%
The methods for formulating the recommendations are clearly described.	50% (5)	40% (4)	10% (1)	0%
The symptom definition(s) are clear and comprehensive.	40% (4)	60% (6)	0%	0%
There is an explicit link between the supporting evidence and the recommendations.	30% (3)	70% (7)	0%	0%
Recommendations based on SMG expert consensus are clearly identified.	30% (3)	70% (7)	0%	0%
The source from which the recommendations are extracted is clearly identified.	40% (4)	60% (6)	0%	0%
The recommendations are in agreement with my understanding of the evidence.	30% (3)	70% (7)	0%	0%
The recommendations are specific and unambiguous.	40% (4)	60% (6)	0%	0%
The recommendations are easily identifiable.	50% (5)	50% (5)	0%	
The recommendations are achievable.	30% (3)	60% (6)	10% (1)	0%
The different options for management of the condition are clearly presented.	30% (3)	70% (7)	0%	0%
The Guide-to-Practice is supported with tools for application.	20% (2)	80% (8)	0%	0%
The Guide-to-Practice is user friendly.	20% (2)	50% (5)	30% (3)	0%
The working group includes individuals from all the relevant professions.	20% (2)	70% (7)	10% (1)	0%

Question	**Very Likely** (Response count)	**Not Very Likely** (Response count)	**Not Applicable** (Response count)
How likely would you be able to apply these recommendations to the clinical care decisions for which you are professionally responsible?	90% (11)	0%	10% (1)

Question	**Differ greatly** (Response count)	**Differ slightly** (Response count)	**In Line** (Response count)	**Not Applicable** (Response count)
How do the recommendations compare to your current clinical practice?	0%	40% (4)	50% (5)	10% (1)

External Review

The external review process consisted of I) a Targeted Peer Review, intended to obtain direct feedback on the draft guides from a small number of specified content experts and II) a Professional Consultation, that intended to disseminate the draft guide as widely as possible to its intended readership, provide a forum for recipients to explain any disagreement with the recommendations, and to further ensure the quality and relevance of the document.

Targeted Review

Twenty-two reviewers were invited to participate in the external target review for the Oral Care Guide-to-Practice. Seven respondents provided survey responses (Table 10 and 11), while two submitted general comments via email.

Table 10. Overview of the Oral Care targeted peer reviewers

Guide	Sample	Results
Oral Care	**Reviewers:** 3 Physicians 2 Radiation Oncologists 2 Medical Oncologists 1 Surgeon 4 Dentists 2 Nurses 2 Dietitians 2 Pharmacists 2 Advance Practice Radiation Therapists 2 Research Methodologists	**Responses:** 1 Physicians 1 Radiation Oncologists 1 Medical Oncologists 2 Dentists 2 Nurses 1 Dietitians 1 Research Methodologists

Table 11. Responses to key questions on the Oral Care target peer review survey (7 respondents)

Question	1 **Lowest Quality** % (Response count)	2 % (Response count)	3 % (Response count)	4 % (Response count)	5 **Highest Quality** % (Response count)
Rate the Guide-to-Practice development methods.	0%	14.3% (1)	0%	57.1% (4)	28.6% (2)
Rate the Guide-to-Practice presentation.	0%	14.3% (1)	14.3% (1)	28.6% (2)	42.9% (3)
Rate the Guide-to-Practice recommendations.	0%	0%	14.3% (1)	57.1% (4)	28.6% (2)
Rate the completeness of the reporting.	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)
Does this document provide sufficient information to inform your decisions?	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)
Rate the overall quality of the Guide-to-practice.	0% (0)	14.3% (1)	0% (0)	42.9% (3)	42.9% (3)
Question	**1 Strongly Disagree** % (Response count)	**2** % (Response count)	**3** % (Response count)	**4** % (Response count)	**5 Strongly Agree** % (Response count)
I would make use of this Guide-to-Practice in my professional decisions.	14.3% (1)	0% (0)	0% (0)	42.9% (3)	42.9% (3)
I would recommend this Guide-to-Practice for use in practice.	14.3% (1)	0% (0)	14.3% (1)	14.3% (1)	57.1% (4)

Professional Consultation

The Professional Consultation consisted of a sample of approximately 1000 health care practitioners*, including palliative care physicians, family physicians, radiation oncologists, medical oncologists, surgeons, dental oncologists, nurses, pharmacists, dietitians, radiation therapists, physiotherapists and administrators. Participants were contacted by email and asked to read the guides and complete a brief corresponding electronic survey. One hundred and nineteen responses were received for all three guides. Thirty-four respondents reviewed the Oral Care Guide (Table 12 and 13)

* Participant were encouraged to forward the electronic survey to interested colleagues, hence the total sample size is only an estimate.

