



## Recent Update on Management of Xerostomia: A Narrative Review

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### ABSTRACT

**Background:** Xerostomia is a multifactorial condition with significant consequences for oral function and quality of life. While conventional diagnostic and treatment strategies remain essential, rapid advances in salivary diagnostics, imaging technologies, artificial intelligence, and regenerative therapies have expanded the clinical landscape. However, the clinical utility and translational readiness of these emerging approaches remain incompletely synthesised.

**Objectives:** To review conventional and emerging diagnostic and therapeutic approaches for xerostomia and evaluate their clinical utility, translational readiness, and limitations.

**Methods:** A narrative literature review was conducted using Google Scholar, MEDLINE, and PubMed databases. English-language publications from 2000 to 2025 were retrieved using combinations of keywords related to xerostomia, diagnosis, management, biomarkers, imaging, and emerging therapies. Clinical studies, systematic reviews, meta-analyses, and relevant narrative reviews were included.

**Results:** Conventional diagnostic methods, including symptom assessment, clinical examination, and sialometry, remain essential but have limitations. Emerging approaches such as salivary biomarkers, advanced imaging, wearable sensors, and artificial intelligence show improved diagnostic potential. Traditional treatments focus on symptom relief and salivary stimulation, while novel therapies—including acupuncture, low-level laser therapy, intraoral devices, and regenerative approaches—demonstrate promising outcomes. However, their clinical application is limited by cost, accessibility, and insufficient validation.

**Conclusion:** Conventional and emerging approaches should be viewed as complementary rather than competing strategies in xerostomia management. Although novel technologies offer substantial promise for improving diagnostic precision and therapeutic outcomes, further clinical validation and long-term evidence are required before widespread integration into routine practice.

**Keywords:** Xerostomia; Hyposalivation; Salivary gland dysfunction; Diagnosis; Salivary biomarkers; Emerging therapies

### INTRODUCTION

Xerostomia is a common clinical complaint encountered in dental practice and refers to the subjective sensation of oral dryness.<sup>1</sup> Although both conditions are interrelated, xerostomia does not necessarily indicate hyposalivation, which is an objective reduction in salivary flow rate.<sup>1</sup> The feeling of xerostomia often results when saliva production is reduced by 30 to 50 per cent.<sup>2</sup>

Saliva plays significant roles in oral lubrication, taste perception, chewing, swallowing, digestion, and protection against infections.<sup>3, 4</sup> Consequently, reduced salivary secretion can significantly impair oral health and negatively affect quality of life.<sup>5</sup>

The prevalence of xerostomia varies across different populations, with recent global estimates ranging from 22% to 30%.<sup>6</sup> Studies have revealed higher prevalence amongst the older age group and the female gender.<sup>7-9</sup> This age-related increased predisposition is attributed to polypharmacy, systemic diseases, and age-related physiological changes.<sup>9, 10</sup>

Factors implicated in the development of xerostomia include medication use,<sup>11</sup> head and neck radiotherapy,<sup>12</sup> systemic diseases such as diabetes mellitus, and autoimmune disorders including Sjögren's syndrome (SS), amongst others.<sup>13</sup> Patients with xerostomia face increased risk of dental caries, oral candidiasis, mucosal discomfort, and difficulties with speech, swallowing, and taste.<sup>6</sup> Further details on causes can be found in Table 1.



**Table 1: Causes of Xerostomia**

Category	Specific Causes	Notes / Examples	Clinical Relevance
<b>Medications</b>	Anticholinergics, antihistamines, antidepressants, diuretics, antihypertensives	Many commonly prescribed drugs reduce salivary flow rate; e.g., atropine, SSRIs, furosemide	Dose-dependent; often reversible
<b>Systemic diseases</b>	Diabetes mellitus, Sjögren's syndrome, rheumatoid arthritis, HIV/AIDS	Autoimmune or metabolic disorders impair salivary gland function	Requires treatment of underlying condition
<b>Radiation / chemotherapy</b>	Head and neck radiotherapy, chemotherapy	Radiation can directly damage salivary glands; chemotherapy may reduce secretion temporarily	Often irreversible; dose-related
<b>Lifestyle factors</b>	Tobacco use, alcohol consumption, dehydration	Smoking, alcohol, and insufficient fluid intake worsen dryness	Modifiable
<b>Local / other causes</b>	Mouth breathing, salivary gland obstruction, oral infections	Structural or local issues can impede saliva flow; e.g., sialolithiasis, candidiasis	Often treatable

The multifactorial aetiology and varied presentation can make diagnosis and management challenging.<sup>14</sup> Accurate diagnosis of these conditions is germane to providing adequate and comprehensive treatment for affected patients.<sup>5, 14</sup> Conventional diagnostic approaches include patient-reported symptom assessment, salivary flow rate measurement, and clinical examination of the oral cavity. Management strategies traditionally focus on treating underlying causes, stimulating salivary secretion, and providing symptomatic relief using salivary substitutes and pharmacological agents.

