# Investigating the Influence of Periodontal Disease on the Association Between Complex Multimorbidity and Health: A Cross-Sectional Study 

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Aims and Objectives: The aim of this study was to evaluate whether periodontal disease (PD) moderates the association between complex multimorbidity (MM) and fair/poor general health in a US representative sample of older individuals. Materials and Methods: This study identified 937 participants who were at least 60 years of age from the 2013-2014 National Health and Nutrition Examination Survey. A multivariable logistic regression model was used to estimate the association between complex MM (including chronic conditions, functional limitations, and geriatric syndromes) and self-reported fair/poor general health. Subsequently, we specified interactions between complex MM and PD to determine whether PD moderates the effect of complex MM on fair/poor general health. Results: Nineteen percent of participants reported fair/poor general health. Complex MM was associated with 2.2 times greater odds of self-reported fair/poor health. However, PD was neither independently associated with fair/ poor health nor an effect modifier for the association between complex MM and fair/poor general health. Age, white race, those with at least a high-school education level, a family income-to-poverty ratio of at least 2, former smoking status, and being married were significantly associated with fair/poor general health. Conclusion: Complex MM, but not PD, was associated with greater odds to report fair/poor general health, and PD did not moderate the association between complex MM and fair/poor general health. People with complex MM are more likely to have worse general health; however, PD did not strengthen this association. Further studies are needed to evaluate whether treatment for PD for people vulnerable to the development of complex MM has a positive effect on their general health.

Keywords: Activities of daily living, aged, health status, multimorbidity, NHANES, periodontal disease

## Introduction

$\eta \mathrm{n}$ US middle-aged and older adults, complex L multimorbidity (MM)-the co-occurrence of chronic conditions, functional limitations, and geriatric syndromes-has beenshown to beassociated with several adverse health outcomes, ${ }^{[1-3]}$ including self-reported fair/poor health. ${ }^{[4]}$ In the context of periodontal disease (PD), and among participants with complex MM of a nationally representative sample of NHANES, we

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showed that combinations of sociodemographic factors and functional limitation are associated with PD. ${ }^{[5]}$ Furthermore, given the multifactorial inflammatory

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[^0]nature of PD, ${ }^{[6]}$ this condition has been associated with several chronic conditions. ${ }^{[7-9]}$ For instance, biomarkers like transforming growth factor-Beta 1 (TGF-1) and vascular endothelial growth factor (VEGF) have been identified as they have an early role in assessing the risk for periodontitis and rheumatic disease. ${ }^{[10]}$ In addition, severe periodontitis, tooth loss, and cardiovascular disease all resulted in an increase in the number of circulating endothelial progenitor cells. ${ }^{[11]}$ Therefore, due to competing priorities in their care, individuals with PD who may have functional limitations and or geriatric syndromes are less likely to attend to their oral care regularly and less likely to adhere to regular periodontal maintenance visits.
Despite the known association between complex MM and general health, ${ }^{[4]}$ and the potentially widespread effects of the inflammatory process of PD, little is known about the conjoint effects of the co-occurrence of PD and complex MM on general health. We hypothesize that PD moderates the association between complex MM and self-reported fair/poor general health. Identifying people who have complex MM and PD will make monitoring their periodontal health easier as they are more likely to be concerned about their overall well-being.
Therefore, the aim of this study was to evaluate whether the association between complex MM and fair/poor general health is moderated by PD in a US representative sample of older individuals.

