



# Diabetes and Oral Health: Summary of Current Scientific Evidence for Why Transdisciplinary Collaboration Is Needed

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This Perspective provides a brief summary of the scientific evidence for the often two-way links between hyperglycemia, including manifest diabetes mellitus (DM), and oral health. It delivers in a nutshell examples of current scientific evidence for the following oral manifestations of hyperglycemia, along with any available evidence for effect in the opposite direction: periodontal diseases, caries/periapical periodontitis, tooth loss, peri-implantitis, dry mouth (xerostomia/hyposalivation), dysbiosis in the oral microbiome, candidiasis, taste disturbances, burning mouth syndrome, cancer, traumatic ulcers, infections of oral wounds, delayed wound healing, melanin pigmentation, fissured tongue, benign migratory glossitis (geographic tongue), temporomandibular disorders, and osteonecrosis of the jaw. Evidence for effects on quality of life will also be reported. This condensed overview delivers the rationale and sets the stage for the urgent need for delivery of oral and general health care in patient-centered transdisciplinary collaboration for early detection and management of both hyperglycemia and oral diseases to improve quality of life.

**Keywords:** diabetes mellitus, early diagnosis, health care costs, interdisciplinary communication, interprofessional relations, periodontal diseases, prevention and control, referral and consultation

## INTRODUCTION

Regrettably, dentistry was separated from general health care and became an independent profession (1), leaving little education and awareness regarding oral health and its links to general health among the other health professions (2–10).

The most prevalent chronic diseases share the same “common risk factors” (11–13) (**Figure 1**) and hence often occur in the same patients, regardless of whether causal links and not merely associations exist. Nonetheless, rapidly emerging scientific evidence demonstrates that oral diseases and hyperglycemia (elevated blood glucose concentration), including manifest diabetes mellitus (DM), independently and mutually affect each other.

The term “transdisciplinary” is used to include practitioners of all health care disciplines, such as physicians, assistants of the physician, nurses, nurse practitioners, midwives, dietitians, DM educators, speech therapists, social workers, etc., in contrast to “interprofessional” that implicitly accepts the siloed approach regarding dentistry and general health care as separate professions.

This research summarizes, in a nutshell, the current evidence for links between oral diseases and DM to support the need for transdisciplinary collaboration.

## HYPERGLYCEMIA/DM AND ORAL HEALTH MUTUALLY AFFECT EACH OTHER

While type 1 DM (T1DM) is due to no or insufficient insulin production affecting about 5% of patients with DM, type 2 DM (T2DM) is a syndrome characterized by elevated blood glucose levels due to insufficient insulin production, insufficient insulin uptake, or both (15–17). About 463 million (9.3%) adults suffer from DM, with 700 million (10.9%) expected by the year 2045 (18, 19). An additional 374 million people have prediabetes (preDM) and are at risk of developing T2DM (18).

Systemic hyperglycemia causes complications such as retinopathy; nephropathy; neuropathy; heart, peripheral arterial, and cerebrovascular disease; obesity, cataracts; erectile dysfunction; and non-alcoholic fatty liver disease (20). Regardless of DM type, it is the hyperglycemia, not the diagnosis of DM *per se*, that leads to several oral complications (21) and oral health-related decreased quality of life (QoL) (22).

These oral manifestations are described, followed by any effects in the opposite direction.

For succinct brevity, DM is used for any type of diabetes or hyperglycemia; and the comparison group is non-traditionally omitted. For example, in the sentence “*People with DM have greater xxxx,*” the comparison “*than people without DM*” is implicit, but not shown.

### Periodontal Diseases

Periodontal diseases affect up to 90% of adults globally, with the reversible form, gingivitis, affecting almost everybody (23). In contrast, periodontitis is chronic, irreversible destruction of soft and hard tissues around the teeth that results from an interplay between polymicrobial dysbiosis in the plaque microbiome in the gingival sulcus and the especially susceptible host (24, 25). Periodontitis affects 42.2% of US dentate adults (26), likely varies globally, and is the 12th of 291 most prevalent diseases worldwide (27), with “severe” periodontitis being the sixth most prevalent disease (28), affecting 11.2% of adults (28).

