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RESEARCH ARTICLE

Healthy lifestyle is associated with reduced cardiovascular disease, depression and mortality in people at elevated risk of sleep apnea

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Summary

We assessed: (1) the independent and joint association of obstructive sleep apnea risk and healthy lifestyle with common consequences (excessive daytime sleepiness, depression, cardiovascular disease and stroke) of obstructive sleep apnea; and (2) the effect of healthy lifestyle on survival in people with increased obstructive sleep apnea risk. Data from 13,694 adults (median age 46 years; 50% men) were used for cross-sectional and survival analyses (mortality over 15 years). A healthy lifestyle score with values from 0 (most unhealthy) to 5 (most healthy) was determined based on diet, alcohol intake, physical activity, smoking and body mass index. In the cross-sectional analysis, obstructive sleep apnea risk was positively associated with all chronic conditions and excessive daytime sleepiness in a dose–response manner (p for trend < 0.001). The healthy lifestyle was inversely associated with all chronic conditions (p for trend < 0.001) but not with excessive daytime sleepiness (p for trend = 0.379). Higher healthy lifestyle score was also associated with reduced odds of depression and cardiovascular disease. We found an inverse relationship between healthy lifestyle score with depression (p for trend < 0.001), cardiovascular disease (p for trend = 0.003) and stroke (p for trend = 0.025) among those who had high obstructive sleep apnea risk. In the survival analysis, we found an inverse association between healthy lifestyle and all-cause mortality for all categories of obstructive sleep apnea risk (moderate/high- and high-risk groups [p for trend < 0.001]). This study emphasises the crucial role of a healthy lifestyle in mitigating the effects of obstructive sleep apnea risk in individuals with an elevated obstructive sleep apnea risk.

KEYWORDS
cardiovascular disease, depression, excessive daytime sleepiness, healthy lifestyle, mortality, sleep apnea

1 | INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep disorder where the upper airway is obstructed repetitively, resulting in inadequate breathing and sleep disruption. OSA is very common, and is estimated to affect one billion people globally (Benjafield et al., 2019; Lechat et al., 2022). Adverse health outcomes of OSA include excessive daytime sleepiness (EDS; Bjorvatn et al., 2015), depression (Mjelle et al., 2022), cardiovascular disease (CVD; Dong et al., 2013) and stroke (Jehan et al., 2018). Potential mechanisms by which OSA affects health include metabolic dysfunction and inflammation (Jun & Polotsky, 2009), due to exposure of organs to intermittent hypoxia, as well as reduced quality and duration of sleep.

Continuous positive airway pressure (CPAP) is the first-line treatment of OSA. Although CPAP can reduce EDS and symptoms of depression (Povitz et al., 2014), it has not been shown to reduce the incidence of primary or secondary CVD and all-cause mortality (Khan et al., 2018; McEvoy et al., 2016; Sánchez-de-la-Torre et al., 2020). In addition, CPAP is often associated with poor compliance due to patients' physiological characteristics (Gray et al., 2017), device design, and psychological and social factors (Sawyer et al., 2011). Further, CPAP treatment reduces symptoms without addressing the root causes of airway collapse.

There is an ongoing need to identify and support alternative interventions for OSA to reduce the burden on health systems and individual quality of life. Healthy lifestyle interventions remain a potentially important intervention pathway to reduce the risk of OSA (Georgoulis et al., 2021; Melaku et al., 2022) and its associated adverse health outcomes. This is particularly imperative as lifestyle interventions more specifically target not only underlying causes of sleep apnea, but also some of the consequences, such as obesity and inflammation (Melaku et al., 2022).

Previous studies (Carneiro-Barrera et al., 2019; Georgoulis et al., 2021), including our recent work (Melaku et al., 2022), have demonstrated that healthier lifestyles (i.e. not smoking, moderate alcohol consumption, healthy body mass index [BMI], healthy eating and exercise) are associated with reduced risk and severity of OSA, independently of most common traditional risk factors such as older age and male sex (Thompson et al., 2022). However, evidence on whether healthy lifestyles reduce the adverse health consequences of OSA, or improve survival in people with OSA, is scarce.

In this study, we aimed to: (1) assess independent and joint association of OSA risk and healthy lifestyle with common health consequences of OSA (EDS, depression, CVD and stroke); and (2) to determine the effect of healthy lifestyle on survival in people with increased risk of OSA.