## Materials and Methods

This study examined data from the 2013-2014 National Health and Nutritional Examination Survey (NHANES), the most recent years for which NHANES collected data on oral health. The NHANES is a reliable and comprehensive source of information as it uses a complex, multistage probability design to sample the population of the 50 states and DC. This helps to reduce any potential sources of bias, making the findings more reliable. Thus, a nationally representative sample of adults 60 years of age or older participants was analyzed in this study $(n=937)$ in 2021. Based on our previous study, ${ }^{[5]}$ we calculated the minimum sample size for multivariate logistic regression to be at least 900 subjects with a power of $80 \%$ and a significance level of 0.05 . In addition, we limited our analysis to older adults because complex MM data are available only for individuals in older age groups. The NHANES 2013-2014 excluded edentulous individuals who lost their teeth since a periodontal examination could not be performed. The Case Western Reserve University Institutional Review Board approved this
study and determined to be exempted from human subjects research (\#2021-0469).
Our outcome of interest was self-reported fair/poor general health, indicating the state of their health condition (compared to excellent, very good, or good).
Our main independent variables were PD and complex MM. PD was categorized based on the clinical attachment loss (CAL) value (mild $\mathrm{PD}=1-2 \mathrm{~mm}$, moderate $\mathrm{PD}=3-4 \mathrm{~mm}$, and severe $\mathrm{PD}=\geq 5 \mathrm{~mm}) .{ }^{[12]}$ Conditions constituting complex MM included chronic conditions, functional limitations, and geriatric syndromes. ${ }^{[13]}$ Self-reported chronic conditions included hypertension, diabetes, arthritis, coronary heart disease, overweight, stroke, hyperlipidemia, asthma, COPD, emphysema, chronic bronchitis, cancer, liver condition, weak or failing kidneys, thyroid problems, and psoriasis. For functional limitations, we used selfreported data to assess participants' ability to perform activities of daily living (ADL), instrumental activities of daily living (IADL), leisure and social activities, lower-extremity mobility, and general physical activity activities. Geriatric syndromes were defined by conditions frequently seen among older participants, including depression (based on a Patient Health Questionnaire [PHQ-9] score of at least 10), cognitive impairment (a digital symbol substitution test score falling in the lowest quartile of the study population [33]), and self-reported data on urinary incontinence, visual impairment, hearing impairment, fracture, and osteoporosis.
Age was classified in five categories (60-64, 65-69, $70-74,75-79,>80$ ). Participant's sex included male and female. We grouped race/ethnicity into the following three categories: White, Black, and Other. Marital status was defined as married, divorced, and other. The ratio of family income to poverty included ( $<2,2-3.99,>4$ ). Years of Education were categorized into three groups (high school or below, some college or associate degree, college graduate or above). In addition, we accounted for smoking (Current, Former, None) insurance status (Medicare, Private Insurance, and others), alcohol use (Yes, No), vigorous recreational activities (Yes, No), and insurance coverage for dental procedures. Body mass index was dichotomized as nonobese $(<30)$ and obese ( $>30$ ).
We performed a descriptive analysis for all variables included in this study. We used a multivariable logistic regression model to evaluate the association between complex MM and fair/poor general health after adjusting for demographic and socioeconomic. In addition, we added an interaction term between PD
and complex MM to determine to what extent PD moderates the effect of complex MM on fair/poor general health. Moreover, we conducted stratified analysis by PD to determine whether PD modified the association between complex MM and fair/poor general health. Using the Mantel-Haenszel test, we also evaluated PD as a potential confounding variable by considering differences $>10 \%$ between the MantelHaenszel odds ratio and the crude odds ratio. R version 3.6.2. were used for all analyses.

## Results

Table 1 shows the population's characteristics of the present study. Approximately $19 \%$ of the study's participants had fair/poor general health. Among people with fair/poor general health, $65 \%$ presented with PD. A higher prevalence of fair/poor general health was among those who were younger than 75 years of age, without PD and with severe PD, those with a marital status other than married and divorced, without vigorous physical activity, those who were obese, and former and current smokers. Conversely, participants of the white race, with higher education level, higher family income to poverty ratio, nonsmoker, and those with private insurance had a low prevalence of fair/poor general health.
Findings from Table 2 show that the most common chronic conditions were hypertension (62.1\%), hyperlipidemia ( $59.4 \%$ ), arthritis ( $47.0 \%$ ), and being overweight ( $37.6 \%$ ). In addition, nearly one-third of study participants had urinary incontinence and about $14 \%$ had cognitive impairment. Limitations in general physical activities were the top condition among functional limitations variables ( $49.0 \%$ with limitations). The prevalence of fair/poor general health was generally low among individuals with chronic conditions except for stroke, liver, and kidney. Conversely, the prevalence of fair/poor general health among participants with limitations in ADL, IADL, and leisure and social activities exceeded $40 \%$. In addition, approximately $60 \%$ of people with depression had fair/poor general health.