In recent years, advances in biomedical research have led to the development of emerging diagnostic and therapeutic strategies aimed at improving the evaluation and management of xerostomia. These include salivary biomarker analysis, advanced imaging techniques, wearable saliva monitoring devices, and regenerative medicine approaches such as stem cell therapy and gene therapy. These innovations have the potential to enhance early diagnosis and provide more effective treatment options for patients suffering from xerostomia.

Despite growing research on xerostomia, existing literature frequently addresses either diagnostic methods or therapeutic interventions in isolation, with limited emphasis on integrating conventional approaches with rapidly emerging technologies. Recent advances in salivary biomarkers, artificial intelligence, wearable monitoring systems, regenerative medicine, and minimally invasive therapies have considerably expanded the diagnostic and therapeutic landscape; however, their translational readiness, clinical applicability, and limitations remain incompletely synthesised. Furthermore, clinicians (particularly in resource-limited settings) require practical guidance regarding the comparative strengths, feasibility, and evidence maturity of available approaches.

Accordingly, this narrative review was undertaken to provide a comprehensive and clinically oriented synthesis of conventional and emerging diagnostic and therapeutic strategies for xerostomia, highlighting their utility, limitations, and future translational potential. The review follows SANRA (Scale for the Assessment of Narrative Review Articles) guidelines for reporting transparency.

## METHODS

### Search Strategy

A comprehensive literature search was conducted in October 2025 using electronic databases including Google Scholar, MEDLINE, and PubMed. The search terms combined included MeSH terms and free-text keywords with Boolean operators:



("xerostomia" OR "hyposalivation" OR "dry mouth") AND ("diagnosis" OR "management" OR "treatment")

("xerostomia" OR "hyposalivation") AND ("biomarkers" OR "salivary diagnostics" OR "imaging")

("xerostomia" OR "hyposalivation") AND ("acupuncture" OR "laser therapy" OR "stem cells" OR "gene therapy")

Additional articles were identified through manual screening of reference lists of relevant publications.

### **Inclusion and Exclusion Criteria**

Articles published in English between 2000 and 2025 were considered. Human studies evaluating diagnostic methods, therapeutic interventions, salivary biomarkers, imaging modalities, or management strategies for xerostomia and hyposalivation were included. The types of studies considered included clinical trials, observational studies, systematic reviews, meta-analyses, and narrative reviews. Exclusion criteria included animal studies, case reports (single case, <5 patients), conference abstracts without full text, and non-English publications.

### **Study Selection**

Two reviewers (OF, FE) independently screened titles and abstracts. Full texts of potentially relevant articles were retrieved and assessed. Disagreements were resolved by consensus or by a third reviewer (EO). Being designed as a narrative review, formal quantitative synthesis and structured risk-of-bias assessment were not undertaken. Reference lists of included articles were hand-searched for additional relevant publications.

### **Synthesis Approach**

Findings were organised thematically into diagnostic methods (conventional and emerging) and therapeutic approaches (conventional and emerging). Emerging technologies were stratified by translational readiness using an evidence maturity framework (Table 2).

## **Conventional and Emerging Diagnostic Measures**

### **I. Conventional Diagnostic Measures**

Accurate diagnosis combines subjective assessment with objective clinical findings. This assists the clinician in identifying the cause—autoimmune disease, drugs, or iatrogenic—and guides treatment and interventions for individual patients.

Conventional diagnostic methods are first-line and invaluable and form the basis for novel diagnostics. However, they have some limitations, which include variable reproducibility and poor interchangeability.<sup>15</sup> Methodological details and validation evidence also differ, fostering these limitations.

Many papers and research documentations have emphasised the use of conventional diagnostic measures, which include history, clinical examination, use of questionnaires, sialometry, and targeted imaging.