2 | METHODS

2.1 | Study design and sample

Data from four cycles of the National Health and Nutrition Examination Survey (NHANES; 2005–2008 and 2015–18) were used (Center for Disease Control and Prevention, 2020). Data to determine OSA risk were not available for other waves. NHANES is a USA-based repeated cross-sectional study that uses interviews, medical assessment and laboratory investigations to collect data. A total of 39,722 adults, aged 20–78 years, participated in the four cycles, and data from 13,694 participants were used for both cross-sectional and survival analyses (Figure 1). Nevertheless, all participants with a sample weight were incorporated into the analysis, regardless of missing data, to properly account for the sample design and obtain the correct variance estimates. Ethical approvals for NHANES were provided by the National Center for Health Statistics Ethics Review Board (McQuillan et al., 2015).

2.2 | Healthy lifestyle score

We have previously described detailed methods for scoring healthy lifestyle using NHANES data (Melaku et al., 2022). Briefly, the healthy lifestyle score was composed of five lifestyle factors (Li et al., 2015; Shan et al., 2018): diet, alcohol intake, physical activity, smoking and BMI. Dietary intake data were assessed using a 24-hr recall method over 2 days through both face-to-face and telephone interview (Ahluwalia et al., 2016). In this study, we used only data collected during the face-to-face interview, as in-person interviews have higher response rates and lower item non-response rates than phone interviews, which result in more complete and accurate data. In addition, in-person interviews may be more effective at capturing detailed and nuanced dietary information than phone interviews. The US Department of Agriculture Food and Nutrient Database for Dietary Studies was used to determine micro- and macronutrient contents of food (Perloff et al., 1990). In addition, participant data were linked with the USDA Food Patterns Equivalents Database (US Department of Agriculture and Department of Health and Human Services, 2020). Overall diet quality was assessed using the healthy eating index (HEI-2015; Krebs-Smith et al., 2018) based on 14 dietary components. Components and related scoring of the HEI-15 are provided in Table S1. Alcohol intake was also based on the 24-hr recall dietary data (reported in grams), as we also previously used (Melaku et al., 2022).

The Global Physical Activity Questionnaire (Armstrong & Bull, 2006) was used to assess physical activity, and MET (metabolic equivalents of task)-minutes per week were estimated based on the number of minutes that participants spent each week doing moderate to vigorous activities requiring at least 4 MET units per hour (Du et al., 2019). Smoking status was categorised as never, former (smoked > 100 cigarettes in lifetime but does not currently smoke) and current (smoked > 100 cigarettes in lifetime and smokes currently). BMI was the ratio of measured body mass (kg) to measured height (metres) squared.

A detailed method of assessment, definition and scoring of healthy lifestyle is provided in Table S2. We defined low-risk lifestyle factors as: HEI-2015 in the upper two-fifths; ≤ 1 standard drink per day (women); ≤ 2 standard drinks (men; one drink contains 14 g of ethanol; National Health Service, 2019; US Department of Agriculture and Department of Health and Human Services, 2020; Zhang et al., 2021); moderate or sufficient physical activity (≥ 600 MET-minutes per week); never smoking; and BMI between 18.5 kg m^{-2} and 25 kg m^{-2}. For each healthy lifestyle factor, participants received a score of 1 if they met the criterion or 0 otherwise (Li et al., 2015; Shan

