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Association between adherence to life's simple 7 metrics and risk of obstructive sleep apnea among adults in the United States

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Abstract

Background We aimed to explore the impact of adherence to Life's Simple 7 (LS7) metrics on risk of obstructive sleep apnea (OSA), and the impact of inflammation on the association, in adults in the United States.

Methods Data from 13,825 community-dwelling adults aged ≥ 20 years recruited in the National Health and Nutrition Examination Surveys (NHANES) 2005–2008, 2015–2018 was analyzed. The LS7 score was calculated based on the AHA definition of LS7 metrics. The diagnosis of OSA was based on self-reported symptoms of sleep disturbance using a standard questionnaire. The Multivariable Apnea Prediction (MAP) Index score was also calculated to assess the risk of OSA. Log-binominal regression and negative binomial regression were performed to estimate the associations between LS7 and OSA and MAP index, with odds ratios (ORs) and prevalence ratios (PRs) and their 95% confidence intervals (CIs) calculated. Mediation analysis was performed to estimate the mediating effects of inflammatory indicators on the associations.

Results A total of 4473 participants (32.4%) had OSA, and the mean MAP index was 0.39. In fully adjusted log-binominal regression models, with total score < 6 as the reference, the ORs (95% CIs) for risk of OSA were 0.90 (0.73, 1.10), 0.76 (0.65, 0.89), 0.78 (0.64, 0.95), and 0.45 (0.38, 0.54) for total score = 6, total score = 7, total score = 8, and total score > 8, respectively (P for trend < 0.001). When LS7 score was analyzed as a continuous variable, each 1-point increase in LS7 score was associated with a 15% decrease in OSA risk ($P < 0.001$). In negative binominal regression models, the adjusted PRs (95% CIs) for the MAP index were 0.93 (0.90, 0.97), 0.87 (0.84, 0.91), 0.80 (0.77, 0.84), and 0.55 (0.53, 0.57) for total score = 6, total score = 7, total score = 8, and total score > 8, respectively (P for trend < 0.001). For each 1-point increase in LS7 score, the risk of OSA decreased by 13% ($P < 0.001$). Consistent results were observed in subgroup analysis. Mediation analysis indicated that inflammatory factors, including blood cell count, neutrophil count, and C-reactive protein, positively mediated the association of LS7 with OSA, with a mediation proportion of 0.022 ($P = 0.04$), 0.02 ($P = 0.04$), and 0.02 ($P = 0.02$), respectively.

Conclusions In a nationally representative sample of US adults, adherence to LS7 metrics was independently associated with reduced OSA risk. Inflammation plays a mediating role in the association between LS7 and OSA.

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Keywords Life's simple 7 metrics, Obstructive sleep apnea, Inflammation, NHANES

Introduction

Obstructive sleep apnea (OSA) is a chronic disorder caused by repeated upper airway collapse during sleep, resulting in recurrent nocturnal asphyxia, fragmented sleep, major fluctuations in blood pressure and increased sympathetic nervous system activity [1, 2]. These episodic cycles of respiratory disruption can cause acute and chronic physiological stressors. It is estimated that one in seven of the world's adult population, or approximately one billion people, suffer from OSA [3]. Obesity and advanced age have been identified as the two major risk factors for OSA [4, 5]. With the prevalence of an ageing population and obesity, vulnerability to OSA increases significantly [6]. OSA is associated with significant comorbidities and mortality and has been established as an important risk factor for a range of cardiovascular diseases, including hypertension, diabetes, coronary heart disease, atrial fibrillation, heart failure, and stroke [7–10]. The importance of OSA extends beyond individual health, directly and indirectly affecting the family and society in terms of productivity and public safety. A better understanding of the pathophysiology of OSA and addressing its risk factors is needed to facilitate the management of this chronic disease and improve overall health outcomes.

Existing literature has shown that a wide range of sociodemographic, physical, biological, lifestyle, and psychological factors are associated with the incidence of OSA [11–13]. Among these factors, some of the modifiable cardiovascular risk factors, such as hypertension, obesity, and alcohol consumption, are critical to the incidence of OSA. In addition, a growing body of evidence suggests that chronic inflammation may play an important role in the pathophysiological process of OSA [14–16]. The Life's Simple (LS7) metrics were initiated by the American Heart Association (AHA) and proposed to promote cardiovascular health (CVH), which includes 7 modifiable cardiovascular risk factors: manage blood pressure (BP), control cholesterol, reduce blood glucose, be physically active, eat better, lose weight and stop smoking [17]. The impact of adherence to LS7 on physical health has been studied in various chronic diseases, and results have shown that higher LS7 scores are associated with better cognitive function, lower risk of atrial fibrillation and depression, and a favorable prognosis after stroke [18–21]. In the field of OSA, the impact of adherence to LS7 on OSA risk in adults has not been investigated, and scarce is known about the mediating effects of inflammation on the association between LS7 and OSA.

The National Health and Nutrition Examination Survey (NHANES) is an ongoing program designed to assess the health and nutritional status of the non-institutionalized civilian population in the US, allowing for the analysis of common health conditions and their risk factors. Given the large and nationally representative sample of the US population, the NHANES program provides an ideal platform to investigate the association between adherence to LS7 and OSA in US adults. In the present study, we aimed to assess the association between adherence to LS7 metrics and risk of OSA in US adults, as well as the mediating effects of inflammation on this association.

Methods

Study design, setting, and participants

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional survey conducted every 2 years by the Center for Disease Control's National Center for Health Statistics. Its purpose is to assess the health and nutritional status of the non-institutionalized civilian population in the United States. The survey uses a stratified multi-stage clustered probability sampling strategy and recruits approximately 5,000 individuals from 15 counties across the country. The survey consists of two parts: face-to-face interviews and physical examinations in a mobile examination center (MEC). Detailed information on NHANES can be accessed at http://www.cdc.gov/nchs/nhanes. The program's protocol is approved by the institutional review board of the National Center for Health Statistics, and all individuals provide written informed consent.

For this study, data were extracted from four cycles of NHANES conducted between 2005 and 2008 and 2015 to 2018, resulting in a total of 116,876 participants. Of these, 17,520 individuals were excluded for being under 20 years old. Further exclusions were made for individuals without data of self-reported symptoms of sleep disorders (n=3998), Life's Simple 7 score (n=2642), marital status (n=5), income-poverty ratio (n=1216), education level (n=2), comorbidity (n=506), and self-reported health status (n=8), resulting in a final sample of 13,825 participants. Participants were categorized into five groups according to their total LS7 score: < 6 (n=2090), = 6 (n=1696), = 7 (n=1957), = 8 (n=2231), and >8 (n=5851) (Fig. 1).

Definition of life's simple 7 metrics

The LS7 metrics, as defined by the AHA, are outlined in Table S1. Each component of the LS7 metrics was assigned a score of 2 for ideal health, 1 for intermediate health, and 0 for poor health. The total LS7 score

