Research Article

# Saliva-Based Digital Biomarkers for Population Oral Health Screening: Current Evidence and Future Perspectives

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**Abstract**

Background: Oral diseases affect more than 3.5 billion people worldwide and remain a major public health concern. Conventional diagnostic methods are often invasive, expensive, and unsuitable for large-scale community screening. Saliva has emerged as an attractive diagnostic biofluid because it contains diverse molecular constituents that reflect both oral and systemic health. Recent advances in salivaomics, biosensor technologies, artificial intelligence (AI), microfluidics, and point-of-care diagnostics have transformed salivary analysis into a promising platform for digital biomarker-based disease detection. Objective: To critically review the current evidence on saliva-based digital biomarkers for population oral health screening, highlight recent technological advances, summarize their applications in major oral diseases, and discuss their potential role in precision dentistry and public health. Methods: A narrative review was conducted using PubMed/MEDLINE, Scopus, Web of Science, Embase, Google Scholar, and the Cochrane Library. English-language studies published primarily between January 2020 and June 2026, including original research, systematic reviews, meta-analyses, consensus statements, and technological reports, were evaluated. Landmark publications published before 2020 were included where appropriate. Results: Evidence indicates that salivary digital biomarkers can identify molecular alterations associated with dental caries, periodontal diseases, oral potentially malignant disorders, oral squamous cell carcinoma, peri-implant diseases, and salivary gland dysfunction. Emerging technologies—including electrochemical biosensors, lab-on-chip systems, microfluidic devices, wearable intraoral sensors, smartphone-assisted diagnostics, and AI-driven analytical platforms—have substantially improved diagnostic sensitivity, specificity, portability, and real-time monitoring. These innovations facilitate decentralized screening, personalized risk prediction, and continuous disease surveillance, making them particularly suitable for school-based programs, rural outreach services, tele-dentistry, and community oral health initiatives. Conclusion: Saliva-based digital biomarkers represent a paradigm shift in oral diagnostics by combining non-invasive sampling with advanced digital technologies. Although further multicenter validation, standardization, regulatory approval, and cost-effectiveness studies are required, these technologies have considerable potential to revolutionize population oral health screening and advance precision public health.

**Keywords:** Saliva; Digital biomarkers; Salivaomics; Oral health screening; Precision dentistry; Biosensors; Artificial intelligence; Point-of-care diagnostics; Microfluidics; Public health dentistry

## 1. Introduction

Oral diseases remain among the most prevalent non-communicable diseases worldwide, affecting approximately 3.5 billion individuals and posing a substantial burden on health systems, economies, and quality of life. Dental caries, periodontal diseases, oral potentially malignant disorders (OPMDs), and oral squamous cell carcinoma (OSCC) continue to be major public health challenges despite advances in preventive and therapeutic dentistry. The burden is disproportionately greater in low- and middle-income countries, where limited access to dental care, delayed diagnosis, and inadequate preventive services contribute to disease progression and associated healthcare costs (1–3).

Early diagnosis remains fundamental to reducing oral disease burden. However, conventional diagnostic approaches rely primarily on clinical examination, radiographic imaging, histopathology, and laboratory investigations, which often detect disease only after significant structural damage has occurred. These methods are frequently invasive, time-consuming, resource-intensive, and impractical for population-based screening programs. Consequently, there is increasing interest in identifying non-invasive biomarkers capable of detecting disease before overt clinical manifestations, enabling earlier intervention and personalized preventive strategies.

Saliva has emerged as one of the most promising diagnostic biofluids because of its ease of collection, minimal invasiveness, low cost, and ability to reflect both oral and systemic physiological conditions. Human saliva contains a complex mixture of proteins, peptides, nucleic acids, extracellular vesicles, metabolites, hormones, electrolytes, antibodies, inflammatory mediators, and microorganisms. Advances in high-throughput analytical technologies have enabled comprehensive characterization of these molecular components, giving rise to the field of **salivaomics**, which integrates proteomics, transcriptomics, genomics, metabolomics, microbiomics, and exosomics to identify disease-specific molecular signatures (4–7).

The convergence of salivaomics with digital health technologies has led to the development of **saliva-based digital biomarkers**. Unlike conventional biomarkers measured solely through laboratory assays, digital biomarkers combine molecular information with biosensors, wearable devices, smartphone-enabled platforms, cloud computing, and artificial intelligence (AI) to provide objective, quantifiable, and real-time physiological information. AI-assisted algorithms can analyze complex multidimensional datasets, enabling rapid disease prediction, automated risk stratification, and clinical decision support (8–10).