We ran the multivariable logistic regression model with and without the interaction term between the presence of PD and complex MM in this study. We estimated the logistic regression model including interaction terms to assess whether the presence of PD moderated the effect of complex MM on fair/poor general health [Table 3]. Compared to individuals with no PD, those with PD had 0.59 odds of having fair/poor general health (adjusted odds ratio [AOR]: $0.59,95 \%$ confidence interval [0.32-1.07]). Participants with complex MM had 2.20 higher odds of having fair/poor general health
(AOR: 2.20, 95\% confidence interval [1.09-4.43]) than those without it. The interaction term between the presence of PD and complex MM was not significant (AOR: 1.41, $95 \%$ confidence interval [0.60-3.29]).
Given that the interaction term was not significant in our model, we further ran a logistic model without interaction term to independently evaluate the main effects of PD and complex MM on fair/poor general health [Table 4]. The main effect of PD on fair/poor general health was not significant ([AOR]: 0.69, 95\% confidence interval [0.45-1.07]). However, there was a statistically significant increased odds of having fair/ poor general health comparing those with complex MM to those without ([AOR]: 2.75, $95 \%$ confidence interval [1.79-4.21]). The slight changes in the results between the two models mean that PD was neither independently associated with fair/poor health nor an effect modifier for the association between complex MM and fair/poor general health.
Several demographic and behavioral variables were associated with fair/poor general health [Table 3]. The odds of having fair/poor general health were low among participants of the white race, among those with at least a high-school level of education, and had a higher family income to poverty ratio of at least 2 (AOR: $0.46,0.44,0.57,0.38$, and 0.67 , respectively). In addition, participants with an increase of 1 year of age were associated with lower odds of having fair/poor general health (AOR: 0.95, 95\% confidence interval [0.92-0.99]). Conversely, married participants and former smokers had higher odds of having fair/poor general health (AOR: 1.88 and 2.20 , respectively).
Given that the interaction term between the presence of PD and complex MM was not significant, we further conducted a stratified analysis to see whether there are differences in the point estimates of PD for the association between complex MM and fair/poor general health [Table 5]. The odds ratio of having fair/ poor general health among participants with conditions constituting complex MM, in the presence of PD, was $2.76,95 \%$ confidence interval [1.83, 4.16]. In the absence of PD, participants with complex MM had a $1.86,95 \%$ confidence interval $[1.05,3.32]$ higher odds of having fair/poor general health than those without it. Despite the fact that the two strata-specific odds ratios were different, both point estimates fall within the confidence interval of the other group indicating that PD was not significant as an effect modifier, which agrees with the interaction effect in the logistic model. Therefore, PD did not moderate the association between complex MM and fair/poor general health.

| Table 1: Characteristics of the study population |  |  |  |
| :---: | :---: | :---: | :---: |
| Demographic characteristics | Excellent/very good/good $\boldsymbol{N}$ (row \%) | Fair/poor $N$ (row \%) | Total N (column \%) |
| No. of subjects | 760 (81.1) | 177(18.9) | 937 (100) |
| Periodontal disease |  |  |  |
| None | 195 (75.9) | 62 (24.1) | 257 (27.4) |
| Mild | 105 (84.0) | 20 (16.0) | 125 (13.3) |
| Moderate | 336 (84.8) | 60 (15.2) | 396 (42.3) |
| Severe | 124 (78.0) | 35 (22.0) | 159 (17.0) |
| Age categories |  |  |  |
| (60-65) | 207 (78.7) | 56 (21.3) | 263 (28.1) |
| (65-70) | 195 (79.3) | 51 (20.7) | 246 (26.2) |
| (70-75) | 148 (77.5) | 43 (22.5) | 191 (20.4) |
| (75-80) | 91 (88.3) | 12 (11.7) | 103 (11.0) |
| (80-81) | 119 (88.8) | 15 (11.2) | 134 (14.3) |
| Sex |  |  |  |
| Male | 351 (81.3) | 81 (18.8) | 432 (46.1) |
| Female | 409 (81.0) | 96 (19.0) | 505 (53.9) |
| Race/ethnicity |  |  |  |
| Other | 167 (73.9) | 59 (26.1) | 226 (24.1) |
| Black | 140 (73.7) | 50 (26.3) | 190 (20.3) |
| White | 453 (86.9) | 68 (13.1) | 521 (55.6) |
| Marital status |  |  |  |
| Other | 186 (85.7) | 31 (14.3) | 217 (23.2) |
| Divorced | 121 (77.6) | 35 (22.4) | 156 (16.6) |
| Married | 453 (80.3) | 111 (19.7) | 564 (60.2) |
| Education |  |  |  |
| High-school graduate or below | 273 (77.0) | 106 (28.0) | 379 (40.4) |
| Some college or associates degree | 253 (86.3) | 40 (13.7) | 293 (31.3) |
| College graduate or above | 234 (88.3) | 31 (11.7) | 265 (28.3) |
| Ratio of family income to poverty |  |  |  |
| $(0,2)$ | 260 (72.2) | 100 (27.8) | 360 (38.4) |
| $(2,4)$ | 246 (87.5) | 35 (12.5) | 281 (30.0) |
| $(4,6)$ | 254 (85.8) | 42 (14.2) | 296 (31.6) |
| Smoking status |  |  |  |
| No | 402 (85.4) | 69 (14.6) | 471 (50.3) |
| Former | 276 (77.3) | 81 (22.7) | 357 (38.1) |
| Current | 82 (75.2) | 27 (24.8) | 109 (11.6) |
| Alcohol use |  |  |  |
| No | 219 (79.1) | 58 (20.9) | 277 (29.6) |
| Yes | 541 (82.0) | 119 (18.0) | 660 (70.4) |
| Body mass index |  |  |  |
| Nonobese < 30 | 514 (83.2) | 104 (16.8) | 618 (66.0) |
| Obese $\geq 30$ | 246 (77.1) | 73 (22.9) | 319 (34.0) |
| Vigorous exercise |  |  |  |
| Yes | 106 (88.3) | 14 (11.7) | 120 (12.8) |
| No | 654 (80.0) | 163 (20.0) | 817 (87.2) |
| Insurance |  |  |  |
| Other | 137 (76.1) | 43 (23.9) | 180 (19.2) |
| Medicare | 392 (81.0) | 92 (19.0) | 484 (51.7) |
| Private | 231 (84.6) | 42 (15.4) | 273 (29.1) |
| Insurance cover the dental procedure |  |  |  |
| No | 742 (81.6) | 167 (18.4) | 909 (97.0) |
| Yes | 18 (64.3) | * | 28 (3.0) |