#### **Clinical assessment**

Clinical assessment of xerostomia encompasses both subjective symptom evaluation and objective clinical examination. Subjective assessment includes comprehensive history taking.<sup>16, 17</sup>

A comprehensive patient history is the cornerstone of diagnosis. This includes the patient's biodata and symptomatology, dental history, medical history, medication history, family and social history, and systemic review. These give a holistic assessment of inherent causes linked to the individual. Symptoms reported often include oral dryness, dry lips or throat, difficulty chewing foods, dysphagia, altered taste, speech impairment, and oral burning sensations. Patients may also report altered taste and a feeling of burning sensation in the mouth. In addition, there may be increased predisposition to dental caries and periodontal complaints.<sup>17-19</sup> Furthermore, medical history of autoimmune diseases such as SS, diabetes, and cancer chemotherapy and radiotherapy is very crucial, as the use of medications in managing systemic diseases contributes immensely to xerostomia.<sup>20</sup> Drug classes such as antihypertensives, antidepressants, anticholinergics, and



antihistamines are commonly implicated.<sup>21, 22</sup> Eliciting lifestyle risk factors such as smoking, alcohol use, and habits such as mouth-breathing and inadequate water intake is also very important. Another advantage of comprehensive history taking is helping to delineate systemic or iatrogenic causes of xerostomia and guiding the clinician on appropriate investigations.

Validated questionnaires—including the Xerostomia Inventory (XI), Fox Questionnaire (FQ), Regional Oral Dryness Inventory (RODI), and Visual Analogue Scale (VAS)—may supplement clinical assessment by quantifying symptom severity and evaluating disease impact on daily functioning.<sup>14, 16, 18, 23-26</sup>

Clinical examination and objective measurements include checking the intraoral sites for signs of dryness on the oral mucosa. The signs of oral dryness based on visual inspection and palpation include dry lips, angular cheilitis, fissured lips, lipstick sign, shining oral mucosa or loss of the normal glistening appearance of the oral mucosa, fissured or lobulated tongue, lack of pooling of saliva in the floor of the mouth, inflamed salivary duct, erosive or ulcerative lesions, opportunistic infection like candidiasis, dental caries especially on the facial surfaces of the teeth, sticking of oral probe or tongue depressor to the oral mucosa, and scanty or reduced salivary flow from the ductal orifices.<sup>14, 27</sup> The clinical signs can be enhanced by tools such as the Clinical Oral Dryness Score (CODS), which helps quantify the extent of dryness in the mouth.<sup>23</sup>

**Sialometry**

Objective assessment includes sialometry, which is the measurement of salivary flow rate. It is the gold standard for objective assessment of salivary gland function.<sup>28</sup> An unstimulated whole salivary flow rate of less than 0.1 mL/min or a stimulated whole salivary flow rate of less than 0.5 mL/min is regarded as hyposalivation.<sup>2, 17</sup> Stimulation of saliva can be done mechanically by chewing paraffin wax or chemically by using 1% citric acid.<sup>29</sup> These tests are usually performed at the chairside. They are simple, reproducible, and non-invasive.

**Sialochemistry**

Sialochemistry is another form of objective measurement to analyse saliva biochemical composition, but it is not routinely performed and is necessary only when systemic disease is suspected. It can assess the buffering capacity, pH, and electrolyte and protein content of saliva.<sup>28</sup>

**Imaging**

Objective assessment also includes imaging such as sialography and ultrasound.<sup>30-32</sup>

Additionally, labial salivary gland biopsy and serology are performed in cases of Sjögren's syndrome for confirmatory diagnosis.<sup>33</sup>

**II. Emerging Diagnostic Methods**

Emerging methods of diagnosis include profiling of salivary biomarkers, proteomics, advanced imaging techniques, point-of-care assays, wearable saliva sensors, artificial intelligence including machine learning, and stem cell regenerative monitoring.<sup>34-36</sup> Table 2 stratifies emerging diagnostics by translational readiness.

**Table 2: Translational Readiness of Emerging Diagnostic Modalities**

Modality	Readiness Level	Key Evidence	Limitations
Salivary proteomics	Early translational	Case-control studies	No external validation
Salivary metabolomics	Experimental	Pilot studies	Reference ranges undefined
Microbiomics	Early translational	Cross-sectional studies	Causality unclear
AI/machine learning	Early translational	Retrospective cohorts	No prospective validation
Wearable sensors	Experimental	Proof-of-concept	Clinical data lacking
Advanced imaging	Clinical (specific)	Validated in radiation-	Cost, availability

### Salivary biomarkers (Omics Technologies)

Recent advances in salivary diagnostics have introduced omics-based approaches, including salivary proteomics, transcriptomics, metabolomics, and microbiomics. These technologies allow comprehensive analysis of salivary components such as specific cytokines, metabolites, proteins, and genetic materials in the saliva, which correlate with identifiable causes of xerostomia. This facilitates the identification of novel biomarkers associated with xerostomia and salivary gland dysfunction, improving diagnostic accuracy and enhancing the understanding of the molecular mechanisms underlying xerostomia.