Table 12. Overview of the Professional Consultation Sample

Profession	Count
Family Physician	9
Nurse	11
Medical Oncologist	5
Dietitian	3
Radiation Therapist	2
Dentist	1
Physiotherapist	1
Administrator	1
Oral Medicine/oncology	1
Total:	**34**

Table 13. Responses to key questions on the Professional Consultation survey (34 respondents)

Question	**1 Strongly Disagree** % (Response count)	**2** Percent (Response count)	**3** Percent (Response count)	**4** Percent (Response count)	**5 Strongly Agree** % (Response count)
I would make use of this Guide-to-Practice in my professional decisions.	0%	11.8% (4)	14.7% (5)	26.5% (9)	47.1% (16)
I would recommend this Guide-to-Practice for use in practice.	0%	2.9% (1)	11.8% (4)	29.4% (10)	55.9% (19)
Question	**1 Lowest Quality** % (Response count)	**2** Percent (Response count)	**3** Percent (Response count)	**4** Percent (Response count)	**5 Highest Quality** % (Response count)
Rate the overall quality of the Guide-to-Practice.	0%	0%	8.8% (3)	35.3% (12)	55.9% (19)

Appendix C: Assessment Scales

1) The Kayser-Jones Brief Oral Health Status Examination (BOHSE)
Link: http://www.annalsoflongtermcare.com/pdfs/altc1008TryThis_NoCrops.pdf

2) Radiation Therapy Oncology Group (RTOG) Mucositis Rating (40)

0	1	2	3	4
None	Erythema of the muscosa	Patchy reaction <1.5 cm, noncontiguous	Confluent reaction >1.5 cm, contiguous	Necrosis or deep ulceration, ± bleeding

3) World Health Organization (WHO) Assessment Scale for Oral Mucositis (41)

0	1	2	3	4
None	Soreness ± erythema	Erythema, ulcers and patient can swallow solid food	Ulcers with extensive erythema and patient cannon swallow solid food	Mucositis to the extent that alimentation is not possible

Appendix D: Presentation of Oral Infections

Table 14. Presentation of Oral Infections *(adapted from CCNS (1) and MASCC/ISOO (6)).*

Oral Infection	Appearance and Characteristics
Fungal Infections	Oral candidiasis accounts for vast majority of oral fungal infections, which have a number of clinical presentations: **Pseudomembranous candidiasis (thrush)** • Presents as white curd-like pseudomembranes, which can be removed with some pressure, leaving behind an erythematous mucosa. **Erythematous candidiasis** • Presents as intensely red inflamed areas of the oral mucosa, often under a denture or following antibiotic therapy. **Angular cheilitis** • Presents as erythema, fissuring, and crusting of the commissures (angles) of the lips. • Chronic hyperplastic candidiasis: presents as a hyperkeratotic white patch, with or without hyperplasia of epithelial tissue, which cannot be removed by scraping.
Bacterial Infection	• **Periodontitis or gingivitis** usually appears as reddened, boggy gums which bleed easily on probing. • **Acute periodontal abscess** may cause intraoral swelling or mucopurulent drainage. • **Dental caries** can be initiated or exacerbated in the presence of salivary hypofunction that leads to enamel demineralization, cavitation and ultimately tooth loss. The altered bacterial and fungal flora can potentiate a more aggressive form of dental decay. • **Odontogenic infections** in acute stage can be associated with intraoral or facial swelling and mucopurulent drainage. • **Pre-existing dental disease**. When the nerves inside teeth lose their vitality due to dental decay or periodontal disease, it may remain quiescent and asymptomatic. In the presence of immunosuppresion and myelosuppression these teeth may activate from a chronic to acute infection. When the natural flora is affected by cancer therapy, some of the bacteria may proliferate and invade the gastrointestinal, cardiovascular, renal, or respiratory systems, resulting in systemic infections (such as bacterial endocarditis or glomerulonephritis). Local infections in the oral cavity may provide foci for systemic infection.
Viral Infection	**Herpes Simplex** • A prodrome of pain, burning, or itching. Symptomatic primary infection, with multiple, small, clustered vesicles in numerous locations, can occur anywhere in the oral cavity, on the perioral skin, on the lips, or on the pharynx, and can be extremely painful. • Vesicles often break quickly, so the lesions may appear as small clustered ulcers. Recurrent herpes lesions (or cold sores) occur on keratinized mucosa (usually the lips, attached gingiva, and/or the hard palate) and are commonly unilateral in appearance; atypical sites and patterns may occur in immunsuppressed /myelosuppressed patients. **Varicella-Zoster** • A prodrome of pain, burning, or itching that mimics a toothache may occur. Recurrent varicella (also known as herpes zoster or shingles) results in a vesicular rash that usually affects a single dermatome. Inside the oral cavity, this may be observed as vesicles or ulcerations that stop sharply at the midline. • After the resolution of the rash, postherpetic neuralgia may linger for a month or longer, especially in patients who are immunosuppressed. **Cytomegalovirus** • Cytomegalovirus infection may cause esophagitis, which is occasionally accompanied by oral ulcerations or erythema. Oral ulcerations are clinically nonspecific; a biopsy is required for definitive diagnosis.

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Post-amble

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A wide variety of health professionals were invited to participate in the development of this Guide-to-Practice, input from professions not represented on the working group was sought out during the external review. Every effort was made to ensure representation from relevant professions.

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