



Glycemic Control and Periodontal Health in Uncontrolled Diabetes and Periodontitis Using an Electric Toothbrush with a Smart Mobile Application: A Randomized Controlled Trial

Citation

Thanasuwat, Burinrutt. 2026. Glycemic Control and Periodontal Health in Uncontrolled Diabetes and Periodontitis Using an Electric Toothbrush with a Smart Mobile Application: A Randomized Controlled Trial. Masters Thesis, Harvard University School of Dental Medicine.

Link

<https://dash.harvard.edu/handle/1/42736779>

Terms of use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material (LAA), as set forth at

<https://harvardwiki.atlassian.net/wiki/external/NGY5NDE4ZjgzNTc5NDQzMGIzZWZhMGFIOWI2M2EwYTg>

Accessibility

<https://accessibility.huit.harvard.edu/digital-accessibility-policy>

Share Your Story

The Harvard community has made this article openly available.

Please share how this access benefits you. [Submit a story](#)

Master of Medical Sciences Thesis

Presented by

Burinrutt Thanasuwat, DDS

to the Faculty of Medicine

Research Mentor:

Chia-Yu Chen, DDS, DMSc., Assistant Professor/Pre-Doctoral Director

Project Title:

Glycemic Control and Periodontal Health in Uncontrolled Diabetes and Periodontitis Using an

Electric Toothbrush with a Smart Mobile Application:

A Randomized Controlled Trial



Abstract

Background: Periodontitis and type II diabetes mellitus (T2DM) are both chronic inflammatory diseases and have been shown to have a bidirectional relationship. Periodontal inflammation can worsen glycemic control, while hyperglycemia can raise baseline inflammatory load and worsen periodontal tissue breakdown.

Aim: To evaluate whether an electronic toothbrush with a smartphone application, used as an adjunct to scaling and root planing (ScRP), improves glycemic control and periodontal outcomes, compared to a manual toothbrush.

Methods: Adults ≥ 35 -year-old with stage II-III periodontitis and T2DM with HbA1c $\geq 7\%$ were included for the study. Patients received ScRP and oral hygiene instruction, and frequent periodontal maintenance. Patients were randomized into either (1) manual toothbrush (control) or (2) electronic toothbrush with smartphone application (test) group. Patients receives periodontal maintenances at follow-ups visits at 3, 6, 9, and 12 months. Oral hygiene instruction and periodontal maintenance was provided at follow-up visits at 3, 6, 9, and 12 months. The primary outcome was HbA1c changes from baseline. Secondary outcomes included changes in probing pocket depth (PPD), residual deep pocket, bleeding on probing (BOP), plaque index (PI), and inflammatory biomarkers collected from gingival crevicular fluid (GCF).

Results: 32 participants were enrolled; 23 were included in the final analysis (11 control, 12 test). The mean age was 62-year-old for both groups. HbA1c declined initially for both groups and then increased again at the end of 12-month follow-up. In the control group, the greatest mean HbA1c reduction of 0.51% was at 6 months. In the test group the greatest mean HbA1c reduction of 0.85% was at 3 months. Overall, HbA1c level changes did not demonstrate a statistically significant difference between the two groups over time. For periodontal clinical parameters, PPD reduction were significant across all time points for both control and test groups, however, no between-group differences were observed. End point parameter of residual deep pockets showed significant differences across all time points within-group and a significant difference at 9 months between two groups, favoring the test group. BOP showed statistically significant within-group reduction across all time points for test group but only significant at 2 and 6 months for control group. Between-group difference was statistically significant at 9 months, favoring the test group. PI showed no statistical significance between the two groups. GCF biomarker analyses were completed for 14 inflammatory biomarkers. Statistically significant between-group differences at the $p < 0.05$ threshold were limited to TNF α , IL-2, IL-4, IL-5, and VEGF.

Conclusions: Electronic toothbrush with smartphone application when used as adjunct to nonsurgical periodontal therapy with regular maintenance enhanced periodontal clinical outcomes. However, the effects on HbA1c are comparable between two groups.

Introduction/Background

Periodontitis is a chronic, microbially-associated, host-mediated inflammatory condition affecting the supporting soft and hard tissue around teeth.¹ In 2017, the American Association of Periodontology together with the European Federation of Periodontology, developed a new classification system for periodontal and peri-implant diseases to provide an evidence-based strategy for diagnosing and treatment planning. The classification system characterizes periodontitis by stage (I-IV), based on the severity, complexity and extent of the disease, and by grade (A-C), based on the risk and progression of the disease.¹ According to Bernabe et al. 2020, findings from the Global Burden of Disease 2017 study considered severe periodontitis (Stage III-IV) to have major impacts on the population on a global scale, affecting roughly 796 million individuals worldwide.² Based on an NHAES 2009-2014 study, it was estimated that 42.2% of U.S. population aged 30 years or older were affected with periodontitis, of which 7.8% had severe periodontitis.³ The most recent meta-analysis showed that approximately 61.6% of dentate population between 2011-2020 was diagnosed with periodontitis, of which 23.6% was diagnosed with severe periodontitis.⁴ Periodontitis is not only a common chronic inflammatory disease of the oral cavity, but also a condition with significant consequences for patients' quality of life and systemic health.

The American Diabetes Association (ADA) described type 2 diabetes mellitus (T2DM) as a metabolic disorder characterized by insulin resistance or deficiency in association with progressive loss of β -cells' insulin secretion ability.⁵ T2DM account for approximately 90-95% of

all diabetes cases.⁵ Globally, an estimated 537 million people are living with T2DM, and this number is projected to rise to 783 million by 2045.⁶ In the United States, approximately 40.1 million adults are diagnosed with T2DM, with an additional estimated 11 million individuals remaining undiagnosed according to the Center of Disease Control and Prevention.⁷

Both periodontitis and diabetes are chronic diseases and linked by a bidirectional relationship.⁸ A heightened inflammatory background is a shared features of both diseases. Both chronic conditions showed increased in inflammatory biomarkers along with an increased in bone resorption markers and oxidative stress.⁸ There is strong evidence that periodontitis patients have increased risk for developing T2DM.⁸ Patients with periodontitis have been shown to have elevated levels of interleukin-1- β (IL-1 β), tumor necrosis factor- α , and IL-6, which can contribute to poorer metabolic regulation and insulin resistance.^{8,9} On the other hand, diabetes and hyperglycemia have been reported to promote advanced glycation end products and their receptors (AGE-RAGE) signaling, delayed wound healing, and impaired neutrophil functions, all of which can contribute to the development of periodontitis.¹⁰

Periodontal therapy has been shown to reduce systemic inflammatory burden and improve other systemic conditions, including insulin resistance and glycemic control in diabetic patients.^{8,11} An HbA1c reduction of 0.29% at 3-4 months post subgingival instrumentation or nonsurgical periodontal therapy has been reported.¹¹ Another study concluded that nonsurgical periodontal therapy could reduce HbA1c level of approximately 0.43% at 3-4 months postoperatively.¹¹ Similarly, a randomized clinical trial by D'Aiuto et al. in 2018 showed a

sustained HbA1c reduction of about 0.6% up to 12 months follow-up.¹² However, another large randomized clinical trial did not demonstrate a significant differences in HbA1c levels between diabetic patients treated with periodontal therapy and those in the control group.¹³ A landmark study by Grossi et al. in 1997 compared patients with diabetes who received periodontal therapy with or without adjunctive antimicrobial regimen and demonstrated significant reductions in HbA1c levels across all groups at 3 months, with decreases close to 10% from pre-treatment HbA1c level.¹⁴ They also reported improvements in all clinical parameters, including reduction of periodontal pathogen such as *Porphyromonas gingivalis*, when analyzing subgingival plaque.¹⁴ While the current findings are not definitive, the available evidence supports a biologically plausible role of periodontal therapy in improving glycemic control and reducing inflammatory burdens in patients with chronic inflammatory diseases such as T2DM.

While the evidence for a direct effect of improved glycemic control on periodontal conditions remains limited, a key study in 2013 by Katagiri et al. reported that an effective glycemic control improved bleeding on probing (BOP) lesions in type 2 diabetic patients with periodontitis.¹⁵ Another by Tseng et al in 2022, evaluated diabetic medications, metformin, and concluded that long-term use of metformin is associated with a significant reduced risk of gingival and periodontal diseases.¹⁶ Therefore, improvement in diabetic control may have a beneficial influence on periodontal conditions.

