

Review

Radiation-induced xerostomia in nasopharyngeal carcinoma survivors: psychosocial burden, survivorship implications, and the potential role of malic acid

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Abstract: Radiation-induced xerostomia is a common late effect of radiotherapy for nasopharyngeal carcinoma (NPC). It can impair oral comfort, eating, swallowing, speech, and sleep, with adverse consequences for oral health-related quality of life (OHRQoL). Xerostomia, the subjective sensation of oral dryness, should be distinguished from objectively measured salivary gland hypofunction, although the two frequently coexist. This structured narrative review examines the clinical and psychosocial burden, pathophysiology, assessment, and management of radiation-induced xerostomia in NPC survivors. It also evaluates malic acid as a candidate topical sialogogue. The literature indicates that assessment should combine patient-reported measures, clinical examination, and unstimulated and stimulated salivary flow measurements. Management requires a multidisciplinary framework that distinguishes prevention or preservation of gland function from treatment of established hypofunction and symptomatic relief. Short-term studies of low-concentration malic acid formulations in non-cancer xerostomia populations have reported improvements in perceived dryness or salivary flow, but their relevance to irradiated NPC survivors remains uncertain and long-term dental safety is insufficiently characterised. NPC-specific trials should define eligibility, formulation, dose, and treatment duration and prespecify patient-centred outcomes and oral-safety monitoring.

Keywords: radiation-induced xerostomia; nasopharyngeal carcinoma; patient-reported outcomes; quality of life; psychosocial burden; malic acid

1. Introduction

Nasopharyngeal carcinoma (NPC) is a major head and neck malignancy in endemic regions of southern China, and cases in China account for a substantial proportion of the global burden [1,2]. Radiotherapy, alone or as part of combined-modality treatment, remains the principal curative treatment [3]. Irradiation of the major and minor salivary glands can produce salivary gland hypofunction, while patients may report xerostomia even when objective flow reduction is less marked. These related but non-equivalent outcomes should be assessed separately. Radiation-induced oral dryness may persist after treatment despite modern intensity-modulated radiotherapy (IMRT) [4,5] and can contribute to taste alteration, difficulty forming a food bolus, impaired swallowing, disturbed sleep, oral infection, dental disease, and reduced oral health-related quality of life (OHRQoL) [6,7]. From a survivorship perspective, the clinical importance of xerostomia therefore extends beyond salivary output to patient-perceived symptoms, daily functioning, and self-management [8].

Emerging computational methods may complement conventional clinical and

patient-reported assessment by refining individualised risk estimates for radiation-induced xerostomia. In NPC, magnetic resonance imaging-based delta-radiomics and integrated radiomics–dosimetrics have combined salivary gland imaging with clinical and radiation-dose data for risk prediction [9–12]. Methods developed for biomedical image analysis, self-supervised representation learning, and multimodal modelling may be transferable to xerostomia prediction, particularly for feature extraction and the integration of heterogeneous data [13–15]. Future models should be interpretable and integrate longitudinal salivary flow measurements, salivary gland dose–volume and spatial-dose features, oral and dental findings, and patient-reported outcome measures (PROMs). Most published models, however, are retrospective or single-centre and require prospective external validation, calibration, and evidence of added clinical value. Improved prediction could support surveillance and patient selection, but it does not replace practical symptom-directed care for established xerostomia.

Gustatory stimulation may augment salivary output when residual glandular tissue remains, although repeated acidic exposure may pose risks to dental enamel and sensitive oral tissues. Malic acid has been used as a food acidulant and evaluated in topical xerostomia formulations, but food-use status does not establish therapeutic efficacy or long-term oral safety in irradiated NPC survivors. Its relevance therefore depends on residual salivary function, oral and dental status, formulation characteristics, and the transferability of evidence from other populations.

Current guidelines address the prevention, assessment, and management of salivary gland hypofunction and xerostomia across cancer populations [16–18]. They provide less detailed guidance for persistent xerostomia in NPC survivorship, particularly its functional and psychosocial effects, the discordance between perceived dryness and measured salivary function, and the possible role of malic acid. Existing reviews address parts, but not the full combination, of these questions [8,19]. This review therefore examines the burden of xerostomia after NPC treatment using four evidence categories: direct NPC evidence, indirect head and neck cancer evidence, indirect non-cancer evidence, and mechanistic evidence. It organises assessment and management around patient needs and evaluates the rationale, patient-selection criteria, oral safety, and research priorities for malic acid, including the role of nurse-coordinated assessment, education, and follow-up.

2. Methods of literature search and evidence selection

2.1. Search strategy

This review was undertaken as a structured narrative review. PubMed, Scopus, China National Knowledge Infrastructure (CNKI), and Wanfang Data were searched for records published from 1 July 2021 to 30 June 2026, with the final search update completed on 30 June 2026. Database-specific strategies combined Medical Subject Headings (MeSH) in PubMed, where applicable, with free-text terms, and the search syntax was adapted to the indexing structure and search functions of each database. Search concepts were organised into seven domains: (1) nasopharyngeal carcinoma, head and neck cancer, radiotherapy, intensity-modulated radiotherapy, and intensity-modulated proton therapy; (2) xerostomia, dry mouth, salivary gland hypofunction, hyposalivation, salivary flow, and salivary gland volume; (3) malic acid, L-malic acid, sour taste, gustatory stimulation, the gustatory–salivary reflex, and sialogogues; (4) xerostomia assessment, clinical oral dryness, sialometry, validation studies, patient-reported outcome measures, and electronic symptom monitoring; (5) health-related and oral health-related quality of life, nutrition, food choice, social eating,

swallowing, communication, sleep, anxiety, depression, fear of cancer recurrence, financial toxicity, social support, supportive care needs, treatment adherence, and self-management; (6) oral and dental safety, including dental erosion, caries, enamel demineralisation, dentine hypersensitivity, oral mucosal effects, oral pH, and salivary buffering capacity; and (7) computational imaging and risk prediction, including magnetic resonance imaging, functional magnetic resonance imaging, radiomics, delta-radiomics, dosiomics, artificial intelligence, machine learning, multimodal modelling, and predictive modelling. The disease and xerostomia domains were combined with one or more topic-specific domains as appropriate. Searches for malic acid in non-cancer xerostomia populations and for the oral safety of acidic formulations were conducted without requiring an NPC-related term. English and Chinese equivalents were used, with search syntax adapted to the requirements of each database. Publications in English or Chinese were considered.

