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Leisure-time and occupational physical activity demonstrate divergent associations with periodontitis: A population-based study

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Abstract

Aim: To evaluate the association between leisure-time/occupational physical activity (LTPA/OPA) and periodontitis in a nationally representative sample of the U.S. population.

Materials and Methods: Data from 10,679 adults were retrieved from NHANES 2009–2014 database. Physical activity was assessed through the Global Physical Activity Questionnaire, and accordingly, subjects were classified as performing either high or low LTPA/OPA. Periodontal status was assessed through a full-mouth periodontal examination, and subjects were classified according to the AAP/CDC criteria (no, mild, moderate, or severe periodontitis). Simple and multiple regression analyses were applied to study the association between LTPA/OPA and periodontitis/severe periodontitis.

Results: Multiple regression analyses identified high LTPA as a protective indicator for periodontitis (odds ratio [OR] = 0.81; 95% confidence interval [CI]: 0.72–0.92), while high OPA was found to be a significant risk indicator (OR = 1.16; 95% CI: 1.04–1.30). The combination low LTPA/high OPA showed a cumulative independent association with periodontitis (OR = 1.47; 95% CI: 1.26–1.72). Moreover, both high LTPA (OR = 0.72; 95% CI: 0.58–0.90) and high OPA (OR = 1.29; 95% CI: 1.09–1.53) were significantly associated with stronger estimates of severe periodontitis; the same was observed for the combination of low LTPA/high OPA (OR = 1.66; 95% CI: 1.29–2.15). **Conclusions:** LTPA and OPA showed divergent associations with periodontitis.

KEYWORDS

epidemiological factors, exercise, National Health and Nutrition Examination Survey, periodontal diseases

Clinical Relevance

Scientific rationale for study: While leisure-time physical activity (LTPA) can reduce low-grade systemic inflammation and oxidative stress, scientific evidence indicates that occupational physical activity (OPA) has the opposite effect. Hence, a divergent association of LTPA/OPA with periodontitis may be hypothesized.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes. © 2023 The Authors. *Journal of Clinical Periodontology* published by John Wiley & Sons Ltd. *Principal findings*: High LTPA was found to be a protective indicator for periodontitis/severe periodontitis, while high OPA turned out to be a risk indicator. The combination of low LTPA and high OPA showed a cumulative independent association with periodontitis and severe periodontitis.

Practical implications: The possible beneficial effects of LTPA also on periodontal health may be relevant for future iterations of physical activity guidelines.

1 | INTRODUCTION

Leisure-time physical activity (LTPA) refers to bodily movements performed during free time and not required as part of the essential activities of daily living. It is performed at the subject's discretion and includes activities such as sports, exercise, and recreational walking. LTPA is regarded as a preventive factor for most chronic non-communicable diseases (NCDs; Katzmarzyk et al., 2022). Indeed, LTPA-associated dynamic movements and psychological well-being have been linked with improved cardiometabolic function and reduced state of low-grade systemic inflammation (LGSI; Hamer et al., 2012; H. Li et al., 2021). Conversely, LTPAinactive subjects have shown higher prevalence of cardiovascular diseases (CVDs), type II diabetes mellitus, cancer, depression, and, in general, shortened life expectancy (Lee et al., 2012).

Occupational physical activity (OPA) refers, instead, to bodily movements made as part of the subject's professional tasks (e.g., carrying/lifting heavy loads, digging or construction work, household chores, etc.). OPA often involves long-lasting static load and repetitive working postures, with detrimental consequences on psycho-physical health and on the LGSI balance. Therefore, in contrast to LTPA, high OPA was shown to increase the incidence of several NCDs (Holtermann et al., 2013; Hallman et al., 2017; Holtermann et al., 2021).

Since LGSI has been bi-directionally linked with periodontitis (Pink et al., 2015; Romandini et al., 2018; Hajishengallis & Chavakis, 2021), the association between physical activity and periodontitis has been analysed in several epidemiological studies, which, however, reported conflicting results (Merchant et al., 2003; Ferreira et al., 2019; Marruganti et al., 2022). Nonetheless, these investigations did not differentiate between LTPA and OPA, and this aspect may provide a possible explanation to these contradictory findings. Clarifying the possible preventive role of physical activity on periodontitis would be relevant for oral healthcare providers, since this could represent a target for intervention as part of Step 1 of periodontal therapy (Ramseier et al., 2020). Therefore, the aim of the present study was to separately investigate the relationship between LTPA/OPA and periodontitis, analysing a nationally representative sample of the U.S. population.

2 | MATERIALS AND METHODS

The present cross-sectional study is reported according to the STrengthening the Reporting of OBservational studies in

Epidemiology (STROBE) guidelines (Vandenbroucke et al., 2007; von Elm et al., 2007).