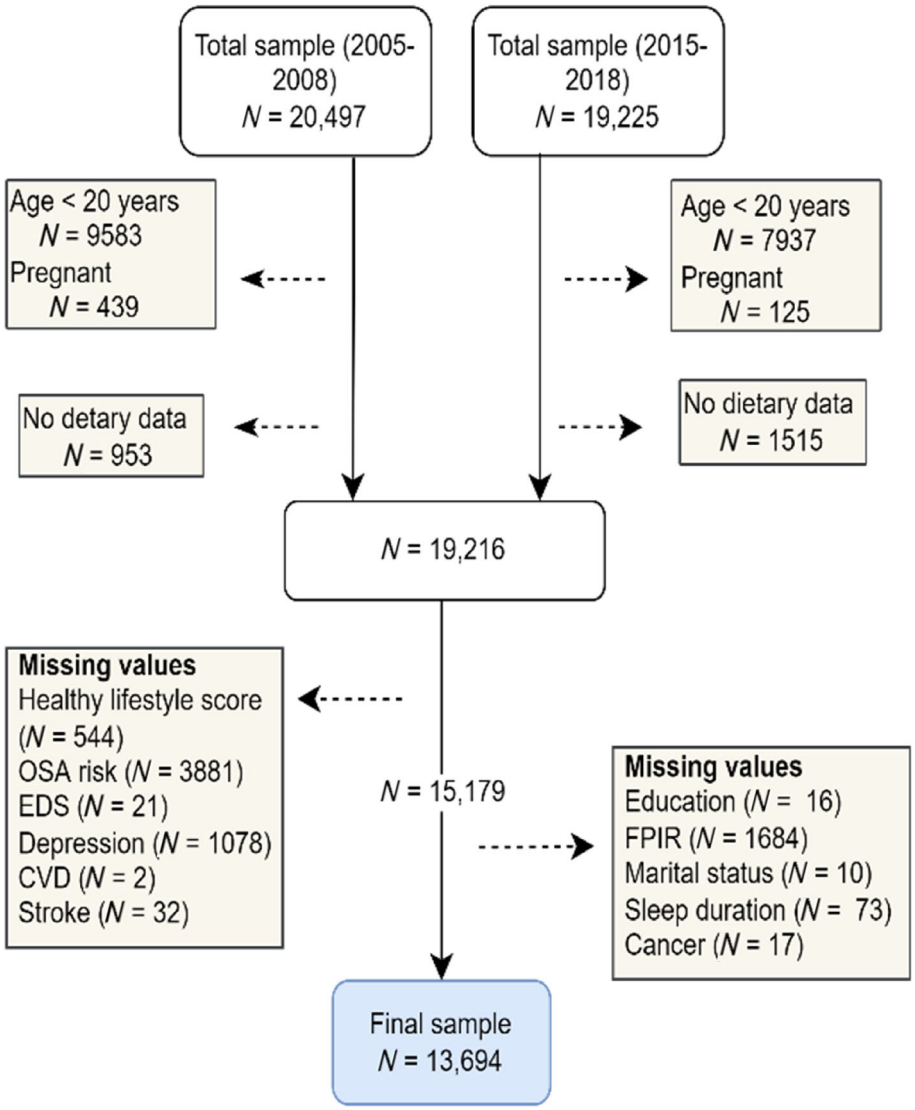

FIGURE 1 Sampling scheme. CVD, cardiovascular disease; EDS, excessive daytime sleepiness; FPIR, family-to-poverty income ratio; OSA, obstructive sleep apnea.

et al., 2018). Therefore, possible scores range from 0 (most unhealthy) to 5 (most healthy). Because there were a small number of participants in the extreme scores of healthy lifestyle, we combined scores 0 and 1, and 4 and 5 for both cross-sectional and survival analyses.

2.3 | OSA risk

In the main analysis, OSA risk definition was based on the STOP-BANG (Snoring, Tired, Observed apnea, blood Pressure, Body mass index, Age, Neck circumference, Gender) tool. Details on methods of assessment of each component, scoring criteria and frequency are provided in Table S3, and more detailed explanation of how questions from NHANES were used can be found in our previous work (Melaku et al., 2022; Sweetman et al., 2021). Briefly, observed apneas were determined based on a question: "In the past 12 months, how often did you snort, gasp, or stop breathing while you were asleep?" Waist circumference was used as a substitute as there were no data on neck circumference (described and used previously; Melaku et al., 2022). These two measurements are highly correlated ($r = 0.64$; Joshipura et al., 2016). STOP-BANG scores range from 0 to 8. Scores < 2, 3–4 and > 5 are considered low, moderate and high risk, respectively. Unless specified, all results of this study are based on this criterion. A systematic review by Pivetta et al. (2021) demonstrated that a STOP-BANG score of at least 3 has excellent sensitivity (90%) in the USA. The negative predictive values were calculated to be 78% and 91% for moderate to severe and severe OSA, respectively. Furthermore, the diagnostic accuracy of a STOP-BANG score of at least 3 to detect moderate to severe OSA was also found to be 0.89 for both moderate to severe and severe OSA (Pivetta et al., 2021). These findings suggest that the STOP-BANG questionnaire is a reliable tool for identifying individuals at risk of moderate to severe and severe OSA, despite low specificity (54%; Chung et al., 2016).