Recent advances in biosensor engineering, nanotechnology, lab-on-chip systems, microfluidics, and point-of-care (POC) diagnostics have further expanded the clinical applicability of salivary diagnostics. Modern portable devices require only microliter quantities of saliva and provide rapid, multiplex biomarker analysis within minutes. Integration with tele-dentistry and electronic health records enables decentralized screening and longitudinal monitoring, making these technologies particularly attractive for school oral health programs, tobacco cessation clinics, rural outreach services, and national oral health surveillance systems.

Although numerous reviews have independently discussed salivary biomarkers, biosensors, AI, or salivaomics, relatively few have comprehensively integrated these rapidly evolving fields within the context of **population oral health screening**. This narrative review therefore synthesizes current evidence on saliva-based digital biomarkers, summarizes recent technological developments, evaluates their applications in major oral diseases, and discusses future opportunities and implementation challenges for precision public health.

## 2. Literature Search Strategy

A comprehensive narrative review was performed to summarize contemporary evidence regarding saliva-based digital biomarkers for population oral health screening. Electronic databases including **PubMed/MEDLINE, Scopus, Web of Science, Embase, Google Scholar, and the Cochrane Library** were searched for articles published between **January 2020 and June 2026**. Seminal studies published before 2020 were additionally included to provide historical context.

Search terms included combinations of Medical Subject Headings (MeSH) and free-text keywords such as *saliva*, *salivary biomarkers*, *digital biomarkers*, *salivaomics*, *oral health screening*, *biosensors*, *microfluidics*, *lab-on-chip*, *point-of-care diagnostics*, *wearable sensors*, *artificial intelligence*, *machine learning*, *oral cancer*, *periodontal disease*, *dental caries*, *precision dentistry*, and *public health dentistry* using Boolean operators (AND, OR).

Original research articles, systematic reviews, meta-analyses, randomized clinical trials, consensus statements, and technological reports published in English were eligible for inclusion. Conference abstracts, editorials, letters, duplicate publications, and studies lacking methodological rigor were excluded. Reference lists of eligible articles were manually screened to identify additional relevant publications. The selected evidence was critically appraised and synthesized narratively with emphasis on clinical relevance, technological innovation, and potential applications in community-based oral health programs.

## 3. Saliva as a Diagnostic Biofluid

Saliva has become an increasingly important diagnostic medium because it offers a safe, inexpensive, and non-invasive alternative to blood and tissue sampling. Whole saliva is secreted mainly by the parotid, submandibular, sublingual, and minor salivary glands and contains more than 2,000 proteins and peptides in addition to nucleic acids, metabolites, hormones, antibodies, extracellular vesicles, electrolytes, inflammatory mediators, and a diverse oral microbiome. Many of these constituents enter saliva through passive diffusion, active transport, or ultrafiltration from the bloodstream, allowing saliva to reflect systemic physiological and pathological changes while simultaneously capturing local alterations within the oral cavity(5).

The major advantages of saliva include painless collection, minimal risk of infection transmission, reduced need for specialized personnel, and excellent patient acceptability. These features make saliva particularly suitable for children, older adults, medically compromised individuals, and patients requiring repeated longitudinal monitoring. Saliva collection is also highly feasible in school-based screening programs, rural outreach camps, nursing homes, and community health centers where conventional laboratory infrastructure may be unavailable (6).

Advances in molecular diagnostics have significantly expanded the clinical utility of saliva. Sensitive analytical techniques can now detect disease-associated proteins, messenger RNAs, microRNAs, circulating cell-free DNA, metabolites, cytokines, microbial signatures, and extracellular vesicles at extremely low concentrations. Salivary biomarkers have demonstrated diagnostic potential in dental caries, periodontal diseases, oral cancer, autoimmune disorders such as Sjögren syndrome, diabetes mellitus, cardiovascular disease, and viral infections. Consequently, saliva is increasingly regarded as a cornerstone of precision diagnostics(9).

Despite these advantages, several factors influence salivary biomarker concentrations, including circadian rhythm, age, hydration status, smoking, medication use, systemic disease, dietary habits, and methods of saliva collection and storage. Standardized protocols for sample collection, processing, transportation, and analysis remain essential before widespread clinical implementation can be achieved.

