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Oral Complications of Systemic Therapies: A Narrative Review of Interdisciplinary Prevention and Management

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Abstract

Background: Systemic cancer therapies, including chemotherapy, targeted agents, and immunotherapies, frequently induce oral complications that significantly impair patients' quality of life, nutritional status, and treatment adherence. These complications range from oral mucositis and xerostomia to immune-related oral adverse events, requiring coordinated interdisciplinary management. **Aim:** This narrative review synthesizes current evidence on the prevention, assessment, and management of oral complications associated with systemic cancer therapies, with emphasis on interdisciplinary collaboration among oncology nurses, dentists, pharmacists, and laboratory professionals. **Methods:** A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science for peer-reviewed articles published between 2010 and 2024, focusing on oral complications, assessment tools, preventive strategies, and interprofessional interventions. **Results:** Evidence demonstrates that professional oral health care and patient education programs significantly reduce oral mucositis incidence and severity. Dental pre-treatment optimization, particularly allowing ≥2 weeks healing time for extractions, reduces osteoradionecrosis risk. Immune checkpoint inhibitors are associated with distinct oral toxicities, including xerostomia (5% prevalence), mucositis (3%), and dysgeusia (3%). Laboratory biomarkers, including single-nucleotide polymorphisms in XRCC1 and inflammatory cytokines, show promise for predicting mucositis risk. Pharmacist-led medication management and nursing assessment tools are essential for early detection and intervention. **Conclusion:** Effective management of oral complications requires integrated interdisciplinary approaches, standardized assessment protocols, and personalized preventive strategies. Future research should focus on validating predictive biomarkers and optimizing interprofessional care models.

Keywords: oral mucositis, immunotherapy-related oral complications, targeted therapy adverse effects, dental oncology, interdisciplinary care

Introduction

Cancer remains a leading cause of mortality worldwide, with systemic therapies playing an increasingly central role in treatment paradigms. Chemotherapy, targeted agents, and immunotherapies have dramatically improved survival outcomes but are frequently accompanied by debilitating oral complications that profoundly impact patients' quality of life, nutritional status, and treatment adherence (Elad et al., 2022). The oral cavity, with its rapid epithelial cell turnover and diverse microbiome, is particularly vulnerable to the toxic effects of antineoplastic agents, making oral complications among the most common and distressing adverse effects reported by patients undergoing cancer treatment (Lalla et al., 2014).

The significance of oral complications extends beyond symptomatic discomfort. Severe oral mucositis affects approximately 80% of patients receiving radiotherapy for head and neck cancer, and 34% of those undergoing conventional radiotherapy develop severe (grades 3-4) mucositis (Thornton et al., 2022). These complications can necessitate treatment interruptions, dose reductions, or discontinuation of potentially curative therapy, directly impacting oncological outcomes (Sonis, 2021). Moreover, oral complications increase healthcare utilization, with prolonged hospitalizations, increased analgesic

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requirements, and greater need for nutritional support (Berger et al., 2018).

The landscape of cancer therapy has evolved substantially over the past decade, with immune checkpoint inhibitors (ICIs) and targeted therapies joining traditional cytotoxic chemotherapy as standard treatments across numerous malignancies. These newer agents are associated with distinct oral toxicity profiles that differ from those of conventional chemotherapy. Immune-related oral adverse events (irOAEs), including lichenoid reactions, bullous pemphigoid, and severe xerostomia, have been increasingly recognized, yet their prevalence and management remain inadequately characterized (Srivastava et al., 2024). Similarly, targeted therapies such as mTOR inhibitors and tyrosine kinase inhibitors produce unique oral manifestations requiring specialized management approaches (de Bataille et al., 2021).

Effective prevention and management of oral complications necessitate coordinated interdisciplinary collaboration. The complexity of modern cancer care means that no single professional group possesses all the expertise required to address the multifaceted challenges posed by oral toxicities. Dentists bring expertise in pre-treatment oral optimization and management of dental complications; nurses provide frontline assessment, patient education, and daily supportive care; pharmacists contribute medication management expertise, including analgesic optimization and antimicrobial stewardship; and laboratory professionals enable biomarker-driven risk stratification and monitoring (Epstein et al., 2012).

This narrative review aims to synthesize current evidence regarding oral complications of systemic cancer therapies, with particular emphasis on the distinct toxicity profiles of novel agents, evidence-based preventive strategies, and the essential roles of different healthcare professionals in interdisciplinary management. By integrating findings from recent systematic reviews, meta-analyses, and clinical studies, we provide a comprehensive overview that can inform clinical practice and guide future research directions.

Oral Complications of Novel Cancer Therapies

Immune Checkpoint Inhibitor-Associated Oral Toxicities

Immune checkpoint inhibitors have revolutionized cancer treatment by harnessing the immune system to combat malignancies (Table 1). However, their mechanism of action—blocking inhibitory pathways that regulate immune responses—can lead to immune-related adverse events (irAEs) affecting multiple organ systems, including the oral cavity (Martins et al., 2019). Unlike traditional chemotherapy-induced toxicities, irAEs result from uncontrolled immune activation and may present with distinct clinical features, delayed onset, and prolonged duration (Postow et al., 2018).