One consistent element across the previously cited periodontal literature was routine supportive periodontal therapy (SPT) after any periodontal treatment. Strict supportive

periodontal therapy, or professional dental hygiene therapy (PDHT), is aimed at preventing periodontal disease recurrence, enabling early detection, and maintaining periodontal stability over time. The 2020 European Federation of Periodontology (EFP) S3 level clinical practice guideline determines that patient education, oral hygiene instruction, and regular SPT are the foundation of periodontal care.¹⁷ This highlights the importance of patients' homecare as a fundamental factor to the success of any periodontal therapy. Based on a systemic review by Lee et al in 2015, compliance with SPT is one of the strongest determinants of long-term tooth retention.¹⁸ The byproducts from dental plaque have been reported to be associated with higher risk of periodontitis, while regular SPT and daily brushing were reported as a protective factor from developing periodontitis.¹⁹ Home use of interdental cleaning devices, in addition to toothbrushing, were also shown to reduce gingival and periodontal diseases development.²⁰ Another study reported that patients who received instruction in flossing technique (adapted horizontal vertical flossing technique, AHVFT), demonstrated greater reductions in interproximal BOP when compared to patients who did not received the same instruction, further emphasizing the importance of patient education.²¹ Currently, no single brushing technique has been shown to have definitive superiority across all studies, although the Bass intrasulcular technique showed short term benefits of reduction in gingival inflammation, BOP, and gingival index.²²⁻²⁴

A systematic review and meta-analysis found that mobile application maybe beneficial as an adjunct to oral home care, although definitive or conclusive evidence cannot yet been drawn.²⁵ The smart mobile application can provide real-time feedback on brushing time, surfaces,

pressure, and brushing frequency, all of which can help patients improve compliance to oral hygiene routine at home. One randomized clinical trial reported that a smartphone application used with electric toothbrush improved full-mouth plaque index.²⁶ Tonetti et al. in 2020 reported that smartphone application usage was associated with lower plaque scores.²⁷ Another randomized clinical trial testing artificial intelligence (AI) enabled electric toothbrush with application reported better inflammation resolution across multiple clinical markers.²⁸ These findings provide valuable insights into the potential usage of technology to improve home oral hygiene routine for patients.

Therefore, a better understanding on prevention and treatment of periodontal disease, such as plaque control, can greatly decrease disease burdens not only for periodontitis but also for type II diabetes mellitus and potentially for other chronic inflammatory diseases. Currently, there are no studies demonstrating the impact of an electric toothbrush with mobile phone smart application in controlling periodontal disease and treatment outcomes in diabetic patients.

Specific Aims

- (1) To investigate the efficacy of an electric toothbrush with a mobile smart application as an adjunct to periodontal therapy on the improvement of glycemic control in patients with stage II-III chronic periodontitis and type II diabetes mellitus, compared to a manual toothbrush.
- (2) To investigate the efficacy of an electric toothbrush with a mobile smart application as an adjunct to periodontal therapy on the improvement of periodontal outcomes and

inflammatory biomarkers in patients with chronic severe periodontitis and type II diabetes mellitus, compared to a manual toothbrush.

Methods

Study Design: The study is a prospective randomized controlled clinical trial. The subjects are divided into two groups: (1) using a standard manual toothbrush (control group) and (2) using an electric toothbrush with mobile smart application (test group). All patients were randomized into either the control or test group, using a computer-generated randomization list. All participants were seen at the Harvard Dental Clinic and followed a three-month periodontal maintenance protocol following a course of non-surgical therapy (scaling and root planing) and re-evaluation. At every study visit, participants in both study arms received standardized oral hygiene instruction. Oral hygiene practices were reviewed at each appointment, and participants' techniques were observed and corrected when necessary. All participants were provided with oral hygiene materials at baseline and at each follow-up visit. The control group received Oral-B® 3D White Vivid manual toothbrush with polishing cups in 35 soft (UPC: 300416684673), while the test group received Philips Sonicare DiamondClean Smart 9700® (HX9957/51). Participants in the test group were additionally provided with soft-bristle replacement brush heads (Phillips Sonicare G3 two-in-one, HX9052/77) at the 3-, 6-, and 9-month visits. In both groups, participants received an identical 3-month supply of toothpaste (Crest Cavity Protection toothpaste gel Cool Mint, PPAX1237155), floss (Oral-B Glide Pro-Health Deep Clean dental floss Cool Mint, UPC: 037000203391), and interproximal brushes (GUM Sunstar Proxabrush Go-Betweens model, 3612) at baseline and at each subsequent follow-up

visit. The smartphone application, Philips Sonicare app, was asked to be downloaded and instructed to connect to the electric toothbrush to the app via Bluetooth. The Philips Sonicare app is a smartphone-based companion designed to support daily oral hygiene by pairing with compatible Sonicare electric toothbrushes. The application provides real-time feedback during brushing, including pressure monitoring, visual representation of surfaces covered, and alerts for excessive scrubbing. It also tracks brushing frequency and duration and generates progress reports and reminder notifications, which may promote better adherence to the recommended homecare routines. In the context of this clinical trial, the application functioned as a behavioral support tool that may enhance patient compliance with homecare and improve self-monitoring of the brushing performance and plaque removal.

All participants were instructed in the Bass intrasulcular toothbrushing technique according to the method described by Ausenda et al. (2019), with a recommended brushing duration of 2 minutes.²⁴ In addition, participants received instruction in interdental cleaning, including flossing with the adaptive horizontal vertical flossing technique (AHVFT) as described by Basali et al. (2023), as well as the proper use of interdental brushes.²¹ Periodontal charting was completed using the 15 UNC periodontal probe, and gingival-crevicular fluid (GCF) was collected (using PerioPaper GCF Collection Strips 1.2 µl, Oraflow Inc., 593520) at initial presentation and each maintenance appointment. Professional periodontal hygiene therapy were completed at 3-, 6-, 9-, and 12-month visits, using EMS AIRFLOW® Prophylaxis Master with Piezon® and AIRFLOW® Max handpieces, along with hand scalers.

Two calibrated examiners performed the clinical measurements for the entire study. Prior to the study, probing measurements were calibrated between examiners until a Kappa statistic of 0.8 or greater was achieved.

The study protocol was approved by the Harvard Medical School Institutional Review Board (IRB 21-0148) and is registered on ClinicalTrials.gov (NCT05260814). Written informed consent was obtained by all participants prior to their enrollment in the clinical trials.

Inclusion Criteria: Patients of at least 35 years or older were included in this study. All patients were diagnosed with generalized stage II-III periodontitis with uncontrolled type II diabetes mellitus (HbA1c >7%). The diagnosis of periodontitis was made following the criteria created by the 2017 AAP/EFP World Workshop. All patients received an initial comprehensive periodontal examination with a radiographic full-mouth series (FMX) at appointment #1. Patients included into the study were treatment planned at minimum 2 quadrants of scaling and root planing. The diagnosis of uncontrolled type II diabetes mellitus was confirmed using medical record from patients' medical provider and HbA1c blood test at Quest Diagnostics.

Randomization: Forty (40) patients diagnosed with stage II or stage III periodontitis with T2DM were recruited and randomized into a control or test group, with twenty (20) participants per group, using a computer-generated randomization list.

Treatment Protocol:

Appointment 1 (T0) – Comprehensive periodontal consultation, full-mouth series (FMX), GCF collection, blood test, and Oral hygiene instruction.

Appointment 2 (T1) – Non-surgical therapy (scaling and root planing)

Appointment 3 (T2) – Re-evaluation appointment (PDHT, periodontal charting, GCF collection, blood test)

Appointment 4 (T3) – 3-month periodontal maintenance (PDHT, periodontal charting, GCF collection, blood test)

Appointment 5 (T4) – 6-month periodontal maintenance (PDHT, periodontal charting, GCF collection, blood test)

Appointment 6 (T5) – 9-month periodontal maintenance (PDHT, periodontal charting, GCF collection, blood test)

Appointment 7 (T6) – 12-month periodontal maintenance (PDHT, periodontal charting, GCF collection, blood test)

Sample size calculation: The sample size was calculated on power of 80% and alpha level of 5% using the primary outcome variable: changes in HbA1c level. Based on standard deviation of 0.18% and difference of 0.36% according to a meta-analysis, the minimum total sample size will be 8 for each group¹³.

Clinical parameters: Probing pocket depths (PPDs) were measured with a UNC probe at six sites per tooth. Full mouth bleeding on probing (BOP) and plaque index (PI) were recorded. Time spent brushing (TB) by the patient was recorded chairside for the control group and recorded

from the smart application for the test group. The clinical measurements and brush time were recorded at the screening visit.