2.2. Eligibility criteria and study selection

Evidence considered for inclusion comprised clinical practice guidelines and consensus statements; systematic, scoping, and narrative reviews; randomised and non-randomised clinical studies; observational studies; validation studies of xerostomia assessment instruments; digital symptom-monitoring studies; imaging-based prediction-model studies; and mechanistic studies relevant to salivary secretion, radiation-induced salivary gland injury, or acidic stimulation.

One author conducted the initial screening of titles and abstracts and subsequently assessed potentially relevant full-text articles. The database searches identified 12,035 records. After removal of 3,589 cross-database duplicates, 8,446 unique records underwent title and abstract screening, of which 7,397 were excluded. A focused title, abstract, and metadata assessment of the remaining 1,049 records excluded a further 657 records, leaving 392 potentially relevant database-derived reports for full-text assessment. Reference-list screening and forward citation tracking identified an additional 17 earlier foundational reports that were not captured within the prespecified database search period. In total, 409 full-text reports were assessed, of which 333 were excluded and 76 were included in the final narrative synthesis.

The 7,397 records excluded during title and abstract screening were judged to be clearly outside the predefined clinical or methodological scope. During the focused assessment of the remaining 1,049 records, 657 were excluded. The principal reasons were insufficient relevance to xerostomia, salivary gland function, or the prespecified patient-centred outcomes ($n = 398$); a non-cancer context without sufficient relevance to the review questions ($n = 129$); and the absence of a separable xerostomia or salivary-function outcome ($n = 99$). The remaining 31 records were excluded because they were protocols without completed results, ineligible publication types, generic computational studies without direct relevance, retracted publications, or studies of ineligible interventions or topics. At full-text assessment, 333 reports were excluded, primarily because they provided overlapping or redundant evidence, made a limited incremental contribution to the review questions, or had limited applicability to NPC survivorship. Both authors reviewed the final evidence set, and uncertainties regarding eligibility or relevance were resolved through discussion and consensus.

2.3. Evidence appraisal and classification

Given the narrative scope of the review, no quantitative synthesis or formal grading of evidence certainty was undertaken. The evidence was appraised qualitatively with reference to study design, sample size, comparator, validity and relevance of outcome measures, duration of follow-up, consistency of findings, and

applicability to NPC survivors. Evidence was categorised as direct evidence from NPC survivors, indirect evidence from other head and neck cancer populations, indirect evidence from non-cancer xerostomia populations, or mechanistic and theoretical evidence.

3. Psycho-oncological burden and patient-centred outcomes in NPC survivors

Concurrent chemoradiotherapy remains a standard treatment for locoregionally advanced NPC, with induction or adjuvant chemotherapy selected according to disease stage and risk [3,20]. Current treatment paradigms include induction chemotherapy followed by concurrent chemoradiotherapy, concurrent chemoradiotherapy followed by adjuvant chemotherapy, and definitive concurrent chemoradiotherapy alone. Advances in IMRT, concurrent chemoradiotherapy, and multimodal treatment have substantially improved survival outcomes. In the IMRT era, 5-year overall survival exceeds 80% and approaches 85% in large institutional cohorts [21,22]. Although estimates vary by disease stage and cohort composition, improved survival has increased the importance of late toxicity, functional recovery, psychosocial adjustment, social participation, and health-related quality of life (HRQoL).

IMRT enables highly conformal dose delivery according to the three-dimensional geometry of the target volume, thereby maintaining target coverage while reducing unnecessary irradiation of adjacent organs at risk [20]. Despite its dosimetric advantages over conventional radiotherapy, patients receiving IMRT for NPC may still experience a broad spectrum of treatment-related toxicities. Radiation dermatitis has been reported in approximately 95% of patients [23], while radiation-induced oral mucositis may occur in nearly all patients during treatment [24]. Oral mucositis is frequently accompanied by clinically significant oral pain, which can impair oral intake and compromise HRQoL [25]. Malnutrition and progressive weight loss are also prevalent during treatment [26]. Although dermatitis and mucositis are predominantly acute toxicities, their effects on oral intake, nutritional status, treatment experience, and functional recovery emphasise the need for comprehensive supportive care. Moreover, some oral complications, particularly xerostomia and salivary gland hypofunction, may persist long after the completion of radiotherapy and become important components of survivorship care. These persistent complications may extend beyond oral discomfort to affect daily functioning, emotional well-being, social participation, and the resumption of valued activities.

3.1. Functional and social-eating consequences

Xerostomia refers to the subjective sensation of oral dryness, whereas salivary gland hypofunction denotes an objectively measurable reduction in salivary secretion. Although the two conditions frequently coexist following radiotherapy, they are not interchangeable, because patients with comparable salivary flow rates may report markedly different levels of perceived dryness and functional burden. Patients with xerostomia commonly report persistent oral dryness, thirst, pronounced nocturnal or morning discomfort, and frequent reliance on water during eating, speaking, or sleep. These subjective complaints and related behaviours may coexist with objectively reduced salivary output, which should be interpreted as evidence of salivary gland hypofunction rather than as a defining symptom of xerostomia. Additional coexisting manifestations may include chapped lips, sticky saliva, burning sensations affecting the pharyngeal, lingual, labial, or buccal mucosa, hypogeusia or dysgeusia, mucosal sensitivity, and swallowing difficulty [8,19].

Reduced salivary lubrication can impair bolus formation and make dry, hard, or sticky foods more difficult to masticate and swallow. Patients may consequently require frequent water sipping, modify food preparation, restrict food texture or variety, or avoid foods that are difficult to chew and swallow. These adaptations can prolong mealtimes, reduce eating enjoyment, and compromise oral nutritional intake. Prospective and long-term studies indicate that salivary dysfunction and associated patient-reported symptoms may persist for months or years after radiotherapy [27,28]. Objective salivary flow and mouth-opening measurements have been reported to explain only a limited proportion of the variation in patient-reported eating, drinking, distress, and salivation outcomes, indicating that physiological measurements alone cannot fully represent the burden experienced by individual patients [29].

NPC-specific evidence further demonstrates the importance of late symptom burden. In a cross-sectional survey of 200 evaluable NPC survivors, dry mouth was the highest-rated late symptom, while greater overall symptom burden was associated with poorer HRQoL and greater unmet needs for symptom management [30]. Because the analysis evaluated overall symptom burden, the independent contribution of xerostomia to impaired HRQoL could not be isolated. This limitation does not diminish the clinical relevance of xerostomia; rather, it indicates that its psychosocial significance should be examined within an interconnected symptom network rather than interpreted as an isolated determinant of HRQoL.