## 4. Salivaomics and Digital Biomarkers

The emergence of **salivaomics** has transformed saliva from a simple oral fluid into a comprehensive source of molecular information. Salivaomics encompasses the integrated study of salivary proteomics, genomics, transcriptomics, metabolomics, microbiomics, lipidomics, and exosomics, enabling identification of disease-specific molecular signatures that precede clinical manifestations.

Proteomics evaluates alterations in proteins, enzymes, cytokines, chemokines, and matrix metalloproteinases associated with inflammation and tissue destruction. Transcriptomics investigates messenger RNA and microRNA profiles that regulate cellular signaling and oncogenesis, while genomics identifies host genetic polymorphisms, microbial DNA, and circulating tumor DNA. Metabolomics analyzes low-molecular-weight metabolites reflecting biochemical alterations during disease progression, whereas microbiomics characterizes changes in oral microbial ecology associated with dysbiosis and chronic inflammation(4).

Digital biomarkers extend the utility of these molecular signatures by integrating them with biosensors, wearable devices, smartphone applications, cloud computing, and AI-based analytical platforms. According to the U.S. Food and Drug Administration, digital biomarkers are objective, quantifiable physiological or biological data collected through digital devices that can predict, detect, or monitor health conditions. In dentistry, saliva-based digital biomarkers combine molecular information with computational algorithms to facilitate rapid diagnosis, risk prediction, and personalized treatment planning.

Artificial intelligence has become central to digital biomarker development. Machine learning algorithms can analyze complex multidimensional biomarker datasets, identify hidden disease patterns, improve diagnostic accuracy, and support automated clinical decision-making. Integration of salivaomics with AI therefore represents a significant step toward precision dentistry and personalized preventive care(8).

## 5. Digital Technologies in Salivary Diagnostics

Recent advances in digital health technologies have transformed salivary diagnostics from laboratory-based investigations into portable, rapid, and point-of-care diagnostic systems. Biosensors form the foundation of these innovations by converting biological interactions into measurable electrical, optical, or electrochemical signals capable of detecting proteins, nucleic acids, metabolites, inflammatory mediators, and microbial biomarkers with remarkable sensitivity.

Nanotechnology-enhanced electrochemical biosensors improve analytical performance while reducing sample volume and detection time. Microfluidic and **lab-on-chip (LOC)** platforms miniaturize multiple laboratory procedures onto a single disposable chip, enabling multiplex biomarker analysis using only a few microliters of saliva. These systems reduce reagent consumption, improve portability, and provide diagnostic results within minutes, making them highly suitable for community-based screening (11).

Point-of-care devices integrated with smartphone applications facilitate wireless data transmission, cloud-based storage, and tele-dentistry consultations. Such systems enable healthcare providers to perform chairside diagnostics in dental clinics, schools, rural outreach programs, and mobile health units while simultaneously supporting centralized surveillance through electronic health records. Emerging wearable technologies—including smart mouthguards, intraoral sensors, and intelligent dental appliances—offer continuous monitoring of salivary pH, glucose, inflammatory mediators, hydration status, and microbial activity. These devices have the potential to shift oral healthcare from episodic diagnosis to continuous disease surveillance(11).

Artificial intelligence further enhances these technologies by integrating multiple biomarkers into predictive algorithms capable of automated diagnosis, disease risk stratification, and personalized clinical decision support. As biosensors become more affordable and portable, saliva-based digital diagnostics are expected to play an increasingly important role in preventive dentistry, public health surveillance, and precision oral healthcare.

**Table 1. Major Salivary Biomarkers in Oral Diseases(9,12)**

| Disease | Representative Salivary Biomarkers | Clinical Utility |
|---|---|---|
| Dental caries | *Streptococcus mutans*, Lactobacillus spp., sIgA, salivary pH, buffering capacity | Caries risk prediction |
| Periodontitis | IL-1β, IL-6, TNF-α, MMP-8, MMP-9, RANKL | Early diagnosis and disease activity |
| OPMDs | miR-21, miR-31, TP53 mutations, IL-8, EGFR | Malignant transformation risk |
| Oral squamous cell carcinoma | IL-8, Cyfra 21-1, CD44, miR-31, ctDNA | Early cancer detection |
| Peri-implant disease | MMP-8, IL-1β, osteocalcin, calprotectin | Monitoring peri-implant inflammation |
| Xerostomia | Lactoferrin, mucins, aquaporins, amylase | Assessment of salivary gland dysfunction |