A comprehensive meta-analysis of 95 clinical trials examining oral toxicities associated with single-agent ICI therapy provided the most robust estimates to date of irOAE prevalence (Srivastava et al., 2024). The weighted pooled prevalence was 5% (95% CI: 4-6%) for xerostomia, 3% (95% CI: 3-4%) for mucositis/stomatitis, 3% (95% CI: 2-3%) for dysgeusia, 2% (95% CI: 1-2%) for dysphagia, and 3% (95% CI: 2-4%) for oropharyngeal/oral pain. Oral infections, including candidiasis, occurred in 2% (95% CI: 1-3%) of patients, and angular cheilitis in 2% (95% CI: 0-4%). Subgroup analyses revealed minimal differences based on specific ICI agents, suggesting class-wide effects rather than drug-specific toxicities.

Importantly, the meta-analysis identified a significant gap in the literature regarding severe oral mucosal reactions. Despite clinical reports describing oral lichenoid reactions, bullous pemphigoid, mucous membrane pemphigoid, erythema multiforme, and Stevens-Johnson syndrome-like reactions in ICI-treated patients (de Bataille et al., 2021), no trials in the meta-analysis reported these outcomes (Srivastava et al., 2024). This discrepancy highlights the critical need for systematic collection and reporting of oral morbidity data in immunotherapy trials, as current reporting practices likely underestimate the true burden of irOAEs.

The pathogenesis of ICI-associated oral toxicities differs fundamentally from that of chemotherapy-induced mucositis. While chemotherapy directly damages rapidly dividing epithelial cells, irOAEs result from T-cell-mediated attack on oral tissues, often resembling autoimmune or hypersensitivity reactions (Jacob et al., 2021). This mechanistic difference has important therapeutic implications: corticosteroids and other immunosuppressive agents may be required for management, rather than the growth factors and cytoprotective agents used in conventional mucositis (Asan et al., 2021).

Targeted Therapy-Related Oral Complications

Targeted therapies, including tyrosine kinase inhibitors (TKIs), mTOR inhibitors, and anti-angiogenic agents, produce distinct oral toxicity profiles that reflect their specific molecular mechanisms. mTOR inhibitors such as everolimus and temsirolimus are associated with aphthous-like stomatitis, which differs clinically from conventional mucositis. mTOR inhibitor-associated stomatitis (mIAS) typically presents as well-demarcated, painful ulcers resembling aphthous stomatitis, often appearing within the first week of treatment (Peterson et al., 2016). The prevalence of mIAS ranges from 24% to 78% depending on the specific agent and dose, and it represents a common reason for dose modification or treatment discontinuation (Rugo et al., 2016).

Tyrosine kinase inhibitors, particularly those targeting vascular endothelial growth factor receptors (VEGFR-TKIs), are associated with dysgeusia, stomatitis, and mucosal inflammation. Sorafenib and

sunitinib, widely used in renal cell carcinoma and hepatocellular carcinoma, produce oral adverse effects in 20-40% of patients (Hwang et al., 2020). Dysgeusia, often described as a metallic or altered taste sensation, can significantly impair appetite and nutritional intake, contributing to cancer-related weight loss and cachexia (Hovan et al., 2010).

Epidermal growth factor receptor (EGFR) inhibitors, including cetuximab and panitumumab, are associated with distinctive oral complications. Beyond the well-characterized cutaneous rash, EGFR inhibitors frequently cause mucositis, xerostomia, and dysgeusia. The oral mucosa expresses high levels of EGFR, and inhibition of this receptor disrupts epithelial homeostasis, impairing wound healing and increasing susceptibility to secondary infection (Lacouture et al., 2021). Severe oral complications may necessitate treatment interruptions, potentially compromising oncological outcomes in patients where these agents are critical components of therapy.

Chemotherapy-Induced Oral Complications: Persistent Challenges

Despite advances in targeted and immunotherapeutic approaches, conventional chemotherapy remains a cornerstone of cancer treatment, and chemotherapy-induced oral mucositis continues to pose significant clinical challenges. The pathogenesis of chemotherapy-induced mucositis involves a complex five-phase process: initiation, primary damage response, signal amplification, ulceration, and healing (Al-Dasooqi et al., 2013). This multifactorial process involves direct DNA damage, oxidative stress, inflammatory cytokine activation, and alterations in the oral microbiome (Al-Dasooqi et al., 2013).

The incidence and severity of chemotherapy-induced mucositis vary considerably depending on the specific agents used, dosing intensity, and patient-related factors. Antimetabolites such as methotrexate and 5-fluorouracil, alkylating agents including cyclophosphamide, and anthracyclines like doxorubicin are particularly associated with mucositis (Lalla et al., 2019). High-dose chemotherapy regimens used in hematopoietic stem cell transplantation conditioning produce mucositis in virtually all patients, with severe (grades 3-4) mucositis affecting 70-80% (Chaudhry et al., 2016).