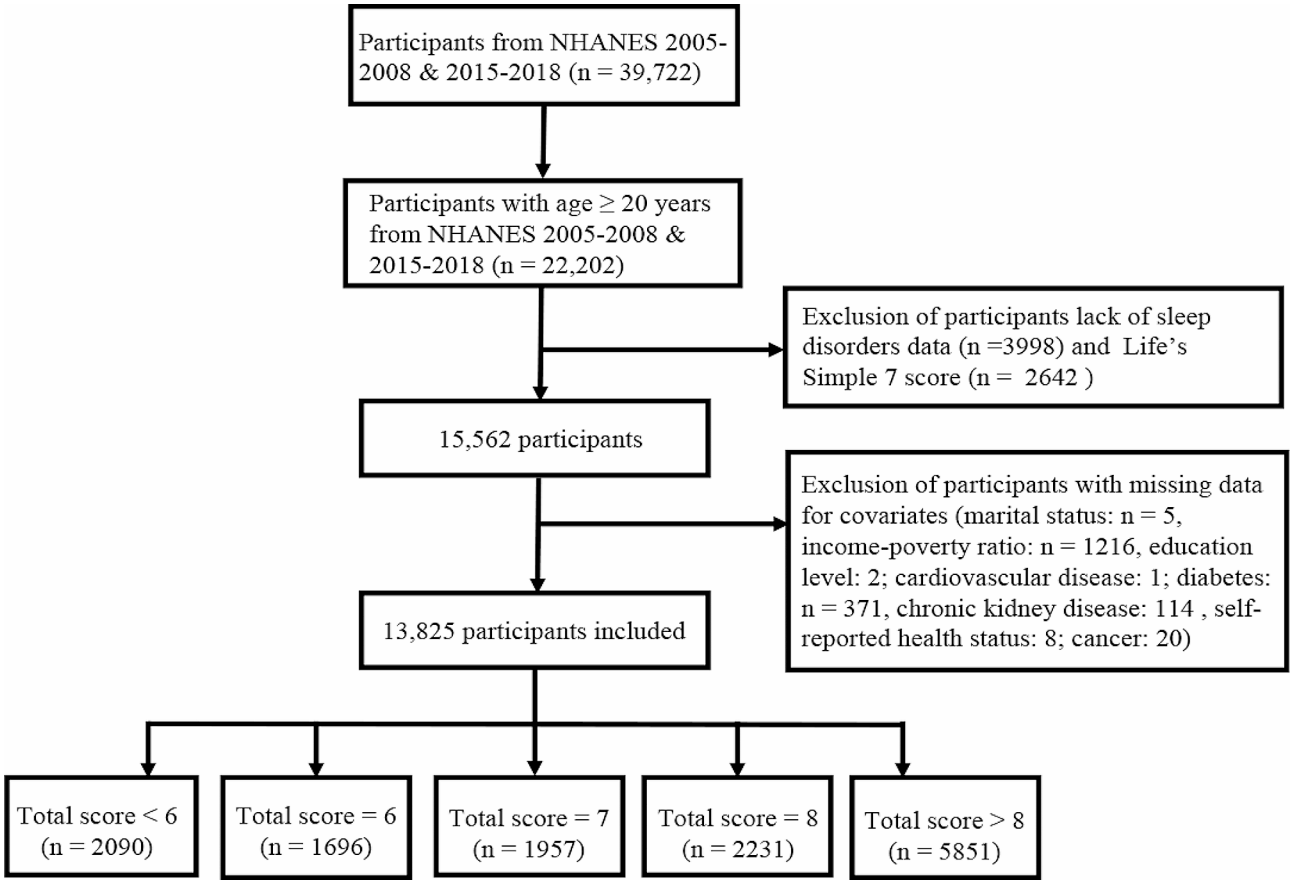

Fig. 1 Study enrolment flowchart. NHANES, National Health and Nutrition Examination Survey

ranged from 0 to 14 points, with higher scores indicating better CVH. Blood pressure (BP) was measured in the MEC according to a standardized protocol, and the average of three consecutive readings was calculated for scoring. Ideal health for BP was defined as untreated BP < 120/80 mmHg and not on antihypertensive medication; intermediate health as BP 120 to 139/80 to 89 mmHg or < 120/80 mmHg on antihypertensive medication; and poor health as BP ≥ 140/90 mmHg. Hemoglobin A1c (HbA1c), instead of fasting plasma glucose, was used to assess diabetic health, due to a significant proportion of NHANES participants did not fast. Ideal health for HbA1c was defined as HbA1c < 5.7% and not on glucose-lowering medication; intermediate health as HbA1c 5.7–6.4% or < 5.7% on glucose-lowering medication; and poor health as HbA1c ≥ 6.5%. For cholesterol, ideal health was defined as untreated total serum cholesterol < 200 mg/dL; intermediate health as untreated total serum cholesterol 200 to 239 mg/dL or treated to < 200 mg/dL; and poor health as total serum cholesterol ≥ 240 mg/dL. Weight and height were measured at the MEC using standard protocols, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Ideal health for BMI was defined as BMI < 25 kg/m^2; intermediate health as BMI 25 to 29.9 kg/m^2; and poor health as BMI ≥ 30 kg/m^2. For smoking, ideal health was defined as never smokers who had never smoked or had smoked < 100 cigarettes in their lifetime; intermediate health as former smokers who had smoked ≥ 100 cigarettes in their lifetime but did not currently smoke; and poor health as current smokers who had smoked ≥ 100 cigarettes in their lifetime and currently smoke some days or every day. Physical activity was quantified by calculating the total number of minutes of moderate or vigorous activity per week. Ideal health for physical activity was defined as ≥ 150 min/week of moderate or vigorous activity; intermediate health as 1 to 149 min/week of moderate or vigorous activity; and poor health as 0 min/week of moderate or vigorous activity. Dietary intake was assessed by two 24-hour dietary recall interviews by trained interviewers. The first interview was conducted in person at the MEC, and the second interview was conducted by telephone 3 to 10 days after the first interview. The Food and Nutrient Database for Dietary Studies from the United States Department of Agriculture (USDA) was utilized to calculate the nutritional content and components of all food items. The Healthy Eating Index (HEI) version 2015 developed by the USDA

was calculated to assess diet quality, which comprised 13 components categorized into Adequacy and Moderation, and each component was evaluated against specific standards, with scores ranging from 0 to 5 based on adherence to dietary recommendations [22]. The summation of these component scores yields a total score between 0 and 100, with higher scores indicating better diet quality. In this study, the daily intake of HEI components for each participant is determined by averaging the results of their two dietary recalls. The total nutrient intakes on the first day are used to calculate the 13 components of HEI-2015. Food components, excluding fatty acids, are scored based on density (per 1,000 kcal or as a percentage of energy), while fatty acids are evaluated as a ratio of unsaturated to saturated fatty acids (Table S22). Ideal dietary health was defined as an HEI > 80; intermediate health was defined as an HEI 50 to 80; and poor health was defined as an HEI < 50.

Definition of OSA

According to the four signs/symptoms recommended by the American Academy of Sleep Medicine for OSA screening [23], the diagnosis of OSA was based on self-reported symptoms of sleep disorders using a standard questionnaire (how often have you snored, gasped, or stopped breathing while sleeping in the past year?) and a self-reported diagnosis of hypertension. The frequency of occurrence was categorized as follows: never, rarely (1 to 2 nights per week), occasionally (3 to 4 nights per week), and frequently (5 to more nights per week). According to the STOP screening questionnaire for OSA [24], participants were classified as being at high risk of OSA if they reported ≥ 2 positive reactions to the following: snoring, daytime fatigue, witnessed apneas, and hypertension, and they also had to experience snoring, daytime fatigue, and witnessed apneas 'frequently'. Otherwise participants were categorized as low risk for OSA. Participants at high risk of OSA were considered to have a diagnosis of OSA. In addition, risk of OSA was evaluated with an adaptation of the multivariable apnea prediction (MAP) index with NHANES variables [25]. In the original MAP index, the three OSA symptoms of loud snoring, breath-holding, and sneezing and/or wheezing were rated on a 5-point Likert scale, with '0' = never to '4' = always (i.e., 5 or more times per week). Two NHANES questions on frequency of 'snoring' and 'snort or stop breathing' that were recorded to approximate the original MAP sleep questions. As with the original MAP index, an apnea index was calculated as an average of non-missing responses and entered into the adapted MAP algorithm along with age, gender, and BMI to produce a continuous score from no sleep apnea (0) to OSA (1).

Assessment of covariates

Data on age, gender, race, marital status, education, poverty income ratio (PIR), alcohol consumption, self-reported health status, and comorbidities including cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and cancer were collected through household interviews using standardized questionnaires. Alcohol consumption was classified as non-drinker, low-to-moderate drinker (< 3 drinks per day for women, < 4 drinks per day for men, or binge drinking on less than 5 days per month), or heavy drinker (≥ 3 drinks per day for women, ≥ 4 drinks per day for men, or binge drinking on ≥ 5 days per month). CVD was defined as a composite of self-reported diagnosis of coronary heart disease, congestive heart failure, heart attack, angina, and stroke. COPD was defined as self-reported diagnosis of emphysema, ratio of forced expiratory volume in 1 s to forced vital capacity < 0.7 after bronchodilator, or use of anti-inflammatory drugs in subjects age ≥ 40 years with a history of smoking or chronic bronchitis. CKD was defined as an estimated glomerular filtration rate < 60 mL/min/1.73 m^2 or urine albumin to creatinine ratio ≥ 30 mg/g.