Blood test: HbA1c level and high-sensitivity C-reactive protein (hsCRP) were collected to assess the severity of diabetes and the level of glycemic control. Blood assays were performed at baseline and every three months thereafter until 12 months (Quest Diagnostics Clinical Laboratories, Inc.).

Gingival crevicular fluid: Four sites with the deepest probing pocket depths ($\geq 5\text{mm}$) were selected for the collection of GCF with absorbent strips. The strips were placed in the same sites at each subsequent visit and left in place for 30 to 60 seconds or until adequate collection was determined according to manufacturer's instructions (Periopaper, ORAFLow). The GCF samples were stored in 1.5mL Eppendorf tubes at -20 degrees Celsius. Multiplex protein analysis of the GCF samples was performed by the Multiplex Core Facility at The Forsyth Institute (Cambridge, MA). The samples were analyzed for the following inflammatory cytokines: Granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon gamma (IFN- γ), interleukin 1 beta (IL-1 β), interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 5 (IL-5), interleukin 6 (IL-6), interleukin 8 (IL-8), interleukin 10 (IL-10), interleukin 12p70 (IL-12 p70), Tumor necrosis factor (TNF- α), and Vascular endothelial growth factor (VEGF). In addition, C-reactive protein (CRP) and Advanced Glycosylation End-Product Specific Receptor (RAGE/AGER) were also quantified.

Statistical analysis: HbA1c and high sensitive C-reactive protein (hs-CRP) were reported as mean percentage $\pm$ standard deviation (SD) and milligrams per liter (mg/L), respectively. Clinical periodontal parameters, PPD (mm), residual pocket (%), BOP (%), and PI (%) were reported as mean $\pm$ SD. Inflammatory cytokine concentrations (pg/mL) were reported as mean $\pm$ SD. Longitudinal associations between treatment groups and time were evaluated using generalized estimated equation (GEE) models. Each model included treatment groups, time, and their interaction term as fixed effects, with an exchangeable working correlation structure to account for within-subject correlations arising from repeated measurements over time.

Results

Patient population:

A total of 40 patients were initially enrolled in the study, with 20 allocated to the control group and 20 to the test group. After accounting for attrition and dropouts over the course of the study, 23 patients were included in the analysis, comprising of 11 patients in the control group and 12 participants in the test group. The mean age of participants in both groups was 61.9 years.

In the control group, 9 of 11 patients completed the 6-month follow-up, resulting in a 6-month retention rate of 81.8%, while 7 patients completed the 12-month follow-up, corresponding to a 12-month retention rate of 63.6%. In the test group, all 12 patients completed the 6-month

evaluation (100% retention rate), and 7 patients completed the 12-month follow-up (58.3% retention rate).

Clinical Evaluations:

- Probing pocket depth (PPD)

Both groups demonstrated statistically significant within-group reductions in mean pocket probing depth across all time points. The control group reported mean PPD at 3.65 ± 0.45 mm, 3.15 ± 0.33 mm, and 3.23 ± 0.24 mm at baseline, 6 months, and 12 months, respectively. The test group reported 3.57 ± 0.34 mm, 3.04 ± 0.63 mm, and 3.06 ± 0.70 mm at baseline, 6 months, and 12 months, respectively. Between-group differences were not statistically significant at any timepoint.

- Residual deep pockets

Residual deep pockets were defined as any periodontal pockets ≥ 5 mm. Non-bleeding PPD ≤ 4 mm are considered clinical end point for periodontal therapy.²⁹ Both groups showed statistically significant reduction in residual deep pockets across all timepoints. The control group showed a reduction from $39 \pm 8.6\%$ to $29.5 \pm 6.8\%$ from baseline to 12 months. The test group showed a reduction from $35.8 \pm 5.5\%$ to $23.5 \pm 18.0\%$ from baseline to 12 months. Between-group differences show a statistically significant difference at 9 months, favoring the test group ($p < 0.05$).

- Bleeding on probing (BOP)

The test group demonstrated statistically significant within-group reductions in bleeding on probing across all timepoints. The test group's BOP decreased from $63.5 \pm 37.5\%$ at baseline to

43.8 ± 27.2% at 12 months follow-up ($p < 0.05$). In contrast, the control group showed statistically significant within-group reductions at only two timepoints; at 2 months and 6 months follow-up. Between-group differences show a statistically significant difference at 9 months, favoring the test group ($p < 0.05$).

- Plaque index (PI)

Only the test group showed statistically significant within-group reductions at 2 months, 3 months, and 6 months. The control group showed no significant reduction in PI at any timepoints. Between-group differences for PI were not statistically significant at any timepoint.

Blood analysis:

- HbA1c

In the test group, HbA1c values demonstrated the greatest reduction between baseline and the 3-month visit, followed by a gradual increase returning to approximately baseline levels by 12 months. A similar pattern was observed in the control group, with an initial decrease followed by an upward trend, and the most pronounced reduction occurring between baseline and 6 months. Changes in HbA1c levels were not statistically significant in either group.

- High-sensitivity C-reactive protein (hsCRP)

Both the control and test groups exhibited an overall decreasing trend in hsCRP levels over the study period; however, these reductions were not statistically significant within-group or between-group. The control group showed a decrease from 5.41 ± 3.59 mg/L to 4.07 ± 3.39

mg/L. The test group demonstrated a decrease from 3.07 ± 2.83 mg/L to 2.87 ± 3.43 mg/L, corresponding to a reduction of 0.74 mg/L.

Gingival crevicular fluid:

Among the 14 inflammatory biomarkers were analyzed from GCF samples, statistically significant between-group differences at the $p < 0.05$ threshold were limited to TNF α , IL-2, IL-4, IL-5, and VEGF. Compared to the control group, the test group demonstrated higher TNF α at 2 months (67.89 ± 29.24 vs 35.65 ± 12.65 pg/ml, $p < 0.05$) and 9 months (64.21 ± 21.85 vs 29.43 ± 8.60 pg/ml, $p < 0.05$). At 12 months, IL-4 and IL-5 levels were significantly higher in the test group than in the control group (21.76 ± 1.40 vs 26.95 ± 5.14 pg/ml, $p < 0.05$, and 0.46 ± 0.06 vs 0.56 ± 0.01 pg/ml, $p < 0.05$, respectively). In contrast, the test group showed significantly lower IL-2 and VEGF levels when compared to the test group (4.02 ± 0.21 vs 3.46 ± 0.07 pg/ml, $p < 0.05$, and 597.87 ± 148.82 vs 536.51 ± 216.11 pg/ml, $p < 0.05$). No significant between-group differences at any timepoint were observed for GM-CSF, IFN-g, IL-1b, IL-6, IL-8, IL-10, IL-12 p70, CRP, and RAGE/AGER.

Discussion and Limitations

This study addresses a clinically important problem involving two highly prevalent chronic inflammatory diseases, periodontitis and diabetes mellitus. Periodontitis is the most common non-communicable chronic disease worldwide with approximately 1.1 billion cases.³⁰ The global burden of periodontal disease continue to rise, with an estimate of 8.44% increase between

1990 and 2019.³⁰ On the other hand, diabetes mellitus affects 536.6 millions adults worldwide, of whom an estimated 239.7 million are unaware of their diagnosis.³¹ These conditions share a bidirectional relationship in which each condition can exacerbate the other and contribute to worsening prognosis and disease severity. Given a substantial burden imposed by both of conditions, even modest improvements in plaque control, periodontal inflammation, concordance to periodontal maintenance, or compliance to home care practices could translate to a meaningful impact or reduction in the overall burden of both diseases. The findings of this study demonstrated greater reductions in all evaluated all evaluated clinical parameters, suggesting that the use of an electric toothbrush combined with a smart mobile application may be a practical strategy for supporting clinical improvements and recuing the disease burden associated with both diabetes and periodontitis.

The significant improvements observed in the study across all clinical parameters in both the control and test groups indicate that standard periodontal therapy with frequent periodontal maintenance was effective independent of study arm. This study demonstrated significantly better results in clinical endpoint outcomes and BOP in the test group at 9 months compared to the control group. Taken together in conjunction with the broader pattern of statistically more consistent clinical improvements observed in test group, these findings suggest that the use of mobile phone enabled smart application with electric toothbrush can improve adherence to oral hygiene routine at home, which in turn enhances periodontal health and may have a potential to support improvements in diabetes-related outcomes.