Xerostomia, or subjective sensation of dry mouth, represents another prevalent and distressing complication of chemotherapy. While often overshadowed by mucositis, xerostomia affects up to 78% of patients with advanced cancer and is associated with significant functional impairment, including difficulties with speech, swallowing, and taste perception (Oneschuk et al., 2000, as cited in Wilberg et al., 2012). In palliative care populations, xerostomia becomes increasingly prevalent as patients approach the end of life, with one study reporting 78% prevalence in patients with short estimated survival compared to 54% in those with longer survival (Matsuo et al., 2016, as cited in Wilberg et al., 2012).

Oral infections, particularly candidiasis, represent a common complication of cancer therapy. The combination of immunosuppression, mucosal disruption, xerostomia, and broad-spectrum antibiotic use creates an environment conducive to fungal overgrowth. Davies et al. (2008, as cited in Wilberg et al., 2012) found microbiological evidence of Candida in 70% of patients with advanced cancer, with clinical manifestations present in 13%. Importantly, non-albicans species, including C. glabrata with reduced azole susceptibility, are increasingly prevalent in cancer populations, reflecting prior antifungal exposure and the selection of resistant strains (Bagg et al., 2003, as cited in Wilberg et al., 2012).

Table 1. Prevalence of Oral Complications Associated with Systemic Cancer Therapies

Complication	Chemotherapy	Immune Checkpoint Inhibitors	Targeted Therapies	Key References
Oral Mucositis	40-80% (severe: 34-80%)	3% (95% CI: 3-4%)	mTOR inhibitors: 24-78%; TKIs: 20-40%	Thornton et al., 2022; Srivastava et al., 2024; Peterson et al., 2016
Xerostomia	56-88% (advanced cancer)	5% (95% CI: 4-6%)	VEGFR-TKIs: 30-50%	Wilberg et al., 2012; Srivastava et al., 2024; Oneschuk et al., 2000
Dysgeusia	40-70%	3% (95% CI: 2-3%)	EGFR inhibitors: 40-60%	Hovan et al., 2010; Srivastava et al., 2024
Oral Candidiasis	26-86% (microbiological)	2% (95% CI: 1-3%)	Similar to chemotherapy	Wilberg et al., 2012; Srivastava et al., 2024; Davies et al., 2008
Dysphagia	20-43% (advanced cancer)	2% (95% CI: 1-2%)	Reported but prevalence unclear	Wilberg et al., 2012; Srivastava et al.,

				2024; Matsuo et al., 2016
Oropharyngeal/Oral Pain	16-67%	3% (95% CI: 2-4%)	Variable by agent	Wilberg et al., 2012; Srivastava et al., 2024; Oneschuk et al., 2000
Immune-Related Oral Reactions	Not applicable	Rare (<1% in trials, underreported)	Not applicable	Srivastava et al., 2024; de Bataille et al., 2021

Dental Pre-Treatment Optimization

Pre-treatment dental optimization represents a critical opportunity to reduce the risk and severity of oral complications during subsequent cancer therapy. The rationale is straightforward: eliminating potential sources of infection, addressing pre-existing dental pathology, and establishing optimal oral hygiene before immunosuppression and mucosal injury can prevent complications that would otherwise necessitate treatment interruptions or pose infection risks during neutropenia (Spijkervet et al., 2021).

A rapid systematic review examining the optimal timing of dental procedures before oncological treatment provided important evidence to guide clinical practice (Mazzetti et al., 2022). The review, which included three retrospective observational studies, specifically evaluated the relationship between timing of dental extractions and subsequent osteoradionecrosis (ORN) risk. Meta-analysis demonstrated a significantly higher risk of ORN development in patients undergoing extractions less than two weeks before oncological treatment compared to those with extractions performed between two weeks and one month before therapy (relative risk 1.29; 95% CI 1.12-1.48; $p < 0.01$) (Mazzetti et al., 2022).

This finding has important clinical implications, supporting the recommendation that dental extractions should be performed at least two weeks before initiating radiotherapy or chemotherapy to allow adequate mucosal healing. However, the authors cautioned that the included studies had serious to critical risk of bias, with very low certainty of evidence, highlighting the need for higher-quality prospective studies to confirm these findings (Mazzetti et al., 2022).

For periodontal treatment and professional oral hygiene procedures, the evidence regarding optimal timing is less clear. The review identified a higher prevalence of oral mucositis in patients receiving periodontal treatment within three weeks of oncological therapy compared to those treated more than three weeks before, but the limited evidence precluded definitive recommendations (Mazzetti et al., 2022). Nevertheless, the biological plausibility of allowing healing time before mucosal injury supports a conservative approach, favoring earlier intervention when possible.

Components of Comprehensive Dental Evaluation

A comprehensive pre-treatment dental evaluation should include several key components. Clinical examination should assess for potential sources of infection, including carious lesions, periodontal disease, impacted teeth, and ill-fitting prostheses (Epstein et al., 2012). Radiographic evaluation, typically with panoramic imaging supplemented by periapical views as needed, is essential for identifying periapical pathology, impacted teeth, and other occult disease (Brennan et al., 2017).

Risk stratification should consider the planned cancer therapy in addition to dental findings. Patients scheduled for high-dose radiotherapy to fields including the jaw face substantially higher risks of ORN and radiation caries, warranting more aggressive preventive interventions (Mazzetti et al., 2022). Similarly, patients undergoing high-dose chemotherapy with prolonged neutropenia require meticulous elimination of infection sources before immunosuppression (Elad et al., 2020).

