Received: 1 November 2022 | Revised: 21 March 2023 | Accepted: 24 March 2023

DOI: 10.1111/jcpe.13813

ORIGINAL ARTICLE

Journal of Clinical Periodontology WILEY

Healthy lifestyles are associated with a better response to periodontal therapy: A prospective cohort study

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Abstract

Aim: To evaluate the association between lifestyle behaviours and clinical periodontal outcomes following Steps 1/2 of periodontal therapy.

Methods: A total of 120 subjects with untreated Stage II/III periodontitis participated in this study. At baseline, questionnaires were administered to assess the following lifestyle behaviours: adherence to Mediterranean diet (MD), physical activity (PA) and stress levels, sleep quality, smoking and alcohol use. Participants received Steps 1/2 of periodontal therapy and were re-evaluated after 3 months. A composite outcome of the endpoint of therapy (i.e., no sites with probing pocket depth [PPD] ≥4 mm with bleeding on probing, and no sites with PPD ≥ 6 mm) was regarded as the primary outcome. Simple and multiple regression analyses were used to evaluate the association between lifestyle behaviours and clinical periodontal outcomes. Disease severity at baseline, body mass index, diabetes, household disposable income and plaque control were considered as confounders.

Results: Multiple regression analyses showed significantly lower odds of achieving the endpoint of therapy in subjects with poor sleep quality (odds ratio [OR] = 0.13; 95% confidence interval [CI]: 0.03–0.47; $p < .01$), smoking (OR = 0.18; 95% CI: 0.06–0.52; $p < .05$) and alcohol use above the suggested intake (OR = 0.21; 95% CI: 0.07–0.63; $p < .01$). Subjects with a combination of 'unhealthy lifestyles' (low adherence to MD and low PA levels and high levels of stress and poor sleep quality) showed higher proportions of residual PPD≥6 mm (MD = 1.51; 95% CI: 0.23–2.80; $p < .05$) and lower odds of achieving the endpoint of therapy (OR = 0.85; 95% CI: 0.33–0.99; $p < .05$) at re-evaluation.

Conclusions: Subjects with unhealthy lifestyle behaviours showed worse clinical outcomes 3 months after Steps 1/2 of periodontal therapy.

KEYWORDS

Mediterranean diet, periodontal diseases, periodontal therapy, physical activity, stress

Clinical Relevance

Scientific rationale for study: Several epidemiological studies have reported a higher prevalence and severity of periodontitis in subjects with unhealthy lifestyle behaviours. However, the association between lifestyle behaviours and response to periodontal therapy has not been evaluated yet.

Principal findings: Subjects with poor sleep quality, smoking and alcohol use above the suggested intake showed significantly lower odds of achieving the endpoint of therapy at 3 months.

Practical implications: Given the modifiable nature of lifestyle behaviours, they could represent potential targets of interventions in the context of the Step 1 of periodontal therapy.

1 | INTRODUCTION

Unhealthy lifestyle behaviours are at the root of the global burden of non-communicable diseases (NCDs), which account for about 63% of all deaths (Marrero et al., 2012). Unhealthy lifestyle behaviours include poor nutrition, physical inactivity, poor sleep quality, high stress and tobacco/alcohol use (Kushner & Sorensen, 2013). Each of these lifestyle behaviours constitute the multiple determinants of 'health' as defined by the U.S. Department of Health and Human Services. Over the past several years, there has been an increased interest in evaluating the benefit of adhering to healthier lifestyle behaviours in the development of morbidity and mortality (Kushner & Sorensen, 2013). In many epidemiological studies, patterns of healthy lifestyle behaviours, characterized by high diet quality (e.g., high adherence to Mediterranean diet [MD]), adequate frequency of physical activity (PA) and not smoking, were associated with a lower risk of NCDs onset, cardiovascular events and mortality when compared to subjects with unhealthy lifestyles (Chiuve et al., 2011; Ford et al., 2009; Stringhini et al., 2010).

The detrimental impact of unhealthy lifestyles on systemic health may be mainly ascribed to the induction of a state of low-grade systemic inflammation (LGSI) and to the overproduction of reactive oxygen species (ROS), leading to oxidative stress (Esposito et al., 2004; Frodermann et al., 2019). Since LGSI has been bi-directionally linked with periodontitis (D'Aiuto et al., 2010; Romandini et al., 2018), the association between lifestyle behaviours and periodontitis has been analysed in several epidemiological studies, which frequently reported a higher prevalence and a more severe disease phenotype in subjects with unhealthy lifestyle behaviours (Coelho et al., 2020; Karaaslan & Dikilitaş, 2019; Marruganti et al., 2022; Marruganti, Baima, Grandini, et al., 2023; Morales et al., 2022; Romandini et al., 2017). On these premises, unhealthy lifestyles may also negatively influence the efficacy of the Steps 1 and 2 of periodontal therapy through the molecular pathways of LGSI imbalance and ROS overproduction. Although the detrimental impact of each single unhealthy lifestyle behaviour on periodontal treatment outcomes has been investigated in previous longitudinal studies (Bakri et al., 2013; Bartha et al., 2022; Chang et al., 2021; Costa et al., 2020; Dommisch et al., 2018; Leite, Nascimento, Baake, et al., 2018; Leite, Nascimento, Scheutz, & López, 2018; Marruganti et al., 2022; Woelber et al., 2019), little is known regarding their combined effect on such outcomes. Moreover, while on one hand the latest treatment guidelines recommend smoking cessation interventions as part of Step 1, it is still unclear whether other lifestyle interventions, such as dietary counselling and increase in PA, may provide an added benefit to periodontal therapy, as evidence is still scarce (Sanz et al., 2020). Therefore, the aim of this prospective cohort study was to investigate the association between lifestyle behaviours and the efficacy of the Steps 1/2 of periodontal therapy.

2 | MATERIALS AND METHODS

The present study is reported according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines for cohort studies (von Elm et al., 2008). The research protocol was approved by the local Ethical Review Board (ERB; protocol number: 19037/2021) and was registered on Clinicaltrials.gov before commencing recruitment (NCT04769622).