2.1 | Study sample: NHANES 2009-2014

Data for the present study were drawn from the 2009–2014 cycles of the National Health and Nutrition Examination Survey (NHANES), a nationwide, stratified, multi-stage probability survey conducted by the Centers for Disease Control and Prevention (CDC) and designed to be representative of the civilian non-institutionalized U.S. population. Each cycle consists of questionnaires administered in the home of the participants, followed by an examination performed in a designated room at a mobile examination centre (MEC). Detailed information regarding the survey, its contents, and sampling methods are provided elsewhere (Dye et al., 2019). All NHANES cycles were ethically approved by the CDC's National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB), and all survey participants gave written informed consents.

2.2 | Physical activity assessment

All survey participants aged 2 years or more were eligible for the physical activity assessment, which was based on self-reported answers to the World Health Organization-validated "Global Physical Activity Questionnaire" (GPAQ) (National Health and Nutrition Examination Survey, 2009-2010; 2011-2012; 2013-2014; Armstrong & Bull, 2006). The GPAQ had previously shown moderate reliability (x 0.67- 0.73) and correlation with the International Physical Activity Questionnaire (IPAQ) (x 0.45-0.65) (Bull et al., 2009). Briefly, participants were asked to report the frequency and duration of moderate and vigorous physical activity during a typical week, discriminating between LTPA and OPA (Hallman et al., 2017; Holtermann et al., 2021). The specific GPAQ questions used to assess LTPA and OPA are reported in the Appendix. The total weekly LTPA and OPA (in minutes) were calculated as the amount of moderate-intensity activity in a week (in minutes) plus twice the reported weekly amount of vigorous-intensity activity (in minutes; Wiebe et al., 2018). Participants were then categorized, separately for LTPA and OPA, as being inactive (no, moderate, or vigorous activity), insufficiently active (<150 min/week), sufficiently active (150-300 min/week), or highly active (>300 min/week), according to the current guidelines (U.S. Department of Health and Human Services, 2018; Wiebe et al., 2018).

For analytical purposes, only subjects aged at least 30 years were considered (because of the availability of a periodontal examination

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Mediators

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level of significance at 5%.

WILEY while educational level and family poverty level (FPL) were considered as additional a priori confounders for OPA. Putative confounders included educational level and FPL (only for LTPA), ethnicity, marital status, alcohol intake, sleep duration, and frequency of self-performed inter-proximal hygiene. The assessment methods of confounders, their category boundaries, and evidence supporting their possible role are reported in the Appendix and in Figure 1. Potential mediators comprised biomarkers of systemic inflammation (platelet and white blood cells [WBC] counts), body mass index (BMI), diabetes, and hypertension. Assessment methods of the mediators, their category boundaries, and the evidence supporting their possible role are reported in the Appendix and in Figure 2. Statistical analyses All statistical analyses were performed using an ad hoc statistical software (STATA BE, version 17.1, StataCorp LP, TX, USA), setting the

Continuous variables were expressed as mean (linearized standard error, SE), while categorical variables were presented as proportions (SE). Prevalence (SE) values of periodontitis/severe periodontitis according to the different combinations of LTPA and OPA were plotted; simple and multiple logistic regression models were then built to

result), and the four categories of physical activity were merged to consider participants as either performing high (highly/sufficiently active) or low (insufficiently active/inactive) LTPA and OPA.

2.3 Periodontitis assessment

All survey participants aged at least 30 years, presenting at least one tooth (excluding third molars) and not meeting any of the health exclusion criteria (Dye et al., 2014) were eligible for a full-mouth periodontal examination, which was performed by trained dental hygienists (cycle 2009-2010) and general dentists (cycles 2011-2012 and 2013-2014) using a colour-coded periodontal probe (PCP2, HuFriedy). Gingival recession and probing pocket depth were measured at six sites per tooth (excluding third molars) and the clinical attachment level was then calculated. The periodontal examiners were trained and calibrated before the surveys and then periodically 2-3 times a year. Further details on the periodontal examination are reported elsewhere (Dve et al., 2019).

Only participants with a complete periodontal examination were considered for the present study. Periodontitis was identified applying the AAP/CDC criteria, categorizing its severity as mild, moderate, or severe (Eke et al., 2012).

2.4 Confounders

Based on external knowledge, age, gender, and smoking (pack-year) were considered as a priori confounders for both LTPA and OPA,

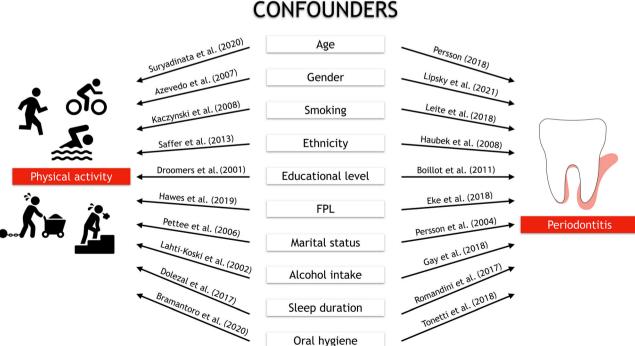


FIGURE 1 Evidence supporting the role of the selected putative confounders. FPL, family poverty level.