Periodontitis and hyperglycemia share the same risk factors (29, 30) and hence often occur in the same individuals with compromised immune systems or exhibiting hyperinflammatory responses; and they additionally adversely affect each other.

A much greater proportion of people with DM suffer from periodontitis (31–33), and the severity of periodontitis is much greater, especially in poorly or uncontrolled DM (31, 34, 35). Citing clinical studies from Denmark (36), Australia (37), Finland (38), Argentina (39), and the US (40, 41), including among the Pima Indians in Arizona (42–46), periodontitis was declared the sixth complication of DM in 1993 (47), but with negligible effect on the medical and dental communities.

In the opposite direction, people with periodontitis are much more likely to have T2DM (33, 48). Periodontitis, *via* bacteremia (49, 50) and inflammatory responses of which

hyperglycemia is a normal part (Figure 1), is a risk factor for DM, that is, incident T2DM, gestational DM, poorer glycemic control in existing DM, and more severe DM complications (51, 52). Furthermore, periodontitis is increasingly regarded as an independent risk factor for the macro-vascular DM complications cardiovascular disease (CVD) (53–58) and ischemic stroke (54, 56), and is associated with the microvascular DM complications: neuropathy (54, 59), nephropathy (54, 60–62), and retinopathy (54, 60).

### Cognitive Impairment in DM

Alzheimer’s disease has been named “type 3 DM” (63) as a DM complication (64) partly due to glucose hypometabolism causing cognitive decline (65). Novel research supports the role of especially *Porphyromonas gingivalis* (Pg), a key periodontitis-associated bacterium, in Alzheimer’s disease (66–72), with promising experimental treatment with gingipain inhibitors to reduce Pg brain colonization and neurodegeneration reported (73).

### COVID-19

With DM being a risk factor for COVID-19, oral manifestations of the SARS-CoV-2 virus (74, 75) are reported in DM, such as painful ulcers (76, 77) and necrotizing periodontitis (78).

In COVID-19, a radiographic study found periodontitis to be associated with more intensive unit admissions, increased ventilation needs, and mortality in COVID-19 (79), and gingivitis is also reported (80). This is probably the case also in DM with its weakened immune system. Likely, periodontal pockets (81, 82), gingival crevicular fluid (83), and saliva acting as reservoirs for SARS-CoV-2 virus (81, 84–86) may even facilitate COVID-19 development (87), persistence (88), and mortality especially in people with DM (89).