Statistical analysis

All statistical analyses were performed using R software (version 3.3.3, S. Urbanek & H.-J. Bibiko, © R Foundation for Statistical Computing). A P value < 0.05 (2-tailed) was considered significant. As NHANES is designed as a complex, multi-stage, probability sampling study to select participants representative of the US civilian non-institutionalized population, it is important to consider sample weights, clustering, and stratification in the statistical analysis. Following NHANES analytical guidelines, a 4-year MEC weight (2005–2008 & 2015–2018) was used for the 2005 to 2008 and 2015 to 2018 subsamples, and weights were recalculated (divided by 4) after combining NHANES 2005 to 2008 with 2015 to 2018 to obtain weighted percentages adjusted to the US adult population.

Descriptive analysis was used to describe the characteristics of the study population. Continuous normally distributed variables were expressed as means ± standard errors, continuous non-normally distributed variables were expressed as medians and interquartile ranges, and categorical variables were expressed as numbers and percentages. Comparisons of baseline characteristics classified by the total LS7 score were performed using one-way analysis of variance for continuous variables and the Rao-Scott $\chi 2$ test for categorical variables, with adjustment for sampling weights. The prevalence of ideal, intermediate, and poor levels for each LS7 component was described, and the proportion of different numbers in ideal and poor levels of LS7 components was calculated.

Survey-weighted log-binominal regression analysis and negative binomial regression analysis were performed to estimate the associations between LS7 score and OSA and MAP index [26, 27]. OSA was treated as a binary outcome variable ('OSA') in log-binomial regression analysis and as a count variable ('MAP index score') in negative binomial regression analysis. To obtain integer values without changing the distribution, MAP index score was multiplied by 100 and included in the negative binominal regression models. Three models were constructed for each method of analysis. The first model was unadjusted; the second model was adjusted for age, sex and race; the third model was additionally adjusted for marital status, education level, PIR, alcohol consumption, self-reported health, CVD, COPD, CKD and cancer. Due to the potential confounding effects of inflammation on the association between adherence to LS7 metrics and OSA, we conducted a sensitivity analysis to further adjust for inflammatory indicators including white blood cell count, neutrophil count, lymphocyte count, and C-reactive protein (CRP) on the basis of model 3. The associations of each incremental ideal and poor item of the LS7 with OSA were also analyzed, adjusting for variables in the third model as well as other components. Finally, we examined the associations of different clusters of behavioral factors (physical activity, smoking, BMI, diet) and biological factors (BP, HbA1c, total serum cholesterol) with OSA. Results of the regression analyses were reported as odds ratios (ORs) with their respective 95% confidence intervals (CIs) for log-binomial regression analysis, and prevalence ratios (PRs) with their respective 95% CIs for negative binomial regression analysis.

Subgroup analyses were performed by age (< 65 years, ≥ 65 years), sex (male, female), race (non-Hispanic white, other races), BMI (<30 kg/m^2, ≥ 30 kg/m^2), smoking status (never smoked, former/current smoker), alcohol status (non-drinker, drinker) and self-reported health (poor to fair, good to excellent). In these subgroup analyses, the total LS7 score was included in the regression models as a continuous variable to assess the significance of interactions. Causal mediation analysis was further performed to assess the potential mediating effect of inflammatory indicators on the relationship between total LS7 score and risk of OSA. Survey-weighted generalized linear regression models were constructed and adjusted for variables including age, sex, race, BMI, marital status, education level, PIR, smoking status, alcohol consumption, self-reported health and comorbidities. The direct effect, indirect effect, total effect, and mediated proportion were calculated. Significance tests were performed using 1,000 bootstrapping iterations [28].

Results

Baseline characteristics of all participants, categorized by total LS7 score, are shown in Table 1. The survey-weighted mean age of all participants was 46.9 years, and 50.7% were male. Compared with individuals with low total LS7 scores, those with high total LS7 scores were more likely to be younger, non-black, highly educated, well paid and in good health. They also had a lower prevalence of smoking and chronic comorbidities. In the total sample of participants, 4473 individuals (32.4%) had OSA. There was a significant reduction in the proportion of individuals with OSA as the total LS7 score increased, and the MAP index score was significantly reduced as the LS7 score increased.

Examining the individual components of the LS7 score, smoking (54.7%) and HbA1c (62.0%) had a high prevalence of ideal levels, while the prevalence of ideal diet was less than 3%. For both diet and BMI, the prevalence of poor levels was over 35%. Only 20 participants achieved ideal levels for all 7 components, and 4 participants had poor values for all 7 components. The proportions of participants achieving ideal levels in 0–1, 2–4, and ≥4 were 21.2%, 64.6%, and 14.2%, respectively (Fig. 2).

Table 2 shows the association between LS7 score and OSA as well as the MAP index. When OSA was considered as the outcome variable, there was a significant decrease in the risk of OSA with increasing LS7 score in the unadjusted log-binominal regression models. After adjustment for age, sex, and race in the second models, the ORs did not show significant changes. After further adjustment for marital status, education level, PIR, smoking status, alcohol consumption, self-reported health status and chronic comorbidities, with total score<6 as the reference, the ORs (95% CIs) for OSA were 0.86 (0.71, 1.04), 0.70 (0.60, 0.82), 0.69 (0.58, 0.82), and 0.36 (0.31, 0.42) for total score=6, total score=7, total score=8, and total score>8, respectively. In the fully adjusted models analyzing LS7 score as a continuous variable, each 1-point increase in LS7 score was associated with a 15% decrease in the risk of OSA ($P<0.001$). Consistent results were obtained when the MAP index was considered as the outcome variable. In the fully adjusted negative binomial regression models, with total score<6 as the reference, the PRs (95% CIs) for MAP index were 0.93 (0.90, 0.97), 0.87 (0.84, 0.91), 0.80 (0.77, 0.84), and 0.55 (0.53, 0.57) for total score=6, total score=7, total score=8, and total score>8, respectively. In addition, for each 1-point increase in LS7 score, the risk of MAP index decreased by 13% ($P<0.001$). Our sensitivity analysis by incorporating inflammatory indicators in model 3 for adjustment did not alter these associations (Table S3).

Table 3 shows the association between components of the LS7 metrics and OSA and MAP index. Both higher lifestyle and biometric scores were significantly

Table 1 Baseline characteristics of participants according to Life's simple 7 score in NHANES 2005–2008 & 2015-2018[a]