MEDIATORS

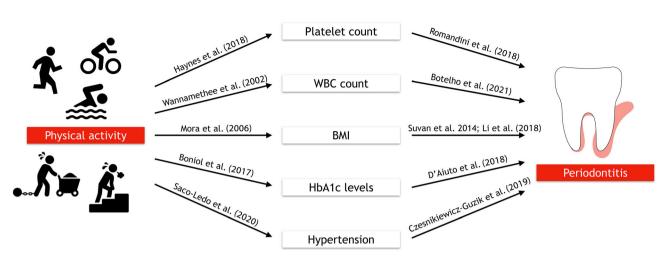


FIGURE 2 Evidence supporting the role of the selected putative mediators. CVD, cardiovascular disease; HbA1c, glycated haemoglobin; WBC, white blood cells count.

separately evaluate the crude and adjusted estimates of association between the levels of LTPA/OPA (as well as their combinations) and periodontitis/severe periodontitis. For the multiple analyses, age, gender, and smoking (as well as educational level and FPL for models involving OPA) were considered as a priori confounders, while the potential role of all the putative confounders was separately tested using the change-in-estimate strategy (Maldonado & Greenland, 1993). Only variables showing a change of 10% or more, compared to the model adjusted only for the a priori confounders, were retained in the final model (Appendix). Results from logistic regression models are expressed as odds ratios (ORs) with 95% confidence intervals (Cls).

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Moreover, age (<60 or \geq 60 years), gender (male, female), and smoking status (non-smokers, smokers) were considered as a priori effect modifiers; accordingly, the results from the respective subgroup analyses are reported.

Furthermore, a mediation analysis was performed by calculating the percentage (%) of excess odds explained (K. Han et al., 2016; Romandini et al., 2017).

Finally, to explore the possible presence of a dose-response relationship, sensitivity analyses were performed using the four different frequencies of LTPA and OPA as exposure (highly/sufficiently/insufficiently active and inactive).

3 | RESULTS

The sampling strategy led to the selection of 30,468 subjects; of them, 10,679 participants had a complete periodontal examination as well as LTPA/OPA data, and they were then included, representing a weighted population of approximately 431.1 million civilian non-institutionalized U.S. adults aged 30 years or more.

3.1 | Descriptive statistics

Table 1 shows the descriptive statistics of the study sample, while Table S1 reports the missing data. The weighted mean age was 50.8 (SE = 0.24) years; most of the participants were females (weighted 51.1%) and non-smokers (weighted 82.7%). The weighted prevalence of periodontitis and severe periodontitis was 42.3% and 7.8%, respectively.

With regard to LTPA, the largest proportion of participants were inactive (weighted 46.3%), while the remaining ones were categorized as insufficiently active (17.3%), sufficiently active (14.9%), or highly active (21.4%).

With regard to OPA, although most of the participants were also inactive (weighted 58.5%), a relevant proportion of the study population was considered as highly active (weighted 26.8%); only a minority of the included subjects was finally considered as either sufficiently or insufficiently active (weighted 6.8% and 7.7%, respectively).

3.2 | LTPA/OPA and periodontitis

Simple and multiple logistic regression analyses for the association between LTPA/OPA and periodontitis are reported in Table 2, while the confounder selection is reported in Table S2.

Multiple logistic regression analyses indicated a statistically significant association between high LTPA and lower odds of suffering from periodontitis (OR = 0.81), with similar estimates observed in subgroup analyses by age, gender, and smoking.

Conversely, high OPA was associated with higher adjusted odds of periodontitis (OR = 1.16); an effect modification by smoking, but not by age and gender, was, however, observed, with stronger estimates in current smokers (OR = 1.59).