For example, genetic markers such as anti-cyclic citrullinated peptide (anti-CCP) antibodies are correlated with autoimmune diseases such as rheumatoid arthritis and could predict xerostomia risk.<sup>20, 36</sup> Radiation damage to acinar cells of the salivary gland can be identified by measurable cytokines such as IL-1, TNF- $\alpha$ , and CRP, indicating inflammation linked to oral dryness.<sup>37</sup> Salivary proteins such as  $\alpha$ -amylase precursor, carbonic anhydrase VI, and epidermal fatty acid binding protein are key biomarkers of primary SS discovered through proteomics analyses.<sup>38</sup> Additionally, salivary aquaporin-3 (AQP-3) has been reported as a screening biomarker of xerostomia in patients with periodontal diseases.<sup>37</sup> Increased risk and severity of xerostomia can also be detected by reduced levels of nitric oxide in saliva.<sup>39</sup> Furthermore, alterations in salivary microbiota—including *Candida albicans* overrepresentation—have been associated with oral dryness and may provide adjunctive diagnostic information.<sup>40</sup>

Preliminary evidence indicates that these biomarkers show potential for improving early disease detection, aetiologic differentiation, and treatment monitoring of xerostomia and salivary gland dysfunction. Nevertheless, broader clinical implementation remains limited by insufficient external validation, lack of standardised reference thresholds, and variability across patient populations.

### Advanced Imaging Techniques

Advanced imaging techniques such as MRI, scintigraphy, PET scan, and ultrasound elastography are being explored. Alteration in fat composition in salivary gland tissue can be detected with MRI and is suggestive of reduced acini cells heralding radiation-induced xerostomia. Late-onset xerostomia from radiation therapy could also be predicted with <sup>18</sup>F-FDG PET, which measures metabolic activity in the salivary gland when standardised uptake values are low.<sup>41</sup> These techniques offer high-resolution images and help visualise salivary architecture and monitor functions more accurately. They can detect subclinical changes in the salivary glands before symptoms arise.<sup>30, 31</sup> However, widespread implementation remains constrained by cost, availability, and limited standardisation.

### Point-of-Care Assays and Wearable Sensors

Further development and validation of point-of-care assays for real-time salivary analysis are necessary to enhance their clinical utility. These chairside devices can provide immediate information on salivary composition, pH, and biomarker levels, potentially supporting timely diagnosis, disease monitoring, and treatment personalisation. An example is the SillHa Oral Wellness System.<sup>34</sup>

Wearable saliva sensors are intraoral devices that sense oral dryness or wetness; they can also sense alterations in salivary flow and composition and provide real-time feedback, thereby initiating or sensitizing algorithms for adaptive treatment delivery and modification.<sup>34</sup> However, clinical validation remains limited, and most available systems remain at proof-of-concept or early translational stages.

### Artificial Intelligence and Machine Learning

AI models trained on large data involving patient history, imaging reports, and responses to questionnaire surveys can predict the risk of xerostomia and determine the severity of the disease and prognosis. If properly designed and validated, these systems can be employed in large-population automated screening for xerostomia and could function well in personalized diagnosis and treatment.<sup>35</sup> Current evidence is largely derived from retrospective datasets, and prospective validation studies remain limited.

### Regenerative Monitoring

Regenerative monitoring with stem cell therapy is a very promising endeavour in healthcare for many disorders. Monitoring this process involves using biosensors and tissue-engineered models that simulate the behaviour of salivary gland tissue.<sup>41</sup>



These show promising usefulness but have limited clinical validation. They tend to be more of a complement to conventional measures rather than stand-alone tools in diagnosis.<sup>42</sup>

## **Conventional and Emerging Therapies for Xerostomia**

### **I. Conventional Therapies for Xerostomia**

Traditional treatment measures for xerostomia are usually aimed at alleviating symptoms and/or increasing salivary flow in order to improve the oral health of affected individuals and prevent resulting oral complications. They include patient education and counselling; symptomatic treatment; use of systemic and topical salivary stimulants; removal and treatment of the underlying cause; and preventive measures.<sup>14, 43, 44</sup>

#### **Patient Education and Counselling**

This entails equipping patients with adequate information on the possible causes and the identified cause of their symptoms. Potential sequelae of dry mouth, such as dental caries, candidiasis, altered taste, and oral infections, should also be discussed. In addition, patients should be counselled about self-care measures such as adequate hydration by frequent sipping of water, use of lime water, reducing the intake of alcohol and caffeinated drinks, avoiding the consumption of hard-textured foods and use of irritating dentifrices, and the use of sugar-free chewing gums.<sup>43, 45</sup> Definitive treatment measures, as well as preventive therapies for oral complications, should also be made known to patients.