2.1 | Participants

Participants were selected from among those identified in the baseline (BL) study (Marruganti et al., 2022) according to the following inclusion criteria:

Presence of untreated Stage II/III periodontitis, either localized or generalized (Tonetti et al., 2018), with at least one site with probing pocket depth (PPD) ≥ 4 mm; presence of at least 20 remaining teeth; age between 18 and 70 years; and ability and willingness to give informed consent.

The exclusion criteria were as follows: current pregnancy or lactation; periodontal therapy received during the previous 12 months; antibiotics intake within the previous 6 months; and inability to effectively communicate in Italian.

Participants were recruited between February 2021 and August 2021 and were enrolled in the study after they had read and signed a written informed consent, in accordance with the Declaration of Helsinki.

2.2 | Assessment of study variables

2.2.1 | Lifestyle behaviours

Lifestyle behaviours were assessed by interviewers at BL by asking structured questions and giving the explanations provided by each questionnaire. In >90% of the cases, the interviewers were trained undergraduate students not involved in the study of clinical examination procedures; in <10% of the cases, the interviews were conducted by the same clinical examiners (CM, CG) because of COVID-19 restrictions. The following four validated questionnaires were administered: (i) adherence to Mediterranean diet questionnaire (QueMD) (Gnagnarella et al., 2018); (ii) International Physical Activity Questionnaire (IPAQ) (Mannocci et al., 2010); (iii) Perceived Stress Score (PSS) questionnaire (Cohen et al., 1983) and (iv) Pittsburgh Sleep Quality Index (PSQI) questionnaire (Mondo et al., 2021). According to the scores obtained in each questionnaire, participants were categorized as having either high or low adherence to MD; moderate/high or low PA level; low or moderate/high PSS; and good or poor sleep quality. Details regarding the thresholds selected for all categories are provided in Appendix S1. In addition, smoking status and frequency of alcohol consumption were also assessed; thus, participants were further categorized as being non-smokers versus smokers and consuming alcohol below versus above the suggested intake. Further details regarding the structure of the questionnaires and their score assessment methods are reported in Appendix S1.

2.2.2 | Clinical periodontal variables

A full-mouth periodontal examination was performed at BL and 3 months (3 M) after completing the Steps 1/2 of periodontal therapy by two previously calibrated examiners (CM, CG). The clinical examiners were different from the interviewers in >90% the cases, and they were therefore blinded with respect to lifestyle assessment in most cases. Calibration of the examiners was performed for both PPD and recession (REC) on two non-study subjects suffering from periodontitis, and it was considered satisfactory only when an agreement in least 95% of measurements (with a maximum of 2 mm difference) was recorded between the two examiners (CM, CG). Inter-examiner agreement resulted in ICC = 0.98 ($p < .001$) for PPD and ICC = 0.96 ($p < .001$) for REC. For the first examiner, intra-examiner agreement resulted in ICC = 0.89 ($p = .002$) for PPD and ICC = 0.92 ($p = .001$) for REC; for the second one, intra-examiner agreement resulted in ICC = 0.94 ($p < .001$) for PPD and ICC = 0.98 ($p < .001$) for REC. PPD, REC, plaque (O'Leary et al., 1972) and bleeding on probing (BoP) (Ainamo & Bay, 1975) were recorded with a standardized periodontal probe (UNC 15 probe, HuFriedy Group, Chicago, IL, USA) at six sites per tooth, with third molars excluded. Clinical attachment levels (CALs) were computed. Tooth mobility was measured according to the Miller index (Miller & Boenheim, 1938).

2.2.3 | Other variables

Socio-demographic characteristics (age, gender, body mass index [BMI], education) and diabetes status were collected. Household disposable income was approximated from the participant's post code. Details of the assessment method are reported in Appendix S1.

2.3 | Periodontal therapy

The included participants received Steps 1/2 of periodontal therapy by two therapists (CM, CG). Briefly, Step 1 included oral hygiene instructions (OHIs) and motivation, as well as supragingival professional mechanical plaque removal (PMPR) performed with ultrasonic instruments (Cavitron Select SPS, Dentsply Sirona, Rome, Italy) (Step 1). Moreover, smokers received simple counselling in the form of advice to limit or possibly quit smoking (Sanz et al., 2020). No interventions aimed at modifying the other lifestyles behaviours were implemented. Step 2 of periodontal therapy included quadrant-wise subgingival instrumentation performed with both ultrasonic and hand instruments (Gracey curetters, HuFriedy, Chicago) under local anaesthesia (articaine 4% with epinephrine 1:100,000) (Sanz et al., 2020). One month after the completion of the Steps 1/2, participants received a reinforcement of OHIs and motivation.

2.4 | Study outcomes

The primary outcome of this study was the presence of a composite measure of 'endpoint of therapy' defined at the patient level as the absence of sites with residual PPD ≥ 4 mm with BoP and of sites with PPD ≥ 6 mm. Additional patient-level outcomes encompassed full-mouth plaque score (FMPS), full-mouth bleeding score (FMBS), percentage of sites with PPD ≥ 5 mm and percentage of sites with PPD ≥ 6 mm and the number of teeth with mobility ≥1. Moreover, site-level PPD, REC, CAL changes (3 M−BL) and BoP at 3M were also considered.

2.5 | Statistical analyses

Analyses were performed using a statistical software (STATA BE, version 17, StataCorp LP, Texas, USA), a priori setting the level of significance at 5%. Sample size calculation had been performed for the BL study (Marruganti et al., 2022); no specific a priori power analysis was done for this follow-up examination, since all the patients identified in the BL study fulfilling the inclusion criteria were included in the present analysis. Continuous variables were described as mean and standard deviation (SD), while the categorical ones were expressed as number of observations (%).