The decision to extract versus retain teeth with a questionable prognosis requires careful consideration of multiple factors. Teeth with moderate to severe periodontal disease, periapical pathology, or extensive caries may warrant extraction if they pose an infection risk during therapy. However, extractions themselves carry risks, particularly in patients who will receive radiotherapy, where extraction sites may heal poorly and serve as nidi for ORN (Nabil & Samman, 2011). A study examining tooth-level predictors of post-radiation tooth loss found that allowing at least three weeks for healing after extraction was preferable to the commonly recommended two-week window, with a mean difference of 6.6 days in healing time associated with better outcomes (Mazzetti et al., 2022).

Challenges in Implementation

Implementing comprehensive pre-treatment dental optimization faces numerous challenges in clinical practice. Time constraints are perhaps the most significant barrier: the urgency to initiate cancer therapy often conflicts with the desire for optimal dental preparation. Multidisciplinary coordination among oncology teams, dental professionals, and patients is essential but frequently logistically challenging (Zrubáková et al., 2020). Access to dental care represents another substantial barrier, particularly in healthcare systems where dental services are not

integrated with cancer care. Patients may lack dental insurance, face financial barriers to necessary treatment, or reside in areas with limited access to dental professionals with expertise in oncology (Threet et al., 2023). These disparities in access to pre-treatment dental care may contribute to inequities in cancer outcomes.

Patient-related factors, including dental anxiety, functional limitations, and competing medical priorities, can further complicate pre-treatment optimization. Effective communication among the interdisciplinary team and with patients is essential to prioritize interventions and develop feasible care plans that balance oncological urgency with dental preparation needs (Fischer et al., 2014, as cited in Wilberg et al., 2012).

The Critical Role of Nursing in Oral Complication Management

Nurses serve as frontline healthcare providers in oncology settings, positioned to conduct regular oral assessments, provide patient education, implement preventive interventions, and detect complications at early stages when intervention is most effective. The nursing role in oral care for cancer patients has been recognized for decades, yet significant gaps remain in nursing education, standardized assessment, and evidence-based protocol implementation (Gillam et al., 2006, as cited in Wilberg et al., 2012).

A scoping review examining the roles of clinical pharmacists and nurses in managing oral mucositis in head and neck cancer patients identified nine publications focused on nursing monitoring of adverse reactions (Zerillo et al., 2018). These studies demonstrated that nursing interventions, including regular oral assessment, patient education, and implementation of oral care protocols, can significantly reduce mucositis severity and improve patient outcomes. However, the review also highlighted substantial heterogeneity in nursing practices and the need for standardized, evidence-based approaches.

The European Oral Care in Cancer Group emphasizes that oral care should be central to preventing and minimizing oral complications during and after cancer treatment, with nurses playing essential roles in the oral care team alongside dental professionals, dietitians, physicians, and pharmacists (Zerillo et al., 2018). Effective communication among team members and with patients forms the core of successful care plans.

Oral Symptom Assessment Tools

Accurate assessment of oral complications is essential for guiding interventions and monitoring treatment response. A scoping review of oral symptom assessment tools in patients with advanced cancer identified four validated scales suitable for clinical use (Cleary et al., 2022). These included the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Oral Health 15 (EORTC QLQ-OH15), a cancer-specific quality of life scale; the Oral Health Impact Profile (OHIP), a generic tool assessing the social impact of oral problems; the Memorial Symptom Assessment Scale (MSAS), a cancer-specific generic symptom assessment scale; and the Oral Symptom Assessment Scale (OSAS), a cancer-specific oral symptom assessment tool.

The OSAS has undergone rigorous validation, with studies supporting its criterion validity against the EORTC QLQ-OH15 and demonstrating reliability in patients with advanced cancer (Cleary et al., 2022). This tool enables systematic assessment of multiple oral symptoms, including pain, dryness, taste alteration, and functional difficulties, facilitating comprehensive evaluation and tracking over time. The Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO) has published clinical practice statements on assessing salivary gland hypofunction and xerostomia in cancer patients (MASCC/ISOO, 2021, as cited in Cleary et al., 2022). These recommendations summarize common investigator- and patient-reported instruments and provide guidance on best practices for clinical assessment, emphasizing the importance of both objective measures (e.g., salivary flow rates) and subjective patient-reported outcomes.

Despite the availability of validated tools, significant gaps remain in clinical implementation. Oneschuk et al. (2000, as cited in Wilberg et al., 2012) found that while 56% of patients reported oral pain to caregivers and 44% reported dry mouth, medical documentation captured only one pain complaint and five dry mouth complaints. This documentation gap highlights the need for systematic assessment protocols and better integration of patient-reported outcomes into clinical documentation.

Nursing Interventions for Oral Complication Prevention and Management

Basic oral hygiene represents the foundation of oral complication prevention. Regular tooth brushing with a soft-bristled toothbrush, flossing when feasible, and use of non-irritating oral care products help maintain mucosal health and reduce infection risk (McGuire et al., 2013). For patients unable to tolerate mechanical cleansing due to pain or bleeding, foam swabs or soft oral sponges may serve as alternatives, though they are less effective at plaque removal.