TABLE 1 Characteristics of the study population



Characteristics	Ν	Weighted N in millions	Overall	No periodontitis ^a	Periodontitis
Age (years), mean (SE)	10,679	431.1	50.8 (0.25)	48.1 (0.28)	54.6 (0.34)
Gender, % (SE)					
Male	5264	210.5	48.9 (0.01)	24.3 (0.01)	24.6 (0.01)
Female	5415	220.6	51.1 (0.01)	33.5 (0.01)	17.7 (0.01)
Smoking, % (SE)					
Non-smokers	8672	356.3	82.7 (0.003)	51.2 (0.01)	31.4 (0.01)
Smokers	2002	74.7	17.3 (0.001)	6.5 (0.003)	10.9 (0.005
Pack-year smoking, mean (SE)	10,645	430.4	3.3 (0.15)	1.6 (0.11)	5.8 (0.26)
Ethnicity, % (SE)					
Non-Hispanic Black	2213	45.9	10.7 (0.01)	4.6 (0.004)	6.0 (0.01)
Non-Hispanic White	4580	295.0	68.4 (0.02)	43.1 (0.02)	25.3 (0.01)
Mexican	1518	34.8	8.1 (0.01)	3.3 (0.004)	4.8 (0.01)
Other	2368	55.3	12.8 (0.01)	6.8 (0.005)	6.1 (0.01)
Educational level, % (SE)					
Less than high school	2496	66.1	15.3 (0.01)	5.4 (0.004)	9.9 (0.01)
High school graduate	2298	89.7	20.8 (0.01)	9.9 (0.005)	10.9 (0.01)
College degree or more	5872	275.0	63.8 (0.01)	42.5 (0.02)	21.4 (0.01)
Family poverty level, % (SE)					
<100	1889	48.2	11.2 (0.01)	4.7 (0.003)	7.2 (0.01)
100-199	2497	76.6	17.8 (0.01)	8.8 (0.005)	10.2 (0.01)
200-399	2567	115.8	26.9 (0.01)	15.9 (0.01)	12.9 (0.01)
≥400	2831	161.9	37.6 (0.01)	28.7 (0.01)	11.5 (0.01)
Marital status, % (SE)					
Married	6226	273.0	63.3 (0.01)	39.4 (0.01)	23.9 (0.01)
Widowed	766	22.9	5.3 (0.002)	2.2 (0.002)	3.1 (0.002
Divorced	1352	53.4	12.4 (0.004)	6.5 (0.003)	5.9 (0.004
Separated	412	11.1	2.6 (0.002)	1.0 (0.001)	1.6 (0.002
Never married	1224	44.3	10.3 (0.005)	5.7 (0.004)	4.6 (0.003
Living with a partner	696	26.3	6.1 (0.004)	2.9 (0.003)	3.1 (0.003
Alcohol intake, % (SE)			(י,		(
Below suggested intake	5660	226.3	56.1 (0.01)	58.0 (0.01)	53.4 (0.01)
Above suggested intake	4194	177.4	43.9 (0.01)	42.0 (0.01)	46.6 (0.01)
Sleep duration, % (SE)				,	
<7 h	4239	154.9	35.4 (0.01)	19.3 (0.01)	16.7 (0.01)
7-8 h	2901	131.4	30.5 (0.01)	19.0 (0.01)	11.5 (0.005
>8 h	3527	144.3	33.5 (0.01)	19.4 (0.01)	14.1 (0.007
Frequency of self-performed inter-proxima			0010 (0101)	1777 (0101)	1 112 (01007
0 days/week	3393	119.6	27.7 (0.01)	13.0 (0.005)	14.7 (0.01)
1-6 days/week	3735	169.7	39.4 (0.01)	25.3 (0.01)	14.1 (0.01)
7 days/week	3551	141.9	32.9 (0.01)	19.5 (0.01)	13.4 (0.01)
Platelet count (1000 cells/μl), mean (SE)	10,315	420.1	237.2 (0.97)	238.0 (0.99)	235.9 (1.55)
WBC count (1000 cells/μl), mean (SE)	10,315	420.1	7.1 (0.04)	6.9 (0.04)	7.3 (0.05)
BMI (kg/m ²), mean (SE)	10,318	429.2	29.2 (0.11)	28.9 (0.13)	29.5 (0.05)
Diabetes, % (SE)	10,010	727.2	27.2 (0.11)	20.7 (0.13)	27.3 (0.13)
Yes	1834	56.2	13.0 (0.004)	5.2 (0.003)	7.8 (0.01)
	1034	JU.2	13.0 (0.004)	5.2 (0.003)	7.8 (0.01) (Contin

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TABLE 1 (Continued)

Characteristics	N	Weighted N in millions	Overall	No periodontitis ^a	Periodontitis ^b
Hypertension, % (SE)					
Borderline hypertension	4249	171.1	39.7 (0.01)	23.9 (0.01)	19.9 (0.01)
Yes	1155	38.1	8.8 (0.003)	3.9 (0.003)	5.8 (0.004)
LTPA, % (SE)					
Highly active	1987	92.4	21.4 (0.01)	14.6 (0.01)	6.9 (0.004)
Sufficiently active	1427	64.2	14.9 (0.01)	9.4 (0.01)	5.5 (0.004)
Insufficiently active	1731	74.4	17.3 (0.01)	10.8 (0.01)	6.5 (0.004)
Inactive	5529	199.9	46.3 (0.01)	22.9 (0.01)	23.4 (0.009)
OPA, % (SE)					
Highly active	2722	115.5	26.8 (0.01)	34.9 (0.01)	23.7 (0.01)
Sufficiently active	630	29.3	6.8 (0.001)	4.7 (0.003)	3.0 (0.002)
Insufficiently active	750	33.3	7.7 (0.002)	3.9 (0.003)	2.8 (0.002)
Inactive	6561	252.1	58.5 (0.01)	14.2 (0.005)	12.6 (0.01)
Combination of LTPA and OPA, % (SE)					
High LTPA/low OPA	2182	97.7	22.7 (0.01)	15.5 (0.01)	7.2 (0.004)
High LTPA/high OPA	1229	58.9	13.7 (0.01)	8.5 (0.004)	5.2 (0.004)
Low LTPA/low OPA	5126	187.7	43.5 (0.01)	24.1 (0.01)	19.5 (0.01)
Low LTPA/high OPA	2122	85.9	19.9 (0.01)	9.7 (0.004)	10.3 (0.01)

Abbreviations: BMI, body mass index; LTPA, leisure-time physical activity; (m²); OPA, occupational physical activity; SE, standard error; WBC, white blood cell count.