The functional effects of xerostomia may extend into social eating. Dependence on water, prolonged chewing, restricted food choices, difficulty speaking while eating, and concern about swallowing may make shared meals more demanding. Some patients may become reluctant to eat in restaurants or in front of others, particularly when xerostomia coexists with dysphagia, oral pain, taste disturbance, fatigue, or nutritional impairment. Evidence from longitudinal studies of mixed head and neck cancer cohorts indicates that difficulties with social eating, oral pain, weight loss, psychological distress, and changes in social circumstances are associated with different HRQoL trajectories [31,32]. Xerostomia may therefore contribute to restricted social eating and participation as part of a broader symptom cluster, through both perceived dryness and interference with valued activities, social roles, and interpersonal interactions.

Clinical assessment should consequently extend beyond salivary flow measurements. Relevant questions include the duration of meals, reliance on water during eating, restriction of food texture, avoidance of shared meals, and distress associated with eating in front of others. The links between these functional and social consequences and the wider sleep, emotional, and behavioural burden provide the basis for the hypothesised psycho-oncological framework presented below.

3.2. A hypothesised psycho-oncological framework

Taken together, the available evidence supports a hypothesis-generating psycho-oncological framework rather than an established linear causal pathway. Radiation-induced salivary gland injury may reduce salivary secretion; however, perceived xerostomia severity is not determined by salivary flow alone [29]. The proposed model posits that xerostomia may influence survivorship outcomes through functional interference, including difficulties with eating, swallowing, speaking, sleeping, and oral self-management. These limitations may be accompanied by frustration, symptom-related worry, embarrassment, and emotional distress. Avoidance of shared meals and other symptom-sensitive situations may restrict social participation [31]. Functional impairment, emotional distress, and reduced social participation may,

individually or jointly, contribute to poorer HRQoL [30,32].

The relationships within this framework may also be reciprocal. Emotional distress may heighten attention to oral symptoms and increase their perceived burden, whereas persistent functional limitations and social withdrawal may further intensify distress. Co-occurring physical symptoms may add to the functional and psychosocial burden [32]. Fear of cancer recurrence and pre-existing psychosocial vulnerability may shape emotional responses [33,34], whereas financial burden may further affect HRQoL [35]. Coping resources, social support, and access to supportive care are therefore conceptualised as potential modifiers rather than established determinants. Accordingly, the framework situates xerostomia within a broader network of physical, psychological, and social influences and does not assume that xerostomia independently causes psychological morbidity or social withdrawal (**Figure 1**).

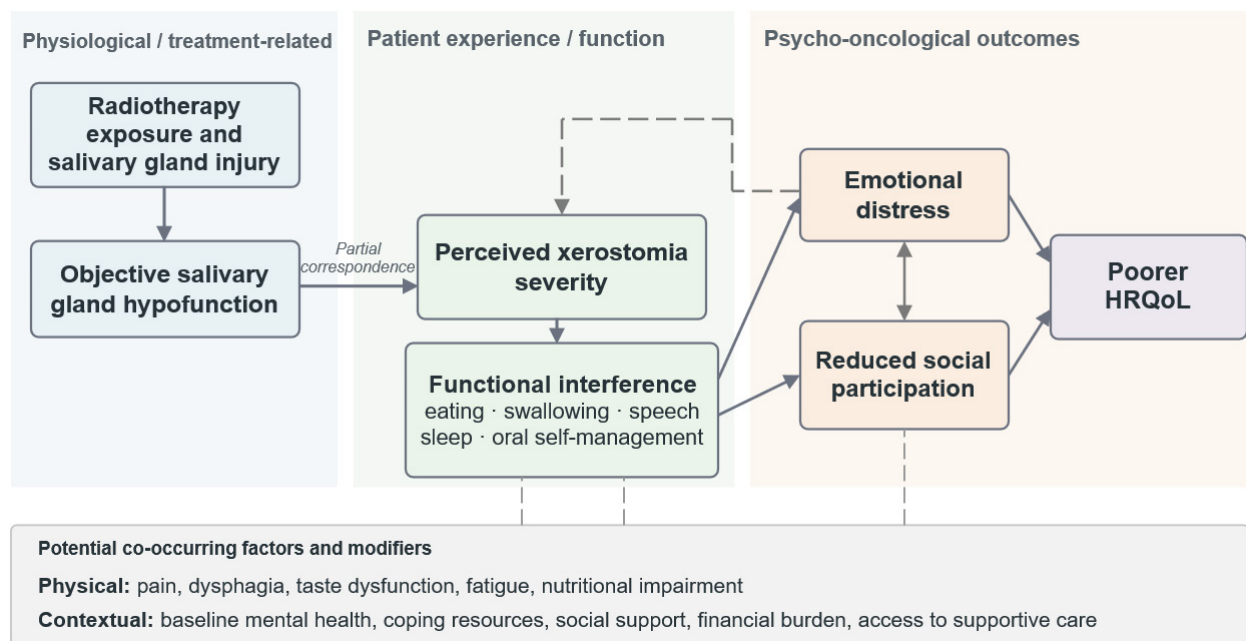


Figure 1. Hypothesised psycho-oncological framework linking radiation-induced xerostomia to functional, emotional, social, and quality-of-life outcomes among survivors of NPC.

Objective salivary gland hypofunction and perceived xerostomia are related but distinct constructs. Solid arrows indicate the principal hypothesised pathways; the bidirectional arrow indicates a potentially reciprocal relationship between emotional distress and social participation; and the dashed arrow indicates possible feedback from emotional distress to perceived xerostomia severity. The lower band identifies co-occurring physical and contextual factors that may influence several stages of the framework. The model is hypothesis-generating and does not represent established causal relationships.

3.3. Sleep, emotional distress, and unmet psychosocial needs

Nocturnal oral dryness may coexist with repeated waking, frequent water consumption, throat discomfort, and difficulty returning to sleep. In a symptom-enriched dental-clinic sample of 120 survivors of various head and neck cancers who had undergone radiotherapy, approximately 79% met the study criterion for hyposalivation, and 55% had both hyposalivation and sleep disturbance [36]. Because the cohort included several tumour sites and recruited patients with oral-dryness or sleep-related symptoms, these estimates represent indirect evidence and may not generalise to NPC survivors. Clinically, sleep disturbance should be assessed alongside pain, fatigue, anxiety, medication effects, nocturnal breathing problems,

and other treatment-related sequelae. Within the proposed framework, nocturnal dryness may contribute to daytime fatigue and reduced coping capacity, with possible consequences for social functioning.