*Cells with counts <11 were masked

We presented two logistic regression analyses for the association between complex MM and fair/poor general health in the presence and absence of PD,
respectively, adjusting for other covariate variables in Supplemental Material. Complex MM was associated with fair/poor general health, regardless of PD. In

| Table 2: Distribution of the study population by conditions constituting multimorbidity |  |  |  |
| :---: | :---: | :---: | :---: |
| Conditions constituting MM | Excellent/very good/good | Fair/poor | Total |
| No. of subjects | 760 | 177 | 937 |
| Chronic conditions |  |  |  |
| Hypertension | 456 (78.4) | 126 (21.6) | 582 |
| Hyperlipidemia | 453 (81.3) | 104 (18.7) | 557 |
| Diabetes | 166 (70.9) | 68 (29.1) | 234 |
| Arthritis | 347 (78.9) | 93 (21.1) | 440 |
| Coronary heart disease | 60 (71.4) | 24 (28.6) | 84 |
| Overweight | 281 (79.8) | 71 (20.2) | 352 |
| Stroke | 30 (63.8) | 17 (36.2) | 47 |
| Asthma | 97 (79.5) | 25 (20.5) | 122 |
| Chronic obstructive pulmonary disease | 37 (71.2) | 15 (28.8) | 52 |
| Emphysema | 15 (71.4) | * | 21 |
| Bronchitis | 44 (72.1) | 17 (27.9) | 61 |
| Cancer | 182 (84.3) | 34 (15.7) | 216 |
| Liver | 24 (66.7) | 12 (33.3) | 36 |
| Thyroid | 141 (81.5) | 32 (18.5) | 173 |
| Psoriasis | 22 (81.5) | * | 27 |
| Kidney | 18 (58.1) | 13 (41.9) | 31 |
| Functional limitations |  |  |  |
| Activities of daily living (ADL) | 51 (53.1) | 45 (46.9) | 96 |
| Instrumental activities of daily living (IADL) | 74 (56.5) | 57 (43.5) | 131 |
| Leisure and social activities (LSA) | 46 (54.1) | 39 (45.9) | 85 |
| Lower extremity mobility (LEM) | 145 (67.8) | 69 (32.2) | 214 |
| General physical activities (GPA) | 339 (73.9) | 120 (26.1) | 459 |
| Geriatric syndromes |  |  |  |
| Cognitive impairment | 89 (67.9) | 42 (32.1) | 131 |
| Hearing impairment | 68 (74.7) | 23 (25.3) | 91 |
| Visual impairment | 29 (65.9) | 15 (34.1) | 44 |
| Urinary incontinence | 241 (76.5) | 74 (23.5) | 315 |
| Depression | 22 (39.3) | 34 (60.7) | 56 |
| Osteoporosis | 104 (83.2) | 21 (16.8) | 125 |
| Fractures | 85 (86.7) | 13 (13.3) | 98 |

*Cells with counts $<11$ were masked
addition, we further ran two logistic models for the association between PD and fair poor/general health, in the presence and absence of complex MM, respectively, adjusting for other covariate variables. PD was not statistically associated with fair/poor general health, regardless of complex MM. However, the magnitude of the association between PD and fair/poor general health was higher in the presence of complex MM ( $\mathrm{OR}=1.08$ vs. 0.69 ), as shown in Tables $1 \mathrm{~S}-4 \mathrm{~S}$ in Supplementary Material.

## Discussion

Using NHANES data for a US representative sample of older adults, we evaluated whether the association between conditions constituting complex MM and fair/poor general health was stronger in the presence of PD. Complex MM was strongly associated with fair/poor general health; however, the relationship between complex MM and fair/poor general health did
not differ in the presence and absence of PD. Several sociodemographic and behavioral factors, including white race, higher level of education, higher family income to poverty ratio, and older age, were negatively associated with fair/poor general health. However, being married and former smoking status were positively associated with fair/poor general health.
The odds of self-reported fair/poor health were not statistically significantly associated with PD after adjusting for all other covariates. Sixty-five percent of the study's participants with fair/poor general health presented with PD. Since PD was identified as a long-life condition that needsperiodicclosemonitoring, ${ }^{[14]}$ itsurprised us not to find an association between PD and general health. Numerous studies have outlined some of the potential mechanisms that could account for the association between PD and several systemic diseases, including circulating endothelial progenitor cells and biomarkers like transforming growth factor-Beta 1 (TGF-1) and VEGF. ${ }^{[17,12,1,13]}$ Conversely,