^aNo periodontitis: N = 5210; weighted N in millions = 249.1.

^bPeriodontitis: N = 5469; weighted N in millions = 182.1.

Sensitivity analyses employing the four different frequencies of physical activity as exposure indicated an inverse dose-response relationship between the amount of LTPA and the odds of periodontitis (Tables S3 and S4).

3.3 | LTPA/OPA and severe periodontitis

Results of simple and multiple logistic regression analyses for the association between LTPA/OPA and severe periodontitis are reported in Table 3; confounder selection is reported in Table S5.

As with periodontitis, high LTPA was found to be a protective indicator for severe periodontitis in the adjusted models (OR = 0.72), while high OPA was a risk indicator (OR = 1.29). These results were consistent in all subgroup analyses, except for smoking: indeed, a stronger estimate of the association between OPA and severe periodontitis was present in current smokers (OR = 1.69).

The same dose-response relationship observed between the amount of LTPA and the odds of periodontitis was also found in the sensitivity analyses for severe periodontitis (Tables S6 and S7).

3.4 | Combination of LTPA and OPA

The weighted prevalence of periodontitis and severe periodontitis in subjects performing high LTPA/low OPA was 31.8% and 4.7%, respectively; these proportions doubled in low LTPA/high OPA participants (51.6% and 12.4%, respectively; Figure 3).

Multiple regression models indicated how the odds of both periodontitis (Table 2) and severe periodontitis (Table 3) gradually increased when shifting from the reference group (high LTPA/low OPA) to the high LTPA/high OPA (OR = 1.10 and OR = 1.13, respectively) and the low LTPA/low OPA groups (OR = 1.35 and OR = 1.15, respectively), reaching their peak for the subjects performing low LTPA/high OPA (OR = 1.47 and OR = 1.66, respectively).

3.5 | Mediation analysis

Table 4 shows a series of ORs after further adjusting the final models for the putative mediators.

The association between high LTPA and periodontitis was partially mediated by biomarkers of systemic inflammation (platelet count and WBC), BMI, and diabetes. Their presence in the final model attenuated the estimate of association by 21.1%. With regard to severe periodontitis, in addition to the same variables, also hypertension showed a mediator effect (10.7%).

Conversely, the magnitude of the association between high OPA and periodontitis/severe periodontitis was not attenuated by any of the putative mediators considered.

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		Age		Gender		Smoking	
	Overall	<60 years	≥60 years	Males	Females	Non-Smokers	Smokers
LTPA							
High LTPA (vs. low LTPA)							
Crude	0.58 (0.52-0.65)***	0.57 (0.50-0.65)*	0.68 (0.54–0.85)	0.52 (0.45-0.60)*	0.57 (0.50-0.66)	0.61 (0.55–0.69)*	0.62 (0.47–0.88)**
Adjusted ^b	0.81 (0.72–0.92)**	0.81 (0.70-0.93)**	0.70 (0.55-0.88)**	0.78 (0.65-0.93)**	0.85 (0.73-1.02)	0.83 (0.72-0.94)**	0.77 (0.54–1.09)
OPA							
High OPA (vs. low OPA)							
Crude	1.26 (1.15–1.37)**	1.49 (1.33-1.68)**	1.03 (0.77-1.38)	1.18 (1.05-1.32)**	1.09 (0.95-1.27)	1.11 (0.99-1.25)	1.52 (1.19–1.94)*
Adjusted ^b	1.16 (1.04-1.30)***	1.15 (1.00-1.32)*	1.12 (0.80-1.57)	1.14 (0.98-1.32)	1.19 (1.01–1.39)*	1.08 (0.96-1.22)	1.59 (1.22-2.07)**
Combination of LTPA and OPA	PPA						
High LTPA/low OPA	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High LTPA/high OPA							
Crude	1.29 (1.07–1.57)*	1.54 (1.18–1.99)**	0.94 (0.56–1.56)	1.35 (1.05-1.72)*	1.06 (0.82-1.35)	1.65 (1.01-2.71)*	1.15 (0.93-1.40)
Adjusted ^b	1.10 (0.90-1.34)	1.26 (0.97–1.62)	0.90 (0.51–1.57)	1.25 (0.97, 1.61)	1.10 (0.86–1.42)	1.03 (0.83-1.28)	1.43 (0.80–2.55)
Low LTPA/low OPA							
Crude	1.74 (1.52–1.98)**	1.79 (1.5–2.10)**	1.39 (1.05–1.83)*	2.10 (1.78-2.48)**	1.69 (1.4-2.03)**	1.68 (1.09-2.59)*	1.63 (1.41–1.88)*
Adjusted ^b	1.35 (1.15–1.68)*	1.76 (1.48-2.09)**	1.44 (1.08-1.92)*	1.53 (1.35–1.87)*	1.46 (1.20-1.77)*	1.60 (1.33-1.86)*	1.19 (0.71–2.00)
Low LTPA/high OPA							
Crude	2.28 (1.96–2.66)**	2.76 (2.27–3.35)**	1.65 (1.15-2.37)*	2.29 (1.93–2.73)***	2.08 (1.67–2.59)**	2.64 (1.59-4.37)**	1.88 (1.59–2.23)**
Adjusted ^b	1.47 (1.26–1.72)***	1.48 (1.22-1.80)***	1.40 (0.93–2.12)	1.47 (1.19–1.82)**	1.46 (1.1–1.86)**	2.34 (1.13-4.58)**	2.04 (1.15–3.62)*