**Table 2. Emerging Digital Technologies in Salivary Diagnostics (11,13)**

| Technology | Principle | Major Applications |
|---|---|---|
| Electrochemical biosensors | Electrical signal detection | Multiplex biomarker analysis |
| Optical biosensors | Fluorescence/colorimetric detection | Oral cancer biomarkers |
| Lab-on-chip devices | Integrated microfluidic analysis | Rapid point-of-care diagnostics |
| Smartphone-based platforms | Mobile image and data analysis | Community screening and tele-dentistry |
| Wearable intraoral sensors | Continuous salivary monitoring | Real-time disease surveillance |
| Artificial intelligence | Predictive analytics and pattern recognition | Risk prediction and clinical decision support |

## 6. Current Evidence for Saliva-Based Digital Biomarkers in Oral Diseases

Recent advances in salivaomics, digital biosensing, nanotechnology, and artificial intelligence (AI) have significantly enhanced the diagnostic utility of saliva for oral diseases. Unlike conventional clinical examinations that primarily detect established disease, saliva-based digital biomarkers identify early molecular alterations associated with inflammation, microbial dysbiosis, oxidative stress, tissue destruction, and malignant transformation. The integration of multiplex biomarker panels with biosensors, microfluidic platforms, and machine learning algorithms has improved diagnostic accuracy while enabling rapid, non-invasive, and chairside assessment. These technologies are increasingly being investigated for precision dentistry and population-level oral health screening.

### 6.1 Dental Caries

Dental caries is a chronic, biofilm-mediated disease resulting from complex interactions among cariogenic microorganisms, fermentable carbohydrates, host susceptibility, and environmental factors. Conventional diagnosis relies on visual-tactile examination and radiography, which primarily detect established lesions rather than early biological changes. Salivary biomarkers offer an opportunity to identify individuals at high risk before irreversible demineralization occurs.

Several salivary biomarkers have demonstrated associations with caries activity. Elevated counts of *Streptococcus mutans* and *Lactobacillus* species remain the most extensively validated microbial indicators of caries risk. In addition, decreased salivary pH, reduced buffering capacity, diminished salivary flow rate, and altered calcium and phosphate concentrations contribute to enamel demineralization and disease progression. Host-derived biomarkers, including secretory immunoglobulin A (sIgA), β-defensins, histatins, lactoferrin, and inflammatory cytokines such as interleukin (IL)-6, IL-8, and tumor necrosis factor-alpha (TNF-α), reflect the host immune response to cariogenic biofilms. Recent metabolomic investigations have further identified organic acids, amino acid derivatives, and oxidative stress metabolites associated with active carious lesions(14).

Digital diagnostic technologies have accelerated the translation of these biomarkers into clinical practice. Electrochemical biosensors and microfluidic devices can quantify cariogenic bacteria, salivary pH, and inflammatory proteins within minutes using minimal sample volumes. AI-driven predictive models integrating salivary biomarkers with demographic, dietary, and clinical variables have demonstrated higher predictive accuracy for future caries development than conventional risk assessment tools. Smartphone-enabled point-of-care devices are particularly promising for school-based screening programs, allowing rapid identification of high-risk children who may benefit from preventive interventions such as fluoride varnish application, pit-and-fissure sealants, and individualized oral health education.

Despite encouraging findings, variability in sampling techniques and the multifactorial nature of dental caries remain important challenges. Future research should focus on validating multiplex biomarker panels rather than relying on individual biomarkers to improve predictive performance across diverse populations.

### 6.2 Periodontal Diseases

Periodontal diseases are chronic inflammatory disorders characterized by destruction of the gingiva, periodontal ligament, cementum, and alveolar bone. Traditional diagnosis depends on periodontal probing and radiographic assessment, which primarily reflect historical tissue destruction rather than current disease activity. Salivary biomarkers provide valuable information regarding ongoing inflammatory processes and tissue breakdown, offering opportunities for earlier diagnosis and personalized disease monitoring.

Inflammatory cytokines including IL-1β, IL-6, IL-8, TNF-α, prostaglandin E2 (PGE2), and C-reactive protein (CRP) consistently demonstrate elevated concentrations in patients with periodontitis. Matrix metalloproteinases, particularly MMP-8 and MMP-9, have emerged as robust biomarkers of collagen degradation and active periodontal destruction. Bone remodeling markers such as receptor activator of nuclear factor kappa-B ligand (RANKL), osteoprotegerin (OPG), osteocalcin, and alkaline phosphatase provide additional information regarding alveolar bone metabolism(15).