Patient education is a core nursing responsibility with demonstrated effectiveness in reducing oral complication severity. A systematic review of oral care interventions found that patient education programs consistently demonstrated beneficial effects, with over 75% of studies reporting significant reductions in oral mucositis incidence and severity (Thornton et al., 2022). Effective education should cover the rationale for oral care, proper techniques, warning signs requiring professional attention, and strategies for managing discomfort.

Nurses play essential roles in implementing evidence-based preventive protocols. Professional oral health care (POHC), which includes regular professional cleaning, fluoride applications, and preventive interventions, has demonstrated the strongest evidence for reducing oral mucositis incidence and severity (Thornton et al., 2022). While dentists and dental hygienists typically provide POHC, nurses coordinate referrals, reinforce recommendations, and support patients in maintaining oral health between dental visits.

For patients receiving specific therapies associated with oral complications, targeted nursing interventions may be indicated. For ICI-treated patients, nurses should be vigilant for signs of immune-related oral reactions, including lichenoid changes, blistering, or unusual mucosal lesions, and facilitate prompt evaluation by appropriate specialists (Asan et al., 2021). For patients receiving targeted therapies, nurses should educate about expected oral effects and strategies for management, including topical analgesics and dietary modifications.

In palliative care settings, where patients may be unable to articulate symptoms or participate in complex oral care regimens, nursing assessment and intervention become particularly critical. Wilberg et al. (2012) found that only 22% of patients with advanced cancer had received information about oral adverse effects of cancer treatment, and only 38% had received guidance on managing xerostomia. These findings underscore the need for proactive nursing assessment and education, even—and perhaps especially—in patients with limited life expectancy.

Expanding Roles of Clinical Pharmacists in Oncology Supportive Care

Clinical pharmacists have increasingly assumed essential roles in oncology supportive care, applying their expertise in pharmacology, medication safety, and therapeutic optimization to manage treatment-related adverse effects. A scoping review examining pharmacist and nurse roles in oral mucositis management identified three publications specifically addressing clinical pharmacist interventions (Zerillo et al., 2018). These studies demonstrated that pharmacists providing pharmaceutical care to patients undergoing chemoradiotherapy can significantly improve symptom management and quality of life. The direct care model implemented by pharmacists effectively alleviates symptoms and enhances quality of life, fostering better treatment outcomes and patient satisfaction (Zerillo et al., 2018). Pharmacist interventions typically include comprehensive medication review, optimization of analgesic regimens, antimicrobial stewardship, and patient education about medications used for oral complication management.

The European Oral Care in Cancer Group guidelines explicitly include pharmacists as essential members of the oral care team, alongside dental professionals, dietitians, nurses, and physicians (Zerillo et al., 2018). This recognition reflects the complexity of medication management in patients with oral complications, who may require multiple agents for pain control, infection management, and symptom relief while continuing their antineoplastic therapy.

Pharmacist-Led Interventions for Oral Mucositis

Pain management represents a primary focus of pharmacist intervention in oral mucositis. Severe mucositis pain can be debilitating, interfering with oral intake, sleep, and quality of life. The MASCC/ISOO guidelines recommend topical 0.2% morphine mouthwash for pain associated with oral mucositis in head and neck cancer patients (Zerillo et al., 2018). Pharmacists play essential roles in preparing appropriate formulations, ensuring correct dosing, and monitoring for efficacy and adverse effects. Systemic analgesics, including non-steroidal anti-inflammatory drugs, acetaminophen, and opioids, may be required for moderate to severe mucositis pain. Pharmacists assess individual patient factors, including organ function, concomitant medications, and substance use history, to select appropriate agents and doses. They also monitor for adverse effects, including constipation, sedation, and respiratory depression, implementing preventive strategies such as bowel regimens and dose adjustments (Walko et al., 2016).

Infection management represents another critical domain for pharmacist intervention. Oral mucositis disrupts mucosal barriers, creating portals of entry for bacterial, fungal, and viral pathogens. The selection of appropriate antimicrobial agents requires consideration of likely pathogens, local resistance patterns, patient allergy history, and potential drug interactions with antineoplastic therapy (Thomsen & Vitetta, 2018). For oral candidiasis, topical antifungals such as nystatin or clotrimazole are typically first-line, with systemic azoles reserved for refractory or extensive disease. However, the increasing prevalence of non-albicans species with reduced azole susceptibility complicates treatment selection. Bagg et al. (2003, as cited in Wilberg et al., 2012) found that while *Candida albicans* remained the most common isolate (79%), *C. glabrata*—often less susceptible to fluconazole—was increasingly prevalent.

Pharmacists' knowledge of local antifungal resistance patterns and antifungal pharmacology is essential for optimizing treatment. Antiviral prophylaxis may be indicated for patients at high risk of herpes simplex virus reactivation, particularly those undergoing hematopoietic stem cell transplantation or receiving highly immunosuppressive regimens. Pharmacists ensure appropriate dosing, monitor renal function for agents requiring dose adjustment (e.g., acyclovir), and assess for drug interactions.