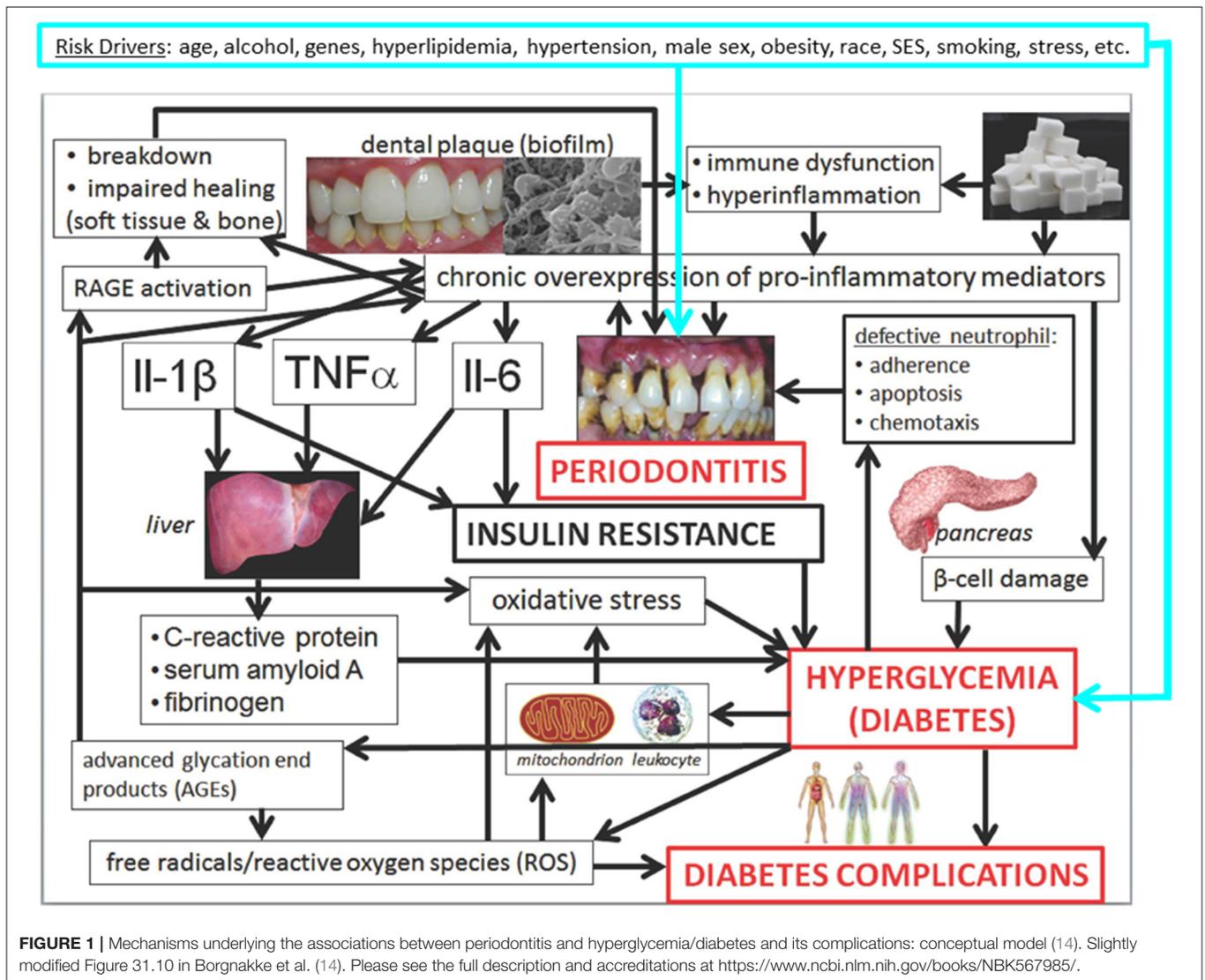
### Caries/Periapical Periodontitis

Untreated caries in permanent teeth is the most prevalent condition of the world affecting 2.4+ billion people (90). The evidence for links to DM is mixed, although adolescents with DM have 2- and 3-fold greater numbers of filled teeth and teeth with untreated caries, respectively (91). Patients with DM receiving hemodialysis have more caries (92); and periapical infections and their abscesses seem to be more prevalent in DM (93, 94).

### Tooth Loss

Worldwide, people with DM have lost many more teeth (36, 37, 95–101), [about twice the magnitude (102)], especially if uncontrolled (103), and at an earlier age (96).

Tooth loss is a risk factor for hyperglycemia that is not usually mentioned as such, even though this has possibly the greatest immediate importance for DM management. Having loose teeth (due to periodontitis), sensitive teeth (due to deep caries lesions), few teeth left (104), or removable dentures will automatically cause problems with mastication, resulting in people not being able to eat crisp foods that need biting off or proper mastication. That is, such people are simply unable to follow the recommendations for a proper diet intended for controlling their DM by consuming appropriate



amounts and kinds of healthy nutrients (105–107). In contrast, they resort to soft, processed food items with high Glycemic Index scores (108) and high Dietary Inflammatory Index scores (105, 106), typically laden with fat, sugar, and salt but deficient in fibers and vitamins (109), as opposed to fresh vegetables and fruit and whole-grain products. Alone for this reason, sincere efforts to prevent tooth loss should be invested in transdisciplinary DM management including dietitians (109).