Microbiomic analyses have further strengthened salivary diagnostics by identifying increased abundance of periodontal pathogens including *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*, and *Fusobacterium nucleatum*. Integration of host inflammatory biomarkers with microbial signatures has substantially improved diagnostic sensitivity and specificity(16).

Digital biosensor platforms capable of multiplex detection of inflammatory mediators have shown excellent agreement with conventional laboratory assays while requiring only microliter quantities of saliva. Lab-on-chip devices provide rapid chairside analysis within 10–15 minutes, facilitating routine periodontal risk assessment in clinical practice. AI algorithms incorporating salivary biomarker profiles, clinical periodontal parameters, and radiographic features have demonstrated excellent predictive performance for disease progression and treatment outcomes.

From a public health perspective, saliva-based digital diagnostics may enable opportunistic periodontal screening in primary healthcare settings, particularly among individuals with diabetes mellitus, cardiovascular disease, and tobacco use, where periodontitis contributes significantly to systemic disease burden.

### 6.3 Oral Potentially Malignant Disorders (OPMDs)

Oral potentially malignant disorders—including leukoplakia, erythroplakia, oral submucous fibrosis, and oral lichen planus—represent important precursors of oral squamous cell carcinoma (OSCC). Early identification of lesions with high malignant potential remains a major challenge because conventional diagnosis relies on clinical examination followed by invasive biopsy.

Recent advances in salivaomics have identified numerous biomarkers associated with malignant transformation. Salivary microRNAs, particularly miR-21, miR-31, miR-184, and miR-375, exhibit altered expression patterns during early carcinogenesis and have demonstrated promising diagnostic performance. Increased concentrations of IL-8, IL-1β, vascular endothelial growth factor (VEGF), epidermal growth factor receptor (EGFR), CD44, TP53 mutations, oxidative stress markers, and extracellular vesicle-derived nucleic acids have also been associated with OPMDs(17).

Biosensor technologies capable of detecting multiple biomarkers simultaneously have enhanced the feasibility of non-invasive community screening. Optical biosensors and nanotechnology-based immunosensors demonstrate high analytical sensitivity, while AI-assisted image analysis combined with salivary biomarker profiles enables improved risk stratification of suspicious lesions. Such integrated diagnostic approaches may reduce unnecessary biopsies while facilitating early referral of high-risk individuals.

Although promising, most biomarkers remain at the validation stage. Large multicenter prospective studies are required before widespread implementation in national oral cancer screening programs.

### 6.4 Oral Squamous Cell Carcinoma

Oral squamous cell carcinoma accounts for nearly 90% of oral malignancies worldwide. Delayed diagnosis remains the principal determinant of poor survival, particularly in low- and middle-income countries where access to specialist care is limited. Saliva-based diagnostics have emerged as attractive non-invasive alternatives for early detection and surveillance.

Current evidence supports several validated salivary biomarkers including IL-6, IL-8, Cyfra 21-1, CD44, matrix metalloproteinases, p53 antibodies, circulating tumor DNA (ctDNA), exosomal proteins, metabolomic signatures, and microRNAs such as miR-31, miR-125a, and miR-200a. Individual biomarkers often demonstrate moderate diagnostic performance; however, multiplex biomarker panels analyzed using AI algorithms have reported sensitivities and specificities exceeding 85–90%(17).

Machine learning has become increasingly important in oral cancer diagnostics. Deep learning algorithms integrating salivary biomarkers, demographic characteristics, tobacco exposure history, and clinical photographs significantly improve early detection and prediction of malignant transformation. Portable biosensor devices capable of providing diagnostic results within minutes offer considerable potential for screening high-risk populations, particularly tobacco and areca nut users.

From a public health perspective, saliva-based screening may substantially reduce diagnostic delays by facilitating decentralized detection of high-risk lesions in community outreach programs and primary healthcare centers.

**6.5 Peri-implant Diseases**

The increasing global use of dental implants has been accompanied by a rising prevalence of peri-implant mucositis and peri-implantitis. Early diagnosis remains challenging because clinical signs often appear after considerable peri-implant tissue destruction has occurred.