Emotional distress is an important component of survivorship assessment. Compared with the general population, patients with head and neck cancer have been reported to experience higher levels of depression, anxiety, and fatigue, together with poorer quality of life [37]. In a prospective study of patients with NPC assessed before, during, and shortly after radiotherapy, symptom distress and depression were most pronounced towards the end of treatment and were associated with quality-of-life outcomes [38]. Although the follow-up period was relatively short, these findings support the integration of emotional-distress assessment into care during treatment and early survivorship. Longer-term studies are required to determine whether persistent xerostomia predicts subsequent emotional distress, whether pre-existing distress increases the perceived burden of xerostomia, or whether these relationships operate reciprocally over time.

Much of the available evidence is cross-sectional, while longitudinal evidence often comes from mixed head and neck cancer populations. In these cohorts, xerostomia forms part of an interacting physical, psychological, and social symptom burden [32]. Anxiety, depression, fear of cancer recurrence, and pre-existing psychosocial vulnerability may coexist with physical symptoms and influence subsequent distress [33,34]. Clinical symptoms and treatment-related factors may contribute to the same functional and quality-of-life outcomes [32,38]. Financial strain and unmet supportive care needs may further shape the burden experienced during survivorship [35,39]. The available evidence therefore shows association but does not establish xerostomia as an independent cause of depression, anxiety, or social withdrawal. Prospective studies should examine how xerostomia interacts with these factors and which functional or social pathways determine its importance for individual survivors.

NPC survivors may have unmet psychosocial needs that extend beyond the management of individual physical symptoms. These may include emotional support, clear and accessible information, assistance with social and occupational reintegration, nutritional and swallowing rehabilitation, and coordinated access to dental, psychological, and supportive care. In an NPC survivorship survey, greater overall late-symptom burden was associated with poorer HRQoL and greater unmet needs for symptom management [30]. In the broader head and neck cancer literature, supportive-care needs may persist into mid- to long-term survivorship [39]. Xerostomia may compound these needs by making eating, speaking, sleeping, and oral self-care more effortful and by increasing reliance on water, dietary modification, and other coping strategies. When these adaptations are difficult to manage in social settings, patients may experience embarrassment, avoid shared meals, or withdraw from valued activities. Assessment should therefore address not only xerostomia severity but also the activities that patients have stopped or become reluctant to undertake, the relationships or social roles affected, and the supportive-care needs that remain unmet.

Self-management burden represents a related but distinct survivorship issue, although direct evidence linking xerostomia to reduced adherence to anticancer treatment in NPC remains scarce. Treatment adherence in head and neck cancer is multifactorial and may be influenced by socioeconomic circumstances, disease characteristics, treatment complexity, cumulative toxicity, symptom burden, and

psychological factors [40]. Xerostomia may add to the practical burden of self-management through the need for frequent hydration, oral care, dietary adaptation, and symptom-relief measures, particularly when pain, dysphagia, fatigue, nutritional compromise, or emotional distress coexist. Current evidence therefore supports considering xerostomia as a potential contributor to symptom-management burden but does not establish it as an independent predictor of missed radiotherapy fractions, systemic-treatment discontinuation, or poorer oncological outcomes.

In a mixed head and neck cancer population, structured counselling improved adherence to preventive swallowing exercises during radiotherapy [41]. Although this outcome differs from completion of anticancer treatment, the study illustrates how structured behavioural support can strengthen adherence to symptom-management activities. These observations support the inclusion of sleep, emotional distress, unmet psychosocial needs, coping resources, and adherence to symptom-management activities within nurse-coordinated, multidisciplinary survivorship assessment, without implying that xerostomia independently determines completion of anticancer treatment.

3.4. Patient-reported outcome measures and their clinical value

PROMs are particularly important in the assessment of xerostomia because subjective oral dryness cannot be reliably inferred from salivary flow measurements or clinician-rated toxicity alone. The limited proportion of patient-reported functional impairment explained by objective salivary and oral measurements reinforces the need to assess both physiological dysfunction and the patient's lived experience [29]. PROMs can capture symptom severity, interference with eating and speaking, sleep disturbance, emotional distress, social participation, and changes over time that may otherwise remain unrecognised during routine clinical consultations. Within the proposed framework, PROMs may be particularly informative for examining the pathways through which physiological dysfunction becomes subjectively and socially consequential.

No single instrument captures all relevant dimensions. Xerostomia-specific instruments, such as the Xerostomia Questionnaire, provide a focused assessment of oral dryness. The Chinese version of the Xerostomia Questionnaire (XQ-C) has demonstrated acceptable reliability and validity in patients with NPC receiving radiotherapy [42]. Broader head and neck cancer symptom inventories and multidimensional quality-of-life instruments can additionally assess swallowing, nutrition, fatigue, sleep, emotional distress, and social functioning. For example, the Chinese versions of the MD Anderson Symptom Inventory–Head and Neck Module (MDASI-HN) and the Functional Assessment of Cancer Therapy–Head and Neck (FACT-H&N) were used to characterise late symptom burden and quality of life in NPC survivors [30]. Combining a xerostomia-specific PROM with a broader head and neck cancer or HRQoL instrument is therefore likely to be more informative than relying on either approach alone.

Where feasible, PROMs should be collected longitudinally at baseline, during treatment, at the completion of radiotherapy, and throughout survivorship follow-up. A high or worsening xerostomia score should trigger targeted clinical assessment and, where appropriate, referral for oral, nutritional, swallowing, sleep, or psychosocial support. Depending on the associated difficulties, subsequent evaluation may include salivary gland function, oral and dental health, swallowing safety, nutritional intake, sleep, emotional distress, social participation, financial difficulties, and access to supportive care. Repeated PROM assessment may also help clinicians distinguish persistent symptoms from emerging late effects and identify patients who require referral to dental, nutritional, speech and swallowing, sleep, or psychosocial services.

Questions concerning avoided activities, changes in family or social roles, confidence in shared eating, available support, and unmet supportive-care needs may provide clinically relevant information that is not captured by symptom-intensity scores alone.