Variables	All participants (*n* = 13825)	Life's Simple 7 score				
		Total score < 6 (*n* = 2090)	Total score = 6 (*n* = 1696)	Total score = 7 (*n* = 1957)	Total score = 8 (*n* = 2231)	Total score > 8 (*n* = 5851)
Age, years	46.9 ± 0.4	55.9 ± 0.2	53.6 ± 0.5	51.4 ± 0.6	48.4 ± 0.6	41.4 ± 0.4
Male, n (%)	7012 (50.7)	1118 (52.0)	912 (53.7)	1006 (50.9)	1193 (52.3)	2783 (46.7)
Ethnicity, n (%)						
Mexican American	2264 (16.4)	346 (7.6)	261 (8.1)	339 (8.4)	380 (8.2)	938 (7.8)
Non-Hispanic White	6055 (43.8)	902 (69.8)	704 (67.0)	841 (68.5)	998 (71.1)	2610 (70.3)
Non-Hispanic Black	2818 (20.4)	569 (13.4)	422 (12.8)	418 (10.6)	450 (10.2)	959 (8.0)
Other	2688 (19.4)	273 (9.2)	309 (12.1)	359 (12.5)	403 (10.5)	1344 (13.9)
Marital status, n (%)						
Married or living with a partner	8895 (64.3)	1285 (66.2)	1070 (68.4)	1243 (67.1)	1474 (70.4)	3823 (67.8)
Widowed/divorced/separated	2676 (19.4)	594 (23.9)	447 (20.8)	466 (21.3)	441 (16.8)	728 (11.0)
Never married	2254 (16.3)	211 (9.9)	179 (10.8)	248 (11.7)	316 (12.9)	1300 (21.2)
Education, n (%)						
Less than high school	1340 (9.7)	295 (7.3)	194 (5.5)	239 (6.0)	213 (4.4)	399 (3.3)
High school or equivalent	5121 (37.0)	943 (45.0)	713 (41.9)	789 (39.0)	881 (36.9)	1795 (26.6)
College or above	7364 (53.3)	852 (47.7)	789 (52.6)	929 (55.0)	1137 (58.7)	3657 (70.1)
Family income-poverty ratio	3.15 ± 0.04	2.77 ± 0.06	3.00 ± 0.07	3.02 ± 0.06	3.16 ± 0.06	3.31 ± 0.04
Smoking status, n (%)						
Never smoker	7570 (54.8)	565 (25.2)	678 (36.9)	928 (43.1)	1174 (51.5)	4225 (70.6)
Former smoker	3432 (24.8)	752 (36.6)	568 (33.5)	591 (33.5)	551 (25.2)	970 (18.2)
Current smoker	2823 (20.4)	773 (38.2)	450 (29.6)	438 (23.4)	506 (23.4)	656 (11.2)
Drinking status, n (%)						
Nondrinker	7654 (55.4)	1292 (55.4)	998 (53.8)	1083 (50.0)	1247 (50.6)	3034 (46.7)
Low to moderate drinker	4053 (29.3)	519 (28.6)	460 (30.2)	571 (32.1)	603 (31.6)	1900 (36.9)
Heavy drinker	2118 (15.3)	279 (16.0)	238 (16.0)	303 (17.9)	381 (17.8)	917 (16.4)
Self-reported health status, n (%)						
Poor to fair	3149 (22.8)	892 (35.0)	546 (26.0)	507 (19.8)	479 (14.9)	725 (8.0)
Good	5009 (36.2)	763 (40.3)	673 (39.7)	794 (41.9)	848 (36.3)	1931 (29.4)
Very good to excellent	5667 (41.0)	435 (24.8)	477 (34.3)	656 (38.3)	904 (48.9)	3195 (62.6)
Self-reported chronic diseases, n (%)						
Cardiovascular disease	1475 (10.7)	494 (19.7)	304 (14.6)	242 (10.9)	203 (7.0)	232 (2.9)
Diabetes mellitus	2494 (18.0)	1044 (44.6)	539 (26.1)	428 (17.4)	259 (8.9)	224 (2.8)
Hypertension	5759 (41.7)	1601 (74.7)	1093 (59.6)	1035 (50.0)	932 (40.2)	1098 (17.0)
Hypercholesterolemia	9816 (71.0)	1968 (95.6)	1502 (90.2)	1629 (85.3)	1681 (77.8)	3036 (51.8)
Chronic kidney disease	2437 (17.6)	748 (31.2)	452 (20.8)	390 (15.8)	345 (12.8)	502 (7.2)
COPD	610 (4.4)	201 (8.6)	104 (5.7)	88 (5.2)	94 (3.7)	123 (1.8)
Cancer	1255 (9.1)	272 (13.3)	208 (12.8)	207 (12.1)	223 (11.1)	345 (6.1)
Body mass index, kg/m^2	29.1 ± 0.1	34.1 ± 0.2	32.3 ± 0.3	31.2 ± 0.3	29.9 ± 0.2	26.2 ± 0.1
Systolic blood pressure, mmHg	122.2 ± 0.2	135.4 ± 0.6	130.3 ± 0.5	127.3 ± 0.5	123.4 ± 0.5	115.3 ± 0.2
Diastolic blood pressure, mmHg	71.4 ± 0.3	75.0 ± 0.5	72.8 ± 0.5	73.2 ± 0.4	72.3 ± 0.4	69.4 ± 0.3
HbA_{1c}, %	5.58 ± 0.01	6.46 ± 0.05	5.93 ± 0.02	5.72 ± 0.03	5.47 ± 0.02	5.26 ± 0.01
Total cholesterol, mg/dl	194.1 ± 0.7	211.3 ± 1.4	206.4 ± 1.8	202.1 ± 1.7	198.3 ± 1.4	183.4 ± 0.7
Physical activity, minutes per week	827.2 ± 22.9	547.1 ± 41.2	633.9 ± 39.2	796.6 ± 41.7	825.2 ± 39.3	897.8 ± 28.4
Healthy eating index-2020	49.6 ± 0.4	43.6 ± 0.4	45.4 ± 0.4	47.6 ± 0.4	48.1 ± 0.5	53.2 ± 0.4
MAP index	0.39 ± 0.00	0.59 ± 0.01	0.54 ± 0.01	0.49 ± 0.01	0.43 ± 0.01	0.27 ± 0.00
OSA, n (%)	4473 (32.4)	935 (46.2)	690 (42.4)	693 (37.5)	796 (37.1)	1359 (23.6)

[a] All estimates accounted for sample weights and complex survey designs, and means and percentages were adjusted for survey weights of NHANES

COPD chronic obstructive pulmonary disease, *HbA_{1c}* glycated hemoglobin A_{1c}, *MAP index* multivariable apnea prediction index, *OSA* obstructive sleep apnea

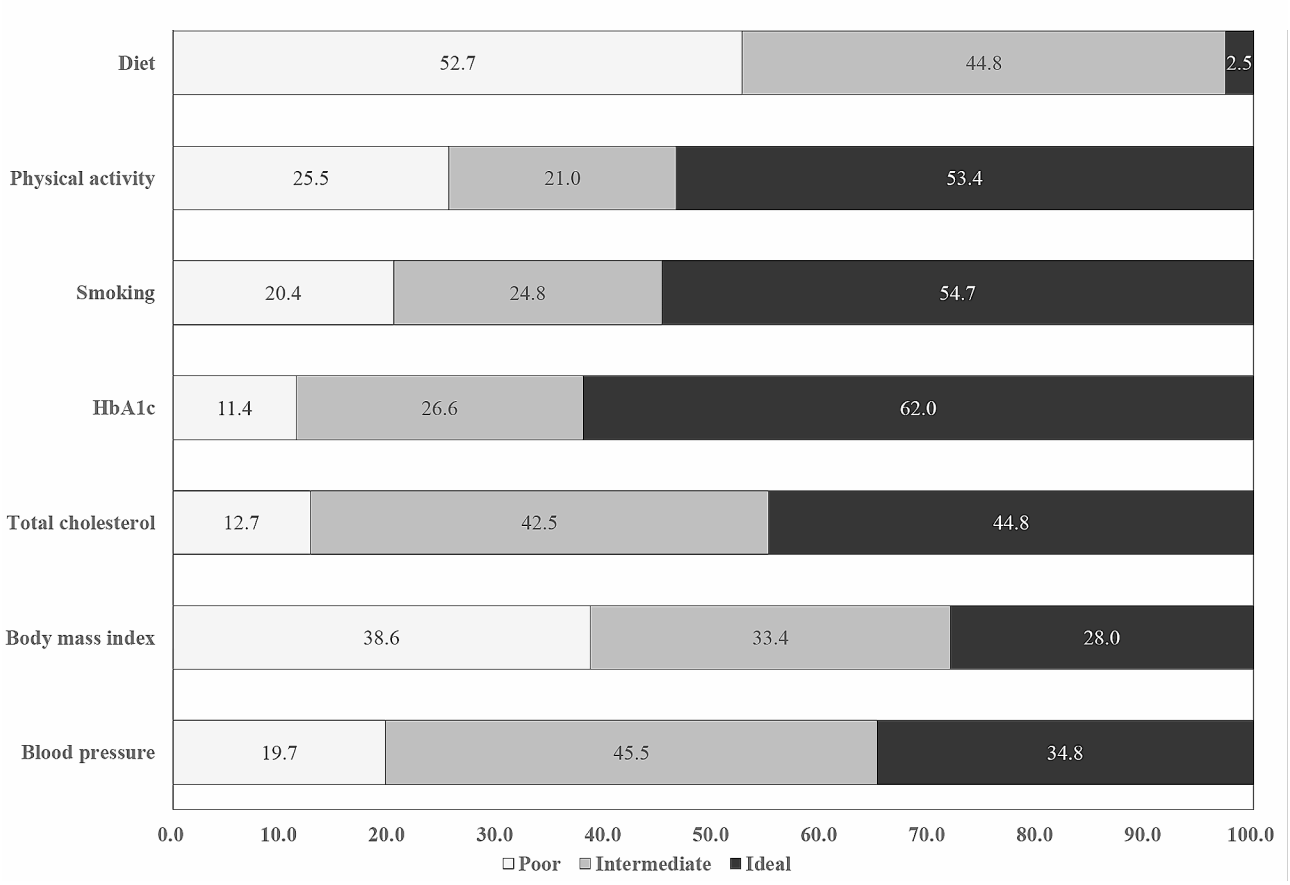

Fig. 2 Distribution of overall and the seven components of ideal cardiovascular health metrics