Consensus evidence reports that periodontal therapy in patient with T2DM could improve glycemic control, with reported HbA1c reductions of approximately 0.29% to 0.43% in 3-4 months.⁸ Although the between-group differences are not significant for the changes in HbA1c levels, the findings of this study is consistent with previously published data. The control group showed a reduction of 0.23% at 3 months post scaling and root planing, from 8.18% to 7.95%, while the test group showed 0.85% reduction at 3 months, from 8.40 to 7.55%. At 12 months, HbA1c for both groups remained mostly unchanged, despite significant periodontal improvements. The significant improvements in clinical parameters with unchanged systemic inflammatory markers (HbA1c and hsCRP) could suggest that the magnitude of periodontal improvement may not reach the threshold needed to influence systemic inflammatory burden or glycemic control.

The biomarker findings suggest selective, time-dependent differences between groups rather than a broad, divergence across the full biomarker panel. The most recurrent signal was higher TNF α observed at 2 and 9 months for test group. At 12 months, IL-2 and VEGF were lower in the test group and higher IL-4 and IL-5 levels in the test group. Because of the smaller sample size, these isolated significant findings should be considered exploratory, rather than conclusive evidence.

Taken together, these findings support a more integrated model of care in which periodontal assessment, diabetes management, and behavioral support are addressed together. The most recent consensus report from the EFP and the World Organization of Family Doctors (WONCA)

directly linked periodontal diseases with diabetes, along with cardiovascular and respiratory diseases.³² The consensus also recommended closer collaboration between oral health care professionals and family doctors for early disease detection and management.³² This study has limitations, including a small sample size and relatively high attrition rate. In addition, as a single-center, non-blinded randomized clinical trial, there were also potential introduction of performance and detection bias. In addition, adherence to at-home oral hygiene practices could not be comprehensively measured or captured, limiting the ability to fully assess the behavioral contribution to the observed outcomes. Lastly, since all of the participants' T2DM was managed by their medical doctors, the effects of different medications or medication changes on the study outcomes could not be excluded.

Conclusion

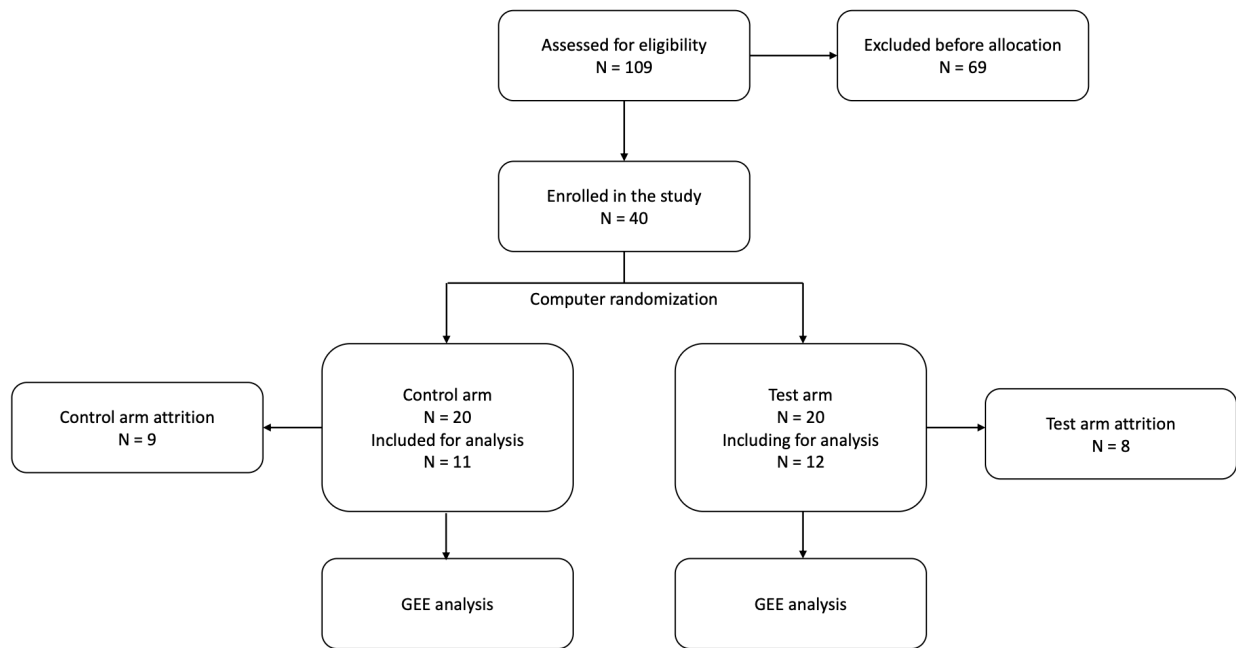
Both study groups demonstrated significant improvements in periodontal clinical parameters over time following non-surgical periodontal therapy and strict periodontal maintenance care. Reductions in PI, PPD, residual pockets, and BOP were observed in both groups, with the test group generally showing greater improvements in trends in these clinical parameters, although not statistically significant. The test group demonstrated statistically significant improvement in BOP and residual pocket at 9-month when compared to the control group. However, the use of an electric toothbrush with smartphone application did not result in statistically significant additional benefits in glycemic control, systemic inflammatory markers, or periodontal outcomes compared to manual toothbrush. The absence of significant differences in most other measured biomarkers further suggests that any biological effect captured in this analysis was

not generalized. Within the limitations of this study, these findings suggest that structured periodontal therapy and reinforcement of oral hygiene are effective, while the adjunctive digital oral hygiene approach may offer some clinical benefits in periodontal outcomes.

Funding information

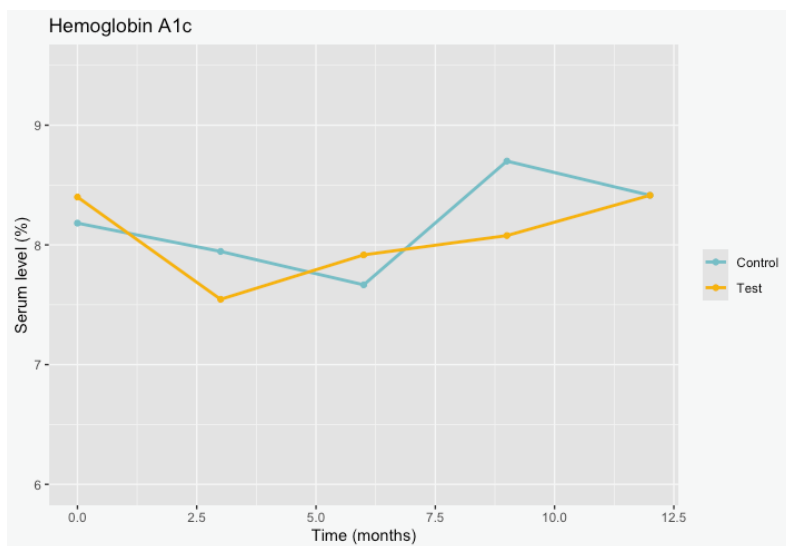
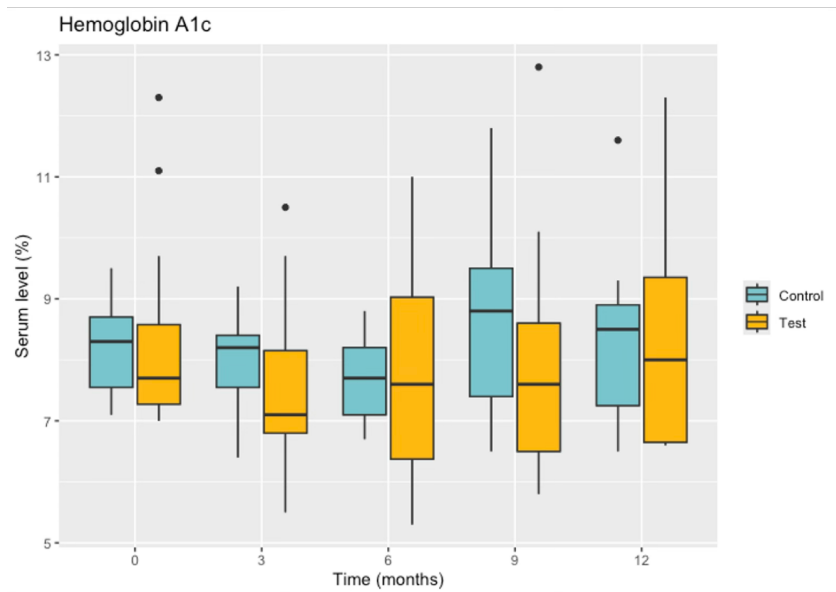
This study was supported by a grant from Philips Oral Healthcare (GMAS project #8057109-01, award number A45389).