In further sensitivity analyses, the STOP score (high-risk subcriteria without BMI, age, waist circumference or gender) ≥ 2 was used to define increased risk of OSA (Chung et al., 2016). The OSA-50 tool was also used as an alternative approach to determine sleep apnea risk. The OSA-50 has four components: waist circumference (waist circumference > 102 cm if male or > 88 cm if female; 3 points); ever

TABLE 1 Characteristics of participants[a]

Characteristics	Proportion (%)
Female	49.9
Age	46.0 (33.0, 59.0)[a]
Ethnicity	
Mexican American	7.8
Other Hispanic	5.0
Non-Hispanic White	69.7
Non-Hispanic black	10.3
Other race–including multi-racial	7.1
Education	
Less than high school	13.8
High school diploma (including GED)	24.3
More than high school	61.9
Income (FPIR)	3.3 (1.7, 5.0)[a]
Marital status	
Married/living with partner	68.2
Widowed	4.2
Divorced	9.3
Separated	2.3
Never married	16.0
Healthy lifestyle score	
0–1	15.9
2	32.7
3	32.5
4–5	18.9
BMI (kg m^{-2})	29.2 (6.7)
Sleep duration (hr)	7.3 (1.4)[b]
OSA risk (STOP-BANG)	
Low/moderate risk	74.2
High risk	25.8
OSA risk (STOP-BANG)	
Low	49.6
Moderate	24.6
High	25.8
OSA risk (STOP)	
No	73.4
Yes	26.6
STOP score	
0	36.4
1	37.1
2	19.4
3	5.9
4	1.4
OSA risk (OSA-50)	
No	57.4
Yes	42.6
Diabetes	13.1
Cancer	9.6
EDS	22.9
Depression	17.1
CVD (no stroke)	6.1
Stroke	2.5

Abbreviation: BMI, body mass index; CVD, cardiovascular disease; EDS, excessive daytime sleepiness; FPIR, family-to-poverty income ratio; GED, General Education Development; OSA, obstructive sleep apnea; STOP-BANG, snoring, tired, obstructed, pressure, body mass index, age, neck, gender.
[a]Median (interquartile range).
[b]Mean (SD).

snoring (3 points); stopping breathing (2 points); and age (≥ 50 years, 2 points). The score ranges from 0 to 10, and those with scores ≥ 5 were considered to have high sleep apnea risk. With a score of ≥ 5, the OSA-50 has been shown to have a sensitivity of 100% and specificity of 29% to detect moderate-to-severe OSA (Chai-Coetzer et al., 2011).

2.4 | Health outcomes and mortality

2.4.1 | EDS, depression, CVD and stroke

Health outcomes (referred to as chronic conditions hereafter except EDS) were based on self-reported questionnaire. To quantify EDS, participants were asked: "In the past month, how often did you feel excessively or overly sleepy during the day?", with possible responses: "never", "rarely—1 time a month", "sometimes—2–4 times a month", "often—5–15 times a month", and "almost always—16–30 times a month". Those who reported "almost always—16–30 times a month" were considered to have EDS. Depression was assessed using the Patient Health Questionnaire-9, a short questionnaire based on nine questions with four possible responses, and a maximum score of 27 (Kroenke et al., 2010). Those with scores > 5 were classed as prevalent depression cases (Kiely & Butterworth, 2015). CVD was a composite variable determined on questions: "Has a doctor or other health professional ever told you that you had…?" with the following four conditions: (1) congestive heart failure; (2) coronary heart disease; (3) angina/angina pectoris; (4) heart attack (also called myocardial infarction). Participants who reported any of these conditions were considered having CVD. Stroke was assessed using a question: "Has a doctor or other health professional ever told you that you had stroke?"

2.4.2 | All-cause mortality

The US mortality registry was linked with NHANES data using a probabilistic record linkage (Center for Disease Control and Prevention, 2022). Mortality data were updated to 2019 for all waves.