Table 3: The adjusted odds ratios (confidence intervals) from our multivariate logistic regression analysis predicting fair/

|  | poor general health |  |  |  |
| :--- | :---: | :---: | :---: | :---: |
| Variables | Odds ratio | $2.5 \%$ | $97.5 \%$ | $P$ Value |
| Periodontal disease (PD) | 0.59 | 0.32 | 1.07 | 0.08 |
| Multimorbidity (MM) | 2.20 | 1.09 | 4.43 | 0.03 |
| Age | 0.95 | 0.92 | 0.99 | 0.03 |
| Gender female | 1.28 | 0.81 | 2.01 | 0.62 |
| Race Black | 0.93 | 0.53 | 0.79 |  |
| Race White | 0.46 | 0.28 | 0.00 |  |
| Marital divorced | 1.13 | 0.58 | 2.21 | 0.71 |
| Marital married | 1.88 | 1.08 | 3.27 | 0.03 |
| Education college or associates degree | 0.44 | 0.27 | 0.73 | 0.00 |
| Education college graduate | 0.57 | 0.32 | 1.01 | 0.05 |
| Ratio (2,4) | 0.38 | 0.64 | 0.00 |  |
| Ratio (4,6) | 0.67 | 0.38 | 1.18 | 0.17 |
| Smoking behavior former | 2.20 | 1.37 | 3.53 | 0.00 |
| Smoking behavior current | 1.56 | 0.81 | 3.02 | 0.18 |
| Alcohol use | 0.91 | 0.56 | 1.48 | 0.71 |
| BMI group obese | 1.00 | 0.64 | 0.55 | 0.99 |
| No vigorous exercise | 1.69 | 0.81 | 0.516 |  |
| Health insurance medicare | 1.20 | 0.71 | 2.03 | 0.49 |
| Health insurance private | 0.61 | 0.33 | 1.14 | 0.12 |
| No_dental_insurance | 1.21 | 0.48 | 3.06 | 0.68 |
| PD:MM | 1.41 | 0.60 | 3.29 | 0.43 |

Table 4: Multivariate logistic regression analysis predicting fair/poor general health without including interaction term between periodontal disease and multimorbidity

| Variables | Odds ratio | $2.5 \%$ | $97.5 \%$ | $P$ Value |
| :--- | :---: | :---: | :---: | :---: |
| Periodontal disease | 0.69 | 0.45 | 1.07 | 0.10 |
| Multimorbidity | 2.75 | 1.79 | 4.21 | 0.00 |
| Age | 0.95 | 0.92 | 0.99 | 0.03 |
| Gender female | 1.27 | 0.81 | 2.01 | 0.29 |
| Race Black | 0.94 | 0.54 | 1.63 | 0.81 |
| Race White | 0.47 | 0.28 | 0.78 | 0.00 |
| Marital divorced | 1.11 | 0.57 | 2.15 | 0.03 |
| Marital married | 1.86 | 1.07 | 3.24 | 0.71 |
| Education college or associates degree | 0.43 | 0.26 | 1.00 | 0.05 |
| Education college graduate | 0.56 | 0.32 | 0.64 | 0.00 |
| Ratio (2,4) | 0.38 | 0.22 | 1.18 | 0.16 |
| Ratio (4,6) | 0.67 | 0.38 | 3.56 | 0.00 |
| Smoking behavior former | 2.22 | 1.38 | 0.01 | 0.19 |
| Smoking behavior current | 1.56 | 0.81 | 0.68 |  |
| Alcohol use | 0.90 | 0.56 | 1.47 | 0.99 |
| BMI_group obese | 1.00 | 0.64 | 3.50 | 0.16 |
| No vigorous exercise | 1.69 | 0.81 | 0.06 |  |
| Health insurance medicare | 1.22 | 0.72 | 1.15 | 0.13 |
| health insurance private | 0.62 | 0.33 | 3.16 |  |
| No_dental_insurance | 1.26 | 0.50 | 0.63 |  |

the odds of fair/poor general health were statistically significant with complex MM. Approximately 35.2\% of the study's participants with fair/poor general health presented with complex MM compared to those without complex MM. People with complex MM are more likely to suffer from several conditions that may influence their general health. Additionally, our findings agree with
our previous study that showed the association between complex MM, defined as chronic conditions, functional limitations, or geriatric syndromes, and self-reported fair/ poor general health. ${ }^{[4]}$

Surprisingly, PD did not moderate the effect of complex MM on fair/poor general health. Besides the low percentage of people with conditions constituting