#### **Symptomatic Treatment**

This includes measures that help relieve symptoms such as the use of water, artificial saliva, and other salivary substitutes.<sup>43, 44, 46, 47</sup> Water is the most common substance used to alleviate dry mouth symptoms.<sup>44</sup> However, water does not contain other saliva constituents that contribute to the functions of natural saliva, hence the need for artificial saliva or saliva substitutes.<sup>44</sup> Characteristics of an ideal saliva substitute include close similarity to natural saliva in constituents and functions; cost-effectiveness; being edible and biocompatible; easy swallowing; and a reasonable level of retentiveness in the mouth.<sup>46</sup>

Saliva substitutes can be grouped based on their derivative, which can be carboxymethylcellulose (CMC), hydroxyethylcellulose (HEC), mucin, xanthan gum, linseed oil, or polyethylene oxide.<sup>44, 46</sup> Mucin-based artificial saliva is the most tolerated with the greatest retention amongst others.<sup>44, 46</sup> Affected patients report that mucin- and xanthan gum-based products provide better moisturizing and flow/consistency properties compared with CMC-based agents.<sup>44</sup> Other important constituents of artificial saliva include minerals such as calcium, phosphate, and fluoride ions;<sup>48</sup> natural products such as lycopene-enriched olive oil;<sup>48</sup> and enzymes such as lactoperoxidase, lysozyme, and lactoferrin, among others.<sup>14, 45, 49</sup> All these constituents help in close mimicry of natural human saliva. Artificial saliva/saliva substitutes are available in different forms such as gels, sprays, oral rinses, toothpaste, lozenges, chewing gums, mucoadhesive polymers, swab sticks, and carriers such as denture reservoirs.<sup>46, 50</sup>

#### **Use of Sialogogues**

Sialogogues are agents that stimulate salivary production from the glands. They improve dry mouth symptoms by increasing salivary secretion and flow rate in cases of xerostomia where residual gland function is present.<sup>46</sup> They can act systemically or topically. Examples of topical salivary stimulants include 1% malic acid spray,<sup>51, 52</sup> sugar-free chewing gums and candies,<sup>14, 53</sup> oral spray containing oxygenated glycerol tri-ester,<sup>14</sup> lemon lozenges,<sup>54, 55</sup> and jelly beans.<sup>54</sup> Most of these topical agents contain calcium, phosphate, fluoride, and xylitol, which are bacteriostatic and in turn reduce the incidence of some of the oral complications of xerostomia.<sup>14, 54</sup>

The classic systemic sialogogues approved by the US Food and Drug Administration (FDA) include pilocarpine and cevimeline.<sup>46, 55</sup> Pilocarpine stimulates saliva secretion by binding as a cholinergic agonist to the muscarinic receptors on the salivary glands' acinar cells, thus acting as a parasympathomimetic agent.<sup>46</sup> The dosage is usually 5–10 mg eight-hourly, with a maximum daily dose of 30 mg based on response and tolerance.<sup>56</sup> Side effects of pilocarpine include diarrhoea, sweating, bradycardia, hypotension, blurred vision, and increased smooth muscle tone.<sup>57</sup> Its use is primarily contraindicated in cases of gastrointestinal ulcer, uncontrolled asthma, narrow-angle glaucoma, and acute iritis.<sup>57, 58</sup> Given the risk of treatment discontinuation associated with its systemic adverse effects, topical administration of pilocarpine is emerging as a promising approach for improving tolerability and minimizing adverse effects.<sup>58</sup> Unlike pilocarpine, cevimeline has fewer side effects, being a more specific parasympathomimetic agent with stronger affinity for the M<sub>3</sub> muscarinic receptors and no effect on M<sub>2</sub> receptors.<sup>44, 59</sup> The most common side effect is dyspepsia.<sup>44, 46</sup> Cevimeline provides a longer-lasting effect when compared with pilocarpine, although both medications possess similar contraindications.<sup>59</sup> The dosage recommendation is usually 30 mg eight-hourly, with a maximum daily dose of 200 mg.<sup>46</sup>



Other systemic sialogogues that have shown some efficacy include medications with mucolytic properties such as bromhexine;<sup>46</sup> histamine-2 (H<sub>2</sub>) receptor agonists such as nizatidine alone or with cisapride;<sup>46</sup> other parasympathomimetic drugs such as neostigmine, distigmine, yohimbine, and nicotinic acid;<sup>59</sup> medicinal herbs such as betel nuts and Iceland moss, among others;<sup>61</sup> and immunologic agents such as interferon alpha, rituximab (anti-CD20), and infliximab (anti-tumour necrosis factor), especially in cases of immune-mediated xerostomia such as SS and SLE.<sup>46</sup>