Electronic PROM monitoring may facilitate systematic symptom detection. In a prospective randomised trial involving patients with head and neck cancer undergoing radiotherapy, daily app-based symptom monitoring was feasible, increased the reporting of head and neck symptoms, and improved selected aspects of patient satisfaction [43]. These findings support the use of electronic PROMs to improve symptom detection and patient–clinician communication, while evidence for effects on treatment adherence, survival, and long-term NPC-specific outcomes remains insufficient.

The proposed framework generates several testable hypotheses. First, perceived xerostomia severity may mediate part of the association between radiation dose to the salivary glands or post-treatment salivary hypofunction and social-eating avoidance. Second, functional interference and nocturnal symptom burden may act as sequential mediators of the association between xerostomia severity and emotional distress or poorer HRQoL. Third, social support, coping self-efficacy, baseline mental health, and access to supportive care may moderate the association between xerostomia and social participation. Fourth, within-person reductions in xerostomia severity may predict subsequent improvements in social participation and HRQoL after adjustment for pain, dysphagia, taste dysfunction, fatigue, and nutritional impairment. Testing these hypotheses will require prospective longitudinal studies incorporating repeated xerostomia-specific PROMs, objective measures of salivary function, psychosocial assessments, and prespecified mediation or moderation analyses.

Xerostomia assessment in NPC survivorship should integrate subjective dryness, salivary function, eating and swallowing, sleep, emotional well-being, social participation, nutrition, and barriers to care. Longitudinal studies combining PROMs with objective salivary and psychosocial measures could test the proposed pathways and identify modifiable targets for supportive care.

4. Pathophysiology and residual salivary function

Saliva supports oral comfort, speech, taste, swallowing, food intake, and protection against oral infection and dental disease. The relative contributions of individual salivary glands differ between resting and stimulated conditions, while gland-specific radiation exposure may influence the pattern and persistence of xerostomia [44,45].

Radiotherapy can damage saliva-producing cells and impair tissue repair [46,47]. Microvascular injury may further compromise glandular function [48]. Chronic inflammation and fibrosis may then contribute to persistent loss of salivary function [7,49]. For patients, the clinically important consequence is the extent of residual salivary secretory function, because this influences oral comfort and the likelihood of benefit from stimulation-based approaches.

Because the parotid glands are particularly vulnerable to radiation [50], higher radiation exposure is associated with poorer long-term recovery of salivary function and persistent xerostomia [51]. However, changes in gland size or measured salivary flow do not necessarily parallel patient-reported dryness [29,52]. Recovery also varies with pretreatment gland anatomy and gland-specific radiation exposure [45,53]. Assessment should therefore consider both residual salivary secretory reserve and patient-reported symptoms. Together, these measures inform evaluation of symptom burden, daily functioning, and suitability for gustatory interventions.

5. Patient-centred assessment framework

Assessment should centre on the patient's experience of dryness and its effects on eating, swallowing, speech, sleep, and social participation, while integrating clinical oral findings and measures of salivary function [16]. Clinician-rated toxicity and OHRQoL measures provide complementary information, because no single approach captures the full physiological, symptomatic, functional, and psychosocial burden of xerostomia [18,29]. These assessment domains and their complementary roles are summarised in **Table 1**.

Table 1. Patient-centred framework for assessing radiation-induced xerostomia and salivary gland hypofunction.

Domain	Tool or measure	Clinical question addressed	Strength	Limitation and recommended use
Subjective xerostomia severity	XQ-C [42]	How severe is the patient's xerostomia, and how does it change over time?	Chinese-language reliability and validity reported in patients with NPC receiving radiotherapy	Does not measure objective salivary function; use the same scoring algorithm longitudinally
Rapid symptom intensity	VAS or 0–10 numerical rating scale	How dry does the patient's mouth feel at present?	Brief and suitable for frequent monitoring	Single-item measure; does not capture regional or functional consequences
Regional subjective dryness	RODI [54]	Where in the mouth is dryness most troublesome?	Identifies site-specific perceived dryness	Evidence is mainly derived from heterogeneous dry-mouth populations
Clinician-rated toxicity	RTOG/EORTC criteria [55]	How severe is treatment-related xerostomia according to standard clinician-rated criteria?	Facilitates standardised oncology toxicity reporting	May underestimate patient-experienced burden; combine with a PROM
Clinical oral findings	Standardised oral examination or CODS [54]	What observable clinical signs of oral dryness are present?	Identifies clinical dryness and oral complications	Requires examiner training and calibration
Salivary secretory function	Unstimulated and stimulated whole saliva [18,44]	How much salivary secretion remains at rest and after stimulation?	Provides objective resting and residual-response measures	Sensitive to collection conditions and not equivalent to subjective xerostomia
OHRQoL and multidimensional impact	OHIP-14, EORTC QLQ-H&N35, or validated head and neck cancer PROMs [28,30]	How does xerostomia affect daily functioning, social participation, and well-being?	Captures oral function, eating, pain, social participation, and psychosocial impact	Does not measure salivary physiology; use a validated language version and follow its scoring manual

Abbreviations: CODS, Clinical Oral Dryness Score; EORTC QLQ-H&N35, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Head and Neck 35; NPC, nasopharyngeal carcinoma; OHIP-14, Oral Health Impact Profile-14; OHRQoL, oral health-related quality of life; PROM, patient-reported outcome measure; RODI, Regional Oral Dryness Inventory; RTOG/EORTC, Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer; VAS, visual analogue scale; XQ-C, Chinese version of the Xerostomia Questionnaire.

5.1. Subjective xerostomia measures

Xerostomia should be assessed directly through patient report. The XQ-C has demonstrated acceptable reliability and validity in Chinese patients with NPC receiving radiotherapy and can support longitudinal monitoring when applied consistently [42]. A visual analogue scale (VAS) or 0–10 numerical rating scale allows rapid symptom monitoring, whereas the Regional Oral Dryness Inventory captures the distribution of perceived dryness across oral regions [54]. Whichever instrument is selected, serial assessments should use it consistently and should also consider how dryness affects everyday activities.

5.2. Clinician-rated toxicity

Clinician-rated toxicity scales standardise oncology reporting but may overlook night-time dryness, dependence on water, and difficulty eating socially [55]. They should therefore complement, rather than replace, a xerostomia-specific PROM.

5.3. Clinical oral examination

Clinical oral examination should prioritise findings that affect comfort, oral intake, dental risk, and suitability for topical treatment, including mucosal dryness or injury, altered salivary consistency, candidiasis, caries or erosion, taste disturbance, and swallowing concerns. A structured measure such as the Clinical Oral Dryness Score (CODS) can support consistent documentation [16,54].