Table 5: Distribution of general health status among participants with conditions constituting multimorbidity and without it stratifying by periodontal disease

|  | No pe | riodontal disease ( $n=257$ ) |  | Per | Iontal disease ( $n=680$ ) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Fair/poor general health | Excellent/very good/good general health | Total | Fair/poor general health | Excellent/very good/good general health | Total |
| Multimorbidity |  |  |  |  |  |  |
| Yes | 35 | 80 | 115 | 59 | 156 | 215 |
| No | 27 | 115 | 142 | 56 | 409 | 465 |
| Total | 62 | 195 | 257 | 115 | 565 | 680 |
| Stratumspecific | $\mathrm{OR}=1.86$ (95\% CI: $1.05-3.32)$ |  |  | $\mathrm{OR}=2.76$ (95\% CI: $1.83-4.16)$ |  |  |

Crude OR $=2.51$ ( $95 \%$ CI: 1.80-3.51) and Mantel-Haenszel OR $=2.41$ ( $95 \%$ CI: 1.72-3.36)
complex MM, the prevalence of fair/poor general health was generally low except for depression and functional limitations in ADL, IADL, and leisure and social activities. In addition, participants with complex MM are more likely to have worse general health, which could explain why PD did not moderate this association. Moreover, about $35 \%$ of study participants with fair/poor general health had no PD. Furthermore, using cross-sectional data, we were unable to evaluate whether PD moderated the association between complex MM and general health status as complex MM or general health status worsened.

Given the inflammatory nature of PD and its association with several conditions constituting complex MM, we further evaluated whether PD was a modifier for the relationship between complex MM and fair/poor general health. With the presence of PD, there were 1.3 times higher odds of having fair/poor general health among participants with complex MM compared to those without PD. Although the strataspecific odds ratios of fair/poor general health were different, both point estimates fall within the confidence interval of the other group indicating that PD did not moderate the association between complex MM and fair/poor general health. We further showed that PD did not confound the association between complex MM and fair/poor general health, evidenced by the slight difference between the crude odds ratio and the Mantel-Haenszel odds ratio. Therefore, PD neither moderates the association between complex MM and fair/poor general health nor confounded it.

Several demographic and behavioral factors, including older age, white race, higher level of education, and higher family income to poverty ratio, were negatively associated with fair/poor general health. The low odds of fair/poor general health among older participants is likely because our sub-sample of NHANES for participants with periodontal data may be biased, representing a healthier subgroup of older people. For example, the 2013-2014 NHANES included only
dentate participants; therefore, the edentate people who may have lost their teeth to PD, who were more likely to suffer from complex MM, and who had worse general health, may not have participated in the oral health module of the NHANES and were therefore not represented in our sample. Another explanation could be that older people who were burdened by illness did not participate in the 2013-2014 NHANES. In addition, we do not know whether the well-controlled complex MM conditions were considered in a person's rating of their own perceived general health.

For participants of a white race, the odds of fair/poor general health were low. Our results showed that a large percentage of study participants were of a white race, and only about $13 \%$ of study participants had fair/poor general health. These results agree with an NHANES study by Chasens et al. that found that among participants who were 75 years of age or older, white race participants were more likely to have healthier general health. ${ }^{[15]}$ Regarding the level of education and family income to poverty ratio, the low odds of fair/ poor general health might be due to the healthier status of older participants with higher education levels and higher family income to poverty ratio. Older educated people were more likely to seek information about their health status and healthy lifestyles, ${ }^{[16]}$ given that their general health is at the top of their priority. In addition, older participants with a higher family income to poverty ratio were more likely to have healthcare access due to their ability to cover their medical expenses. Our results showed that more than $40 \%$ of study participants with fair/poor general health had a highschool education level and a family income-to-poverty ratio of at least 2 .