Besides systemic and topical sialogogues, studies have shown transcutaneous electric nerve stimulation (TENS) as a very effective means of increasing the flow rate of whole saliva in patients with diabetes mellitus and postmenopausal women having xerostomia.<sup>62</sup>, <sup>63</sup>

### Removal and Treatment of Underlying Causes

Managing the underlying aetiology of xerostomia is key in treatment. Causes of xerostomia are numerous. They include salivary gland pathologies such as obstructions (e.g., sialolithiasis); infections (e.g., sialadenitis); tumours; immune-mediated conditions such as diabetes mellitus, SS, and SLE; chemotherapy- and radiotherapy-induced salivary gland destruction; salivary centre causes such as stress, anxiety, Parkinson's disease, Alzheimer's disease, and hormonal changes as in menopause; neurological causes such as encephalitis and brain neoplasms; and use of some medications such as antidepressants, antipsychotics, anxiolytics, opioids, antiepileptics, anticholinergics, antihypertensives, and antihistamines, among others.<sup>14</sup>, <sup>44</sup>, <sup>46</sup>

Where any systemic disease has been identified as the cause of xerostomia, the systemic disease should be properly treated in addition to the symptomatic treatment given. Furthermore, if use of medication(s) is the cause, modification of drug dosage or changing to less xerogenic drugs should be considered. The best choice should be made in consultation with the patient's primary physician.

### Preventive Measures for Oral Complications

Measures aimed at preventing complications of xerostomia should be part of the treatment regimen. They include fluoride therapies, low-sugar diet, strict oral hygiene measures, reduction of alcohol and caffeine intake, frequent oral hydration, and regular dental check-ups.

## II. Emerging Therapies

A number of recent methods of stimulating salivary flow as well as glandular regenerative and gene therapies are being introduced. Newer methods of stimulating saliva include the use of acupuncture, intraoral appliances, and low-level laser therapy. Table 3 stratifies emerging therapies by evidence maturity.

**Table 3: Translational Readiness of Emerging Therapies**

Therapy	Readiness Level	Key Evidence	Limitations
Acupuncture	Adjunctive clinical	Systematic reviews, RCTs (small sample)	Sham control difficult; effect size modest
Low-level laser therapy	Adjunctive clinical (mixed evidence)	Pilot studies, systematic review	Lack of consensus; heterogeneity
Intraoral appliances	Early clinical	Uncontrolled trials	Poor acceptance, high cost, requires residual function
Stem cell therapy	Experimental	Preclinical, one human culture study	Safety, efficacy unproven
Gene therapy	Experimental	Phase I/II trial (single)	Safety concerns, ethical issues



### **Acupuncture**

This is a traditional Chinese medical practice that dates back over 3000 years. It entails application of needles to marked body points in close proximity to blood vessels, nerves, periosteum, tendons, and capsules of the joints.<sup>55</sup> The utility of acupuncture as a treatment modality for xerostomia is based on its ability to upregulate calcitonin gene-related peptide (CGRP) release from the nerve endings of the peripheral and autonomic nervous system. This neuropeptide induces vasodilation, which in turn increases salivary gland secretion and salivary flow.<sup>64</sup>

Ghazzaoui et al. observed an increase in salivary flow rate in patients with xerostomia treated with acupuncture.<sup>65</sup> Moreover, an improvement in xerostomia symptoms of patients with SS was observed in a randomised controlled pilot trial of acupuncture as a treatment modality by Jiang et al.<sup>66</sup> A systematic review by Ni et al. also observed alleviation of symptoms with the use of acupuncture in patients with dry mouth.<sup>67</sup>

Acupuncture can be used either as a stand-alone therapy or as an adjunct offering, with marked improvement in oral functions, sleep, and quality of life observed.<sup>55</sup> Acupuncture therapy should be sustained for at least six months, with therapeutic effects reported to last up to three years.<sup>68</sup> Available evidence supporting the efficacy and effectiveness of acupuncture in the management of xerostomia remains insufficient. Therefore, well-designed future studies are required to substantiate and validate its potential benefits for clinical application.