5.4. Objective salivary flow assessment

Unstimulated salivary flow reflects basal secretion, whereas stimulated flow provides an estimate of residual salivary secretory reserve [18,44]. Stimulated flow is therefore particularly relevant when considering gustatory interventions. Measurements should be collected under standardised conditions and interpreted alongside patient-reported benefit, because increased salivary flow does not necessarily translate into clinically meaningful symptom relief [29].

5.5. OHRQoL and multidimensional patient-reported outcomes

OHRQoL measures capture the effects of xerostomia on eating, speech, oral comfort, and daily functioning that symptom severity alone may miss [28,56]. Broader head and neck cancer PROMs can additionally assess pain, sleep, social participation, and emotional well-being [30]. Future trials of gustatory interventions should therefore combine a xerostomia-specific PROM with measures of salivary function, oral safety, and patient-centred functional outcomes.

6. Management framework: from prevention to patient-centred symptom relief

Management can be organised by therapeutic purpose into five categories: prevention during radiotherapy planning and preservation of salivary function; treatment of established salivary gland hypofunction; symptomatic relief of subjective xerostomia; oral, dental, nutritional, and swallowing support; and complementary or emerging interventions. These categories distinguish strategies that prevent tissue injury, stimulate residual glandular tissue, wet and lubricate the oral cavity, or reduce secondary complications [17,18].

6.1. Prevention during radiotherapy planning and preservation of salivary function

Prevention should begin during radiotherapy planning, to limit radiation exposure to salivary tissue without compromising tumour coverage [18,20].

Preserving functional glandular tissue increases the likelihood of maintaining useful salivary function after treatment and may reduce subsequent symptom burden [4,51].

In an NPC trial, a refined parotid-sparing approach was associated with a lower incidence of xerostomia and better preservation of salivary flow, although the between-group difference in Xerostomia Questionnaire scores was not statistically significant [4]. Such objective gains should also be evaluated according to whether they translate into meaningful improvements in comfort and daily functioning.

Submandibular gland transfer may preserve salivary function in carefully selected patients [57,58]. However, the need for surgery, restricted anatomical and oncological eligibility, and uncertain additional benefit alongside modern radiotherapy limit its routine use. Evidence is likewise insufficient to regard the pharmacological and radioprotective strategies evaluated to date as established preventive standards [18].

6.2. Treatment of established salivary gland hypofunction

After radiotherapy, treatment of established salivary gland hypofunction aims to stimulate secretion from remaining functional tissue. Systemic sialogogues, including pilocarpine and cevimeline, may benefit selected patients who retain residual secretory responsiveness [17,18,59]. Non-pharmacological options include sugar-free chewing gum or non-erosive lozenges, gland massage, and gustatory stimulation [17,18]. These interventions do not regenerate permanently damaged glandular tissue, and increased salivary flow does not necessarily result in meaningful relief of dryness [29].

Treatment choice should reflect comorbidities, concomitant medicines, contraindications, anticipated adverse effects, and patient preferences regarding continued treatment. Cholinergic effects such as sweating, urinary frequency, gastrointestinal discomfort, and cardiovascular or respiratory concerns may limit tolerability and long-term acceptability [17,18]. Response assessment should include both salivary flow and patient-reported symptoms.

6.3. Symptomatic relief of subjective xerostomia

When residual salivary function is limited or stimulation is ineffective, management should prioritise artificial wetting and lubrication of the oral and labial surfaces. Saliva substitutes, oral moisturising gels, rinses, sprays, and other topical lubricants may provide temporary relief of oral dryness and improve comfort during speaking, eating, or sleep [17,18,60,61]. These products function as symptomatic supportive measures rather than treatments that restore salivary gland function.

Product selection should consider duration of relief, viscosity, flavour, ease of application, nocturnal symptoms, swallowing ability, mucosal sensitivity, dentition, and patient preference. Frequent sips of water may provide short-term comfort, but the relief is usually brief and does not reproduce the lubricating, buffering, antimicrobial, or remineralising properties of natural saliva. Counselling should set realistic expectations about the purpose and likely duration of symptomatic relief.

The distinction between salivary stimulation and artificial wetting is particularly relevant to the later evaluation of topical gustatory strategies. An acidic topical formulation intended to stimulate residual secretion should not be categorised as a saliva substitute, and its suitability depends on residual salivary secretory reserve, mucosal tolerance, taste acceptance, and oral safety.

6.4. Oral, dental, nutritional, and swallowing support

Management should also address the secondary oral and functional consequences

of salivary dysfunction. Supportive care should include individualised oral-hygiene education, fluoride-based caries prevention where appropriate, regular dental surveillance, and assessment for candidiasis, mucosal injury, dental caries or erosion, periodontal disease, and other radiation-related oral complications [6,17,18]. Dietary and medication review may help identify cariogenic foods, foods that irritate the oral mucosa, inadequate hydration, and concomitant medicines that may aggravate oral dryness.

Patients experiencing difficulty with mastication, bolus formation, swallowing, or maintaining adequate oral intake should receive individualised dietary advice and, where indicated, referral for nutritional and swallowing assessment. Evidence derived mainly from broader xerostomia populations suggests that adaptation of food texture and moisture content and the use of accompanying liquids may improve eating comfort; however, dietary and fluid modification should be guided by nutritional adequacy, mucosal tolerance, dental risk, and swallowing safety rather than xerostomia severity alone [62]. Persistent or uncontrolled pain, suspected aspiration, progressive weight loss, recurrent chest infection, or inability to maintain adequate oral intake should prompt multidisciplinary evaluation [63].

Nurse-led follow-up may include monitoring xerostomia symptoms and oral intake, reinforcing oral self-care and correct product use, supporting adherence to fluoride-based dental-prevention measures, and coordinating timely referral to dental, nutritional, speech and swallowing, sleep, or psychosocial services [63]. Where sleep disturbance or psychosocial distress is identified, referral should be based on a broader survivorship assessment rather than on an assumption that xerostomia is the sole cause [30,39]. Nursing follow-up is one component of multidisciplinary survivorship care. The effects of individual xerostomia interventions on nutritional, swallowing, sleep, and psychosocial outcomes should nevertheless be evaluated separately.