Conversely, the odds of fair/poor general health were high among those who were married and former smokers. Besides the high proportion of married participants ( $n=564$ ) compared to divorced and those with other marital status, $63 \%$ of them had fair/ poor general health ( $\mathrm{n}=111$ ). In addition, about $46 \%$
of participants with fair/poor general health were former smokers. The emergence of demographic and behavioral factors with fair/poor general health is crucial. Our prior work showed that demographic and behavioral factors were significantly associated with the presence and severity of PD using a novel machine learning analysis. ${ }^{[17]}$ Therefore, by controlling these factors, we will improve not only the general health status but also the periodontal condition.
Our findings should be interpreted in light of the following limitations: We used an objective measure for PD, quantified in a uniform fashion for all participants, to predict a self-reported general health status, as perceived by the individual. Similarly, we used self-reported data from the NHANES, including chronic conditions, functional limitations, and geriatric syndromes, which may be subject to response or recall bias. In addition, given the cross-sectional nature of this study, we were unable to evaluate the temporality of PD in relation to general health status, and adding a clinical evaluation could make the results of this study more significant.
Lastly, we note that some of our counterintuitive findings, including the negative association between older age and self-reported fair/poor health may reflect selection factors, given that participation in the oral health module of the NHANES requires that individuals are not edentulous, attesting to better general health in our study population. Edentulous people who were excluded from the NHANES may have already lost their teeth due to PD, thus diminishing our ability to find an effect.
To the best of our knowledge, we are the first to evaluate the effect of PD on general health and to what extent PD may influence the relationship between conditions constituting complex MM and general health. Previously, using machine learning analyses, we showed that functional limitations were associated with PD after incorporating the co-occurrence of chronic conditions, functional limitations, and geriatric syndromes. ${ }^{[5]}$ In addition, we showed that chronic conditions were not strong predictors for PD or severity of PD when accounting for co-occurring chronic conditions. ${ }^{[17]}$ Hence, in this paper, we extend our works to evaluate the independent and interplay effect of PD and complex MM on fair/poor general health. As well, we took advantage of the NHANES data to assess the potential impact of PD on fair/poor general health among a representative sample of older US people with complex MM. Our study has important implications in clinical practice: Persons with complex MM may prioritize general health rather than periodontal care,
which negatively impacts their periodontal care by putting them at a lower priority. In turn, developing a multidisciplinary collaboration of researchers may help design longitudinal studies that account for the dynamic shift of prioritization of health care toward complex MM and PD.

## Conclusion

Complex MM is strongly associated with fair/ poor general health, but PD did not moderate this relationship. Several sociodemographic and behavioral factors were identified as predictors for fair/poor general health. Further studies are needed to build extended models to study PD by including complex MM and other potential factors explaining their cumulative effect on general health.

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## Conflicts of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors report no conflicts of interest related to this study.
AUTHORS CONTRIBUTIONS
HMA and SMK contributed to conception, design, data acquisition, analysis and interpretation, drafted and critically revised the manuscript; KS, NFB and NKS contributed to interpretation, critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work.

Ethical policy and institutional review board statement
This study was deemed research not involving human subjects by the Case Western Reserve University Institutional Review Board (\#2021-0469).

Patient declaration of consent
Not applicable.

## Data availability statement

Not applicable.

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## Supplementary tables

| Table 1S: Multivariate logistic regression analysis predicting fair/poor general health (In presence of periodontal disease) |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| Variables | Odds ratio | 2.5\% | 97.5\% | P -value |
| Multimorbidity | 3.37 | 2.01 | 5.67 | 0.00 |
| Age | 0.97 | 0.92 | 1.02 | 0.26 |
| Gender Female | 1.21 | 0.68 | 2.14 | 0.52 |
| Race Black | 0.80 | 0.40 | 1.60 | 0.53 |
| Race White | 0.49 | 0.26 | 0.91 | 0.02 |
| Marital Divorced | 1.77 | 0.75 | 4.15 | 0.19 |
| Marital Married | 2.78 | 1.32 | 5.86 | 0.01 |
| Education College or AA degree | 0.34 | 0.18 | 0.65 | 0.00 |
| Education College graduate | 0.51 | 0.26 | 0.99 | 0.05 |
| Ratio (2,4) | 0.52 | 0.27 | 0.99 | 0.05 |
| Ratio (4,6) | 0.72 | 0.36 | 1.45 | 0.36 |
| Smoking Behavior Former | 2.05 | 1.17 | 3.60 | 0.01 |
| Smoking Behavior Current | 1.51 | 0.62 | 3.67 | 0.36 |
| Alcohol Use | 0.94 | 0.51 | 1.75 | 0.86 |
| BMI group Obese | 1.34 | 0.79 | 2.28 | 0.28 |
| No Vigorous exercise | 1.68 | 0.70 | 4.06 | 0.25 |
| Health Insurance Medicare | 0.84 | 0.44 | 1.63 | 0.61 |
| Health Insurance Private | 0.75 | 0.36 | 1.54 | 0.43 |
| No_Dental_Insurance | 1.35 | 0.43 | 4.24 | 0.61 |