Medication Management for Xerostomia and Dysgeusia

Xerostomia management requires a multifaceted approach, including both

pharmacological and non-pharmacological interventions. Pharmacists can recommend appropriate saliva substitutes and stimulants based on individual patient factors and preferences. Pilocarpine and cevimeline, cholinergic agonists that stimulate salivary secretion, may be beneficial for patients with residual salivary gland function (Jensen et al., 2019). However, these agents require careful prescribing and monitoring due to potential adverse effects, including sweating, flushing, and cardiovascular effects.

Pharmacists also play essential roles in identifying and managing medications that may exacerbate xerostomia. Many patients receiving cancer therapy take multiple medications with anticholinergic effects, including antidepressants, antipsychotics, antihistamines, and antispasmodics. Comprehensive medication review can identify opportunities to substitute less xerogenic alternatives when clinically appropriate (Yoshida et al., 2021).

For dysgeusia, which affects up to 70% of patients receiving certain chemotherapies (Hovan et al., 2010), pharmacists can recommend strategies to improve food palatability. Zinc supplementation has been investigated for taste alteration prevention and management, though evidence remains mixed (Hoppe et al., 2021). Pharmacists can also advise on the timing of medication administration relative to meals to minimize taste disturbance and recommend flavor enhancements or masking agents.

Drug Interaction and Safety Considerations

Patients receiving cancer therapy are at high risk for drug interactions, given the complexity of their medication regimens and the narrow therapeutic indices of many antineoplastic agents. Pharmacists systematically evaluate potential interactions between medications used for oral complication management and ongoing cancer therapy. For example, azole antifungals used for oral candidiasis are potent CYP3A4 inhibitors that can significantly increase exposure to many kinase inhibitors, potentially enhancing both efficacy and toxicity (Thomsen & Vitetta, 2018). Similarly, opioids used for mucositis pain may interact with other centrally acting medications, increasing sedation risk. Pharmacists' expertise in pharmacokinetics and pharmacodynamics is essential for navigating these complexities and ensuring safe, effective therapy.

Laboratory Biomarkers for Risk Prediction and Monitoring

The Promise of Biomarker-Guided Personalized Prevention

The identification of biomarkers capable of predicting individual patients' risk for severe oral complications holds tremendous promise for personalized supportive care. If high-risk patients could be identified before treatment initiation, preventive interventions could be intensified, treatment regimens could be modified when feasible, and monitoring could be enhanced. Conversely, low-risk patients might be spared unnecessary interventions, focusing resources on those most likely to benefit (Sonis, 2021).

A systematic review and meta-analysis evaluating biomarkers for oral mucositis assessment in head and neck cancer patients examined 26 studies investigating 27 different biomarkers (Normando et al., 2017). The most frequently studied biomarkers included epidermal growth factor (EGF), C-reactive protein (CRP), genetic polymorphisms, tumor necrosis factor alpha (TNF-α), and erythrocyte sedimentation rate (ESR). Meta-analysis revealed expression of polymorphisms in XRCC1 (32.66%), XRCC3 (31.00%), and RAD51 (39.16%) genes in patients with increased risk of developing oral mucositis, as well as expression of protein biomarkers in 39.57% of high-risk patients. The authors concluded that dosing biomarkers before initiating radiation therapy may be a promising method to predict mucositis risk and enable customized treatment for radiosensitive patients (Normando et al., 2017). However, they noted limited evidence to confirm the implementation of serum and salivary biomarkers for correlating with mucositis severity, emphasizing the need for further research.

Genetic Polymorphisms as Predictive Biomarkers

Single-nucleotide polymorphisms (SNPs) represent the most common type of genetic variation and have been extensively investigated as potential predictors of oral mucositis risk. A systematic review examining SNPs as biomarkers for oral mucositis severity in head and neck cancer patients undergoing chemoradiation identified 23 studies analyzing genes from multiple biological pathways (Cavalieri et al., 2024). The DNA damage repair pathways contained the highest number of studied genes, with XRCC1 being the most frequently analyzed. The proinflammatory cytokine pathways evaluated included TNF (three articles) and NF-κB (one article). Most included studies showed potential associations between specific SNPs and high-grade mucositis, suggesting that genetic variation in DNA repair capacity and inflammatory response may influence individual susceptibility to mucosal injury (Cavalieri et al., 2024).

The early identification of patients more likely to develop severe mucositis through genetic analysis represents a promising approach to personalized supportive care. Individuals identified as high-risk could receive preemptive implementation of intensive preventive measures and aggressive supportive care before and during radiotherapy (Cavalieri et al., 2024). However, the authors emphasized that further research is needed to validate these findings and explore the full potential of SNPs in personalized medicine for cancer treatment. The biological plausibility of genetic predictors is supported by the multifactorial pathogenesis of mucositis. Genes involved in DNA damage repair may influence cellular sensitivity to radiation and chemotherapy, while genes regulating inflammatory

cytokines may modulate the intensity of the inflammatory response that amplifies mucosal injury (Sonis, 2021). Variation in drug-metabolizing enzymes may also influence exposure to active chemotherapy metabolites, indirectly affecting mucosal toxicity.