Missing teeth are also associated with DM complications, such as myocardial infarction (110, 111) and retinopathy (36, 112); and lack of proper mastication negatively impacts cognitive function (113, 114).

## Peri-Implantitis

Even though dental implants can osseointegrate, albeit delayed (115), and survive in patients with poorly controlled DM (116), hyperglycemia is a risk factor for peri-implantitis (breakdown

of peri-implant soft and hard tissues) that is independent of smoking (117–119).

## Dry Mouth

Individuals with DM often suffer from dry mouth, meaning xerostomia (subjective feeling of mouth dryness) or hyposalivation (decreased salivary production), decreasing QoL. Patients with DM often suffer from bad breath (halitosis), foul taste, and multimorbidity with polypharmacy (22, 32, 120). All major groups of pharmaceuticals can cause mouth dryness and various periodontal complications (121). Hyposalivation also majorly impacts the oral microbiome composition (122).

Hyposalivation can lead to trouble keeping removable dentures in place, mastication, swallowing (dysphagia), and speech (104); and greater incidence of coronal and root caries and periodontitis, ultimately leading to tooth loss.

In transdisciplinary collaboration, physicians can prescribe fewer or less xerogenic medications or change the dosage

and frequency. Since both hyposalivation and cancer are more prevalent in DM, they should also ensure proper protection of the (unaffected) salivary glands during radiation therapy in the head and neck region.

### Microbiome Dysbiosis

Hyperglycemia causes changes (123) such as in composition (122, 124, 125) and decreased diversity (126, 127) and abundance (126, 128) of certain bacteria in the subgingival microbiome in periodontitis. Moreover, severities of DM and periodontitis are associated (129, 130). DM treatment leads to changes in the salivary microbiome (131).

Oral and gut microbiomes are closely linked (132); even a small number of periodontal bacteria predict change in glucose level in young healthy adults (133). *Pg* alters the gut microbiome and causes metabolic syndrome (134) and preDM (135).

### Candidiasis

DM is an independent predictor of oral candidiasis (136), especially in hyposalivation (137), as DM favors the acidogenic bacteria that in turn promote the development of caries and candidiasis. *Candida albicans*, a commensal yeast in the oral microbiome causing candidiasis, can bind to the oral mucosa and, hence, contribute to the cumulative burden of inflammation, directly or *via* denture stomatitis caused by unclean dentures (138). Over 900 different species of microbes reside in biofilm adhering to dentures (139) and are an important source of sepsis that is largely unnoticed (138).

### Taste Disturbances (Dysgeusia, Ageusia, and Hypogeusia)

Due to hyposalivation, neuropathy of nerves sensing taste, microangiopathy in taste buds or medications, (120), and taste impairment and disorders occur frequently in DM (59). Altered taste (gustatory changes) could be the first sign of T2DM, a useful fact for all health professionals. Ageusia is also a COVID-19 symptom (140).

### Burning Mouth Syndrome

DM can contribute to the complex burning mouth syndrome that likely is caused by neuropathy and other local and systemic factors and, therefore, needs transdisciplinary treatment (32, 120, 141–143).

### Cancer

Cancer is associated with inflammation and occurs more frequently in DM (144), including oral cancer that has a 4.3-fold greater risk of developing and a 2.1 times greater risk of mortality in DM than in non-DM (145). Potentially malignant oral mucosal lesions are also associated with DM, such as leukoplakia, erythroplakia, lichen planus and other lichenoid lesions, and actinic cheilitis (145).

### Other Oral Mucosal Lesions and Conditions

People with DM have a greater risk of traumatic ulcer, infections of oral wounds, delayed wound healing, melanin pigmentation,

fissured tongue, and benign migratory glossitis (geographic tongue), and temporomandibular disorders (21, 32).

### Osteonecrosis of the Jaw (ONJ)

DM is an established risk factor for ONJ in general (146–148) and medication-related ONJ (MRONJ) (149–154). Microvascular complications (angiopathy, ischemia, endothelial cell dysfunction) impair blood circulation and hence bone nutrition and quality with reduced remodeling (155). DM also causes increased apoptosis of osteoblasts and osteocytes and changes in immune cell function, promoting inflammation (155).