6.5. Complementary and emerging interventions

Current guidelines indicate that acupuncture may be offered during or after radiotherapy and that transcutaneous electrical stimulation may be offered after radiotherapy, although the certainty and applicability of the evidence vary [18]. Evidence for other non-pharmacological approaches, including photobiomodulation, remains difficult to interpret because studies use heterogeneous protocols and patient populations [64]. Decisions should therefore take account of patient preference, treatment burden, local expertise, and safety.

Malic acid is best classified as a candidate topical sialogogue that acts through gustatory stimulation and depends on residual salivary secretory reserve. It is distinct from preventive radiotherapy planning, regenerative therapies, and saliva substitutes. Section 7 examines its mechanistic rationale, indirect clinical evidence, eligible population, and oral safety requirements (**Table 2**).

Table 2. Comparison of management strategies for radiation-induced xerostomia and salivary gland hypofunction.

Management category	Representative strategies	What the approach aims to achieve	Who may benefit and when	Principal limitations
Prevention during radiotherapy planning	Salivary gland-sparing IMRT; dose and volume optimisation	Reduce radiation exposure and preserve salivary tissue before injury occurs	Before and during radiotherapy	Must not compromise tumour coverage; anatomical feasibility varies

Continuation Table:

Management category	Representative strategies	What the approach aims to achieve	Who may benefit and when	Principal limitations
Pre-radiotherapy function preservation	Submandibular gland transfer	Preserve functioning glandular tissue outside the radiation field	Highly selected patients before radiotherapy	Surgical morbidity; uncertain incremental benefit with modern IMRT
Treatment of established hypofunction	Pilocarpine, cevimeline, mechanical or gustatory stimulation	Increase secretion from residual functional tissue	Measurable residual secretory reserve	Adverse effects, contraindications, variable response; does not regenerate destroyed tissue
Symptomatic relief	Saliva substitutes, moisturising gels, rinses, sprays, topical lubricants	Artificially wet and lubricate oral surfaces	Limited residual function or insufficient response to stimulation	Usually temporary relief; does not restore gland function
Oral and dental supportive care	Oral hygiene, fluoride prevention, dental surveillance, candidiasis and caries management	Prevent secondary oral complications	Required across severity levels	Requires sustained self-management and access to dental care
Nutritional and swallowing support	Dietary modification, nutritional counselling, swallowing assessment	Preserve oral intake and reduce functional consequences	Eating difficulty, dysphagia, weight loss, or aspiration concern	Requires multidisciplinary assessment
Complementary or emerging interventions	Acupuncture, TENS, photobiomodulation, selected traditional medicine approaches	Prevention, stimulation, or symptom relief depending on modality	Selected patients and locally available programmes	Heterogeneous protocols and evidence; indications remain incompletely defined

Abbreviations: IMRT, intensity-modulated radiotherapy; TENS, transcutaneous electrical nerve stimulation.

7. Emerging candidate interventions: malic acid as a case study

Malic acid is a candidate topical sialogogue for radiation-induced xerostomia. Its biological rationale is plausible, but the clinical evidence is indirect and comes predominantly from non-cancer populations. For NPC survivors, it remains an investigational symptom-directed strategy rather than an established component of post-radiotherapy care.

7.1. Current evidence

Taste dysfunction and xerostomia frequently coexist after head and neck radiotherapy, reflecting salivary gland injury and disruption of the oral environment. When viable glandular tissue remains, sour stimuli may augment salivary secretion through gustatory–salivary reflex pathways. In 59 healthy individuals, Satoh-Kuriwada et al. [65] observed dose-dependent secretion from the labial minor salivary glands following application of the five basic taste stimuli, with sour and umami stimuli eliciting comparatively greater responses.

Responsiveness to gustatory stimulation has also been observed in a murine bioengineered salivary gland model [66], while citric acid has been employed as a physiological challenge to assess salivary flow and composition in patients with myasthenia gravis [67]. Although these findings are mechanistic and cannot establish therapeutic efficacy in irradiated NPC survivors, they support the plausibility of an acid-evoked salivary response when residual functional tissue is present.

Clinical evidence remains limited and derives entirely from non-NPC populations. Short-term trials have evaluated 1% malic acid spray in antihypertensive drug-induced xerostomia [68] and type 2 diabetes-associated xerostomia [69]. A further spray trial enrolled a heterogeneous xerostomia population [70]. Xylitol–malic acid tablets were evaluated separately in a small pilot study of patients with gastro-oesophageal reflux disease [71]. A meta-analysis of five studies involving 244 participants reported short-term reductions in perceived dryness and increases in unstimulated or stimulated salivary flow [72]. However, differences in study populations, formulations, comparators, and outcome measures, together with short follow-up periods and co-formulation with xylitol or fluoride, limit the reported effects specifically. No study identified in this review evaluated malic acid specifically in post-radiotherapy NPC survivors. The available findings therefore support population-specific proof-of-concept evaluation but do not support routine clinical use (Table 3).

Table 3. Clinical studies of malic acid-containing interventions for xerostomia and their applicability to post-radiotherapy NPC survivors.

Study and population	Design, formulation, comparator, and duration	Patient-reported outcomes	Salivary and safety outcomes	Applicability and limitations for NPC survivors
Gomez-Moreno et al. [68]; antihypertensive-associated xerostomia, n = 45	Double-blind randomised trial; spray containing 1% malic acid, xylitol, and fluoride versus placebo; up to eight applications per day for 2 weeks	Patient-reported xerostomia improved in the intervention group	Unstimulated and stimulated salivary flow increased. The short observation period did not permit evaluation of cumulative dental or mucosal effects	Non-cancer, medication-related xerostomia; small sample and short duration. Co-formulation prevents attribution of efficacy or tolerability to malic acid alone
Niklander et al. [70]; heterogeneous xerostomia, 70 enrolled and 60 completed	Double-blind randomised trial; spray containing 1% malic acid, xylitol, and fluoride versus vehicle; 2 weeks	OHRQoL improved within the intervention group	Unstimulated salivary flow improved within the intervention group. Long-term dental safety was not evaluated	Patients with previous head and neck radiotherapy were excluded. Attrition, short follow-up, and co-formulation limit applicability to NPC survivors
Muhammed et al. [69]; type 2 diabetes-associated xerostomia, n = 52	Double-blind randomised controlled trial; 1% L-malic acid spray versus placebo; 2-week treatment with follow-up to week 4	Xerostomia scores improved in the intervention group	Unstimulated salivary flow increased; no adverse events were reported during the study period	Non-cancer population with a different mechanism of salivary dysfunction. Follow-up was insufficient to assess cumulative dental or mucosal safety