Protein and Inflammatory Biomarkers

Beyond genetic polymorphisms, protein biomarkers measurable in blood or saliva have been investigated for their ability to predict or correlate with mucositis severity. Inflammatory markers, including CRP, TNF-α, and interleukins, reflect the systemic inflammatory response that accompanies and amplifies mucosal injury (Al-Dasooqi et al., 2013). Epidermal growth factor (EGF), a protein crucial for epithelial proliferation and wound healing, has been studied as both a predictor and a therapeutic target. Lower salivary EGF levels before treatment have been associated with increased mucositis risk, suggesting that baseline epithelial regenerative capacity may influence susceptibility (Xu et al., 2023).

C-reactive protein, an acute-phase reactant synthesized in response to inflammatory cytokines, rises with mucositis severity and may serve as an objective marker of mucosal injury burden. However, CRP is non-specific and may be elevated due to infection, tumor necrosis, or other inflammatory processes common in cancer patients, limiting its utility as a standalone biomarker (Normando et al., 2017). The meta-analysis by Normando et al. (2017) found expression of protein biomarkers in approximately 40% of patients with increased mucositis risk, but the heterogeneity of studied markers and variability in study quality precluded definitive conclusions. The authors emphasized that while biomarker assessment before treatment shows promise, current evidence is insufficient to recommend routine clinical implementation.

Laboratory Monitoring During Treatment

Laboratory testing during cancer treatment can inform oral complication management in several ways. Complete blood counts identify neutropenia, which increases infection risk and may warrant enhanced oral hygiene measures, antimicrobial prophylaxis, or more aggressive management of suspected infections (Elad et al., 2020). Inflammatory markers such as CRP and ESR may help differentiate infectious from non-infectious causes of oral symptoms, though their non-specificity limits diagnostic utility. In patients receiving ICIs, rising inflammatory markers in conjunction with new oral symptoms may signal immune-related adverse events requiring immunosuppressive intervention (Martins et al., 2019).

Microbiological testing with culture and sensitivity is essential for guiding antimicrobial therapy in patients with suspected oral infections, particularly those with refractory or recurrent symptoms. The increasing prevalence of non-albicans Candida species and azole resistance underscores the importance of species identification and susceptibility testing when feasible (Bagg et al., 2003, as cited in Wilberg et al., 2012). For patients receiving nephrotoxic medications (e.g., amphotericin for fungal infections, high-dose acyclovir, certain antibiotics) or medications requiring renal dose adjustment, monitoring of renal function is essential. Pharmacists and laboratory professionals collaborate to ensure appropriate timing of drug levels, interpretation of results, and dose adjustments based on renal function.

Interdisciplinary Collaboration: Models and Implementation

The complexity of oral complications arising from systemic cancer therapies demands coordinated interdisciplinary collaboration. No single professional group possesses all the knowledge and skills required for optimal prevention, assessment, and management. Dentists bring expertise in oral pathology and dental interventions; nurses provide frontline assessment, education, and daily supportive care; pharmacists contribute medication management and therapeutic optimization; and laboratory professionals enable biomarker-driven risk stratification and monitoring (Epstein et al., 2012).

The European Oral Care in Cancer Group emphasizes that the oral care team may vary by medical setting but should typically include dental professionals, dietitians, nurses, physicians, and pharmacists (Zerillo et al., 2018). The support provided by the team, along with good communication with patients, forms the core of all care plans and is crucial for maintaining patients' oral health throughout cancer treatment (Table 2).

Table 2. Interdisciplinary Roles in Prevention and Management of Oral Complications

Discipline	Prevention	Assessment	Management	Key References
Dentistry	Pre-treatment optimization; elimination of infection sources; professional oral health care; fluoride application	Comprehensive oral examination; radiographic evaluation; risk stratification	Dental extractions; periodontal treatment; management of dental complications; prosthetic care	Mazzetti et al., 2022; Spijkervet et al., 2021; Epstein et al., 2012
Nursing	Patient education; oral hygiene	Regular oral assessment using	Daily oral care; early recognition of	Cleary et al., 2022; Zerillo et

	instruction; implementation of preventive protocols	validated tools (OSAS, EORTC QLQ-OH15); symptom documentation	complications; coordination of referrals; supportive care	al., 2018; Thornton et al., 2022; Wilberg et al., 2012
Pharmacy	Medication review; identification of xerogenic medications; patient education about medications	Assessment of medication-related symptoms; evaluation of drug interactions	Analgesic optimization; antimicrobial stewardship; preparation of specialized formulations; monitoring for adverse effects	Zerillo et al., 2018; Walko et al., 2016; Thomsen & Vitetta, 2018
Laboratory Medicine	Baseline biomarker assessment (investigational); genetic testing for risk prediction (emerging)	Microbiological testing with culture/sensitivity; inflammatory marker monitoring; therapeutic drug monitoring	Guidance for antimicrobial selection, monitoring treatment response, and identifying resistant organisms	Normando et al., 2017; Cavalieri et al., 2024; Al-Dasooqi et al., 2013
Interdisciplinary Collaboration	Coordinated care planning; shared decision-making; integrated clinical pathways	Standardized documentation; regular team communication; shared electronic health records	Combined interventions; coordinated follow-up, and comprehensive supportive care	Epstein et al., 2012; Zrubáková et al., 2020; European Oral Care in Cancer Group, 2020

