

The Importance of

ORAL PERIODONTAL SCREENING

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EXECUTIVE SUMMARY

Over 100M individuals in the US have elevated pathogens in their mouth that can cause gum disease, including periodontitis. Using saliva and an advanced RT-PCR assay, SimplyTest has developed a robust quantitative CAP/CLIA test to screen for periodontal disease and provide insights as to whether any oral bacteria are reaching pathogenic levels. Once these harmful bacteria enter the bloodstream, they can lead to and advance multiple chronic diseases, including cardiovascular, liver, diabetes, cancer, and Alzheimer's.

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INTRODUCTION

Periodontal disease and dental caries are among the most common diseases in the world. The CDC estimates that 47.2% of the general population for individuals over 30, and 70.1% for individuals over 65 have gum disease [1]. Recent studies have identified an association between a variety of microbes in the mouth and increased prevalence of oral diseases such as periodontal disease [2-4]. This association creates an important opportunity for clinicians to introduce to their patients a new form of health screening and treatment. Using advanced real-time PCR (RT-PCR) technologies, routine testing allows a clinician to identify and treat individuals who harbor these organisms in their oral cavity. Importantly, preventive treatments have been shown to mitigate the progression of both gum disease and dental caries when deployed in the early stages of disease [5].

- Periodontal disease is highly prevalent, estimated at 47.2% of the general population for individuals over 30, and 70.1% for individuals over 65.
- Periodontal disease and dental caries (cavities) are driven by communities of bacteria rather than individual species.
- Periodontal disease is a known contributor and potential cause of chronic disease pathogenesis such as cardiovascular disease, diabetes, neurodegeneration and metabolic disease.
- Multiple dental associations and networks are advocating the adoption of such a test to become part of the standard of care.



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SYMPTOMS OF PERIODONTITIS

Healthy gums are firm to the touch and fit snugly around your teeth. In contrast, periodontitis symptoms include:

- Reddish or purplish gums
- Swollen gums
- Gums that bleed easily
- Tender gums
- Bad breath
- Pus (infection) around your gum line
- Loose teeth
- Tooth loss
- Gum recession (when your gums pull away from your teeth)
- Pain when chewing
- New gaps or spaces between your teeth
- Changes in the way your teeth fit together

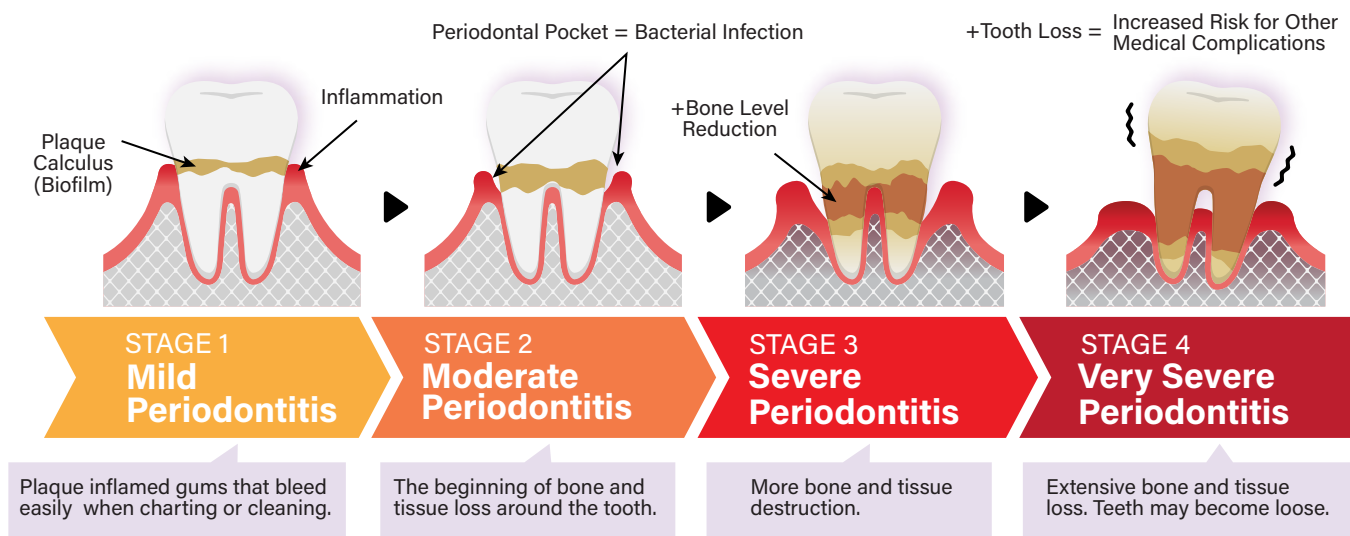
Periodontal disease progresses and becomes more problematic over time. According to the American Academy of Periodontology there are multiple gum disease stages, including:

Gingivitis: This is earliest stage of gum disease and is less severe than periodontitis. With gingivitis, gums become red and irritated, but patients haven't started losing bone around the teeth yet. Gingivitis is reversible with regular dental care and more attentive brushing, flossing and cleaning.