### **Low-Level Laser Therapy**

This entails the application of infrared light with a wavelength of 904 nm to the salivary glands.<sup>69</sup> It is a potentially effective therapy for xerostomia that is non-invasive, affordable, and easy to use.<sup>70, 71</sup> It acts by modulating biometals and biochemical and photophysical processes, transforming the laser light into bioenergy without exerting any mutagenic or photothermal effects on the cells.<sup>71, 72</sup> This laser therapy improves local blood supply, stimulating increased proliferation of cells, cellular respiration, energy production, protein synthesis, and intracellular calcium levels in the salivary glands, hence exerting both stimulating and regenerative effects.<sup>69, 73</sup>

There is a lack of consensus on the improvement offered by the use of low-level laser therapy in xerostomia. More studies are still required to validate its significance in improving xerostomia symptoms.

### **Intraoral Appliances**

The use of intraoral appliances such as the Saliwell Crown device and GenNarino is effective in alleviating the symptoms of xerostomia.<sup>14, 74</sup> These appliances function as saliva stimulation devices and act by increasing saliva production.<sup>74, 75</sup> However, routine clinical use is constrained by poor patient acceptance, compliance-related challenges, high cost, and the need for residual functional glandular tissue.<sup>76</sup>

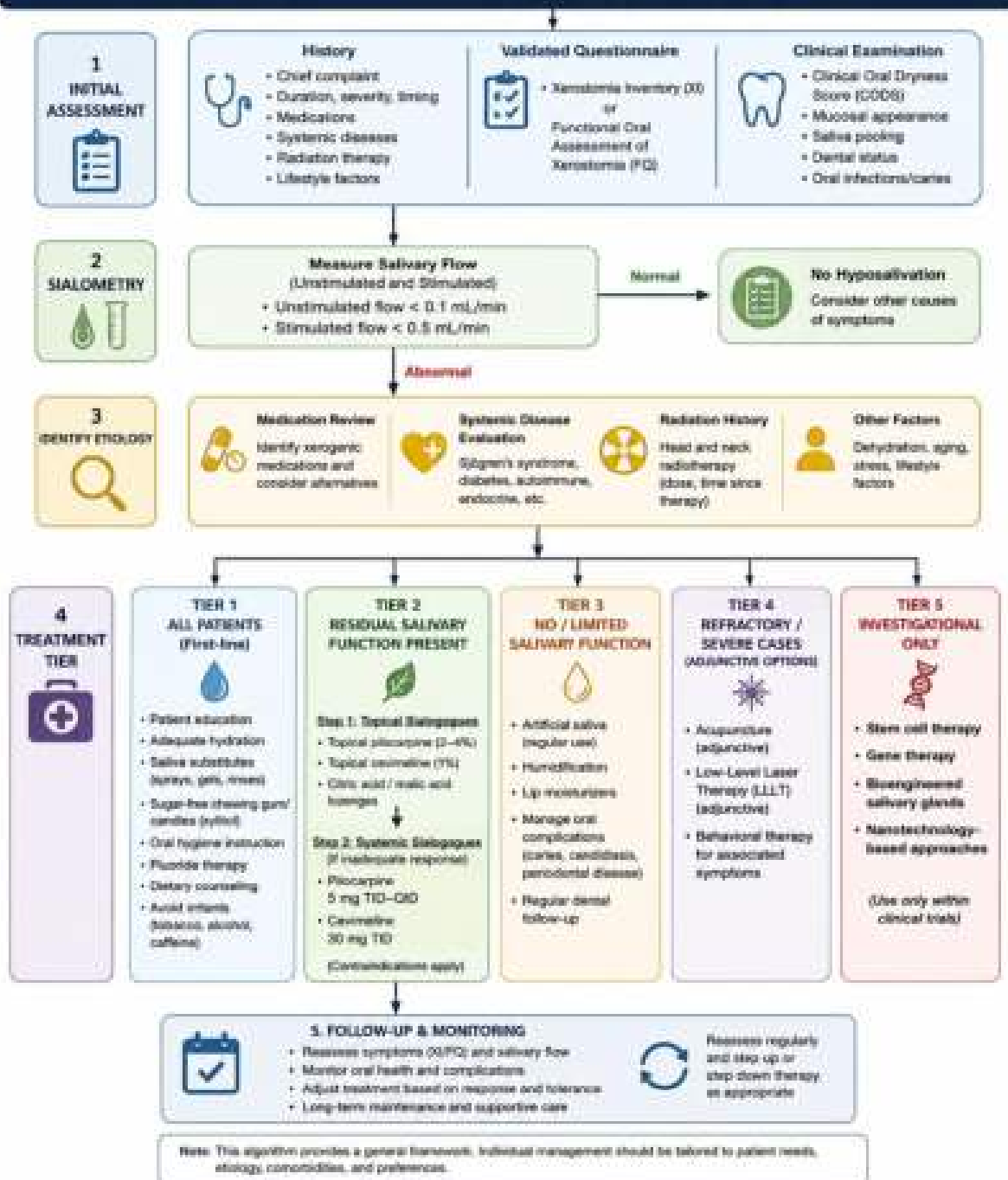
### **Stem Cell Therapy**

This therapy has great potential for repair of salivary glands that are damaged at the cellular level, hence it is a good treatment option for radiation-induced xerostomia.<sup>44, 46</sup> Potential stem cells that have been tried include bone marrow stem cells, adipose tissue-derived stromal cells, and dental pulp cells.<sup>44, 47</sup> Pringle et al. demonstrated the possibility of culturing human salivary stem/progenitor cells derived from parotid and submandibular salivary glands using the salisphere technique, which makes regeneration and restoration of function of damaged salivary glands feasible.<sup>77</sup> This can be achieved by introduction of these progenitor cells into the damaged salivary gland tissues. However, more research work is still required to utilize this great potential.

### **Gene Therapy**

This modality is traditionally used in treating congenital genetic disorders but has found application in inherited and acquired disorders. It entails the introduction of a vector containing a functional gene into the cells for some benefits, which could be for the correction of cellular dysfunction or the induction of a new cellular function.<sup>46, 55</sup> Viral or non-viral vectors can be used for gene transfer. The use of gene therapy in treating xerostomia is effective in alleviating symptoms and providing a better quality of life to patients. Jain et al. reported an increase in parotid salivary flow rate with gene therapy in a phase I/II randomised clinical trial.<sup>78</sup> Its translation into clinical application is still constrained by limited research, insufficient evidence supporting its long-term efficacy, safety concerns, and ethical issues.<sup>79</sup> The summary for the comprehensive management of xerostomia can be found in Figure 1 below.