| Table 2S: Multivariate logistic regression analysis predicting fair/poor general health (In absence of periodontal disease) |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| Variables | Odds ratio | 2.5\% | 97.5\% | P -value |
| Multimorbidity | 2.53 | 1.19 | 5.38 | 0.02 |
| Age | 0.92 | 0.85 | 0.99 | 0.03 |
| Gender Female | 0.63 | 0.27 | 1.46 | 0.28 |
| Race Black | 1.44 | 0.51 | 4.05 | 0.49 |
| Race White | 0.56 | 0.21 | 1.51 | 0.25 |
| Marital Divorced | 1.98 | 0.57 | 6.91 | 0.28 |
| Marital Married | 2.03 | 0.76 | 5.42 | 0.16 |
| Education College or AA degree | 0.64 | 0.26 | 1.56 | 0.33 |
| Education College graduate | 0.70 | 0.22 | 2.24 | 0.54 |
| Ratio (2,4) | 0.28 | 0.11 | 0.70 | 0.01 |
| Ratio (4,6) | 0.61 | 0.22 | 1.74 | 0.36 |
| Smoking Behavior Former | 1.26 | 0.48 | 3.35 | 0.64 |
| Smoking Behavior Current | 1.36 | 0.47 | 3.92 | 0.57 |
| Alcohol Use | 0.38 | 0.15 | 0.96 | 0.04 |
| BMI group Obese | 0.72 | 0.31 | 1.64 | 0.43 |
| No Vigorous exercise | 1.11 | 0.28 | 4.33 | 0.88 |
| Health Insurance Medicare | 2.54 | 0.89 | 7.25 | 0.08 |
| Health Insurance Private | 0.71 | 0.18 | 2.71 | 0.61 |
| No_Dental_Insurance | 0.00 | 0.00 | 0.00 | 0.99 |


| Table 3S: Multivariate logistic regression analysis predicting fair/por | general health | (In presence of multimorlbidity) |  |  |
| :--- | :---: | :---: | :---: | :---: |
|  | Odds ratio | $2.5 \%$ | $97.5 \%$ | P-value |
| PD Yes | 1.08 | 0.57 | 0.82 |  |
| Age | 0.96 | 0.90 | 1.01 | 0.14 |
| Gender Female | 1.12 | 0.57 | 2.21 | 0.74 |
| Race Black | 1.24 | 0.50 | 3.04 | 0.64 |
| Race White | 0.52 | 0.24 | 0.10 |  |
| Marital Divorced | 1.70 | 0.68 | 4.27 | 0.26 |
| Marital Married | 2.18 | 0.97 | 4.90 | 0.06 |
| Education College or AA degree | 0.52 | 0.26 | 1.02 | 0.06 |
| Education College graduate | 0.42 | 0.16 | 1.06 | 0.07 |
| Ratio (2,4) | 0.37 | 0.17 | 0.81 | 0.01 |
| Ratio (4,6) | 0.85 | 0.34 | 2.10 | 0.72 |
| Smoking Behavior Former | 1.43 | 0.72 | 0.31 |  |
| Smoking Behavior Current | 0.91 | 0.35 | 2.40 | 0.86 |
| Alcohol Use | 0.79 | 0.39 | 1.62 | 0.53 |
| BMI group Obese | 1.06 | 0.57 | 1.98 | 0.84 |
| No Vigorous exercise | 1.53 | 0.50 | 4.65 | 0.45 |
| Health Insurance Medicare | 1.26 | 0.61 | 2.58 | 0.53 |
| Health Insurance Private | 0.68 | 0.26 | 1.76 | 0.43 |
| No_Dental_Insurance | 1.18 | 0.33 | 4.25 | 0.80 |


| Table 4S: Multivariate logistic regression analysis predicting fair/poor general health (In absence of multimorbidity) |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  | Odds ratio | 2.5\% | 97.5\% | P -value |
| (Intercept) | 0.79 | 0.01 | 75.68 | 0.92 |
| PD Yes | 0.69 | 0.37 | 1.30 | 0.25 |
| Age | 0.98 | 0.92 | 1.04 | 0.50 |
| Gender Female | 1.01 | 0.53 | 1.92 | 0.98 |
| Race Black | 1.03 | 0.48 | 2.18 | 0.95 |
| Race White | 0.52 | 0.25 | 1.08 | 0.08 |
| Marital Divorced | 1.74 | 0.62 | 4.90 | 0.29 |
| Marital Married | 1.90 | 0.80 | 4.48 | 0.15 |
| Education College or AA degree | 0.51 | 0.24 | 1.06 | 0.07 |
| Education College graduate | 0.76 | 0.33 | 1.71 | 0.51 |
| Ratio (2,4) | 0.39 | 0.18 | 0.82 | 0.01 |
| Ratio (4,6) | 0.56 | 0.26 | 1.22 | 0.14 |
| Smoking Behavior Former | 2.42 | 1.18 | 4.96 | 0.02 |
| Smoking Behavior Current | 2.83 | 1.09 | 7.36 | 0.03 |
| Alcohol Use | 0.61 | 0.30 | 1.24 | 0.17 |
| BMI group Obese | 1.02 | 0.53 | 1.95 | 0.96 |
| No Vigorous exercise | 1.19 | 0.46 | 3.11 | 0.72 |
| Health Insurance Medicare | 1.28 | 0.54 | 3.04 | 0.57 |
| Health Insurance Private | 1.08 | 0.42 | 2.76 | 0.87 |
| No_Dental_Insurance | 0.45 | 0.05 | 4.16 | 0.48 |


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