Abbreviations: CI, confidence Interval; LTPA, leisure-time physical activity; OPA, occupational physical activity; OR, odds ratio.

^aVersus no periodontitis.

^bModel adjusted for age, gender, pack-year smoking (as well as educational level and FPL for models involving OPA), and additional confounders identified with the change-in-estimate strategy (reported in Table S2).

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

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TABLE 3 Si

Severe periodontitis - UK (75% L)	0% CI)						
		Age		Gender		Smoking	
	Overall	Age <60	Age ≥60	Males	Females	Non-smokers	Smokers
LTPA							
High LTPA (vs. low LTPA)							
Crude	0.53 (0.43-0.65)**	0.48 (0.36–0.64)**	0.68 (0.49-0.93)*	0.49 (0.39–0.69)*	0.45 (0.3–0.65)**	0.63 (0.43-0.93)*	0.57 (0.44-0.73)**
Adjusted ^b	0.72 (0.58-0.90)**	0.68 (0.52-0.91)*	0.83 (0.59–1.15)	0.72 (0.55-0.93)**	0.70 (0.47–1.04)	0.75 (0.57, 0.97)*	0.75 (0.49–1.12)
OPA							
High OPA (vs. low OPA)							
Crude	1.49 (1.31-1.71)*	1.66 (1.39–1.99)**	1.31 (0.91-1.88)	1.28 (1.04-1.56)*	1.34 (0.99–1.80)	1.27 (1.08-1.51)*	1.52 (1.12-2.06)*
Adjusted ^b	1.29 (1.09-1.53)**	1.20 (1.00-1.47)*	1.25 (0.85–1.85)	1.26 (0.97–1.62)	1.41 (1.03-1.94)*	1.10 (0.89–1.35)	1.69 (1.19–2.38)**
Combination of LTPA and OPA	PA						
High LTPA/low OPA	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High LTPA/high OPA							
Crude	1.29 (0.94-1.77)	1.47 (1.01–2.13)*	1.05 (0.54–2.06)	1.49 (0.99–2.26)	0.41 (0.21-0.78)*	1.86 (0.92-3.73)	0.95 (0.65–1.39)
Adjusted ^a	1.13 (0.81–1.57)	0.87 (0.57–1.33)	1.14 (0.49–2.65)	1.18 (0.73-1.91)	0.44 (0.23-0.83)*	1.62 (0.76-3.43)	0.72 (0.47–1.46)
Low LTPA/low OPA							
Crude	1.74 (1.35-2.24)**	1.91 (1.39–2.64)**	1.35 (0.91–1.99)	2.23 (1.61–3.09)**	1.48 (0.97–2.25)	1.85 (1.13-3.03)**	1.50 (1.10-2.04)**
Adjusted ^b	1.15 (0.88-1.50)	1.12 (0.79–1.62)	1.09 (0.70-1.71)	1.28 (1.00-1.82)*	0.92 (0.56–1.45)	1.13 (0.81–1.58)	1.30 (0.74-2.28)
Low LTPA/high OPA							
Crude	2.90 (2.28–3.69)***	3.45 (2.48-4.80)**	2.07 (1.26-3.39)**	2.71 (1.99–3.71)**	2.80 (1.74-4.50)**	2.82 (1.61–4.94)**	2.26 (1.68-3.06)**
Adjusted ^b	1.66 (1.29–2.15)***	1.73 (1.19–2.51)***	1.57 (0.83-2.98)	1.67 (1.14–2.44)**	1.77 (1.05, 2.98)*	1.43 (1.03-1.99)**	2.29 (1.22-4.29)*
Note: Significant estimates are indicated in bold font. Abbendiatione: CL confidence interval: LTDA Jointee time abusical activity:	indicated in bold font.		OB odde ratio: ODA occupational physical activity	l abveical activity			

Abbreviations: CI, confidence interval; LTPA, leisure-time physical activity; OR, odds ratio; OPA, occupational physical activity.