Table 2 Associations between total Life's simple 7 score and risk of obstructive sleep apnea in participants from NHANES 2005–2008 & 2015–2018

	Life's Simple 7 score							
	Total score < 6	Total score = 6	Total score = 7	Total score = 8	Total score > 8	*P*-trend	Continuous score	*P* value
Log-binominal regression								
Model 1[a]	Reference	0.86 (0.71, 1.04)	0.70 (0.60, 0.82)	0.69 (0.58, 0.82)	0.36 (0.31, 0.42)	< 0.001	0.82 (0.81, 0.84)	< 0.001
Model 2[b]	Reference	0.86 (0.71, 1.04)	0.70 (0.60, 0.82)	0.69 (0.57, 0.83)	0.37 (0.31, 0.43)	< 0.001	0.82 (0.80, 0.84)	< 0.001
Model 3[c]	Reference	0.90 (0.73, 1.10)	0.76 (0.65, 0.89)	0.78 (0.64, 0.95)	0.45 (0.38, 0.54)	< 0.001	0.85 (0.83, 0.88)	< 0.001
Negative binomial regression								
Model 1[a]	Reference	0.91 (0.87, 0.95)	0.82 (0.79, 0.86)	0.73 (0.70, 0.76)	0.46 (0.44, 0.48)	< 0.001	0.84 (0.84, 0.85)	< 0.001
Model 2[b]	Reference	0.92 (0.89, 0.96)	0.86 (0.82, 0.90)	0.78 (0.75, 0.81)	0.52 (0.51, 0.54)	< 0.001	0.87 (0.86, 0.87)	< 0.001
Model 3[c]	Reference	0.93 (0.90, 0.97)	0.87 (0.84, 0.91)	0.80 (0.77, 0.84)	0.55 (0.53, 0.57)	< 0.001	0.87 (0.86, 0.88)	< 0.001

[a] Model 1 was unadjusted

[b] Model 2 was adjusted for age, sex, and race

[c] Model 3 was further adjusted for education, marital status, family income-poverty ratio, alcohol consumption, self-reported health status, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and cancer

Table 3 Associations between components of Life's simple 7 metrics and obstructive sleep apnea in participants from NHANES 2005–2008 & 2015–2018

	Life's Simple 7 score			
	Poor	Intermediate	Optimal	*P*-trend
Log-binominal regression				
Lifestyle score[a]	Reference	0.68 (0.59, 0.79)	0.46 (0.39, 0.54)	< 0.001
Smoking status [b]	Reference	0.72 (0.62, 0.83)	0.70 (0.61, 0.80)	< 0.001
Body mass index [b]	Reference	0.61 (0.54, 0.69)	0.36 (0.31, 0.42)	< 0.001
Diet [b]	Reference	0.91 (0.82, 1.01)	0.66 (0.45, 0.97)	0.019
Physical activity [b]	Reference	1.12 (0.94, 1.32)	1.03 (0.87, 1.21)	0.961
Biometric score[c]	Reference	0.91 (0.80, 1.03)	0.67 (0.55, 0.82)	< 0.001
Blood pressure [b]	Reference	0.88 (0.77, 0.99)	0.74 (0.61, 0.89)	0.002
Total cholesterol [b]	Reference	0.97 (0.83, 1.13)	0.98 (0.85, 1.12)	0.836
Glycemic status [b]	Reference	0.97 (0.81, 1.17)	0.92 (0.76, 1.11)	0.277
Negative binomial regression				
Lifestyle score[a]	Reference	0.81 (0.79, 0.83)	0.55 (0.53, 0.58)	< 0.001
Smoking status [b]	Reference	0.93 (0.90, 0.97)	0.92 (0.89, 0.95)	< 0.001
Body mass index [b]	Reference	0.58 (0.56, 0.59)	0.33 (0.32, 0.34)	< 0.001
Diet [b]	Reference	0.98 (0.97, 1.00)	0.94 (0.87, 1.02)	0.163
Physical activity [b]	Reference	1.01 (0.98, 1.04)	0.98 (0.95, 1.01)	0.301
Biometric score[c]	Reference	0.95 (0.92, 0.98)	0.77 (0.74, 0.80)	< 0.001
Blood pressure [b]	Reference	1.01 (0.98, 1.03)	0.89 (0.87, 0.92)	< 0.001
Total cholesterol [b]	Reference	0.99 (0.97, 1.02)	0.98 (0.96, 1.01)	0.259
Glycemic status [b]	Reference	1.04 (1.01, 1.07)	0.97 (0.94, 1.00)	0.061

[a] Adjusted for age, sex, race, marriage status, education, income, alcohol consumption, self-reported health status, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cancer, and the biometric score (for the lifestyle score)

[b] Adjusted for age, sex, race, marriage status, education, income, alcohol consumption, self-reported health status, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cancer, and all the other compositions of the LS7 score

[c] Adjusted for age, sex, race, marriage status, education, income, alcohol consumption, self-reported health status, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease cancer, and the lifestyle score (for the biometric score)

associated with lower OSA risk. In terms of specific items, good management of smoking, BMI, and BP was associated with a significantly reduced risk of OSA. When OSA was considered as the outcome variable, with poor score as the reference, the ORs for OSA were 0.72 (0.62, 0.83) and 0.70 (0.61, 0.80) for intermediate and optimal score in smoking status, 0.61 (0.54, 0.69) and 0.36 (0.31, 0.42) for intermediate and optimal score in BMI, and 0.88 (0.77, 0.99) and 0.74 (0.61, 0.89) for intermediate and optimal score in BP management. When MAP index was considered as the outcome variable, with poor score as the reference, the ORs for OSA were 0.93 (0.90, 0.97) and 0.92 (0.89, 0.95) for intermediate and optimal score in smoking status, 0.58 (0.56, 0.59) and 0.33 (0.32, 0.34) for intermediate and optimal score in BMI, and 1.01 (0.98, 1.03) and 0.89 (0.87, 0.92) for intermediate and optimal score in BP management.

When stratified by age, sex, race, BMI, smoking status, alcohol consumption, and self-reported health status, all subgroups consistently showed that higher LS7 scores were associated with a lower risk of OSA (Fig. 3). The results of the causal mediation analysis are shown in Fig. 4. Our results indicate that the LS7 score may reduce the risk of OSA by attenuating inflammatory responses. After adjustment for covariates in model 3, the mediating proportions of white blood cell count, neutrophil count, and CRP were 0.022 (P=0.038), 0.020 (P=0.044) and 0.022 (P=0.020), respectively. However, no significant mediation effects were observed for lymphocytes (P=0.340).

Discussion

In the present study, we examined the association between adherence to LS7 metrics and OSA in a nationally representative sample of US adults. Our main findings were as follows. First, participants with high LS scores were more likely to be in good health and less likely to have chronic comorbidities. Most US adults achieved ideal scores of 2–4, and diet and BMI had a prevalence of poor scores of more than 35%. Second, better adherence to LS7 metrics was independently associated with a lower risk of OSA and lower MAP index scores. The findings were consistent across subgroups categorized by age, sex, race, BMI, smoking status, alcohol consumption, and self-reported health status. Third, further analysis of the association between each component of the LS7 metrics and the risk of OSA showed that poor control of smoking, BMI and BP was associated with a significantly increased risk of OSA. Finally, causal mediation analysis indicated that inflammation plays a mediating role in the association between adherence to LS7 metrics and risk of OSA.