After verification of data distribution, the response to Steps 1/2 of periodontal therapy was evaluated comparing the 3 M and BL

values through the paired Student's *t*-test. At the patient level (uni-level analyses), simple and multiple linear regression were performed to investigate the association between each lifestyle behaviour (binary variables) and continuous periodontal outcomes at 3 M (i.e., FMPS, FMBS, % PPD ≥ 5 mm, % PPD ≥ 6 mm, number of teeth with mobility ≥1), while simple and multiple logistic regression analyses were used to investigate the association between each lifestyle behaviour (binary variables) and the endpoint of therapy (binary outcome). At the site level (multi-level analyses), simple and multiple linear regression were performed to investigate the association between each lifestyle behaviour (binary variables) and the change from baseline (3 M–BL) of continuous periodontal outcomes (i.e., PPD change, PPD change for sites with PPD ≥ 6 mm, REC change and CAL change), while simple and multiple logistic regression were used to investigate the association between each lifestyle behaviour (binary variables) and the presence of BoP at 3 months (binary outcome). Whenever possible, sensitivity analyses using the lifestyle behaviours as continuous variables were also performed. In addition, the binary variable 'unhealthy lifestyles' (=1 whenever each participant had low adherence to MD and low PA level and high perceived stress and poor sleep quality; and =0 otherwise) was built and used as a further exposure variable in the simple/multiple regression models. Multiple regression models were adjusted as follows: (i) Model 1: estimates adjusted for the value of the outcome at baseline (e.g., outcome 'PPD change' adjusted for the PPD value at BL); (ii) Model 2: Model 1 + BMI + diabetes + household disposable income + 3 M FMPS (for patient-level analyses) or plaque at site level (for site-level analyses); (iii) Model 3: Model 2 + other lifestyle behaviours (except for the exposure(s)). Confounders were selected based on previous knowledge of the association with the exposure, the outcome or both (Hsu et al., 2019; Suvan, Harrington, et al., 2020, Suvan, Leira, et al., 2020; Tomasi et al., 2022; VanderWeele, 2019). For each multiple model, multicollinearity was tested using Pearson's correlation coefficient and variance inflation factor (VIF) values; correlation coefficients ≥0.80 or VIF ≥ 5 indicated the presence of multicollinearity and therefore the variable with the highest correlation coefficient/VIF was eventually dropped out from the model. Results from regression analyses were expressed as odds ratios (ORs) or mean difference (MD) with 95% confidence interval (CI).

3 | RESULTS

From the initially selected 235 participants, 120 were included in the present study (Figure S1). Most of the participants were males (58.3%) and had a mean age of 58.8 years. Fifty-five (55.0%) participants had low MD adherence, 42.5% performed low PA, 34.2% had moderate/high PSS, 39.2% had poor sleep quality, 35.8% were smokers and 41.7% consumed alcohol above the suggested intake (Table 1). At 3M, one subject was lost to follow-up because of non-study-related reasons ($n = 119$).

Overall, 76 (63.9%) participants achieved the endpoint of therapy at 3M after Steps 1/2. Steps 1/2 led to a significant reduction of FMPS and FMBS, as well as a significant reduction in the percentage of sites with PPD ≥ 5 mm and PPD ≥ 6 mm ($p < .001$). The mean number of teeth with mobility almost halved from BL to 3 M (Table 2).

Subjects with poor sleep quality (OR = 0.13; 95% CI: 0.03, 0.47; $p < .01$), smokers (OR = 0.18; 95% CI: 0.06, 0.52; $p < 0.05$) and excessive alcohol users (OR = 0.21; 95% CI: 0.07, 0.63; $p < .01$) showed a reduced rate of endpoint of therapy in the fully adjusted model (Model 3), while subjects with low aMed (OR = 0.51; 95% CI: 0.18, 1.46; $p > .05$), low PA (OR = 0.52; 95% CI: 0.18, 1.49; $p > .05$) and moderate/high PSS (OR = 0.65; 95% CI: 0.18, 2.38; $p > .05$) showed the same tendency, even though not statistically significant. Furthermore, smokers had a higher proportion of residual PPD ≥5 mm (Table 3).

At the site level, low aMed and smoking showed a negative association with PPD, REC and CAL changes, while moderate/high PSS and excessive alcohol use showed association only with CAL and PPD (only considering sites with PPD ≥ 6 mm at BL). Moreover, low PA, poor sleep quality and excessive alcohol use were associated with

TABLE 1 Characteristics of the study population.

Variables	Overall ($n = 120$)
Age (years), mean (±SD)	58.8 (±11.2)
Gender, female, *n* (%)	38 (31.7)
Education, *n* (%)	
Elementary/middle school	42 (35.0)
High school	61 (50.8)
College or more	17 (14.2)
Household disposable income, mean (±SD)	18,031.02 (±3415.68)
BMI (kg/m^2), mean (±SD)	27.2 (±4.4)
Diabetes, yes, *n* (%)	15 (12.5)
Low aMed, *n* (%)	66 (55.0)
Low PA, *n* (%)	51 (42.5)
Moderate/high PSS, *n* (%)	41 (34.2)
Poor sleep quality, *n* (%)	47 (39.2)
Smoking, *n* (%)	
Non-smokers	77 (64.2)
Smokers	43 (35.8)
Alcohol use, *n* (%)	
Below the suggested intake	70 (58.33)
Above the suggested intake	50 (41.67)
aMed, mean (±SD)	4.37 (±1.66)
MET-min/week (PA), mean (±SD)	2703.55 (±3840.47)
PSS, mean (±SD)	11.41 (±6.66)
PSQI, mean (±SD)	4.93 (±3.00)

Abbreviations: aMed, alternate Mediterranean diet score; BMI, body mass index; MET-min/week, metabolic equivalent of task in minutes per week; PA, physical activity; PSS, perceived stress score; PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation.

TABLE 2 Periodontal variables at baseline and 3-month follow-up (patient and site level).