Several inflammatory biomarkers—including MMP-8, IL-1β, IL-6, TNF-α, RANKL, osteocalcin, osteopontin, calprotectin, and alkaline phosphatase—correlate strongly with peri-implant inflammation and marginal bone loss. Alterations in peri-implant microbial communities, particularly increased prevalence of anaerobic periodontal pathogens, further enhance diagnostic accuracy (18).

Portable biosensor platforms capable of simultaneous assessment of inflammatory and microbial biomarkers have demonstrated encouraging diagnostic performance for distinguishing healthy implants from peri-implant disease. Integration with digital patient records allows longitudinal monitoring following implant placement and supports personalized maintenance protocols.

Future multicenter studies are needed to establish standardized diagnostic thresholds and validate biomarker panels across different implant systems and patient populations.

**6.6 Xerostomia and Salivary Gland Disorders**

Xerostomia affects millions of individuals worldwide and is commonly associated with Sjögren syndrome, diabetes mellitus, medications, radiotherapy, and aging. Conventional diagnosis depends primarily on subjective symptom assessment and salivary flow measurements, which often lack sensitivity for early disease detection.

Recent investigations have identified multiple salivary biomarkers associated with glandular dysfunction, including lactoferrin, lysozyme, mucins, aquaporins, α-amylase, electrolytes, inflammatory cytokines, autoantibodies, and oxidative stress markers. These biomarkers provide insights into glandular inflammation, secretory dysfunction, and disease progression (19).

Wearable intraoral biosensors capable of continuously monitoring salivary flow rate, electrolyte composition, hydration status, and pH have emerged as promising technologies for real-time assessment. Integration with AI-based predictive models combining patient-reported symptoms and biomarker profiles may improve diagnostic precision while facilitating individualized therapeutic interventions.

Although clinical evidence remains limited, digital salivary diagnostics have considerable potential to improve management of patients receiving head and neck radiotherapy, individuals with autoimmune diseases, and older adults experiencing age-related salivary dysfunction.

**Summary of Current Evidence**

Collectively, current evidence indicates that saliva-based digital biomarkers represent a major advance in precision oral diagnostics. Multiplex biomarker panels integrated with biosensors, lab-on-chip technologies, smartphone-assisted diagnostics, wearable sensors, and artificial intelligence have demonstrated encouraging diagnostic accuracy across a broad spectrum of oral diseases. While continued standardization, multicenter validation, and cost-effectiveness analyses remain essential before routine implementation, these technologies have significant potential to transform population oral health screening by enabling earlier diagnosis, personalized risk assessment, and continuous disease surveillance.

**Table 3. Saliva-Based Digital Biomarkers in Major Oral Diseases (14-19)**

| Oral Disease | Principal Salivary Biomarkers | Emerging Digital Technologies | Clinical Application |
|---|---|---|---|
| Dental caries | *S. mutans*, *Lactobacillus*, sIgA, IL-6, IL-8, salivary pH | Electrochemical biosensors, smartphone-based POC devices | Caries risk assessment |
| Periodontal disease | IL-1β, IL-6, TNF-α, MMP-8, MMP-9, RANKL | Lab-on-chip platforms, AI-assisted multiplex biosensors | Early diagnosis and disease monitoring |
| OPMDs | miR-21, miR-31, EGFR, IL-8, TP53 mutations | Optical biosensors, AI-assisted screening | Malignant transformation risk prediction |
| Oral squamous cell carcinoma | IL-8, Cyfra 21-1, CD44, ctDNA, exosomal miRNAs | Multiplex biosensors, machine learning algorithms | Early cancer detection |
| Peri-implant disease | MMP-8, IL-1β, calprotectin, osteocalcin | Chairside biosensor platforms | Implant maintenance and monitoring |
| Xerostomia | Lactoferrin, mucins, aquaporins, α-amylase | Wearable intraoral sensors, AI-enabled monitoring | Salivary gland function assessment |

## 7. Population Screening Applications

The integration of saliva-based digital biomarkers into population oral health screening represents a paradigm shift from conventional disease detection toward precision public health. Unlike traditional screening methods that rely on clinical examination and radiography, saliva-based diagnostics provide a rapid, non-invasive, and patient-friendly approach capable of identifying molecular alterations before the appearance of clinical disease. The convergence of salivaomics, biosensors, microfluidics, point-of-care (POC) technologies, wearable sensors, and artificial intelligence (AI) has substantially expanded the feasibility of implementing community-based oral disease screening across diverse healthcare settings.