Results and Tables



HbA1c (%) by study visit and treatment group

Time point	Control mean $\pm$ SD	Test mean $\pm$ SD	GEE p-value
Baseline	8.18 $\pm$ 0.77	8.40 $\pm$ 1.72	0.6778
3 months	7.95 $\pm$ 0.91	7.55 $\pm$ 1.51	0.7569
6 months	7.67 $\pm$ 0.72	7.92 $\pm$ 1.85	0.5922
9 months	8.70 $\pm$ 1.83	8.08 $\pm$ 2.19	0.8412
12 months	8.41 $\pm$ 1.70	8.41 $\pm$ 2.17	0.8711

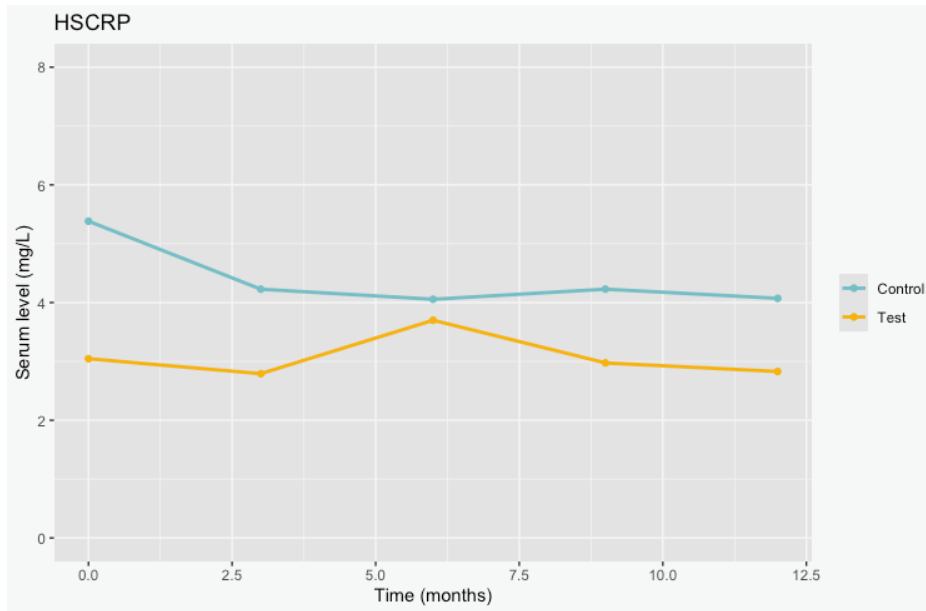
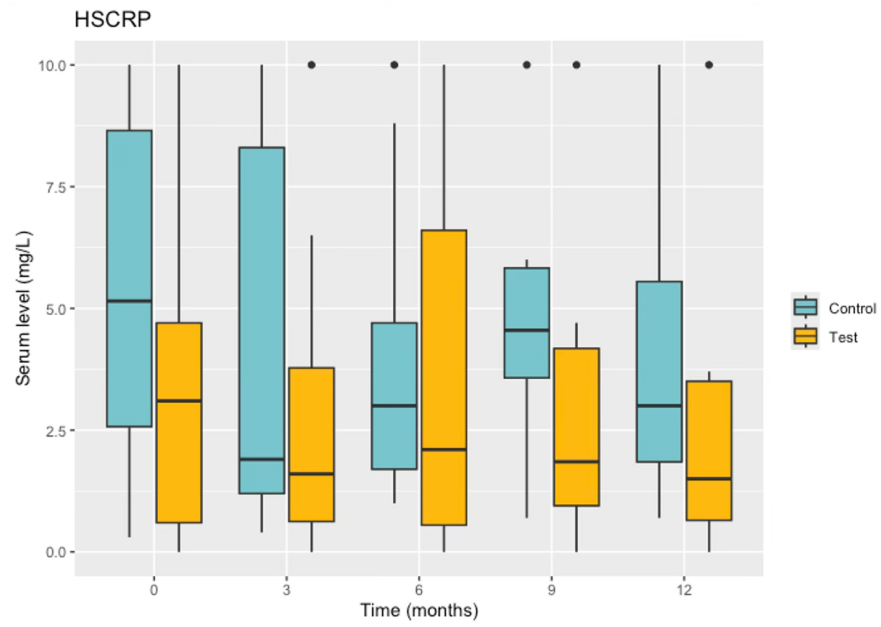


HbA1c (%) within-group change from baseline

Group	Contrast	Estimate	Robust SE	95% CI	GEE p-value
Control	3M - Baseline	-0.236	0.323	(-0.869, 0.396)	0.4640
Control	6M - Baseline	-0.548	0.350	(-1.234, 0.138)	0.1172
Control	9M - Baseline	0.461	0.656	(-0.824, 1.746)	0.4821
Control	12M - Baseline	0.213	0.635	(-1.033, 1.458)	0.7380
Test	3M - Baseline	-0.602	0.314	(-1.218, 0.014)	0.0553
Test	6M - Baseline	-0.483	0.387	(-1.242, 0.275)	0.2118
Test	9M - Baseline	0.061	0.474	(-0.868, 0.990)	0.8978
Test	12M - Baseline	0.142	0.475	(-0.789, 1.072)	0.7655

hsCRP (mg/L) by study visit and treatment group

Time point	Control mean $\pm$ SD	Test mean $\pm$ SD	GEE p-value
Baseline	5.41 $\pm$ 3.59	3.07 $\pm$ 2.83	0.0603
3 months	4.23 $\pm$ 4.06	2.82 $\pm$ 3.14	0.3191
6 months	4.06 $\pm$ 3.29	3.75 $\pm$ 3.81	0.5088
9 months	4.23 $\pm$ 3.32	3.01 $\pm$ 3.27	0.0881
12 months	4.07 $\pm$ 3.39	2.87 $\pm$ 3.43	0.2938



hsCRP (mg/L) within-group change from baseline

Group	Contrast	Estimate	Robust SE	95% CI	GEE p-value
Control	3M - Baseline	-1.112	0.530	(-2.151, -0.074)	0.0358
Control	6M - Baseline	-0.745	0.804	(-2.320, 0.830)	0.3540
Control	9M - Baseline	-0.833	0.717	(-2.239, 0.572)	0.2452
Control	12M - Baseline	-1.208	0.781	(-2.738, 0.322)	0.1217
Test	3M - Baseline	-0.129	0.402	(-0.918, 0.659)	0.7478
Test	6M - Baseline	0.680	0.467	(-0.235, 1.596)	0.1453
Test	9M - Baseline	-0.746	0.529	(-1.783, 0.290)	0.1583
Test	12M - Baseline	-0.243	0.346	(-0.921, 0.434)	0.4816

Average pocket probing depth (mm) by study visit and treatment group

Time point	Control mean ± SD	Test mean ± SD	GEE p-value
Baseline	3.65 ± 0.45	3.57 ± 0.34	0.6401
2 months	3.21 ± 0.64	3.22 ± 0.48	0.9391
3 months	3.20 ± 0.47	3.09 ± 0.60	0.5968
6 months	3.15 ± 0.33	3.04 ± 0.63	0.7377
9 months	3.10 ± 0.31	2.84 ± 0.43	0.1283
12 months	3.23 ± 0.24	3.06 ± 0.70	0.6394

Average pocket probing depth (mm) within-group change from baseline

Group	Contrast	Estimate	Robust SE	95% CI	GEE p-value
Control	2M - Baseline	-0.442	0.145	(-0.727, -0.158)	0.0023
Control	3M - Baseline	-0.448	0.119	(-0.682, -0.214)	0.0002
Control	6M - Baseline	-0.503	0.111	(-0.721, -0.284)	6.38E-06
Control	9M - Baseline	-0.566	0.112	(-0.786, -0.346)	4.58E-07
Control	12M - Baseline	-0.414	0.091	(-0.593, -0.235)	5.98E-06
Test	2M - Baseline	-0.351	0.079	(-0.506, -0.196)	9.35E-06
Test	3M - Baseline	-0.485	0.107	(-0.695, -0.275)	6.21E-06
Test	6M - Baseline	-0.497	0.161	(-0.812, -0.182)	0.0020
Test	9M - Baseline	-0.730	0.135	(-0.995, -0.465)	6.51E-08
Test	12M - Baseline	-0.449	0.203	(-0.846, -0.051)	0.0269