### Quality of Life

DM decreases QoL with a further decrease in oral health-related QoL (OHRQoL) (59, 156–160). Importantly, QoL correlates strongly with OHRQoL (161), so treating oral diseases increases QoL in DM (160, 162, 163).

## DENTAL TREATMENT IN DM

Non-surgical periodontal treatment (NSPT) consisting of scaling and root planing (SRP), or “deep cleaning,” home oral hygiene instruction, and maintenance follow-up visits can be performed in any dental office by dental hygienists or dentists and improves the periodontal health status also in DM (164, 165). However, advanced cases need treatment by periodontists or other especially skilled clinicians. Adults with DM and periodontitis manage to incorporate new, effective oral hygiene measures into daily life (166); and frequent tooth brushing is negatively associated with incident DM (167).

### Glycated Hemoglobin Level

Non-surgical periodontal treatment can lead to a decrease in glycated hemoglobin (HbA1c) level in T2DM after 3 months, which is of clinical significance as it is of the same order of magnitude as adding a second oral antidiabetic medication to metformin (156, 168, 169). Results of meta-analyses upon systematic reviews are displayed in **Table 1**. Greater effect is seen with greater baseline HbA1c levels (186).

Few studies last longer than 3 months. Noteworthy is a definitive 12-months study ( $N = 133$ ) demonstrating that intensive periodontal treatment (including surgery) reduced the crude mean HbA1c level from 8.1 ( $\pm 1.7$ )% to 7.8 ( $\pm 0.2$ )% (187). Upon adjustment, intensive treatment reduced the mean HbA1c value by 0.6 (95% CI; 0.3–0.9)% more than routine NSPT (187).

### Inflammatory Markers

Non-surgical periodontal treatment can lead to decreased levels of inflammatory markers, such as C-reactive protein and leukocyte counts that are risk indicators for CVD (188, 189), and the subgingival periodontal biofilm is disturbed, mitigating periodontitis progression (123).

Full-mouth extraction, the ultimate treatment of terminally periodontally diseased teeth, significantly lowers systemic inflammatory markers (190).

**TABLE 1 |** Effect of non-surgical periodontal treatment (scaling, root planing, and oral hygiene instruction) (NSPT) on glycated hemoglobin (HbA1c) level in type 2 diabetes (T2DM) 3 and 6 months post-intervention: meta-analyses.