Variables	BL ($n = 120$)	3 M ($n = 119$)	3 M–BL
Patient level			
FMPS, %, mean (±SD)	73.15 (±18.78)	18.69 (±14.67)	−54.46 (±16.13)***
FMBS, %, mean (±SD)	37.73 (±20.37)	13.73 (±10.65)	−24.00 (±17.30)***
% PPD ≥ 5 mm, mean (±SD)	10.60 (±9.97)	3.99 (±5.23)	−6.61 (±8.49)***
% PPD ≥ 6 mm, mean (±SD)	4.03 (±6.50)	1.64 (±3.05)	−2.39 (±4.73)***
No. of teeth with mobility ≥1, mean (±SD)	1.96 (±3.16)	1.00 (±2.91)	−0.96 (±3.79)*
% sites with PPD ≥4 mm with BoP, and PPD ≥6 mm	21.41 (±14.23)	4.70 (±5.91)	−16.71 (±7.02)***
Endpoint of therapy[a], yes, *n* (%)	-	76 (63.33)	-
Site level			
PPD, mm, mean (±SD)	2.59 (±1.37)	2.34 (±1.15)	−0.25 (±1.28)**
PPD (sites with PPD ≥ 6 mm), mm, mean (±SD)	6.42 (±0.90)	3.19 (±1.57)	−3.23 (±1.81)*
REC, mm, mean (±SD)	0.10 (±0.61)	0.18 (±0.73)	0.08 (±0.71)**
CAL, mm, mean (±SD)	2.70 (±1.49)	2.53 (±1.34)	−0.17 (±1.46)*

Abbreviations: BL, baseline; FMBS, full-mouth bleeding score; FMPS, full-mouth plaque score; *n*, number; PPD, probing pocket depth; SD, standard deviation; 3 M, 3 months.

[a]Participants with no sites with PPD ≥ 4 mm with BoP, and PPD ≥ 6 mm.

*$p < .05$.**$p < .01$.***$p < .001$.

higher odds of BoP-positive sites at 3 months (Table 4). These trends of association were confirmed also by the sensitivity analyses performed using the exposures—lifestyle behaviours—as continuous variables (Tables S1 and S2).

Subjects with a combination of unhealthy, newly explored lifestyles (low aMed and low PA and moderate/high PSS and poor sleep quality) had a reduced probability of reaching the endpoint of therapy (OR = 0.85; 95% CI: 0.32, 0.99; $p < .05$) even after adjusting for smoking and alcohol. Those subjects also showed a higher proportion of residual PPD ≥ 6 mm and a reduced site-level impact of the Steps 1/2 of periodontal therapy in PPD, REC and CAL changes (Table 5).

4 | DISCUSSION

The results from the present study indicate a significant association between lifestyle behaviours and the clinical outcomes after Steps 1/2 of periodontal therapy. Specifically, poor sleep quality, smoking and alcohol use above the suggested intake were associated with significantly lower rates of endpoint of therapy; the same tendency was also observed for low MD adherence, low PA level and high perceived stress, even though not reaching statistical significance. Moreover, subjects reporting a combination of low MD adherence, low PA level, high perceived stress and poor sleep quality showed reduced rates of endpoint of therapy and a higher proportion of residual PPD ≥ 6 mm.

In the current investigation, Steps 1/2 led to a reduction in the proportion of sites with PPD ≥ 5 mm of around 60%, which is consistent with previous meta-analytical data (Suvan, Leira, et al., 2020). Nonetheless, the proportion of residual pockets achieved in the current study varied widely across subgroups of lifestyle behaviours. These differences were consistent and significant also after adjusting for baseline values, patient compliance (plaque at 3 M), systemic conditions/diseases (i.e., BMI and diabetes) and other tested lifestyle behaviours that could have otherwise influenced the subject's response to Steps 1/2 (Hsu et al., 2019; Suvan, Leira, et al., 2020). Specifically, the magnitude of the association of poor sleep quality and excessive alcohol use was similar or even greater than the one noted for smoking, which is considered as the major behavioural risk factor for periodontitis onset, severity and response to treatment (Chang et al., 2021; Labriola et al., 2005; Leite, Nascimento, Baake, et al., 2018; Leite, Nascimento, Scheutz, & López, 2018). The association between the investigated lifestyle behaviours and the clinical response after Steps 1/2 of periodontal therapy was independent of possible confounders, including plaque control. Hence, a direct biological effect of lifestyle behaviours on the periodontium is suggested. These findings may be relevant for clinicians because those behaviours may represent potential targets of interventions in the context of the Step 1 of periodontal therapy (Sanz et al., 2020), and for researchers because they may represent potential confounders to be considered when analysing the risk factors of periodontitis or its association with systemic diseases (Antonoglou et al., 2023; Baima et al., 2022; Botelho et al., 2022; D'Aiuto et al., 2018; Marruganti, Baima, Aimetti, et al., 2023; Marruganti, Shin, Jim, et al., 2023; Romandini et al., 2020, 2021).

At the local level, previous investigations have indicated that participants under high psychosocial stress showed lower PPD and CAL changes 6 months after Steps 1/2 of periodontal therapy (Bakri et al., 2013). Consistently, the administration of supplemental micronutrients (e.g., vitamin C, D, E, calcium, magnesium, etc.) and specific dietary patterns (e.g., anti-inflammatory or Mediterranean diet) were

TABLE 3 Simple and multiple linear/logistic regression analyses for the association between lifestyle behaviours and periodontal outcomes at 3 M (patient level).