One of the most promising applications is **school oral health programs**, where early identification of children at increased risk of dental caries and periodontal disease remains a public health priority. Portable saliva-based diagnostic devices can rapidly quantify cariogenic microorganisms, inflammatory mediators, salivary pH, buffering capacity, and host immune markers within minutes. Integration of these biomarkers with AI-driven predictive algorithms enables individualized risk stratification, facilitating targeted preventive interventions such as fluoride varnish application, pit-and-fissure sealants, dietary counseling, oral hygiene education, and personalized recall schedules. Such precision prevention strategies may substantially reduce disease incidence and healthcare expenditure.

Saliva-based digital diagnostics also have considerable utility in **community outreach programs and rural healthcare services**, where access to dental specialists and sophisticated laboratory infrastructure is limited. Portable biosensors requiring only microliter volumes of saliva allow rapid screening for periodontal disease, oral potentially malignant disorders (OPMDs), oral squamous cell carcinoma (OSCC), and salivary gland dysfunction. These decentralized diagnostic systems support early referral, improve healthcare accessibility, and reduce diagnostic delays among underserved populations.

High-risk populations—including tobacco users, areca nut chewers, individuals with diabetes mellitus, older adults, immunocompromised patients, and people with limited access to dental care—are particularly suitable candidates for saliva-based screening. Multiplex biomarker panels combining inflammatory mediators, microbial signatures, oncogenic markers, and metabolic indicators enable simultaneous assessment of multiple diseases, thereby maximizing screening efficiency.

The rapid expansion of **tele-dentistry** further enhances the applicability of saliva-based diagnostics. Smartphone-enabled POC devices can securely transmit biomarker data to cloud-based platforms, allowing remote interpretation by specialists and facilitating continuous monitoring of patients residing in geographically isolated regions. Integration with electronic health records (EHRs) enables longitudinal follow-up, automated risk alerts, and population-level epidemiological surveillance.

From a public health perspective, saliva-based digital biomarkers may contribute substantially to strengthening national oral health surveillance systems. Real-time epidemiological data generated through digital platforms can identify disease clusters, monitor temporal trends, evaluate preventive programs, and optimize allocation of healthcare resources. Such data-driven approaches align closely with the principles of precision public health and the World Health Organization's Global Oral Health Action Plan (2023–2030), emphasizing prevention, early detection, equity, and digital health integration.

## 8. Public Health Implications

The emergence of saliva-based digital diagnostics has important implications for the future of public health dentistry. Conventional oral health programs often depend on periodic clinical examinations, which are resource-intensive and difficult to implement at the population level. Saliva-based screening offers an opportunity to transition toward **predictive, preventive, personalized, and participatory (P4) dentistry**, enabling earlier intervention and reducing disease burden before irreversible tissue destruction occurs.

Implementation of saliva-based diagnostics may improve health equity by increasing access to diagnostic services among children, elderly populations, rural communities, and socioeconomically disadvantaged groups. Because saliva collection is painless and non-invasive, patient acceptance is generally high, making repeated surveillance feasible for longitudinal monitoring.

Integration with national health information systems can facilitate evidence-based policymaking by providing real-time epidemiological information regarding disease prevalence, treatment outcomes, and effectiveness of preventive interventions. AI-assisted predictive analytics may enable healthcare planners to identify vulnerable communities and allocate preventive resources more efficiently.

The economic implications are equally significant. Earlier diagnosis and targeted preventive interventions have the potential to reduce restorative treatment costs, minimize productivity losses associated with advanced oral diseases, and improve overall quality of life. Cost-effectiveness studies increasingly suggest that digital point-of-care diagnostics may become economically attractive once standardized multiplex biomarker platforms become commercially available.

Furthermore, saliva-based digital biomarkers may strengthen interdisciplinary healthcare by facilitating collaboration between dentistry, medicine, biomedical engineering, artificial intelligence, epidemiology, and health informatics. Such integration supports the broader concept of **precision public health**, wherein digital technologies are employed to deliver the right intervention to the right population at the right time.

## 9. Challenges and Limitations

Despite remarkable technological progress, several barriers continue to limit the routine clinical implementation of saliva-based digital biomarkers.

One of the most significant challenges is the lack of **standardized protocols** for saliva collection, transportation, storage, processing, and biomarker analysis. Variations in circadian rhythm, hydration status, diet, medications, smoking, systemic diseases, and collection techniques may substantially influence biomarker concentrations, thereby reducing reproducibility across studies.