Models of Interdisciplinary Collaboration

Several models for interdisciplinary oral care in oncology have been described. The integrated care model embeds dental professionals within oncology teams, facilitating regular communication, coordinated treatment planning, and seamless referrals. This model, while ideal, requires substantial institutional commitment and resources that may not be feasible in all settings (Zrubáková et al., 2020). The consultative model relies on referral relationships between oncology teams and dental professionals. This model is more feasible across diverse healthcare settings but requires clear communication pathways, standardized referral criteria, and mechanisms for feedback and follow-up. Challenges include delays in care, incomplete information transfer, and potential fragmentation of care (Threet et al., 2023).

Nurse-led oral care programs, supported by dental and pharmacy consultation as needed, represent another model particularly suited to settings with limited dental access. In this model, nurses conduct initial assessments, implement preventive protocols, and manage uncomplicated oral complications, with referral pathways for complex cases requiring dental or pharmacy expertise (Gillam et al., 2006, as cited in Wilberg et al., 2012). The scoping review of pharmacist and nurse roles in oral mucositis management (Zerillo et al., 2018) provides evidence that direct care models implemented by pharmacists and nurses effectively alleviate symptoms and enhance quality of life. These findings support the expansion of pharmacist and nurse roles in oral complication management, particularly in settings where dental access is limited.

Communication and Care Coordination

Effective communication among interdisciplinary team members and with patients is essential for successful oral complication management. Key elements include clear documentation of oral assessments and interventions, standardized communication tools (e.g., structured referral forms, shared electronic health record documentation), and regular team meetings to discuss complex cases. Patient education and engagement are equally critical. Patients should understand the rationale for oral care recommendations, the importance of reporting symptoms promptly, and strategies for self-management. Educational materials should be culturally appropriate, accessible to patients with varying health literacy levels, and reinforced at multiple time points throughout treatment (McGuire et al., 2013).

The significant gap between patient-reported symptoms and medical documentation identified by Oneschuk et al. (2000, as cited in Wilberg et al., 2012) highlights the need for systematic symptom assessment and documentation protocols. Integrating patient-reported outcome measures into electronic health records, with alerts for concerning symptoms, could improve recognition and timely intervention.

Barriers and Facilitators

Multiple barriers to effective interdisciplinary oral care exist. Time constraints and competing clinical priorities may limit opportunities for comprehensive oral assessment and intervention. Limited access to dental professionals with oncology expertise, particularly in community and rural settings, constrains referral options. Reimbursement structures may not adequately support interdisciplinary care, with dental and medical benefits often siloed (Threet et al., 2023). Facilitators include institutional leadership commitment to supportive care quality, dedicated resources for oral care programs, standardized protocols and order sets, and electronic health record tools that support documentation and communication. Education and training across disciplines, including interprofessional education opportunities, can build knowledge and foster collaborative relationships (Epstein et al., 2012).

Future Research Directions

Several priority areas for future research emerge from this review. First, a systematic collection of oral morbidity data in cancer clinical trials is urgently needed. Standardized reporting of oral adverse events, including severe immune-related mucosal reactions, would improve understanding of true prevalence and risk factors, enabling evidence-based prevention and management. Second, prospective studies examining optimal timing and content of pre-treatment dental interventions are needed. Higher-quality evidence would support evidence-based guidelines and help balance oncological urgency with dental preparation needs.

Third, validation of predictive biomarkers in large, well-characterized cohorts could enable personalized prevention strategies. Multi-institutional collaborations and standardized biomarker assessment protocols are needed to advance this field. Fourth, interventional trials testing specific management strategies, including comparative effectiveness studies of different mouthwash formulations, analgesic approaches, and preventive protocols, would strengthen the evidence base for clinical recommendations. Fifth, implementation science research examining strategies to integrate interdisciplinary oral care into routine oncology practice could identify effective approaches to overcoming barriers and scaling successful models. Sixth, studies examining the oral complications of novel therapies, including antibody-drug conjugates, bispecific T-cell engagers, and cellular therapies, are needed as these agents enter clinical practice.

Conclusions

Oral complications from systemic cancer therapies are common, distressing, and can hinder treatment. The introduction of new agents, like immune checkpoint inhibitors and targeted therapies, has led to unique oral toxicity profiles that require tailored management. Effective outcomes necessitate interdisciplinary collaboration, with dentists addressing pre-treatment optimizations, nurses managing preventive protocols, and pharmacists overseeing medication management. Evidence highlights the benefits of professional oral care and patient education in alleviating oral mucositis and emphasizes the importance of allowing healing time post-dental procedures before starting cancer treatments. However, challenges persist, such as underreported oral toxicity in clinical trials and a lack of high-quality studies on dental intervention timing. Future efforts must focus on systematic data collection of oral morbidity, validation of biomarkers, standardized assessment protocols, and the integration of interdisciplinary care in oncology to enhance patient quality of life and alleviate oral complications.

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