Low aMed—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
FMPS[d], %	0.79 (−5.31, 6.89)	0.37 (−4.81, 5.54)	0.30 (−5.52, 5.00)	−0.23 (−5.72, 5.20)
FMBS, %	2.09 (−1.80, 5.97)	1.47 (−1.86, 4.80)	1.59 (−1.42, 4.66)	1.03 (−2.10, 4.21)
% PPD ≥ 5 mm	3.60 (−0.08, 5.69)	2.62 (−0.04, 5.85)	2.11 (−0.03, 4.24)	1.37 (−0.02, 3.03)
% PPD ≥ 6 mm	0.10 (−0.30, 1.91)	0.10 (−0.27, 1.44)	0.60 (−0.46, 1.28)	0.56 (−0.34, 1.44)
No. of teeth with mobility ≥1, mean (±SD)	−0.68 (−1.75, 0.38)	−0.66 (−1.73, 0.41)	−0.67 (−1.79, 0.44)	−0.60 (−1.76, 0.56)
Endpoint of therapy[d], yes, *n* (%)	0.77 (0.36, 1.63)	0.83 (0.39, 1.79)	0.92 (0.39, 2.11)	0.50 (0.18, 1.47)
Low PA—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
FMPS[e], %, mean (±SD)	5.59 (−0.47, 11.64)	2.82 (−2.41, 8.06)	2.80 (−2.43, 8.04)	1.37 (−4.44, 7.18)
FMBS, %, mean (±SD)	3.35 (−0.52, 7.23)	2.02 (−1.34, 5.38)	1.10 (−2.09, 4.21)	1.87 (−1.52, 5.25)
% PPD ≥ 5 mm, mean (±SD)	1.57 (−0.33, 3.47)	0.73 (−0.92, 2.39)	0.69 (−0.99, 2.37)	0.42 (−1.38, 2.22)
% PPD ≥ 6 mm, mean (±SD)	0.83 (−0.29, 0.02)	0.13 (−0.16, 1.11)	0.34 (−0.41, 0.99)	−0.30 (−1.03, 0.64)
No. of teeth with mobility ≥1, mean (±SD)	0.66 (−0.41, 1.74)	0.49 (−0.60, 1.59)	0.56 (−0.60, 1.69)	0.67 (−0.59, 1.92)
Endpoint of therapy[d], yes, *n* (%)	0.62 (0.29, 1.31)	0.68 (0.32, 1.46)	0.75 (0.33, 1.71)	0.54 (0.19, 1.49)
Moderate/High PSS—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
FMPS[e], %, mean (±SD)	2.89 (−3.53, 9.29)	4.91 (−0.49, 10.30)	4.18 (−1.38, 9.72)	5.14 (−1.30, 11.58)
FMBS, %, mean (±SD)	−2.49 (−6.58, 1.59)	−2.23 (−5.72, 1.26)	−1.81 (−5.09, 1.47)	−0.99 (−4.65, 2.66)
% PPD ≥ 5 mm, mean (±SD)	0.42 (−1.60, 2.44)	0.19 (−1.53, 1.92)	0.04 (−1.73, 1.80)	0.74 (−1.24, 2.71)
% PPD ≥ 6 mm, mean (±SD)	0.15 (−1.02, 1.33)	0.08 (−0.82, 0.99)	0.03 (−0.87, 0.93)	0.11 (−0.95, 1.13)
No. of teeth with mobility ≥1, mean (±SD)	−0.04 (−1.17, 1.10)	−0.18 (−1.34, 0.97)	−0.29 (−1.49, 0.92)	0.05 (−1.35, 1.44)
Endpoint of therapy[d], yes, *n* (%)	1.96 (0.86, 4.46)	0.48 (0.21, 1.11)	**0.34 (0.13, 0.92)***	0.65 (0.18, 2.38)
Poor sleep quality—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
FMPS[e], %, mean (±SD)	−0.37 (−6.58, 5.85)	0.99 (−4.28, 6.26)	0.25 (−5.11, 5.59)	−2.29 (−8.29, 3.70)
FMBS, %, mean (±SD)	**4.20 (0.30, 8.10)***	1.92 (−0.52, 5.38)	1.85 (−0.49, 4.11)	2.01 (−0.37, 4.92)
% PPD ≥ 5 mm, mean (±SD)	1.41 (−0.52, 3.35)	0.78 (−0.89, 2.44)	1.05 (−0.67, 2.72)	1.58 (−0.31, 3.50)
% PPD ≥ 6 mm, mean (±SD)	−0.53 (−1.67, 0.61)	0.32 (−0.58, 1.21)	0.46 (−0.41, 1.37)	0.51 (−0.51, 1.53)
No. of teeth with mobility ≥1, mean (±SD)	−0.39 (−1.48, 0.70)	−0.48 (−1.58, 0.62)	−0.55 (−1.69, 0.60)	−0.64 (−1.99, 0.69)
Endpoint of therapy[d], yes, *n* (%)	**0.31 (0.12, 0.59)****	**0.27 (0.11, 0.65)****	**0.22 (0.08, 0.59)****	**0.13 (0.04, 0.47)****
Smoking—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
FMPS[e], %, mean (±SD)	2.47 (−3.87, 8.81)	1.60 (−3.77, 6.98)	1.50 (−3.88, 6.87)	1.85 (−3.77, 7.47)
FMBS, %, mean (±SD)	−2.19 (−6.24, 1.85)	−0.50 (−4.01, 3.01)	−0.58 (−3.84, 2.72)	−0.42 (−3.76, 2.93)
% PPD ≥ 5 mm, mean (±SD)	**2.89 (0.97, 4.82)****	**2.06 (0.38, 3.74)***	**2.07 (0.38, 3.76)***	**2.26 (0.47, 4.02)***
% PPD ≥ 6 mm, mean (±SD)	**1.19 (0.05, 2.34)***	0.79 (−0.10, 1.68)	0.70 (−0.17, 1.57)	0.87 (−0.06, 1.77)
No.of teeth with mobility ≥1, mean (±SD)	0.48 (−0.63, 1.58)	0.51 (−0.61, 1.62)	0.51 (−0.64, 1.65)	0.48 (−0.75, 1.68)
Endpoint of therapy[d], yes, *n* (%)	**0.33 (0.15, 0.71)****	**0.35 (0.16, 0.77)****	**0.33 (0.14, 0.74)****	**0.18 (0.06, 0.52)***
Alcohol use (above suggested intake)—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
FMPS[e], %, mean (±SD)	−2.12 (−8.26, 4.02)	−3.70 (−8.89, 1.48)	−3.34 (−8.67, 1.97)	−3.84 (−9.37, 1.72)
FMBS, %, mean (±SD)	**5.74 (1.95, 9.54)****	**3.44 (1.23, 5.66)****	**2.74 (1.08, 5.80)***	1.06 (−0.66, 4.65)
% PPD ≥ 5 mm, mean (±SD)	1.10 (−0.83, 3.01)	0.77 (−0.87, 2.42)	0.65 (−1.07, 2.34)	1.08 (−0.64, 2.81)

TABLE 3 (Continued)