Another limitation is the heterogeneity of currently available evidence. Many published studies involve relatively small sample sizes, single-center populations, or cross-sectional designs, limiting generalizability. Large multicenter longitudinal studies involving ethnically diverse populations remain essential for validating diagnostic thresholds and establishing universally accepted reference ranges.

Although numerous biomarkers have demonstrated promising diagnostic performance, few have undergone rigorous external validation or regulatory approval for routine clinical use. Most commercially available platforms evaluate a limited number of biomarkers, whereas oral diseases typically involve complex interactions among inflammatory, microbial, genetic, and metabolic pathways. Consequently, multiplex biomarker panels integrated with AI are likely to provide superior diagnostic performance compared with individual biomarkers.

Technical and economic barriers also remain important. High initial costs of biosensor development, maintenance of digital infrastructure, cybersecurity concerns, interoperability with electronic health records, and requirements for trained personnel may limit adoption, particularly in low-resource settings.

Ethical and legal considerations require careful attention. Digital salivary diagnostics involve collection of biological specimens, genomic information, and cloud-based health data, raising concerns regarding patient privacy, informed consent, data ownership, algorithmic transparency, and cybersecurity. Regulatory frameworks governing AI-assisted diagnostics continue to evolve and must balance innovation with patient safety.

Addressing these challenges will require interdisciplinary collaboration among clinicians, biomedical engineers, epidemiologists, policymakers, regulatory agencies, and industry partners.

## 10. Future Perspectives

The future of saliva-based digital biomarkers lies in the convergence of salivaomics, nanotechnology, biosensors, artificial intelligence, wearable devices, and precision public health. Rather than relying on isolated biomarkers, next-generation diagnostic platforms will integrate proteomic, transcriptomic, genomic, metabolomic, microbiomic, and exosomal datasets to generate comprehensive molecular signatures capable of detecting disease before clinical manifestations become evident (20).

Artificial intelligence and machine learning are expected to become central components of salivary diagnostics. Advanced predictive algorithms capable of analyzing multidimensional datasets will facilitate automated diagnosis, personalized disese risk prediction, therapeutic monitoring, and clinical decision support with minimal operator dependence. Explainable AI approaches may further enhance clinician confidence and regulatory acceptance.

Continuous monitoring through wearable intraoral biosensors represents another promising frontier. Smart mouthguards, dental splints, orthodontic appliances, and implant-supported sensors capable of continuously measuring inflammatory mediators, salivary pH, glucose, hydration status, and microbial activity may transform oral healthcare from episodic clinical assessments to continuous health monitoring.

**Future research should prioritize:**

- Standardization of saliva collection and analytical protocols.
- Large multicenter prospective validation studies.
- Development of affordable multiplex biosensor platforms.
- Cost-effectiveness and implementation research.
- Integration with tele-dentistry and national health information systems.
- Ethical governance and regulatory harmonization.
- Development of AI models with transparent and explainable decision-making.

Successful translation of saliva-based digital diagnostics into routine practice will depend upon close collaboration among oral healthcare professionals, biomedical scientists, engineers, public health experts, policymakers, and industry stakeholders.

## 11. Conclusion

Saliva-based digital biomarkers represent one of the most significant advances in contemporary oral diagnostics. The combination of salivaomics with biosensors, microfluidic technologies, point-of-care devices, wearable sensors, cloud computing, and artificial intelligence has created opportunities for rapid, non-invasive, and highly accurate disease detection that extend beyond traditional laboratory-based diagnostics.

Current evidence supports the application of saliva-based digital biomarkers for early detection and monitoring of dental caries, periodontal diseases, oral potentially malignant disorders, oral squamous cell carcinoma, peri-implant diseases, and xerostomia. Their integration into school oral health programs, community outreach services, tele-dentistry, and national surveillance systems has considerable potential to improve access to care, reduce diagnostic delays, facilitate personalized prevention, and strengthen public health infrastructure.

Nevertheless, widespread implementation requires further multicenter validation, biomarker standardization, regulatory approval, cost-effectiveness evaluation, and ethical governance. Addressing these challenges through interdisciplinary collaboration will accelerate translation from research laboratories to routine clinical practice.

With continued technological innovation and supportive public health policies, saliva-based digital biomarkers are poised to transform precision dentistry and population oral health screening by enabling earlier diagnosis, equitable healthcare delivery, and improved oral health outcomes worldwide.

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