


## COMMENT



Periodontics

# Beyond the mouth: the impact of periodontal disease on dementia

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**A COMMENTARY ON**

**Asher S, Stephen R, Mäntylä P, Suominen A L, Solomon A.** Periodontal health, cognitive decline, and dementia: a systematic review and meta-analysis of longitudinal studies. *J Am Geriatr Soc* 2022; **70**: 2695–2709.

**PRACTICE POINTS**

- Longitudinal studies with lengthy follow-ups validated cognitive assessments, and comprehensive control of confounding are needed to better elucidate the relationship between oral and cognitive health.
- Clinicians should be aware of the potential association between poor oral health and cognition, but the evidence is currently insufficient to recommend specific guidelines for dementia prevention.

**DATA SOURCES:** The authors searched Medline via PubMed, Scopus, CINAHL, Web of Science, and PsycINFO for relevant studies published until April 2022.

**STUDY SELECTION:** Longitudinal studies that assessed periodontal health as the exposure and cognitive decline and/or dementia as the outcome were included. Case reports, reviews, cross-sectional studies, and animal studies were excluded.

**DATA EXTRACTION AND SYNTHESIS:** Two authors independently reviewed studies for inclusion, extracted data, and assessed study quality. Meta-analysis was conducted to generate pooled odds ratios (ORs) for cognitive decline and hazard ratios (HRs) for dementia. Sources of heterogeneity were explored through subgroup analyses.

**RESULTS:** A total of 24 studies were included for cognitive decline and 23 for dementia. Poor periodontal health was associated with increased odds of cognitive decline (OR = 1.23; 95% CI: 1.05–1.44) and dementia (HR = 1.21; 95% CI: 1.07–1.38). Tooth loss also appeared to increase the risk independently. However, significant heterogeneity existed between studies.

**CONCLUSIONS:** Poor periodontal health may increase the risk of cognitive decline and dementia, but the quality of evidence was low. Further high-quality, longitudinal studies with standardized assessments are needed to establish causality.

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**GRADE Rating:** 

**COMMENTARY**

The mouth is the gateway to the body, and emerging studies provide increasing evidence for the bi-directional relationship between oral health and systemic health conditions. Recent research has suggested a noteworthy correlation between periodontal disease and dementia, an association that may have profound implications for both dental and mental health care<sup>1,2</sup>. Periodontal disease, a chronic oral condition, is the 11th most prevalent condition in the world, with a prevalence ranging from 20 to 50% worldwide<sup>3</sup>. It is characterized by the inflammation of the periodontium, the specialized tissues that both surround and support the teeth. An accumulating body of evidence has suggested an intimate link between periodontal disease and dementia, a multifaceted and devastating neurodegenerative condition<sup>1,2,4–8</sup>.

In a 20-year follow-up study, individuals with severe periodontal disease had a 70% increased risk of developing Alzheimer's disease compared to those without periodontal disease<sup>5</sup>. A population-based cohort study by Chen et al. found that dementia and Alzheimer's disease were associated with a higher risk of periodontal disease, dependent on age and independent of systemic confounding factors<sup>9</sup>. A recent meta-analysis of 20 observational studies also showed a strong relationship between periodontitis and cognitive impairment<sup>4</sup>. Asher et al. conducted a systematic review and meta-analysis to investigate the link between poor periodontal health and the risk of cognitive decline and dementia. The study employed appropriate meta-analytic methods and explored potential sources of heterogeneity through subgroup analyses. It also considered the issue of reverse causation to some extent. While the review suggested an association between periodontal disease and cognitive decline, several limitations affected the strength of the conclusions. Significant heterogeneity among studies could not be fully

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explained, and many had a high risk of bias. The definition of cognitive decline varied across studies, and few studies comprehensively adjusted for potential confounders. The review could not fully account for reverse causation, which may impact the observed associations between periodontal disease and cognitive decline. Additional high-quality, longitudinal studies with robust cognitive assessment, longer follow-up, and comprehensive control of confounders are needed to gain better insights. Collecting data on potential effect modifiers and mediators, such as systemic health, medications, dental care access, and social factors, would also benefit.

The suggested link between periodontal disease and dementia is typically explained through systemic inflammation and bacterial spread<sup>1,4</sup>. Periodontal disease triggers a systemic inflammatory response involving the release of cytokines such as tumor necrosis factor-alpha and interleukin-1 beta. These inflammatory mediators may cross the blood-brain barrier and induce the formation of plaques of amyloid peptides and intraneuronal neurofibrillary tangles that activate the glial cells. It finally causes neuroinflammation, a common feature of Alzheimer's disease and other dementias. Moreover, periodontal pathogens such as *Porphyromonas gingivalis* can enter the brain via the bloodstream or nerve routes, leading to direct brain infection and inflammation<sup>7</sup>. These bacteria can produce enzymes such as gingipains that have been found in Alzheimer's brain samples and are believed to be neurotoxic<sup>8,10</sup>. It is worth acknowledging a genetic perspective as well. APOE4 allele, associated with increased risk for Alzheimer's, tends to coincide with higher rates of periodontitis, a severe periodontal disease<sup>11</sup>.

The potential connection between periodontal disease and dementia necessitates dental and mental health care considerations. The prevention and treatment of periodontal disease may be a practical strategy to reduce dementia risk. Oral health care should be integrated into the management plan for patients at risk of or with dementia. At the population level, oral health promotion could potentially contribute to dementia prevention. This approach may be particularly relevant in low- and middle-income countries where both periodontal disease and dementia are prevalent, and resources are limited.

In conclusion, The emerging correlation between periodontal disease and dementia underscores the interconnectedness of oral and systemic health. Further research is required to clarify this association and elucidate the underlying mechanisms. Until then, embracing an integrative approach to oral and mental health care grounded in the prevention and management of periodontal disease may offer a proactive pathway to mitigate the growing burden of dementia.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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