Alcohol use (above suggested intake)—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
% PPD ≥ 6 mm, mean (±SD)	−0.80 (−1.88, 0.36)	−0.21 (−1.09, 0.65)	0.10 (−1.01, 0.76)	0.44 (−0.70, 1.12)
No.of teeth with mobility ≥1, mean (±SD)	−0.84 (−1.92, 0.23)	−0.64 (−1.74, 0.47)	−0.78 (−1.93, 0.40)	−0.73 (−1.94, 0.50)
Endpoint of therapy[d], yes, *n* (%)	0.52 (0.24, 1.12)	0.53 (0.24, 1.18)	**0.39 (0.16, 0.95)***	**0.21 (0.07, 0.63)****

Note: Bold writing indicates statistically significant estimates ($p < 0.05$).
Abbreviations: aMed, alternate Mediterranean diet score; BL, baseline; FMBS, full-mouth bleeding score; FMPS, full-mouth plaque score; PA, physical activity; PPD, probing pocket depth; PSS, perceived stress score; SD, standard deviation; 3 M, 3 months.
[a]Model 1: Adjusted for its baseline value.
[b]Model 2: Model 1 + BMI + diabetes + household disposable income + 3 M FMPS.
[c]Model 3: Model 2 + the remaining five lifestyle behaviours (except for the main exposure).
[d]Participants with no sites with PPD ≥ 4 mm with BoP, and PPD ≥ 6 mm.
[e]Multiple models unadjusted for 3 M FMPS.
*$p < .05$; **$p < .01$.

TABLE 4 Simple and multiple linear/logistic regression analyses for the association between lifestyle behaviours and the changes in periodontal outcomes (3 M−BL) (site level).

Low aMed—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
PPD change, mm	0.17 (−0.005, 0.34)	**0.17 (0.01, 0.34)***	**0.21 (0.05, 0.37)***	**0.17 (0.02, 0.33)***
PPD change (sites with PPD ≥ 6 mm), mm	0.16 (−0.37, 0.68)	0.25 (−0.25, 0.76)	0.33 (−0.17, 0.82)	0.35 (−0.10, 0.82)
REC change, mm	0.02 (−0.06, 0.09)	0.02 (−0.03, 0.07)	**0.04 (0.01, 0.07)***	**0.04 (0.02, 0.08)***
CAL change, mm	0.15 (−0.05, 0.35)	0.15 (−0.06, 0.35)	0.17 (−0.01, 0.34)	**0.17 (0.02, 0.34)***
BoP, yes	**1.10 (1.01, 1.20)***	1.08 (0.99, 1.18)	1.04 (0.96, 1.20)	1.02 (0.92, 1.10)
Low PA—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
PPD change, mm	0.11 (−0.06, 0.28)	**0.24 (0.08, 0.40)****	**0.23 (0.08, 0.39)****	0.16 (−0.01, 0.34)
PPD change (sites with PPD ≥ 6 mm), mm	0.23 (−0.29, 0.75)	0.12 (−0.38, 0.63)	0.17 (−0.30, 0.65)	0.16 (−0.32, 0.69)
REC change, mm	−0.02 (−0.10, 0.06)	−0.01 (−0.10, 0.08)	0.01 (−0.08, 0.12)	0.06 (−0.06, 0.15)
CAL change, mm	0.09 (−0.11, 0.29)	**0.23 (0.02, 0.44)***	**0.22 (0.03, 0.42)***	0.21 (−0.11, 0.41)
BoP, yes	**1.33 (1.22, 1.45)*****	**1.24 (1.13, 1.36)*****	**1.21 (1.11, 1.43)****	**1.19 (1.13, 1.40)***
Moderate/High PSS—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
PPD change, mm	**0.26 (0.09, 0.44)****	**0.22 (0.05, 0.39)***	**0.19 (0.02, 0.36)***	0.16 (−0.03, 0.35)
PPD change (sites with PPD ≥ 6 mm), mm	0.17 (−0.39, 0.73)	0.12 (−0.42, 0.67)	0.03 (−0.51, 0.58)	0.02 (−0.47, 0.50)
REC change, mm	**0.09 (0.006, 0.17)***	**0.10 (0.01, 0.19)***	**0.08 (0.01, 0.17)***	0.06 (−0.05, 0.21)
CAL change, mm	**0.37 (0.17, 0.57)*****	**0.33 (0.12, 0.54)****	**0.28 (0.07, 0.49)****	**0.22 (0.01, 0.45)***
BoP, yes	0.89 (0.78, 1.03)	0.90 (0.82, 1.06)	0.94 (0.84, 1.07)	0.98 (0.89, 1.16)[d]
Poor sleep quality—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
PPD change, mm	**0.28 (0.12, 0.46)****	**0.23 (0.06, 0.29)***	0.12 (−0.07, 0.26)	0.05 (−0.12, 0.24)
PPD change (sites with PPD ≥ 6 mm), mm	0.12 (−0.45, 0.69)	0.09 (−0.59, 0.52)	0.10 (−0.62, 0.43)	0.08 (−0.46, 0.61)
REC change, mm	**0.08 (0.003, 0.17)***	**0.09 (0.002, 0.18)***	0.08 (−0.005, 0.17)	0.09 (−0.02, 0.19)

(Continues)

TABLE 4 (Continued)