Residual pocket probing depth (%) by study visit and treatment group

Time point	Control mean $\pm$ SD	Test mean $\pm$ SD	GEE p-value
Baseline	0.390 $\pm$ 0.086	0.358 $\pm$ 0.055	0.2638
2 months	0.278 $\pm$ 0.154	0.262 $\pm$ 0.112	0.7666
3 months	0.281 $\pm$ 0.136	0.236 $\pm$ 0.126	0.3976
6 months	0.257 $\pm$ 0.090	0.217 $\pm$ 0.148	0.4109
9 months	0.276 $\pm$ 0.091	0.184 $\pm$ 0.114	0.0240
12 months	0.295 $\pm$ 0.068	0.235 $\pm$ 0.180	0.3338

Residual pocket probing depth (%) within-group change from baseline

Group	Contrast	Estimate	Robust SE	95% CI	GEE p-value
Control	2M - Baseline	-0.112	0.038	(-0.187, -0.038)	0.0032
Control	3M - Baseline	-0.110	0.034	(-0.176, -0.043)	0.0012
Control	6M - Baseline	-0.133	0.032	(-0.196, -0.071)	3.04E-05
Control	9M - Baseline	-0.122	0.035	(-0.191, -0.053)	0.0006
Control	12M - Baseline	-0.092	0.030	(-0.150, -0.034)	0.0019
Test	2M - Baseline	-0.096	0.035	(-0.164, -0.028)	0.0056
Test	3M - Baseline	-0.122	0.032	(-0.183, -0.060)	0.0001
Test	6M - Baseline	-0.141	0.039	(-0.218, -0.064)	0.0003
Test	9M - Baseline	-0.188	0.033	(-0.252, -0.123)	1.19E-08
Test	12M - Baseline	-0.117	0.051	(-0.218, -0.017)	0.0225

Bleeding on probing (%) by study visit by treatment group

Time point	Control mean ± SD	Test mean ± SD	GEE p-value
Baseline	0.635 ± 0.375	0.663 ± 0.276	0.8322
2 months	0.407 ± 0.277	0.385 ± 0.182	0.8435
3 months	0.388 ± 0.297	0.340 ± 0.211	0.6417
6 months	0.393 ± 0.130	0.306 ± 0.290	0.3958
9 months	0.391 ± 0.162	0.229 ± 0.147	0.0164
12 months	0.438 ± 0.272	0.351 ± 0.186	0.4321

Bleeding on probing (%) within-group change from baseline

Group	Contrast	Estimate	Robust SE	95% CI	GEE p-value
Control	2M - Baseline	-0.928	0.443	(-1.796, -0.060)	0.0361
Control	3M - Baseline	-1.007	0.569	(-2.122, 0.107)	0.0765
Control	6M - Baseline	-0.986	0.502	(-1.970, -0.002)	0.0495
Control	9M - Baseline	-0.982	0.560	(-2.079, 0.115)	0.0795
Control	12M - Baseline	-0.776	0.683	(-2.114, 0.563)	0.2563
Test	2M - Baseline	-1.123	0.292	(-1.695, -0.550)	0.0001
Test	3M - Baseline	-1.336	0.319	(-1.961, -0.711)	2.78E-05
Test	6M - Baseline	-1.448	0.372	(-2.178, -0.718)	0.0001
Test	9M - Baseline	-1.908	0.392	(-2.675, -1.141)	1.10E-06
Test	12M - Baseline	-1.210	0.453	(-2.098, -0.321)	0.0076

Plaque index (%) by study visit by treatment group

Time point	Control mean $\pm$ SD	Test mean $\pm$ SD	GEE p-value
Baseline	0.583 $\pm$ 0.484	0.622 $\pm$ 0.366	0.8205
2 months	0.366 $\pm$ 0.360	0.319 $\pm$ 0.207	0.6892
3 months	0.513 $\pm$ 0.330	0.299 $\pm$ 0.248	0.0673
6 months	0.463 $\pm$ 0.349	0.235 $\pm$ 0.281	0.0854
9 months	0.474 $\pm$ 0.331	0.401 $\pm$ 0.429	0.6514
12 months	0.576 $\pm$ 0.358	0.403 $\pm$ 0.457	0.3511

Plaque index (%) within-group change from baseline

Group	Contrast	Estimate	Robust SE	95% CI	GEE p-value
Control	2M - Baseline	-0.217	0.147	(-0.505, 0.071)	0.1395
Control	3M - Baseline	-0.070	0.198	(-0.459, 0.319)	0.7239
Control	6M - Baseline	-0.120	0.165	(-0.444, 0.204)	0.4671
Control	9M - Baseline	-0.110	0.184	(-0.471, 0.252)	0.5528
Control	12M - Baseline	-0.008	0.215	(-0.428, 0.413)	0.9708
Test	2M - Baseline	-0.303	0.106	(-0.511, -0.096)	0.0042
Test	3M - Baseline	-0.323	0.097	(-0.513, -0.134)	0.0008
Test	6M - Baseline	-0.376	0.149	(-0.668, -0.085)	0.0114
Test	9M - Baseline	-0.217	0.131	(-0.474, 0.040)	0.0984
Test	12M - Baseline	-0.200	0.168	(-0.530, 0.130)	0.2343

GCF biomarkers by study visit and time point

Biomarker	Time point	Control_n	Control mean $\pm$ SD	Test_n	Test mean $\pm$ SD	GEE estimate (Test-Control)	95% CI	GEE p-value
GM-CSF	Baseline	8	13.80 $\pm$ 5.33	12	17.61 $\pm$ 17.94	3.81	(-6.50, 14.13)	0.469
GM-CSF	2m	6	12.71 $\pm$ 3.91	8	20.80 $\pm$ 16.00	7.18	(-1.86, 16.23)	0.119
GM-CSF	3m	7	13.62 $\pm$ 4.99	8	15.83 $\pm$ 9.63	0.78	(-4.90, 6.45)	0.788
GM-CSF	6m	4	17.38 $\pm$ 9.07	7	14.18 $\pm$ 4.48	-5.16	(-12.85, 2.52)	0.188
GM-CSF	9m	3	15.49 $\pm$ 8.12	4	13.16 $\pm$ 4.87	0.65	(-7.42, 8.72)	0.875
GM-CSF	12m	3	9.16 $\pm$ 1.09	2	12.29 $\pm$ 5.89	4.14	(-2.21, 10.50)	0.202
IFN- γ	Baseline	8	14.10 $\pm$ 1.53	12	15.77 $\pm$ 3.74	1.67	(-0.58, 3.92)	0.146
IFN- γ	2m	6	15.18 $\pm$ 2.46	8	15.17 $\pm$ 3.63	0.26	(-2.45, 2.98)	0.849
IFN- γ	3m	7	14.28 $\pm$ 2.64	8	14.96 $\pm$ 2.73	1.02	(-1.17, 3.21)	0.361
IFN- γ	6m	4	13.93 $\pm$ 0.59	7	14.15 $\pm$ 3.51	0.41	(-1.68, 2.50)	0.701
IFN- γ	9m	3	13.73 $\pm$ 0.40	4	13.21 $\pm$ 3.95	1.86	(-1.29, 5.00)	0.247
IFN- γ	12m	3	14.26 $\pm$ 0.50	2	12.97 $\pm$ 3.59	0.01	(-2.53, 2.55)	0.992
IL-1 β	Baseline	8	5615.71 $\pm$ 1518.54	12	6396.14 $\pm$ 920.12	780.43	(-322.88, 1883.75)	0.166
IL-1 β	2m	6	6420.38 $\pm$ 674.48	8	6658.30 $\pm$ 317.30	247.16	(-354.02, 848.34)	0.420
IL-1 β	3m	7	5163.68 $\pm$ 2158.38	8	6004.88 $\pm$ 1618.07	667.25	(-1137.22, 2471.72)	0.469
IL-1 β	6m	4	4673.37 $\pm$ 1705.59	7	4853.12 $\pm$ 1999.22	-360.65	(-2321.89, 1600.59)	0.719
IL-1 β	9m	3	6011.71 $\pm$ 499.45	4	5780.30 $\pm$ 2132.28	-606.18	(-2298.33, 1085.98)	0.483