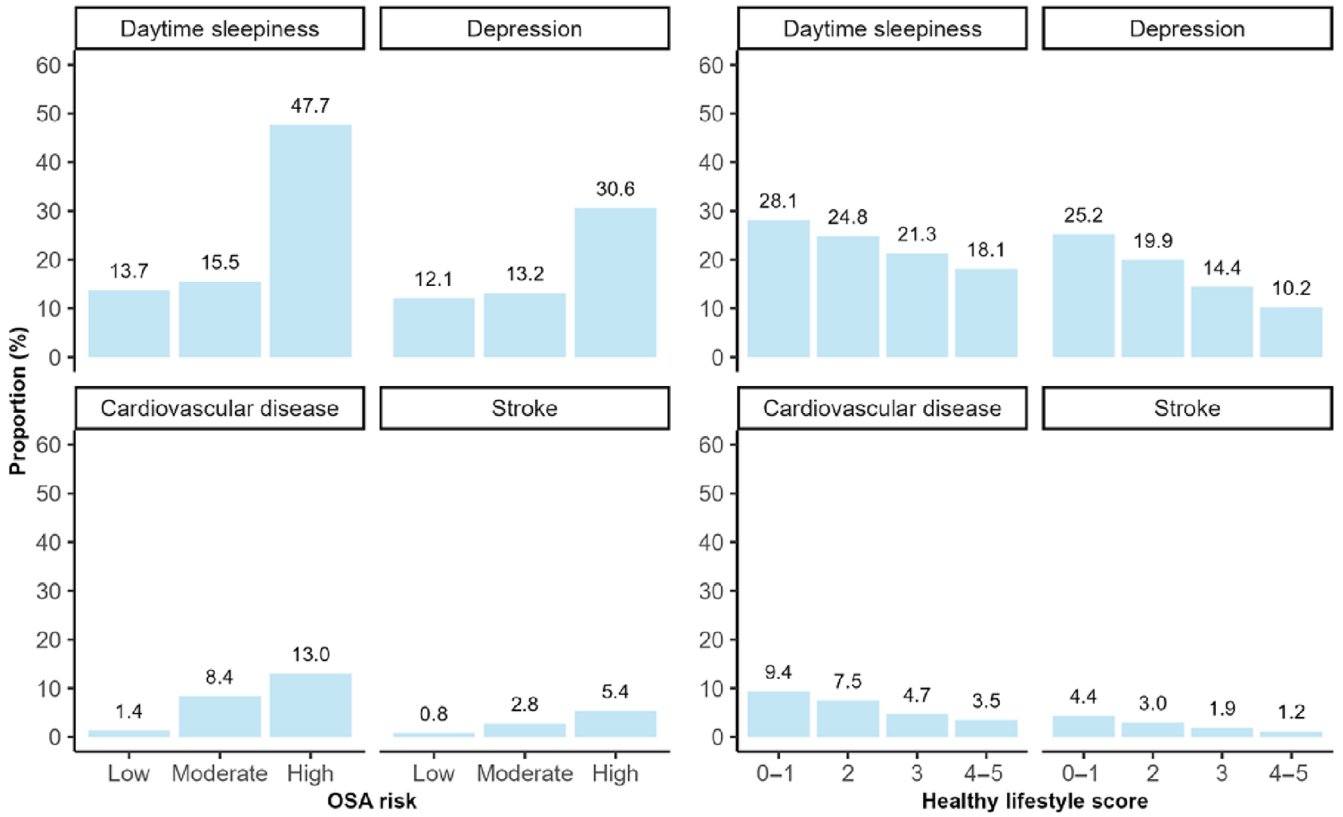

FIGURE 2 Prevalence of excessive day time sleepiness (EDS), depression, cardiovascular disease (CVD) and stroke by obstructive sleep apnea (OSA) risk and healthy lifestyle score (linear trend test [M^2] for all, $p < 0.001$).

2.5 | Statistical analysis

Complex survey design using NHANES-assigned weights, population sampling units and strata were applied to all analyses. Proportion (categorical), mean (SD; continuous and symmetrical) and median (interquartile range; continuous and asymmetrical variables) were used to summarise variables. Chi Square for Trend test (M^2) was used to determine prevalence trend of chronic conditions (depression, CVD and stroke) and EDS across OSA risk and healthy lifestyle scores.