Poor sleep quality—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
CAL change, mm	**0.37 (0.18, 0.56)*** **	**0.21 (0.007, 0.42)***	0.21 (−0.02, 0.39)	0.16 (−0.09, 0.38)
BoP, yes	**1.43 (1.30, 1.56)*** **	**1.31 (1.19, 1.45)****	**1.37 (1.23, 1.52)****	**1.34 (1.19, 1.49)****
Smoking—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
PPD change, mm	0.08 (−0.09, 0.24)	0.15 (−0.02, 0.32)	**0.21 (0.03, 0.43)****	**0.28 (0.02, 0.46)***
PPD change (sites with PPD ≥ 6 mm), mm	**0.64 (0.12, 1.15)***	**0.53 (0.03, 1.03)***	**0.80 (0.31, 1.29)****	**0.85 (0.39, 1.31)*** **
REC change, mm	0.03 (−0.05, 0.11)	0.04 (−0.05, 0.13)	**0.04 (0.01, 0.14)***	**0.06 (0.01, 0.16)***
CAL change, mm	0.12 (−0.09, 0.33)	0.20 (−0.01, 0.42)	**0.18 (0.02, 0.38)***	**0.17 (0.03, 0.38)***
BoP, yes	**0.84 (0.76, 0.92)*** **	**0.89 (0.81, 0.98)***	0.90 (0.83, 1.04)	0.91 (0.79, 1.02)
Alcohol use (above suggested intake)—MD/OR (95% CI)				
Outcomes	**Crude**	**Model 1[a]**	**Model 2[b]**	**Model 3[c]**
PPD change, mm	0.09 (−0.08, 0.27)	0.08 (−0.09, 0.25)	0.08 (−0.10, 0.23)	0.12 (−0.03, 0.29)
PPD change (sites with PPD ≥ 6 mm), mm	0.39 (−0.12, 0.91)	**0.62 (0.13, 1.10)***	0.44 (−0.08, 0.96)	**0.73 (0.23, 1.22)****
REC change, mm	0.05 (−0.03, 0.13)	0.02 (−0.07, 0.11)	0.04 (−0.06, 0.15)	0.05 (−0.04, 0.14)
CAL change, mm	0.14 (−0.06, 0.34)	0.10 (−0.11, 0.31)	0.12 (−0.12, 0.33)	0.11 (−0.09, 0.32)
BoP, yes	**1.43 (1.31, 1.57)*** **	**1.47 (1.34, 1.61)*** **	**1.37 (1.25, 1.51)****	**1.31 (1.19, 1.45)****

Note: Bold writing indicates statistically significant estimates ($p < 0.05$).

Abbreviations: aMed, alternate Mediterranean diet score; BoP, bleeding on probing; BL, baseline; CAL, clinical attachment level; CI, confidence interval; MD, mean difference; OR, odds ratio; PA, physical activity; PPD, probing pocket depth; PSS, perceived stress score; REC, recession; SD, Standard Deviation; 3 M, 3 months.

[a]Model 1: Adjusted for its baseline value.

[b]Model 2: Model 1 + BMI + diabetes + household disposable income + plaque at site level.

[c]Model 3: Model 2 + the remaining five lifestyle behaviours (except for the main exposure).

[d]Smoking was dropped out from the model due to multicollinearity.

*$p < .05$; **$p < .01$; ***$p < .001$.

shown to improve periodontal clinical measures (Bartha et al., 2022; Dommisch et al., 2018; Woelber et al., 2019). At the systemic level, low adherence to MD, low PA, high stress and poor sleep quality were shown to lead to an increased LGSI state through a variety of molecular pathways (Besedovsky et al., 2019; Esposito et al., 2004; Frodermann et al., 2019; Sabbah et al., 2018). In particular, a dietary pattern with low adherence to MD is usually characterized by the frequent consumption of pro-inflammatory foods, such as white flour and processed meats, which also contribute to increasing oxidative stress levels (Christ et al., 2019). Similar molecular pathways leading to an imbalance of LGSI and an overproduction of ROS are also involved in the association between low PA (or sedentary lifestyle), poor sleep quality and periodontitis, respectively (Besedovsky et al., 2019; Frodermann et al., 2019). In addition to these mechanisms, high stress was also found to exert a suppressive action on the immune system (e.g., by reducing lymphocyte proliferation and antibody production) and to trigger other behavioural adaptive changes (e.g., alcohol/drug use, increased smoking, etc.) (Sabbah et al., 2018). Since it has been shown previously that these molecular pathways can negatively influence the periodontium and render the subjects more prone to periodontitis onset and rapid progression (Baima et al., 2021; D'Aiuto et al., 2010; Pink et al., 2015), it can be hypothesized that the same mechanisms can reduce the efficacy of Steps 1/2, as observed in the current investigation.

The biological mechanisms underpinning the detrimental impact of smoking and alcohol on the periodontium are well established. Indeed, several investigations have suggested that smoking is related to a specific pattern of colonization of periodontal pathogens and to high levels of pathogenic species even in shallow sites, while, from an immunoinflammatory standpoint, smoking was shown to increase oxidative stress and to trigger cytokine overproduction through the modification of intracellular signalling mechanisms (Labriola et al., 2005; Nociti et al., 2014). Similarly, the possible mechanisms linking excessive alcohol consumption to periodontitis may be mainly ascribed to the overproduction of cytokines and to the impairment of the host's immunity (i.e., alteration of neutrophils, macrophages and T-cell functioning) (Barr et al., 2016; Szabo & Saha, 2015). From a clinical standpoint, results from the current study are consistent with those of previous longitudinal investigations showing a detrimental impact of smoking and excessive alcohol consumption on periodontal treatment outcomes (Chang et al., 2021; Costa et al., 2020; Ryder et al., 2018).

The present study also indicated how subjects reporting a combination of low MD adherence, low PA, high stress and poor sleep

TABLE 5 Simple and multiple linear/logistic regression analyses for the relationship between the combination of unhealthy lifestyles and the response to periodontal treatment at 3 M (site level and patient level).