The AHA developed the LS7 metrics as a tool to promote the prevention of CVD by encouraging individuals

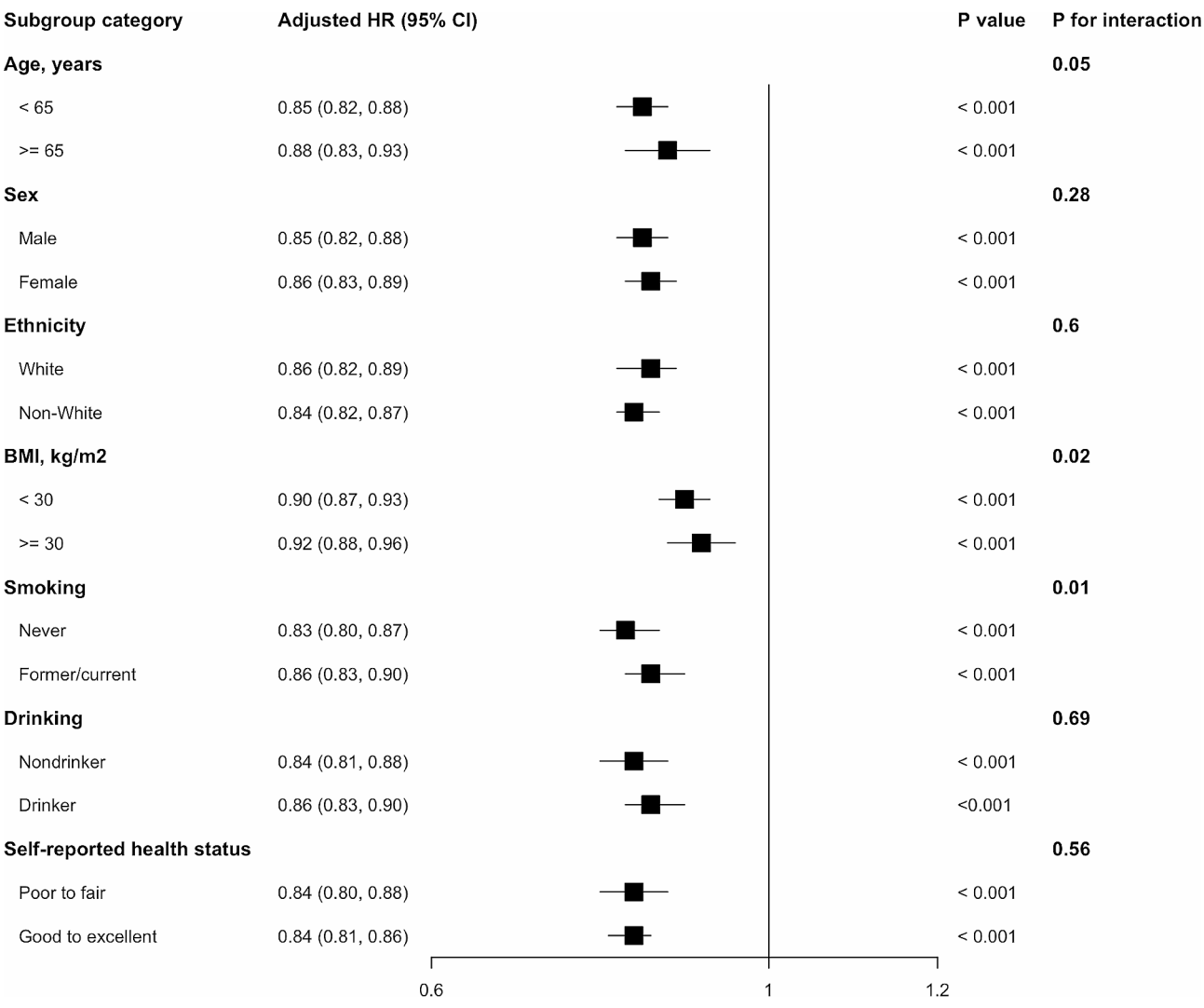

Fig. 3 Subgroup analysis of the association between life's simple 7 metrics and risk of obstructive sleep apnea. Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio

to adopt and maintain healthy lifestyle behaviors. In the meta-analysis conducted by Radovanovic et al. including 21 studies totaling 3,240,660 adults, a higher number of ideal CVH metrics led to a lower risk for CVD and cardiovascular mortality [29]. Unfortunately, the prevalence of CVH metrics has been found to be relatively low. According to a meta-analysis by Younus et al. [30], the percentage of individuals meeting 6 to 7 ideal CVH metrics ranges from as little as 0.5% in African American populations to 12% in employees of a healthcare organization in South Florida. In the present study, only 14.2% of participants achieved ideal values in ≥4 metrics of LS7, and women had significantly higher LS7 scores than men, which is consistent with the above findings. In addition, of the 7 ideal CVH metrics, participants scored lowest on dietary habits and BMI. Only 2.5% of the participants had healthy dietary habits and 28.0% of the participants achieved the ideal level of BMI. These findings highlight significant deficiencies in lifestyle management, i.e., healthy dietary habits and weight management, among US adults, and the need for concurrent targeted interventions.

In addition to its impact on CVD, the association between adherence to LS7 metrics and physical health has also been examined in a variety of non-cardiovascular diseases. Wei et al. examined the association between adherence to LS7 metrics and cognitive function in 2,585 older adults from NHANES and found that higher adherence to LS7 metrics was independently associated with better cognitive function [18]. A recent study evaluated the impact of LS7 on incident depression in 3,231 adults aged 50 years and older and found that higher LS7 scores were inversely associated with depression [19]. Quach et al. examined the associations between midlife LS7 status, psychosocial health, and late-life multidimensional frailty indicators, and showed that a better LS7 score was

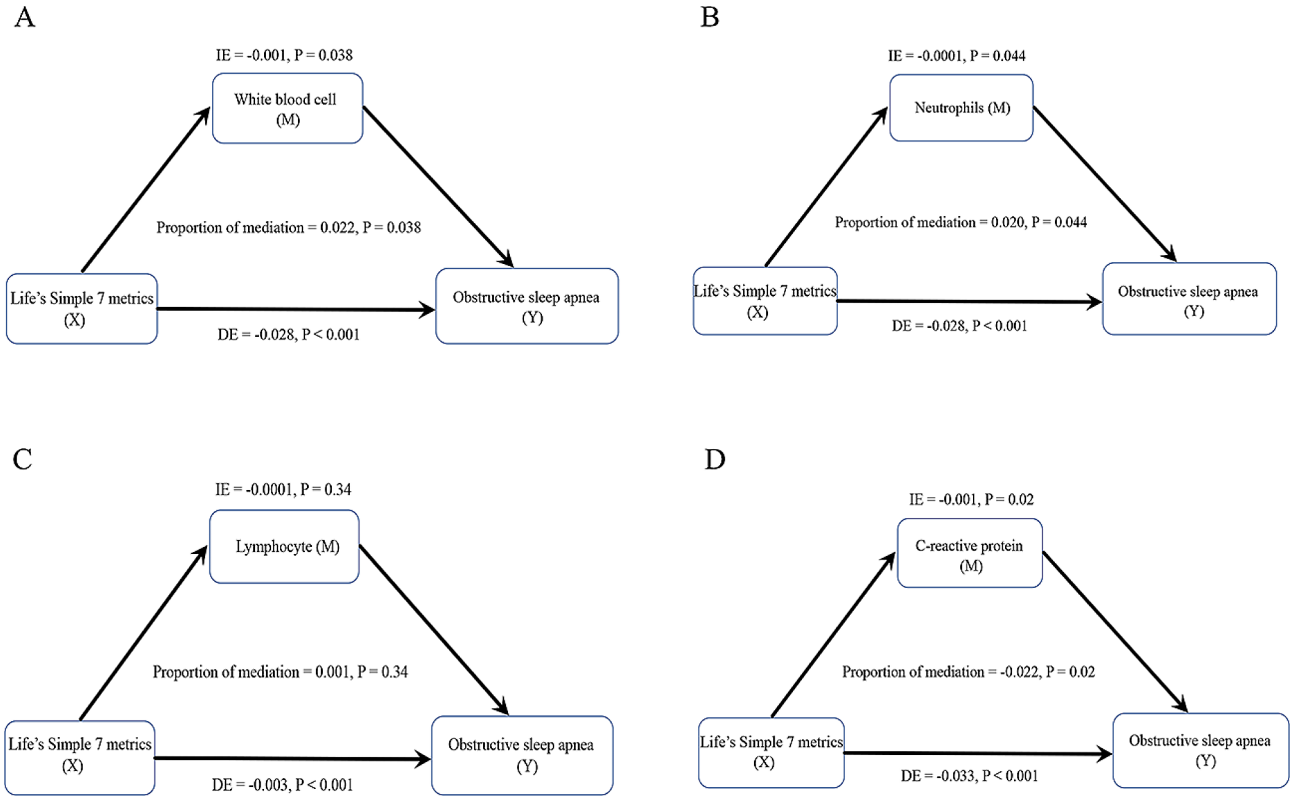

Fig. 4 Mediation effects of inflammatory indicators on the association between Life's Simple 7 metrics and risk of obstructive sleep apnea. (**A**) White blood cell; (**B**) Neutrophils; (**C**) Lymphocyte; (**D**) C-reactive protein. Abbreviations: DE, direct effect; IE, indirect effect