Mild periodontitis (STAGE I): Progressing past gingivitis, a patient will experience mild periodontitis. Within this stage, gums will begin to pull away from the teeth and patients will begin to lose some bone around the teeth. As a result, periodontal pockets will develop where plaque, tartar and bacteria become trapped in these pockets. Within these pockets the toothbrush and floss can't reach so the material persists and can cause more severe stages of periodontitis.

Moderate periodontitis (STAGE II): As periodontitis continues to progress, patients lose even more bone around teeth. Bacteria continue to erode the ligaments and soft tissues that support your teeth and keep them healthy. At this stage, your gums may become sore and tender.

Severe (STAGE III) and Very Severe (STAGE IV) periodontitis: When longer periodontitis exists without treatment, the disease becomes severe. Bone loss continues and the teeth may become loose and potentially fall out. In addition to bleeding gums, there's often pus and infection around your gum line, which can lead to chronic bad breath (halitosis).



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THE ORAL MICROBIOME IN HEALTH & DISEASE

The complex community of bacteria, fungi, and viruses that reside in the oral cavity can dramatically influence overall health and risk of chronic disease. Several species of bacteria have shown to be causally linked to the progression of dental caries and periodontal disease [2-4].

For example, dental caries can occur when sugar is metabolized by specific types of bacteria, such as *Streptococcus mutans*, in the mouth to produce acid, resulting in dental demineralization and damage [6, 7].

Key microbial species such as *Porphyromonas gingivalis*, *Tannerella forsythia*, *Fusobacterium nucleatum* and *Treponema denticola*, are known periodontal pathogens, and their abundance is linked to periodontitis [8, 9]. Furthermore, dozens of other bacterial species have been associated with the progressive stages of periodontal disease such as *Aggregatibacter actinomycetemcomitans* [10].

Importantly, while single bacterial species have been associated with disease, oral health status is influenced by the entire oral microbiome (hundreds of microbial strains), driving the importance of comprehensive profiling of the oral microbiome to assess health status [11].

Finally, the oral microbiome also harbors culturable commensal bacterial species that may reduce the incidence and progression of tooth decay and gum disease [12, 13].

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THE ROLE OF ORAL HEALTH IN SYSTEMIC HEALTH

Gum health has also been shown to play a major role in systemic health. Periodontal disease is associated with adverse outcomes for pregnancy, diabetes, cardiovascular disease, arthritis, and neurological diseases [14-20]. For example, periodontal disease increases a patient's lifetime risk of cardiovascular disease by greater than 19% [21]. In patients 65 years and older, the increased relative risk is as high as 44% [1, 20]. Early detection and active management of periodontal disease is therefore critical to improving overall health and preventing chronic disease associated with morbidity and mortality.

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LABORATORY PROCEDURES

This test utilizes RT-PCR amplification to detect the presence of a microorganism in a saliva sample by amplifying the genomic DNA of the organism(s). SimplyTest laboratory utilizes advanced RT-PCR systems that can simultaneously run up to four 3,072-reaction array plates in about four hours yielding an integrated system can produce up to 110,000 data points or more in an 8-hour day. Internal controls and standards afford the ability to provide quantitative values to the dental or medical clinician for evaluation of periodontal status, microbial burden and treatment options.

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ACCURACY OF RESULTS

Sensitivity (expected on-target amplification) was evaluated based on comparison to well-characterized, normalized genomic DNA, and multi-target synthetic DNA samples. The sensitivity across all assays and days was 100%.

Specificity (off-target amplification) was analyzed by examining potential cross-reactivity with common microflora, related species, and cross-reactivity among targets within the panel, using well-characterized, normalized genomic DNA pools. No Template Controls (NTC) and negative extraction controls (NEC) were evaluated for specificity in the absence of microbial DNA targets. The specificity across all assays was 99.55%.

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CONCLUSION

Periodontitis is a common immune-inflammatory oral disease. Early detection of clinically important microorganisms contribute to the development and progression of periodontal disease. Saliva is easily obtained and is an excellent sample media for reliably and accurately identifying periodontal pathogens and biomarkers. Leveraging salivary specimens, the SimplyTest Perio assay provides a 16-plex microbial snapshot that examines the presence and quantity of multiple organisms that contribute to all stages of periodontal disease. This provides an opportunity to provide early treatment options that can halt and even reverse the progression of periodontitis and its systemic effect on health.

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