2.5.1 | Cross-sectional analyses

The generalised linear model (GLM) with quasi-binomial function and logit link was used to estimate the independent and joint association of OSA and healthy lifestyle with EDS, depression, CVD and stroke. Two models were constructed: Model 1 was adjusted for age (continuous), sex, educational level (less than high school, high school diploma, and more than high school), marital status (married/living with partner, widowed, divorced, separated, never married), family-to-poverty income ratio (FPIR, continuous) and race (Non-Hispanic White, Non-Hispanic Black, Mexican American, Other Hispanic, Other Race–including Multi-Racial); Model 2 was additionally adjusted for sleep duration (continuous, hours), cancer (yes or no), diabetes (yes or no), and mutual adjustment for the outcome variables (EDS, depression, CVD and stroke [yes or no]). A detailed description of covariates is provided in Table S4. Assumptions and confounding selection of these two models are depicted in simple direct acyclic graphs (DAGs; Figures S1 and S2). In the first model (Model 1), we assumed that other chronic conditions, sleep duration and OSA risk/healthy lifestyle were mediators. In Model 2, chronic diseases and OSA risk/healthy lifestyle were considered as confounding factors. Model 2 was also used to determine association of individual components of healthy lifestyle (healthy diet, optimal alcohol intake, physical activity, not smoking and normal BMI) with chronic conditions and EDS in high-risk OSA group. For each component model, additional adjustment was made by creating scores of the components except the component of interest.

For both Model 1 and Model 2, inverse probability of treatment weighting (IPTW; Robins, 1986) was applied to balance the distribution of confounding by weighting each participant using the inverse probability. In this study, we considered both binary exposure for OSA risk (low/moderate risk versus high risk or low and moderate/high risk) and multiple exposure categories for healthy lifestyle scores (ranging from most unhealthy to most healthy) and OSA risk (low, moderate and high). The IPTW method was adapted to balance the distribution of confounding variables across these various exposure groups. Each participant was weighted using the inverse probability of belonging to their specific exposure category—either for OSA risk or healthy lifestyle score.