independently associated with a reduced risk of physical, hospital, and global frailty and that there was a synergistic effect of psychosocial status and LS7 on frailty [31]. However, scarce is known about the influence of adherence to LS7 metrics on the risk of OSA. To our knowledge, the present study is the first comprehensive analysis to evaluate the association between adherence to LS7 metrics and prevalence of OSA in US adults. Our analysis of 13,825 participants from NHANES 2005–2008 and 2015–2018 showed that adherence to LS7 metrics was significantly associated with a reduced risk of OSA, with a negative dose-response relationship, whether OSA was analyzed as a categorical variable using survey-weighted log-binomial regression models or as a continuous variable in the form of MAP using negative binomial regression models.

Our further analysis of the association between each component of the LS7 metrics and the risk of OSA showed that the increased risk of OSA associated with poor adherence to LS7 was mainly concentrated in poor control of smoking, BMI, and BP. Among these components, overweight/obesity has been well established to be an important risk factor for OSA, and weight loss can effectively reduce the incidence and severity of OSA [3]. Besides, the association between hypertension and OSA has been identified to be bidirectional, with elevated BP significantly increasing the incidence of OSA, and OSA also increasing the risk of hypertension, especially resistant hypertension [7]. While studies evaluating the relationship between smoking and OSA have yielded inconsistent results, a recent study conducted by Jang et al. among 3,442 participants of the Korea National Health and Nutrition Examination Survey found a positive dose-dependent relationship between smoking and the risk of OSA, with smoking cessation helping to properly manage sleep quality [32]. As a comprehensive assessment of lifestyle habits, the LS7 metrics may be a superior risk assessment tool for predicting the risk of OSA.

An increasing evidence indicate that ideal CVH is closely associated with a lower inflammatory status, and that poor adherence to LS7 metrics can lead to an activated systemic inflammatory state, which may contribute to the development of a variety of diseases. González-Gil et al. investigated the association between the ideal CVH index and inflammation in European adolescents and found that a higher CVH index was associated with a significantly lower inflammatory profile as constructed by CRP, complement factors C3 and C4, leptin and white blood cell count [33]. Gaye et al. examined the mediating effect of inflammatory and hemostatic blood biomarkers in the association between baseline CVH and incident CVD and found that the association of behavioral CVH

with incident coronary heart disease was partially mediated by high-sensitivity CRP, interleukin-6, and fibrinogen [34]. Fan et al. explored the association of modifiable CVH metrics with physical function in rural older adults in China and the potential role of inflammatory mechanisms in the association, and found that ideal CVH was significantly associated with higher scores on the balance, chair stand, and walking speed tests, and mediation analysis showed that serum interleukin-6 accounted for 14% of the association of CVH with the total Short Performance Physical Battery score and 10% of the association with the walking speed score [35]. Given the existing evidence that inflammation contributes to the pathophysiological process of OSA [14–16], it is reasonable to speculate that inflammation may also play a mediating role in the association between LS7 metrics and risk of OSA. Our results of causal mediation analysis confirmed this speculation and suggested that inflammation mediated the association of adherence to LS7 metrics and risk of OSA.

The major strength of the present study is that it is the first analysis to comprehensively evaluate the association between adherence to LS7 and risk of OSA in a relatively large US adult population. The NHANES program was conducted by professionally trained researchers and the data collection process followed strict standard procedures, which ensured the high quality of the study and the reliability and accuracy of the results. In addition to being analyzed as a dichotomous variable, risk of OSA was also quantified using the MAP index, and consistent results were obtained when the MAP index was analyzed as the target variable in regression analysis, demonstrating the robustness of the results of this study. In addition, covariates were adjusted relatively adequately in multivariate regression models to eliminate the effects of confounding factors on the association between adherence to LS7 and risk of OSA. Finally, the large sample size of this study provided sufficient power for subgroup analyses.

This study has several limitations that should be acknowledged. Firstly, the cross-sectional design inherently limits our ability to establish a definitive causal relationship between good adherence to LS7 and a reduced risk of OSA. Future well-designed prospective cohort studies are needed to provide a more conclusive understanding. Secondly, the diagnosis of OSA in the NHANES program relied on participants' self-reported signs and symptoms using the STOP questionnaire, rather than objective sleep monitoring methods, which may introduce potential misclassifications. Future studies utilizing objective sleep monitoring methods like polysomnography or home sleep apnea testing are crucial to validate our findings. Thirdly, despite adjusting for numerous variables in our multivariate models to address confounding effects, residual and unmeasured confounding variables, such as anatomical abnormalities, neurological disorders, and genetic factors, may still impact the reliability of our results. Prospective studies are necessary to account for these confounding factors. As our study specifically focuses on the US population, caution should be exercised when generalizing our findings to other populations. Additionally, notable variations were observed in the baseline characteristics between the population analyzed and those excluded (Table S4), which may introduce selection bias and influence the precision of our findings. Furthermore, our analysis only suggests that inflammation may mediate the association; however, further research is needed to delve more deeply into the underlying pathways and mechanisms. Lastly, the use of 24-hour dietary recalls in the NHANES project to obtain nutritional data may introduce recall bias, potentially skewing results and affecting the interpretation of the relationship between dietary habits and OSA risk.

Conclusions

In conclusion, the present study demonstrated that poorer adherence to LS7 metrics was significantly associated with increased risk of OSA, which was mainly concentrated in poor control of smoking, BMI, and BP. The findings were consistent across subgroups categorized by age, sex, race, BMI, smoking status, alcohol consumption, and self-reported health status. Causal mediation analysis indicated that inflammation plays a mediating role in the association between adherence to LS7 metrics and risk of OSA. However, given the significant selection bias and recall bias present in this study, the interpretation of our findings should be approached with caution. Future well-designed prospective studies are essential to validate our results.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-024-05990-y.

Supplementary Material 1

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Author contributions

YMY and JZ designed the study and supervised the overall conduct of the study, and they also reviewed and revised the manuscript. SW performed the statistical analysis and drafted the initial manuscript. SW, LLW, WX, SQL, JW, XHS, and HZ contributed to data extraction, data cleaning, and interpretation of the data. All authors reviewed and approved the final manuscript.

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Data availability
The data used in this work was extracted from the NHANES website and is publicly available.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participant
The NHANES protocols were approved by the Ethics Committee of the National Center for Health Statistics, and all participants recruited in the study were informed of the study protocols and signed informed consent form.