References	# Studies	# RCTs	Pooled # Subjects	Mean HbA1c% Change	95% CI	P-value
Janket et al. 2005 (170)	4	1	268	-0.66 <sup>§</sup>	-2.2; +0.9	n.s.
Darré et al. 2008 (171)	9	5	485	-0.46 <sup>†</sup>	-0.82; -0.11	0.01
Simpson et al. 2010 (172) (Cochrane Review)	3	3	244	-0.40	-0.78; -0.01	0.04
Teeuw et al. 2010 (173)	5	3	180	-0.40 <sup>§</sup>	-0.77; -0.04	0.03
Corbella et al. 2013 (174) (3 mos)	15*	15*	678	-0.38	-0.53; -0.23	<0.001
(6 mos)	3	3	235	-0.31	-0.74; 0.11	n.s.
Engelbretson and Kocher 2013 (175)	9	9	775	-0.36	-0.54; -0.19	<0.0001
Liew et al. 2013 (+/-antibiotics) (176)	6 <sup>##</sup>	6 <sup>##</sup>	473 <sup>##</sup>	-0.41 <sup>##</sup>	-0.73; -0.09	0.013
(-antibiotics)	2 <sup>#</sup>	2 <sup>#</sup>	270 <sup>#</sup>	-0.64 <sup>#</sup>	-1.06; -0.23	0.002
(+antibiotics)	4 <sup>#</sup>	4 <sup>#</sup>	203 <sup>#</sup>	-0.09 <sup>#</sup>	-0.52; +0.30	n.s.
Sgolastra et al. 2013 (177)	5	5	315	-0.65 <sup>§</sup>	-0.88; -0.43	<0.05
Wang et al. 2014 (178) (+ doxycycline)	3	3	143	-0.24 <sup>†</sup>	-0.62; +0.14	0.217
Li et al. 2015 (179)	9	9	1,082	-0.27	-0.46; -0.07	0.007
Simpson et al. 2015 (3-4 mos) (Cochrane Review) (180) (6 mos)	14	14	1,499	-0.29	-0.48; -0.10	<0.05
Teshome et al. 2016 (181) (3 mos) (study end)	7	7	940	-0.48	-0.18; -0.78	<0.00001
	7	7	940	-0.53	-0.24; -0.81	<0.00001
Cao et al. 2019 (182) (3-12 mos)	14	14	649	-0.399	-0.088; -0.79	sig.
Jain et al. 2019 (183)	6	6	812	-0.26%	-0.63; 0.11	0.17
Yap and Pulikkotil (184) (+ doxycycline)	6	6	208	-0.13	-0.41; 0.15	n.s.
Baeza et al. 2020 (185) (3 mos × 6 studies; 6 mos × 3 studies)	9	9	623	-0.56	-0.75; -0.36	<0.00001
Chen et al. 2021 (186) (3 mos) (+/- antibiotics; +/- surgery) (6 mos)	19	19	1,660	-0.514 <sup>§</sup>	-0.730; -0.298	=0.000
	10	10	1,441	-0.548 <sup>§</sup>	-0.859; -0.238	=0.000

+/-antibiotics, with or without antibiotics; CI, confidence interval; HbA1c, glycated haemoglobin; mos, months posttreatment; n/a, not available; n.s., nonsignificant; RCT, randomized controlled trial; sig., significant. \*Including one study with 30 T1DM and one study with 12 T1DM. <sup>§</sup>Weighted mean difference (WMD). <sup>†</sup>Standardized mean difference (SMD). <sup>#</sup>Including one study with 6 mos. follow-up only. <sup>##</sup>Including two studies with 6 mos. follow-up only.

## Tooth Loss

Scaling and root planing in patients with T2DM is modeled to significantly decrease tooth loss by 34.1% overall (191) and in microvascular diseases by 20.5% in nephropathy, 17.7% in neuropathy, and 19.2% in retinopathy, respectively (191). Nonetheless, insurance data identify DM as a risk factor for tooth loss during periodontal maintenance (95).

## DENTAL TREATMENT REDUCES HEALTHCARE-RELATED COSTS IN DIABETES

Dental care has been shown to reduce overall medical care costs in people with DM. Acknowledging inherent methodologic issues (192), population studies and analyses of claims data, from people with DM simultaneously insured for dental, medical outpatient care, hospitalization, and pharmacy expenses, report savings in medical care costs, hospitalization, and introduction of insulin among insureds with DM from studies in Germany (193), Japan (194, 195), the Netherlands (196), United Kingdom (197), and the US (191). A correlation between periodontitis severity and

future increases in medical care costs was found among older Japanese (198).

Adults with DM consistently have fewer regular dental check-ups than their non-DM peers (22, 199-208) with between 25 and 60% having had a dental visit the last year. Nonetheless, patients with DM who do receive dental care experience incremental higher costs for more complex treatment and restoration of missing teeth rather than preventive visits (203).

## TRANSDISCIPLINARY CARE

### Transdisciplinary Care Initiated in the Medical Setting

#### Screening for Periodontitis in the Medical Office

Attainment of good oral health deserves the attention of medical care providers as a novel tool in DM management (209, 210). Medical care providers recognize grossly cavitated (caries) teeth and thrush (Candidiasis) and could suspect undiagnosed periodontitis based on evident signs such as having few or loose teeth, bad breath, or swollen and spontaneously bleeding gums.