IL-1 β	12m	3	6172.45 $\pm$ 373.05	2	4324.59 $\pm$ 2759.11	-1590.49	(-3765.05, 584.06)	0.152
IL-2	Baseline	8	3.88 $\pm$ 0.32	12	4.23 $\pm$ 0.53	0.34	(-0.01, 0.69)	0.059
IL-2	2m	6	4.16 $\pm$ 0.28	8	4.10 $\pm$ 0.28	-0.02	(-0.30, 0.26)	0.875
IL-2	3m	7	3.83 $\pm$ 0.68	8	4.04 $\pm$ 0.41	0.21	(-0.31, 0.74)	0.427
IL-2	6m	4	3.69 $\pm$ 0.26	7	3.98 $\pm$ 0.45	0.22	(-0.13, 0.56)	0.216
IL-2	9m	3	3.69 $\pm$ 0.16	4	3.84 $\pm$ 0.25	0.2	(-0.09, 0.50)	0.170
IL-2	12m	3	4.02 $\pm$ 0.21	2	3.46 $\pm$ 0.07	-0.42	(-0.66, - 0.18)	<0.001
IL-4	Baseline	8	20.55 $\pm$ 1.77	12	22.89 $\pm$ 5.51	2.34	(-0.86, 5.53)	0.152
IL-4	2m	6	22.36 $\pm$ 1.39	8	22.39 $\pm$ 2.49	0.38	(-1.41, 2.17)	0.676
IL-4	3m	7	20.43 $\pm$ 2.15	8	22.03 $\pm$ 3.54	1.74	(-0.89, 4.38)	0.195
IL-4	6m	4	20.06 $\pm$ 2.20	7	22.50 $\pm$ 6.60	2.55	(-2.09, 7.19)	0.281
IL-4	9m	3	22.28 $\pm$ 2.51	4	21.42 $\pm$ 5.16	0.7	(-4.42, 5.82)	0.789
IL-4	12m	3	21.76 $\pm$ 1.40	2	26.95 $\pm$ 5.14	6.03	(0.94, 11.13)	0.020
IL-5	Baseline	8	0.52 $\pm$ 0.10	12	0.55 $\pm$ 0.14	0.04	(-0.06, 0.13)	0.480
IL-5	2m	6	0.67 $\pm$ 0.10	8	0.67 $\pm$ 0.35	-0.01	(-0.25, 0.23)	0.951
IL-5	3m	7	0.54 $\pm$ 0.10	8	0.54 $\pm$ 0.15	0.01	(-0.11, 0.13)	0.885
IL-5	6m	4	0.51 $\pm$ 0.07	7	0.58 $\pm$ 0.12	0.06	(-0.04, 0.17)	0.229
IL-5	9m	3	0.53 $\pm$ 0.00	4	0.72 $\pm$ 0.36	0.18	(-0.12, 0.48)	0.250
IL-5	12m	3	0.46 $\pm$ 0.06	2	0.56 $\pm$ 0.01	0.09	(0.04, 0.15)	0.001
IL-6	Baseline	8	13.21 $\pm$ 5.69	12	50.00 $\pm$ 82.91	36.8	(-8.27, 81.86)	0.110
IL-6	2m	6	21.97 $\pm$ 31.75	8	36.55 $\pm$ 31.01	12.35	(-17.69, 42.39)	0.420

IL-6	3m	7	17.34 ± 17.19	8	32.76 ± 45.54	13.49	(-18.67, 45.66)	0.411
IL-6	6m	4	33.12 ± 22.98	7	26.10 ± 25.89	-8.78	(-34.53, 16.96)	0.504
IL-6	9m	3	5.80 ± 1.45	4	52.73 ± 74.19	42.95	(-12.74, 98.63)	0.131
IL-6	12m	3	6.08 ± 2.13	2	41.49 ± 35.43	17.53	(-1.11, 36.18)	0.065
IL-8	Baseline	8	4532.71 ± 341.53	12	4643.57 ± 178.63	110.86	(-130.74, 352.47)	0.368
IL-8	2m	6	4565.50 ± 124.68	8	4603.34 ± 183.87	25.49	(-138.27, 189.25)	0.760
IL-8	3m	7	4641.44 ± 248.16	8	4620.22 ± 208.44	-15.33	(-223.68, 193.03)	0.885
IL-8	6m	4	4596.11 ± 280.76	7	4732.45 ± 240.44	109.8	(-127.04, 346.64)	0.364
IL-8	9m	3	4538.11 ± 266.81	4	4660.59 ± 237.79	198.58	(-65.40, 462.56)	0.140
IL-8	12m	3	4511.98 ± 112.92	2	4559.15 ± 26.73	166.98	(-24.88, 358.84)	0.088
IL-10	Baseline	8	5.92 ± 2.13	12	8.90 ± 8.36	2.98	(-1.75, 7.72)	0.217
IL-10	2m	6	6.73 ± 2.14	8	7.49 ± 3.62	0.88	(-1.87, 3.63)	0.529
IL-10	3m	7	5.45 ± 1.57	8	6.64 ± 2.30	1.09	(-0.60, 2.78)	0.206
IL-10	6m	4	5.96 ± 1.53	7	6.00 ± 2.59	0.1	(-2.21, 2.42)	0.931
IL-10	9m	3	5.92 ± 1.02	4	7.76 ± 5.48	2.48	(-2.24, 7.21)	0.303
IL-10	12m	3	5.42 ± 1.04	2	5.83 ± 2.23	0.69	(-1.92, 3.31)	0.605
IL-12 p70	Baseline	8	15.55 ± 1.81	12	16.14 ± 3.29	0.59	(-1.54, 2.72)	0.589
IL-12 p70	2m	6	14.92 ± 1.82	8	15.37 ± 2.16	0.73	(-1.20, 2.65)	0.458
IL-12 p70	3m	7	15.86 ± 2.03	8	14.79 ± 2.38	-0.68	(-2.65, 1.30)	0.502
IL-12 p70	6m	4	15.64 ± 1.81	7	14.93 ± 1.81	-0.51	(-2.31, 1.29)	0.581
IL-12 p70	9m	3	15.62 ± 1.17	4	15.22 ± 3.16	0.98	(-1.70, 3.66)	0.474

IL-12 p70	12m	3	15.08 ± 1.20	2	15.11 ± 2.47	1.01	(-1.22, 3.23)	0.376
TNFα	Baseline	8	37.98 ± 17.08	12	58.85 ± 27.23	20.87	(2.43, 39.32)	0.027
TNFα	2m	6	35.65 ± 12.65	8	67.89 ± 29.24	27.78	(6.69, 48.87)	0.010
TNFα	3m	7	58.05 ± 60.39	8	47.25 ± 13.39	-12	(-54.13, 30.13)	0.577
TNFα	6m	4	48.43 ± 26.98	7	47.10 ± 22.38	-4.71	(-32.34, 22.93)	0.738
TNFα	9m	3	29.43 ± 8.60	4	64.21 ± 21.85	29.24	(8.62, 49.86)	0.005
TNFα	12m	3	30.60 ± 9.41	2	31.81 ± 14.11	-12.81	(-35.97, 10.34)	0.278
VEGF	Baseline	8	629.43 ± 336.18	12	793.06 ± 343.70	163.63	(-122.98, 450.25)	0.263
VEGF	2m	6	658.95 ± 273.78	8	860.46 ± 412.38	211.01	(-112.05, 534.07)	0.200
VEGF	3m	7	586.74 ± 205.07	8	649.32 ± 220.56	-7.33	(-195.19, 180.53)	0.939
VEGF	6m	4	597.33 ± 231.55	7	725.27 ± 382.73	4.33	(-310.18, 318.84)	0.978
VEGF	9m	3	642.96 ± 313.20	4	1003.70 ± 318.42	111.86	(-268.01, 491.73)	0.564
VEGF	12m	3	597.87 ± 148.82	2	536.51 ± 216.11	-281.18	(-554.57, -7.79)	0.044
CRP	Baseline	8	4180.00 ± 8476.17	12	4371.56 ± 8163.38	191.56	(-6861.23, 7244.36)	0.958
CRP	2m	6	4773.38 ± 6168.26	8	6584.68 ± 11479.26	1370.86	(-5348.15, 8089.86)	0.689
CRP	3m	7	7486.53 ± 11914.32	8	4949.90 ± 7452.54	-4152.28	(-13003.49, 4698.92)	0.358
CRP	6m	4	2781.71 ± 2408.01	7	7225.68 ± 15929.15	1032.91	(-8002.55, 10068.37)	0.823
CRP	9m	3	4713.19 ± 6740.31	4	7145.53 ± 12733.51	-3102.76	(-9660.47, 3454.95)	0.354