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References

1. Patel SR. Obstructive sleep apnea. Ann Intern Med. 2019;171(11):ITC81–96.
2. Veasey SC, Rosen IM. Obstructive sleep apnea in adults. N Engl J Med. 2019;380(15):1442–9.
3. Lyons MM, Bhatt NY, Pack AI, Magalang UJ. Global burden of sleep-disordered breathing and its implications. Respirology. 2020;25(7):690–702.
4. Bonsignore MR. Obesity and obstructive sleep apnea. Handb Exp Pharmacol. 2022;274:181–201.
5. Lee JJ, Sundar KM. Evaluation and management of adults with obstructive sleep apnea syndrome. Lung. 2021;199(2):87–101.
6. Seeger-Zybok RK, Klingelhöfer D, Groneberg DA. Global risk factor evaluation of obstructive sleep apnea in relation to Research Activity and socioeconomic factors. Int J Environ Res Public Health. 2020;17(18):6785.
7. Salman LA, Shulman R, Cohen JB. Obstructive sleep apnea, hypertension, and Cardiovascular Risk: Epidemiology, Pathophysiology, and management. Curr Cardiol Rep. 2020;22(2):6.
8. Bloomgarden Z. Obstructive sleep apnea and diabetes. J Diabetes. 2023;15(11):916–9.
9. Yeghiazarians Y, Jneid H, Tietjens JR, Redline S, Brown DL, El-Sherif N, Mehra R, Bozkurt B, Ndumele CE, Somers VK. Obstructive Sleep Apnea and Cardiovascular Disease: A Scientific Statement from the American Heart Association. Circulation. 2021;144(3):e56–67.
10. Huang B, Liu H, Scherlag BJ, Sun L, Xing S, Xu J, Luo M, Guo Y, Cao G, Jiang H. Atrial fibrillation in obstructive sleep apnea: neural mechanisms and emerging therapies. Trends Cardiovasc Med. 2021;31(2):127–32.
11. Abbasi A, Gupta SS, Sabharwal N, Meghrajani V, Sharma S, Kamholz S, Kupfer Y. A comprehensive review of obstructive sleep apnea. Sleep Sci. 2021;14(2):142–54.
12. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, Nunez CM, Patel SR, Penzel T, Pépin JL, Peppard PE, Sinha S, Tufik S, Valentine K, Malhotra A. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med. 2019;7(8):687–98.
13. Gottlieb DJ, Punjabi NM. Diagnosis and management of obstructive sleep apnea: a review. JAMA. 2020;323(14):1389–400.
14. Orrù G, Storari M, Scano A, Piras V, Taibi R, Viscuso D. Obstructive sleep apnea, oxidative stress, inflammation and endothelial dysfunction-An overview of predictive laboratory biomarkers. Eur Rev Med Pharmacol Sci. 2020;24(12):6939–48.
15. Yi M, Zhao W, Tan Y, Fei Q, Liu K, Chen Z, Zhang Y. The causal relationships between obstructive sleep apnea and elevated CRP and TNF-α protein levels. Ann Med. 2022;54(1):1578–89.
16. Díaz-García E, García-Tovar S, Alfaro E, Jaureguizar A, Casitas R, Sánchez-Sánchez B, Zamarrón E, Fernández-Lahera J, López-Collazo E, Cubillos-Zapata C, García-Río F. Inflammasome activation: a Keystone of Proinflammatory Response in Obstructive Sleep Apnea. Am J Respir Crit Care Med. 2022;205(11):1337–48.
17. Hasbani NR, Ligthart S, Brown MR, Heath AS, Bebo A, Ashley KE, Boerwinkle E, Morrison AC, Folsom AR, Aguilar D, de Vries PS. American Heart Association's life's simple 7: lifestyle recommendations, polygenic risk, and lifetime risk of Coronary Heart Disease. Circulation. 2022;145(11):808–18.
18. Wu J, Xiong Y, Xia X, Orsini N, Qiu C, Kivipelto M, Rizzuto D, Wang R. Can dementia risk be reduced by following the American Heart Association's life's simple 7? A systematic review and dose-response meta-analysis. Ageing Res Rev. 2023;83:101788.
19. Gao B, Song S, Guo J. Associations between life's simple 7 and incident depression among adults aged 50 years and older: a 15-year cohort study. Psychiatry Res. 2023;320:115046.
20. Díaz-Gutiérrez J, Martínez-González MÁ, Alonso A, Toledo E, Salas-Salvadó J, Sorlí JV, Ros E, Fitó M, Estruch R, Arós F, Fiol M, Lapetra J, Gómez-Gracia E, Serra-Majem L, Pintó X, Portolés O, Babio N, Castañer O, Ruiz-Canela M. American Heart Association's life simple 7 and the risk of atrial fibrillation in the PREDIMED study cohort. Nutr Metab Cardiovasc Dis. 2023;33(6):1144–8.
21. Commodore-Mensah Y, Mok Y, Gottesman RF, Kucharska-Newton A, Matsushita K, Palta P, Rosamond WD, Sarfo FS, Coresh J, Koton S. Life's simple 7 at midlife and risk of recurrent Cardiovascular Disease and Mortality after Stroke: the ARIC study. J Stroke Cerebrovasc Dis. 2022;31(7):106486.
22. Reedy J, Lerman JL, Krebs-Smith SM, Kirkpatrick SI, Pannucci TE, Wilson MM, Subar AF, Kahle LL, Tooze JA. Evaluation of the healthy eating Index-2015. J Acad Nutr Diet. 2018;118(9):1622–33.
23. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD. Adult obstructive sleep apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263–76.
24. Patel D, Tsang J, Saripella A, Nagappa M, Islam S, Englesakis M, Chung F. Validation of the STOP questionnaire as a screening tool for OSA among different populations: a systematic review and meta-regression analysis. J Clin Sleep Med. 2022;18(5):1441–53.
25. Kariuki JK, Yang K, Scott PW, Chasens ER, Godzik C, Luyster FS, Imes CC. Obstructive sleep apnea risk is Associated with severity of metabolic syndrome: a secondary analysis of the 2015–2018 National Health and Nutrition Examination Survey. J Cardiovasc Nurs. 2022;37(5):482–9.
26. Lumley T, Scott A. Fitting regression models to Survey Data. Stat Sci. 2017;32:265–78.
27. Hakeem FF, Bernabé E, Sabbah W. Association between Oral Health and Frailty among American older adults. J Am Med Dir Assoc. 2021;22(3):559–e5632.
28. Rijnhart JJM, Lamp SJ, Valente MJ, MacKinnon DP, Twisk JWR, Heymans MW. Mediation analysis methods used in observational research: a scoping review and recommendations. BMC Med Res Methodol. 2021;21(1):226.
29. Radovanovic M, Jankovic J, Mandic-Rajcevic S, Dumic I, Hanna RD, Nordstrom CW. Ideal Cardiovascular Health and Risk of Cardiovascular events or mortality: a systematic review and Meta-analysis of prospective studies. J Clin Med. 2023;12(13):4417.
30. Younus A, Aneni EC, Spatz ES, Osondu CU, Roberson L, Ogunmoroti O, Malik R, Ali SS, Aziz M, Feldman T, Virani SS, Maziak W, Agatston AS, Veledar E, Nasir K. A Systematic Review of the Prevalence and Outcomes of Ideal Cardiovascular Health in US and Non-US Populations. Mayo Clin Proc. 2016;91(5):649 – 70.
31. Wang Q, Zhou C, Dong C, Zhang J, Xie Z, Sun H, Fu C, Hao W, Zhu D. Midlife life's simple 7, Psychosocial Health, and physical Frailty, Hospital Frailty, and Comprehensive Frailty 10 years later. Nutrients. 2023;15(10):2412.
32. Jang YS, Nerobkova N, Hurh K, Park EC, Shin J. Association between smoking and obstructive sleep apnea based on the STOP-Bang index. Sci Rep. 2023;13(1):9085.
33. González-Gil EM, Santabárbara J, Ruiz JR, Bel-Serrat S, Huybrechts I, Pedrero-Chamizo R, de la Gottrand OA, Kafatos F, Widhalm A, Manios K, Molnar Y, De Henauw D, Plada S, Ferrari M, Palacios M, Le Blé G, Siani A, González-Gross M, Gómez-Martínez S, Marcos A, Moreno Aznar LA, HELENA study. Ideal

cardiovascular health and inflammation in European adolescents: the HELENA study. Nutr Metab Cardiovasc Dis. 2017;27(5):447–55.
34. Gaye B, Tafflet M, Arveiler D, Montaye M, Wagner A, Ruidavets JB, Kee F, Evans A, Amouyel P, Ferrieres J, Empana JP. Ideal Cardiovascular Health and Incident Cardiovascular Disease: Heterogeneity across Event Subtypes and mediating effect of blood biomarkers: the PRIME study. J Am Heart Assoc. 2017;6(10):e006389.
35. Fan D, Chen X, Fa W, Liang X, Han X, Wang Y, Cong L, Liang Y, Welmer AK, Hou T, Du Y, Qiu C. Cardiovascular health profiles, systemic inflammation, and physical function in older adults: a population-based study. Arch Gerontol Geriatr. 2023;109:104963.

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