^aVersus no/mild/moderate periodontitis.

^bModel adjusted for age, gender, pack-year smoking (as well as educational level and FPL for models involving OPA), and additional confounders identified with the change-in-estimate strategy (reported in Table S5).

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

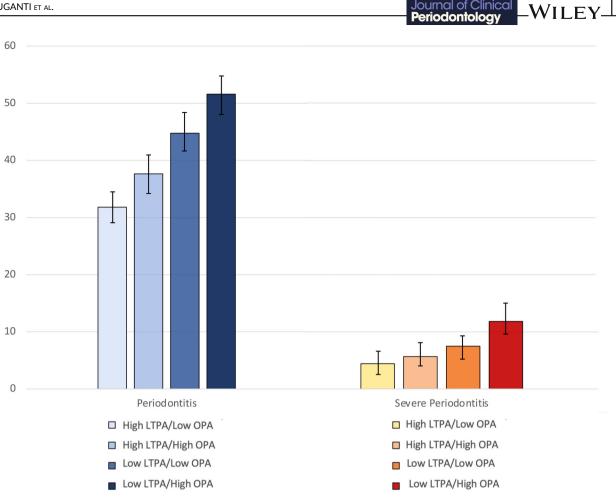


FIGURE 3 Weighted prevalence of periodontitis and severe periodontitis with 95% confidence intervals in subjects performing different combinations of recreational and occupational physical activity. LTPA, leisure-time physical activity; OPA, occupational physical activity.

4 DISCUSSION

The findings from the present population-based study indicate that LTPA represents a protective indicator, while OPA represents a risk indicator, of both periodontitis and severe periodontitis. The association of LTPA with periodontitis/severe periodontitis showed a doseresponse relationship, while the association of OPA with periodontitis/ severe periodontitis was more pronounced in current smokers. Moreover, the associations of LTPA and OPA with periodontitis/severe periodontitis were cumulative, with the highest odds observed in subjects performing both low LTPA and high OPA. Mediation analyses suggested that the association between LTPA and periodontitis/severe periodontitis may be partially mediated by biomarkers of systemic inflammation, BMI, and comorbidities (i.e. diabetes and hypertension).

Previous epidemiological studies had reported an association between high levels of physical activity and periodontitis (Al-Zahrani et al., 2005; Bawadi et al., 2011; S.J. Han et al., 2019). Specifically, a cross-sectional study, also using NHANES data but employing a partial periodontal examination protocol (NHANES III), noted that subjects with normal weight, regular levels of bodily movement, and a better diet quality were 40% less likely to have periodontitis compared to individuals presenting none of these healthy lifestyles (Al-Zahrani et al., 2005). However, other studies have failed to report a significant association between physical activity and periodontitis (Sakki et al., 1995; Sanders et al., 2009). These conflicting results may be explained as due to the use of different case definitions of periodontitis and by the lack of a clear distinction in the quality of the exposure, since previous studies did not differentiate between LTPA and OPA. Notably, the present study showed an inverse tendency of association when LTPA and OPA were analysed separately, with the highest odds for periodontitis found in subjects performing low LTPA and high OPA. This "physical activity paradox" has already been described for the incidence of major cardiovascular events (Holtermann et al., 2021), and therefore it may also hold for periodontitis.

The mechanisms explaining the association between physical activity and NCDs, including periodontitis, are still not clearly understood; however, the modulation of LGSI is regarded as one of the main potential pathways involved (Gleeson et al., 2011). Indeed, high LTPA had been previously found to be associated with a reduction in the levels of both systemic and local (i.e., within the gingival crevicular fluid) inflammatory biomarkers (Kasapis & Thompson, 2005; Sanders et al., 2009; Rombaldi et al., 2015). The results from the present study further underline a possible relevance

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TABLE 4 Mediation analysis for the association between LTPA/OPA and both periodontitis and severe periodontitis