Continuation Table:

Study and population	Design, formulation, comparator, and duration	Patient-reported outcomes	Salivary and safety outcomes	Applicability and limitations for NPC survivors
Liu et al. [72]; systematic review and meta-analysis	Five studies involving 244 participants; primarily short-term trials of 1% malic acid-containing sprays versus placebo or vehicle	Pooled analyses favoured malic acid-containing interventions for patient-reported dryness	Pooled analyses favoured the interventions for unstimulated and stimulated salivary flow. Long-term safety evidence was limited	Small and heterogeneous evidence base involving different xerostomia populations and formulations; no dedicated evidence in irradiated NPC survivors
Sanchez-Blanco et al. [71]; gastro-oesophageal reflux disease, n = 14	Open-label randomised pilot study; xylitol–malic acid tablets plus omeprazole versus omeprazole alone; 6 months	Lower patient-reported xerostomia was observed in the combination group	Greater salivary buffering capacity was reported. The study was not designed to establish the independent or long-term oral safety of malic acid	Very small pilot study; compound intervention, different disease context, and different delivery formulation limit transferability to post-radiotherapy NPC survivors

Abbreviations: NPC, nasopharyngeal carcinoma; OHRQoL, oral health-related quality of life; n, sample size.

The studies provide preliminary evidence that some malic acid-containing formulations may confer short-term symptomatic or physiological benefit in selected xerostomia populations. They do not establish whether malic acid itself accounts for the reported effects, whether benefits persist beyond short treatment periods, or whether similar effects would occur after irradiation of the salivary glands.

7.2. Applicability and oral safety in npc survivors

Malic acid (2-hydroxybutanedioic acid) is a naturally occurring dicarboxylic acid used as an acidulant, flavour modifier, and pH-adjusting agent [73]. Its use in food products does not establish therapeutic effectiveness or long-term safety when it is repeatedly applied to irradiated oral tissues. Oral safety should therefore be assessed in relation to the complete formulation and exposure pattern rather than to malic acid concentration alone. Relevant formulation and administration variables include pH and titratable acidity, contact time, administration frequency, delivery format, and the presence of protective or remineralising components such as xylitol or fluoride.

Dental erosion is multifactorial; acidic oral pH, reduced salivary flow, systemic conditions, dietary acid exposure, and oral-hygiene practices may collectively create an erosion-prone oral environment. Saliva mitigates this risk by diluting and clearing acids, supporting acquired pellicle formation, and supplying substrates for remineralisation [74]. These protective mechanisms may be impaired following irradiation of the salivary glands. No adverse events were reported during the short diabetes-associated study [69]. However, the antihypertensive drug-induced and heterogeneous xerostomia trials were also brief and did not assess cumulative dental or mucosal effects [68,70]. These studies therefore cannot establish the long-term oral safety of repeated malic acid exposure. Similarly, the small pilot study of xylitol–malic acid tablets in patients with gastro-oesophageal reflux disease cannot establish the long-term safety attributable specifically to malic acid [71].

The hypothesised clinical relevance of malic acid would be greatest in NPC survivors with clinically meaningful xerostomia and measurable residual salivary responsiveness. The 2024 MASCC/ISOO Clinical Practice Statement distinguishes stimulation of residual salivary tissue from artificial wetting of oral and labial surfaces [17]. Variation in responses to physical stimulation following head and neck radiotherapy, and observed responses to masticatory, acidic, or olfactory stimulation in chronic dry mouth [75,76].

Clinical evaluation should determine whether any increase in salivary flow is accompanied by patient-perceived and clinically meaningful symptom relief. The secondary domains include OHRQoL, eating and swallowing, speech, nocturnal symptoms, social eating, emotional distress, treatment acceptability, adherence, and dental and mucosal safety.

7.3. Nurse-coordinated support, health literacy, and patient education

Malic acid should be investigated as one component of comprehensive NPC survivorship care rather than as a stand-alone treatment pathway. Until efficacy and longer-term oral safety are established in NPC survivors, evaluation should remain within trials or feasibility studies conducted within a multidisciplinary framework with access to appropriate dental, oral medicine, swallowing, and supportive care expertise.

Within these studies, nurses could coordinate the collection of patient-reported data, patient education, adherence support, adverse-event monitoring, and multidisciplinary referral. Baseline assessment should document xerostomia severity and its effects on daily functioning, including eating, swallowing, speech, sleep, social eating, emotional well-being, and OHRQoL. A validated instrument such as the XQ-C may provide a structured measure of subjective xerostomia severity [42], while practical barriers to self-administration and broader supportive-care needs should also be identified.

Patient education should be tailored to individual health literacy, preferred language, cultural context, and capacity for self-management with plain-language written or visual instructions. Follow-up should assess perceived symptom relief, functional benefit, treatment acceptability, adherence, use of rescue measures, oral adverse effects, and changes in swallowing safety. Problems requiring dental care, nutritional support, swallowing rehabilitation, psychosocial support, or sleep assessment should prompt appropriate multidisciplinary referral.

7.4. Prioritised future research agenda

Future research should address two priorities:

1 (Randomised Trial): In NPC survivors with xerostomia, does a malic acid-containing product improve a patient-reported outcome and improve salivary flow compared with a control group? Can these benefits be achieved without unacceptable dental or mucosal harm?

2 (Longitudinal Observational Safety Study): What are the cumulative dental and mucosal effects of repeated or longer-term exposure, including dental erosion, caries, dentine hypersensitivity, mucosal irritation, and changes in oral tolerance?

8. Conclusion

Radiation-induced xerostomia remains an important survivorship problem after NPC treatment. Because xerostomia and salivary gland hypofunction are related but not interchangeable, follow-up should combine patient-reported symptoms, salivary

testing, and oral examination. Assessment should also address eating, speech, sleep, social participation, emotional distress, and dental complications, while recognising the effects of coexisting symptoms and treatment toxicity.

Malic acid is biologically plausible as a topical gustatory stimulant when residual salivary tissue remains. Current clinical evidence, however, comes from small, short-term studies in non-cancer populations. Heterogeneous formulations and incomplete oral-safety data limit extrapolation of these findings to NPC survivors.

The next step is a randomised controlled trial with clear eligibility criteria and longitudinal dental and mucosal monitoring. Such a trial would determine whether increased salivary secretion produces symptomatic and functional benefits that persist over time.

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