**FIGURE 1. COMPREHENSIVE MANAGEMENT OF XEROSTOMIA**



**CONCLUSION**

Xerostomia is an oral health problem that can be associated with debilitating complications, especially in cases of true hyposalivation. It may arise from several causes such as use of certain medications, head and neck radiotherapy, and systemic diseases including autoimmune conditions and neuropsychiatric disorders.

The successful treatment of this condition is dependent on accurate diagnosis, which should establish the presence or absence of salivary gland hypofunction and the possible causes. Recently, considerable advances in diagnostic and treatment measures have been made, but not without their limitations in clinical applications, especially in resource-limited countries.



A major drawback is the high cost of the technologies and facilities required for these advanced measures, reducing their accessibility and cost-effectiveness. Another challenge is the shortage of manpower with the skills and expertise for effective implementation of these techniques. In addition, many of these emerging methods can only be used in complement with traditional methods for effectiveness.

More importantly, further research such as well-designed clinical trials is required to validate the clinical effectiveness and utility of most of these advanced diagnostic and therapeutic methods *in vivo*.

### Future Directions

Novel diagnostic technologies and regenerative therapies hold great promise for improving the management of xerostomia. Advances in salivary biomarker research, artificial intelligence-assisted diagnostic tools, and regenerative medicine approaches may provide more precise and individualized treatment strategies in the future. However, further clinical trials and long-term studies are required to evaluate the safety, efficacy, and cost-effectiveness of these innovations prior to their full and universal integration for routine clinical practice utility.

### LIST OF ABBREVIATIONS

Abbreviation	Full Form
AI	Artificial intelligence
anti-CCP	Anti-cyclic citrullinated peptide
AQP-3	Aquaporin-3
CGRP	Calcitonin gene-related peptide
CMC	Carboxymethylcellulose
CODS	Clinical Oral Dryness Score
CRP	C-reactive protein
FDG	Fluorodeoxyglucose
FQ	Fox's Questionnaire
HEC	Hydroxyethylcellulose
HIV/AIDS	Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome
IL	Interleukin
LLLT	Low-level laser therapy
mL/min	Millilitres per minute
MRI	Magnetic resonance imaging
PET	Positron emission tomography
pSS	Primary Sjögren's syndrome
RODI	Regional Oral Dryness Inventory
SANRA	Scale for the Assessment of Narrative Review Articles



SLE	Systemic lupus erythematosus
SS	Sjögren's syndrome
TENS	Transcutaneous electric nerve stimulation
TNF- $\alpha$	Tumour necrosis factor alpha
VAS	Visual Analogue Scale
XI	Xerostomia Inventory

## DECLARATIONS

**Ethics approval:** Not applicable.

**Availability of data and materials:** Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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