	High LTPA		High OPA	
	OR (95% CI)	% excess odds explained ^a	OR (95% CI)	% excess odds explained ^a
Periodontitis				
Base model (B)	0.81 (0.72-0.92)	-	1.16 (1.04–1.30)	-
B + platelet count	0.82 (0.73-0.93)	5.3%	1.17 (1.04–1.32)	0.0%
B + WBC count	0.83 (0.74-0.94)	10.5%	1.18 (1.05–1.32)	0.0%
B + BMI	0.83 (0.74-0.94)	10.5%	1.16 (1.04–1.30)	0.0%
B + diabetes	0.83 (0.74-0.93)	10.5%	1.18 (1.05–1.32)	0.0%
B + hypertension	0.81 (0.70-0.93)	0.0%	1.17 (1.04–1.31)	0.0%
$B + platelet\ count + WBC\ count$	0.83 (0.74-0.94)	10.5%	1.18 (1.05–1.32)	0.0%
B + BMI + diabetes	0.85 (0.75-0.95)	21.1%	1.18 (1.05–1.32)	0.0%
$B + platelet\ count + WBC\ count + BMI + diabetes$	0.85 (0.76-0.96)	21.1%	1.19 (1.06–1.34)	0.0%
Severe periodontitis				
Base model (B)	0.72 (0.58-0.90)	-	1.29 (1.09-1.53)	-
B + platelet count	0.73 (0.58-0.91)	3.6%	1.31 (1.10–1.56)	0.0%
B + WBC count	0.74 (0.59–0.93)	7.1%	1.32 (1.11–1.57)	0.0%
B + BMI	0.73 (0.58-0.91)	3.6%	1.29 (1.09–1.53)	0.0%
B + diabetes	0.73 (0.58-0.91)	3.6%	1.31 (1.10–1.56)	0.0%
B + hypertension	0.75 (0.61-0.92)	10.7%	1.32 (1.09–1.59)	0.0%
$B + platelet\ count + WBC\ count$	0.74 (0.59–0.93)	7.1%	1.32 (1.11-1.57)	0.0%
B + BMI + diabetes + hypertension	0.75 (0.61–0.93)	10.7%	1.33 (1.10-1.60)	0.0%
B + platelet count + WBC count + BMI + diabetes + hypertension	0.76 (0.62–0.95)	14.3%	1.35 (1.12-1.64)	0.0%

Note: The base model (B) corresponds to the adjusted model reported in Table 2. Different potential mediators have been added separately to the base model.

Abbreviations: BMI, body mass index; CI, confidence interval; LTPA, leisure-time physical activity; OR, odds ratio; OPA, occupational physical activity; WBC; white blood cell count.

^aNegative values were considered as 0.00% excess odds explained.

of the systemic metabolic/inflammatory axis, since platelet count, WBC, BMI, and diabetes partially attenuated the observed estimates of the association between LTPA and periodontitis within the mediation analyses.

On the other hand, a high occupational workload may contribute to physical deterioration, leading to chronic stimulation of the hypothalamicpituitary-adrenal axis and resulting in the release of high levels of cortisol, pro-inflammatory cytokines, and oxidative stress markers (Tatzber et al., 2022). These blueprints of LGSI have been significantly associated with the incidence and progression of periodontitis (D'Aiuto et al., 2004; Baima et al., 2022). However, OPA is also related to heavy physical labour, which, in turn, is associated with socioeconomic disadvantage, a well-established risk indicator for periodontitis and other NCDs (Borrell et al., 2006). Although the current analyses involving OPA as exposure were adjusted for socioeconomic status, relevant details about specific job type and duration were not available in NHANES, and hence they could not be considered as additional confounders. The present study, therefore, cannot exclude the possibility that the identification of OPA as a risk indicator for periodontitis is spurious.

The results from this study should be regarded with caution due the above-mentioned risk of residual confounding and due to its crosssectional design, which prevents the evaluation of causality and limits the value of the reported mediation analyses. Moreover, a risk of information bias cannot be ruled out because of the self-reported assessment of physical activity and of the use of PCP2 probes for the periodontal examination. Finally, despite the statistical significance, the lower limit of some OPA-related 95% Cls was only marginally higher than 1.0, so such associations (if present) may potentially be of limited clinical relevance. Nonetheless, the present study has the novelty of having differentiated between LTPA and OPA, and the divergent directions of association found with periodontitis may explain the previously reported conflicting results. Moreover, the use of data from a complete periodontal examination protocol minimized the risk of information bias. Finally, the employed sampling procedures allow the generalizability of the present findings to the whole non-institutionalized U.S. population.

5 | CONCLUSIONS

Leisure-time and occupational physical activity showed divergent associations with periodontitis. Both dose-response and cumulative-

type associations were identified, while systemic inflammation, BMI, and co-morbidities may partially explain these relationships. Longitudinal cohort studies are needed to rule out the risk of residual confounding and to verify the temporality of these associations. Furthermore, randomized clinical trials should be carried out to investigate the potential impact of physical activity counselling both on primary prevention of periodontitis and as part of the Step 1 of periodontal therapy.

AUTHOR CONTRIBUTIONS

Crystal Marruganti contributed to the study design, data analysis and interpretation, and manuscript drafting. Giacomo Baima contributed to data interpretation and manuscript drafting. Simone Grandini, Mario Aimetti, Filippo Graziani, and Mariano Sanz contributed to data interpretation and critically revised the manuscript. Mario Romandini contributed to study conception and design, data analysis and interpretation, and manuscript drafting. All the authors gave their final approval of the version to be published and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available at: https://www.cdc.gov/nchs/nhanes/index.htm.

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