CRP	12m	3	2629.26 ± 3078.47	2	11900.65 ± 16493.41	-3283.23	(- 8110.69, 1544.24)	0.183
RAGE/AG ER	Baseline	8	19.50 ± 10.72	11	36.98 ± 31.46	16.7	(-2.15, 35.56)	0.082
RAGE/AG ER	2m	6	26.06 ± 14.62	7	28.95 ± 15.37	1.64	(-11.96, 15.24)	0.813
RAGE/AG ER	3m	6	32.07 ± 11.04	7	30.05 ± 8.91	-3.52	(-12.61, 5.56)	0.447
RAGE/AG ER	6m	4	24.91 ± 11.73	7	35.74 ± 40.01	7.64	(-20.55, 35.83)	0.595
RAGE/AG ER	9m	3	20.06 ± 16.59	4	35.34 ± 33.44	16	(-17.67, 49.68)	0.352
RAGE/AG ER	12m	3	20.14 ± 8.37	2	32.09 ± 10.07	9.82	(-4.55, 24.19)	0.180

References

1. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Periodontology*. 2018;89(S1). doi:10.1002/JPER.18-0006
2. GBD 2017 Oral Disorders Collaborators, Bernabe E, Marcenes W, et al. Global, Regional, and National Levels and Trends in Burden of Oral Conditions from 1990 to 2017: A Systematic Analysis for the Global Burden of Disease 2017 Study. *J Dent Res*. 2020;99(4):362-373. doi:10.1177/0022034520908533
3. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA, Genco RJ. Periodontitis in US Adults: National Health and Nutrition Examination Survey 2009-2014. *J Am Dent Assoc*. 2018;149(7):576-588.e6. doi:10.1016/j.adaj.2018.04.023
4. Trindade D, Carvalho R, Machado V, Chambrone L, Mendes JJ, Botelho J. Prevalence of periodontitis in dentate people between 2011 and 2020: A systematic review and meta-analysis of epidemiological studies. *J Clin Periodontol*. 2023;50(5):604-626. doi:10.1111/jcpe.13769
5. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2026. *Diabetes Care*. 2025;49(Suppl 1):S27-S49. doi:10.2337/dc26-S002
6. Zhang HJ, Feng J, Zhang XT, Zhang HZ. Age at type 2 diabetes diagnosis and the risk of mortality among US population. *Sci Rep*. 2024;14(1):29155. doi:10.1038/s41598-024-80790-8
7. CDC. National Diabetes Statistics Report. Diabetes. January 21, 2026. Accessed March 21, 2026. <https://www.cdc.gov/diabetes/php/data-research/index.html>
8. Sanz M, Ceriello A, Buysschaert M, et al. Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. *J Clin Periodontol*. 2018;45(2):138-149. doi:10.1111/jcpe.12808
9. Polak D, Sanui T, Nishimura F, Shapira L. Diabetes as a risk factor for periodontal disease-plausible mechanisms. *Periodontol 2000*. 2020;83(1):46-58. doi:10.1111/prd.12298
10. Preshaw PM, Alba AL, Herrera D, et al. Periodontitis and diabetes: a two-way relationship. *Diabetologia*. 2012;55(1):21-31. doi:10.1007/s00125-011-2342-y
11. Simpson TC, Clarkson JE, Worthington HV, et al. Treatment of periodontitis for glycaemic control in people with diabetes mellitus. *Cochrane Database Syst Rev*. 2022;2022(4):CD004714. doi:10.1002/14651858.CD004714.pub4

12. D'Aiuto F, Gkranias N, Bhowruth D, et al. Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial. *Lancet Diabetes Endocrinol*. 2018;6(12):954-965. doi:10.1016/S2213-8587(18)30038-X
13. Engebretson S, Kocher T. Evidence that periodontal treatment improves diabetes outcomes: a systematic review and meta-analysis. *J Clin Periodontol*. 2013;40 Suppl 14:S153-163. doi:10.1111/jcpe.12084
14. Grossi SG, Skrepcinski FB, DeCaro T, et al. Treatment of periodontal disease in diabetics reduces glycated hemoglobin. *J Periodontol*. 1997;68(8):713-719. doi:10.1902/jop.1997.68.8.713
15. Katagiri S, Nitta H, Nagasawa T, et al. Effect of glycemic control on periodontitis in type 2 diabetic patients with periodontal disease. *J Diabetes Investig*. 2013;4(3):320-325. doi:10.1111/jdi.12026
16. Tseng CH. Metformin and risk of gingival/periodontal diseases in diabetes patients: A retrospective cohort study. *Front Endocrinol (Lausanne)*. 2022;13:1036885. doi:10.3389/fendo.2022.1036885
17. Sanz M, Herrera D, Kebschull M, et al. Treatment of stage I–III periodontitis—The EFP S3 level clinical practice guideline. *J Clin Periodontology*. 2020;47(S22):4-60. doi:10.1111/jcpe.13290
18. Lee CT, Huang HY, Sun TC, Karimbux N. Impact of Patient Compliance on Tooth Loss during Supportive Periodontal Therapy: A Systematic Review and Meta-analysis. *J Dent Res*. 2015;94(6):777-786. doi:10.1177/0022034515578910
19. Lertpimonchai A, Rattanasiri S, Arj-Ong Vallibhakara S, Attia J, Thakkestian A. The association between oral hygiene and periodontitis: a systematic review and meta-analysis. *Int Dent J*. 2020;67(6):332-343. doi:10.1111/idj.12317
20. Worthington HV, MacDonald L, Poklepovic Pericic T, et al. Home use of interdental cleaning devices, in addition to toothbrushing, for preventing and controlling periodontal diseases and dental caries. *Cochrane Database Syst Rev*. 2019;4(4):CD012018. doi:10.1002/14651858.CD012018.pub2
21. Basali DH, Hong I, Finkleman M, et al. The Effect of Dental Flossing Instructions and Technique on Interproximal Bleeding: A randomized control trial. *J Dent Hyg*. 2023;97(4):36-45.
22. Gibson JA, Wade AB. Plaque removal by the Bass and Roll brushing techniques. *J Periodontol*. 1977;48(8):456-459. doi:10.1902/jop.1977.48.8.456

23. Rajwani AR, Hawes SND, To A, Quaranta A, Rincon Aguilar JC. Effectiveness of Manual Toothbrushing Techniques on Plaque and Gingivitis: A Systematic Review. *Oral Health Prev Dent.* 2020;18(4):843-854. doi:10.3290/j.ohpd.a45354
24. Ausenda F, Jeong N, Arsenault P, et al. The Effect of the Bass Intrасulcular Toothbrushing Technique on the Reduction of Gingival Inflammation: A Randomized Clinical Trial. *J Evid Based Dent Pract.* 2019;19(2):106-114. doi:10.1016/j.jebdp.2019.01.004
25. Toniazзо MP, Nodari D, Muniz FWMG, Weidlich P. Effect of mHealth in improving oral hygiene: A systematic review with meta-analysis. *J Clin Periodontol.* 2019;46(3):297-309. doi:10.1111/jcpe.13083
26. Kay E, Shou L. A randomised controlled trial of a smartphone application for improving oral hygiene. *Br Dent J.* 2019;226(7):508-511. doi:10.1038/s41415-019-0202-1
27. Tonetti MS, Deng K, Christiansen A, et al. Self-reported bleeding on brushing as a predictor of bleeding on probing: Early observations from the deployment of an internet of things network of intelligent power-driven toothbrushes in a supportive periodontal care population. *J Clin Periodontol.* 2020;47(10):1219-1226. doi:10.1111/jcpe.13351
28. Li Y, Wu X, Liu M, et al. Enhanced control of periodontitis by an artificial intelligence-enabled multimodal-sensing toothbrush and targeted mHealth micromessages: A randomized trial. *J Clin Periodontol.* 2024;51(12):1632-1643. doi:10.1111/jcpe.13987
29. Loos BG, Needleman I. Endpoints of active periodontal therapy. *J Clin Periodontol.* 2020;47 Suppl 22(Suppl 22):61-71. doi:10.1111/jcpe.13253
30. Chen MX, Zhong YJ, Dong QQ, Wong HM, Wen YF. Global, regional, and national burden of severe periodontitis, 1990-2019: An analysis of the Global Burden of Disease Study 2019. *J Clin Periodontol.* 2021;48(9):1165-1188. doi:10.1111/jcpe.13506
31. Ogurtsova K, Guariguata L, Barengo NC, et al. IDF diabetes Atlas: Global estimates of undiagnosed diabetes in adults for 2021. *Diabetes Research and Clinical Practice.* 2022;183:109118. doi:10.1016/j.diabres.2021.109118
32. Herrera D, Sanz M, Shapira L, et al. Periodontal diseases and cardiovascular diseases, diabetes, and respiratory diseases: Summary of the consensus report by the European Federation of Periodontology and WONCA Europe. *Eur J Gen Pract.* 2024;30(1):2320120. doi:10.1080/13814788.2024.2320120