Several questionnaires for assessing the risk of periodontitis by self-report exist. For example, the U.S. Centers for Disease

Control and Prevention (CDC) jointly with the American Academy of Periodontology (AAP), developed a set of eight easy-to-pose-and-respond-to items that were validated and found to associate with clinically diagnosed periodontitis (211–213). These or similar questions could be included in the medical visit (22, 214). Such screening in medical practice is well-accepted by both patients (206) and medical professionals (206, 215).

### Guidelines for Medical Care Providers and Their Patients

Acknowledging the importance of good oral health in DM management, several professional organizations have published guidelines for (a) medical care professionals in DM practice: AAP (156); American Diabetes Association (ADA) (20); International Diabetes Federation (IDF) (**Appendix 1**, available online only) (169); and the European Federation of Periodontology (EFP) (156, 169) (**Appendix 1**); and (b) people with DM or at risk for T2DM in medical practice: AAP (156); ADA (216); IDF (169, 217) (**Appendix 1**), and EFP (156, 169) (**Appendix 1**).

### Transdisciplinary Care Initiated in the Dental Setting

#### Screening for T2DM in the Dental Office

Because about half the people with manifest DM and 90% of those with preDM are unaware thereof (18), the dental setting can be important for T2DM screening and referral (218–220), especially for dental patients who do not see a physician regularly (221). It is crucial to identify T2DM in its early stages during which the chances for reversal or mitigation are greatest (222–225). Periodontitis can serve as an early sign of T2DM (226), just like few teeth and recurrent periapical abscesses (93, 94). Random blood glucose or HbA1c levels can be measured chairside by quick finger-prick blood sample analysis (221, 227–241).

Interestingly, 30–54% of dental patients who denied having DM had T2DM with 1.3–5.8% having manifest T2DM as reported from studies in Denmark (227), Saudi Arabia (228), Spain (229), United Kingdom (230, 231), and the US (232–238), aided by electronic health records (239). Whereas, 7.8% of US minority elders (240), 17.2% of patients with Dutch periodontal, and, respectively, 14.6% (241) and 19.1% (221) of Indians had T2DM.

PreDM was found in 9.9% of unaware dental patients in Sweden (242), 28.7% in the US (235), and 46.6% among patients with Dutch periodontal (243).

### Guidelines for Dental Care Providers and Their Patients

Acknowledging the importance of identifying undiagnosed T2DM early in dental patients, several professional organizations have published guidelines for a) dental care professionals in dental practice: AAP (156); EFP (156, 169) (**Appendix 1**); IDF (169) (**Appendix 1**); Indian Society of Periodontology (244); and Research Society for the Study of Diabetes in India (244); and b) people with DM or at risk for DM in dental practice: AAP (156); EFP (156, 169) (**Appendix 1**); and IDF (169) (**Appendix 1**).

Such screening in dental offices is well-accepted by patients (245–247), dentists (246–250) and physicians (251), and their professional organizations (252), and can lead to positive lifestyle changes and decreased HbA1c level (253, 254).

## DISCUSSION

Research to promote the understanding of mechanisms underlying reciprocal links between various aspects of oral health and DM is rapidly emerging. However, the current evidence is sufficient to act. The major causes of tooth loss are the two most common oral diseases, namely caries and periodontitis that occur in great proportions of populations globally. These diseases are associated as their respective prevalence in large population studies are not independent of each other (255). Nonetheless, both are largely preventable or treatable/manageable when developed, resulting in the survival of the teeth. Edentulism (having no natural teeth) is decreasing globally, so people keep their teeth at higher ages (28, 256). Furthermore, life expectancy also increases (28, 256); and the prevalence of DM is increasing rapidly all over the world (18). Consequently, increasing numbers of people with DM worldwide are at risk for the oral manifestations described here.

In conclusion, all health care professionals must join forces. However, such transdisciplinary patient-centered collaboration requires paradigm shifts in awareness, attitude, education, and medical and dental practice delivery systems for all health care professionals.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

## ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

## AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fdmed.2021.709831/full#supplementary-material>

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