Unhealthy lifestyles[a]—MD/OR (95% CI)				
Variables	**Crude**	**Model 1[b]**	**Model 2[c]**	**Model 3[d]**
Patient level				
FMPS, %, mean (±SD)	4.80 (−4.59, 14.19)	6.06 (−1.85, 13.97)	5.53 (−2.43, 13.50)	5.06 (−2.97, 13.12)
FMBS, %, mean (±SD)	0.15 (−5.89, 6.17)	1.54 (−3.62, 6.70)	1.39 (−3.43, 6.20)	1.81 (−3.11, 6.69)
% PPD ≥ 5 mm, mean (±SD)	**3.16 (0.25, 6.06)***	2.18 (−0.32, 4.69)	2.13 (−0.41, 4.66)	1.78 (−0.72, 4.24)
% PPD ≥ 6 mm, mean (±SD)	**2.09 (0.4, 3.78)***	**1.68 (0.39, 2.98)***	**1.59 (0.32, 2.86)***	**1.51 (0.23, 2.80)***
No. of teeth with mobility ≥1, mean (±SD)	0.97 (−0.67, 2.61)	0.96 (−0.67, 2.59)	0.93 (−0.74, 2.59)	0.79 (−0.89, 2.45)
Endpoint of therapy, yes, *n* (%)	0.75 (0.24, 2.31)	0.89 (0.47, 1.28)	**0.81 (0.31, 0.99)***	**0.85 (0.32, 0.99)***
Site level[d]				
PPD change, mm, mean (±SD)	**0.59 (0.35, 0.85)*****	**0.56 (0.32, 0.80)*****	**0.54 (0.31, 0.78)*****	**0.52 (0.30, 0.82)*****
PPD change (sites with PPD ≥ 6 mm), mm, mean (±SD)	0.41 (−0.37, 1.19)	0.50 (−0.25, 1.25)	0.56 (−0.18, 1.23)	0.27 (−0.43, 0.93)
REC change, mm, mean (±SD)	0.07 (−0.05, 0.19)	**0.19 (0.05, 0.33)****	**0.17 (0.04, 0.30)***	**0.17 (0.03, 0.30)***
CAL change, mm, mean (±SD)	**0.67 (0.37, 0.96)*****	**0.77 (0.47, 1.07)*****	**0.74 (0.45, 1.02)*****	**0.73 (0.40, 1.02)*****
BoP, yes	1.11 (0.97, 1.28)	1.07 (0.93, 1.24)	**1.17 (1.10, 1.34)***	**1.10 (1.01, 1.27)***

Note: Bold writing indicates statistically significant estimates ($p < 0.05$).
Abbreviations: BL, baseline; BMI, body mass index; BoP, bleeding on probing; CAL, clinical attachment level; CI, confidence interval; MD, mean difference; PPD, probing pocket depth; REC, recession; SD, standard deviation; 3 M, 3 months.
[a]Binary variable 'unhealthy lifestyles', which equaled 1 whenever each participant had low adherence to Mediterranean diet and low physical activity level and high perceived stress and poor sleep quality; otherwise it equaled 0.
[b]Model 1: Adjusted for its baseline value.
[c]Model 2: Model 1 + BMI + diabetes + household disposable income + 3 M FMPS for patient-level analyses and plaque at the site for site-level analyses.
[d]Model 3: Model 2 + smoking + alcohol.
*$p < .05$; **$p < .01$; ***$p < .001$.

quality had a poorer response to periodontal therapy. These results are in line with the current medical literature focusing on lifestyle behaviours not as independent but instead as closely intertwined entities. Indeed, several prospective cohort studies have highlighted how a combination of unhealthy lifestyle factors (e.g., diet quality, PA level, smoking, stress levels, etc.) was significantly associated with a shorter life expectancy free from multiple chronic diseases, such as diabetes, cardiovascular diseases and cancer (Nyberg et al., 2018; O'Doherty et al., 2016; Stenholm et al., 2016). In addition, it can also be hypothesized that subjects with patterns of unhealthy lifestyle behaviours are less likely to brush regularly and thus unmotivated to maintain oral health (Sabbah et al., 2018; Sakki & Sakki, 1995). Therefore, the promotion of a comprehensive healthy lifestyle, acting jointly on all the major lifestyle-related risk factors, would crucially help reduce the burden of NCDs, including periodontitis (Li et al., 2020).

When interpreting the present findings, some limitations should be considered. They include the limited external validity (due to the inclusion of a non-representative sample), the risk of residual confounding, the inability to attribute causation (due to the observational study design) and the risk of information bias since lifestyle behaviours were assessed through questionnaires, which, although validated, represent self-reported information. Moreover, a risk of information bias, also related to the assessment of periodontal variables, cannot be excluded because, despite calibration, the examiners were not blinded when evaluating a small proportion (<10%) of the included patients. Additionally, because of the potential for type I error due to multiple comparisons, findings for analyses of secondary endpoints should be interpreted as exploratory. Furthermore, no specific sample size calculation was performed for this follow-up examination and the study size may have limited to verifying the statistical significance of MD adherence, PA and stress estimates of association with the endpoint of periodontal therapy. Moreover, the smoking cessation advice intervention, made for ethical reasons as part of the Step 1 of periodontal therapy, may potentially have reduced the magnitude of the association between that behaviour and the reported outcomes. Similarly, lifestyles were monitored only at BL, so it is not possible to exclude whether lifestyle changes may have occurred during the study period. Finally, the validity of the present findings applies only for a short follow-up period (3 months). Overall, the described limitations may have influenced the results in both directions (i.e., lower or higher associations between lifestyles behaviours and periodontal therapy outcomes).

5 | CONCLUSION

The present prospective cohort study showed that unhealthy lifestyle behaviours are associated with a worse response to the Steps 1 and 2 of periodontal therapy. Although randomized clinical trials are warranted to verify whether the modification of those lifestyle behaviours as part of the Step 1 of periodontal therapy may have a significant impact on the clinical outcomes, these results may lay the groundwork

for the implementation of lifestyle interventions as part of Steps 1 and 2 of periodontal therapy.

AUTHOR CONTRIBUTIONS

Crystal Marruganti contributed to study conception, study design, data analysis, data collection and manuscript drafting. Mario Romandini contributed to data analysis, data interpretation and manuscript drafting. Carlo Gaeta contributed to data interpretation and manuscript drafting. Edoardo Ferrari Cagidiaco, Nicola Discepoli, Stefano Parrini and Filippo Graziani contributed to data interpretation and critically revised the manuscript. Simone Grandini contributed to study conception, study design and manuscript drafting.

FUNDING INFORMATION

This research received no specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest related to this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Marruganti, C., Romandini, M., Gaeta, C., Cagidiaco, E. F., Discepoli, N., Parrini, S., Graziani, F., & Grandini, S. (2023). Healthy lifestyles are associated with a better response to periodontal therapy: A prospective cohort study. *Journal of Clinical Periodontology*, 1–12. https://doi.org/10.1111/jcpe.13813