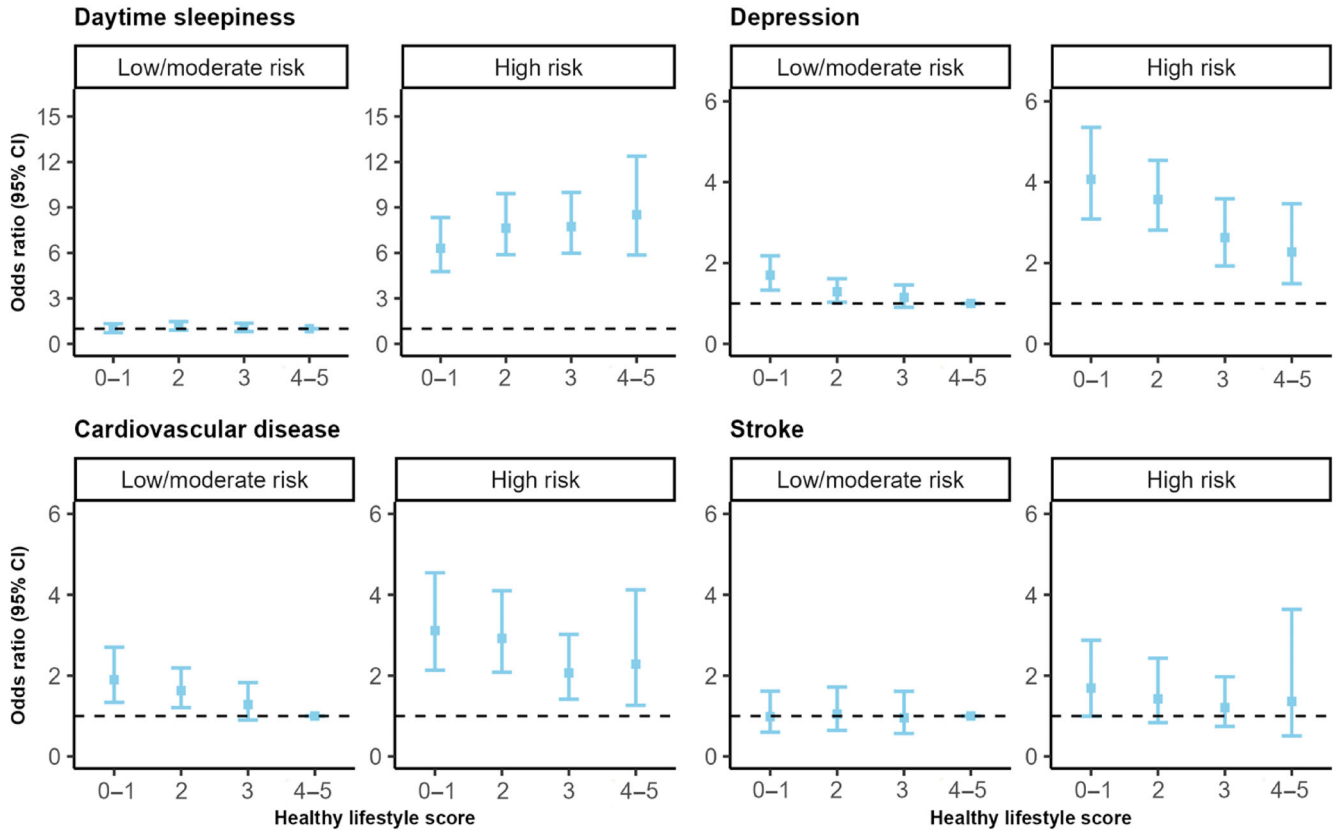

FIGURE 3 Joint association of obstructive sleep apnea (OSA) risk (low/moderate versus high risk) and healthy lifestyle score (0–1 [minimum] to 4/5 [maximum]) with excessive day time sleepiness (EDS), depression, cardiovascular disease (CVD) and stroke. The model was adjusted for age, sex, race, marital status, education, income, cancer, diabetes, sleep duration and mutual adjustment of outcomes (EDS, depression, CVD and stroke). Reference group was low/moderate OSA risk and 4–5 (maximum) healthy lifestyle score.

Working under the assumption that all relevant confounders have been measured and included, IPTW aims to create a "*pseudopopulation*" where these confounders are balanced across the different exposure categories. We calculated weights as the average treatment effect across the entire population, which were then stabilised to mitigate the influence of outliers. To verify the adequacy of our balancing approach, we computed the mean difference between post-IPTW exposure groups as a diagnostic measure. Our analysis indicated a mean difference of 1% or less (data not shown), suggesting that the balance was adequately achieved. IPTW was applied separately for each outcome. The estimates in this study reflect the average treatment effect in the entire population. We investigated the interaction between healthy lifestyle score and OSA risk by specifying a multiplicative term in Model 2, and an interaction test was performed using the likelihood ratio. Estimated associations were reported as odds ratios (ORs) and 95% confidence intervals (CIs). The *p*-value for trend was computed using healthy lifestyle score and OSA risk as continuous variables.

2.5.2 | Survival analyses

The joint association of OSA and healthy lifestyle with all-cause mortality was determined in all participants using linked mortality data that cover a 15-year period. Further, the association between healthy lifestyle and all-cause mortality was determined in subsets of participants with moderate/high and high-risk OSA. A Cox regression model with age as the time scale was used to determine the association between healthy lifestyle score and all-cause mortality by computing the hazard ratios (HRs) and 95% CIs. Two models were constructed: Model 1 was adjusted for age, sex, educational level, marital status, FPIR and race; Model 2 was additionally adjusted for sleep duration, cancer, diabetes, depression and CVD (including stroke). We also determined the association of individual components of healthy lifestyle score with mortality score in Model 2. Although age at baseline was the time scale in our model, we also utilised it as a confounding variable as it was demonstrated to generate a more robust estimate in previous work (Pencina et al., 2007). Figure S3 depicts our assumptions in DAGs for both Model 1 and Model 2. Similar to the cross-sectional analysis, we employed IPTW to achieve a balanced distribution of confounders. To account for differential censoring (Howe et al., 2016), we used stabilised inverse probability of censoring weighting (IPCW; Hernán & Robins, 2020) alongside survey weighting. The same set of confounding variables was utilised in both IPCW and IPTW methods. We used GLM with binomial function to calculate the probabilities of being uncensored. IPCW were truncated between 2.5% and 97.5% to avoid extreme weights.

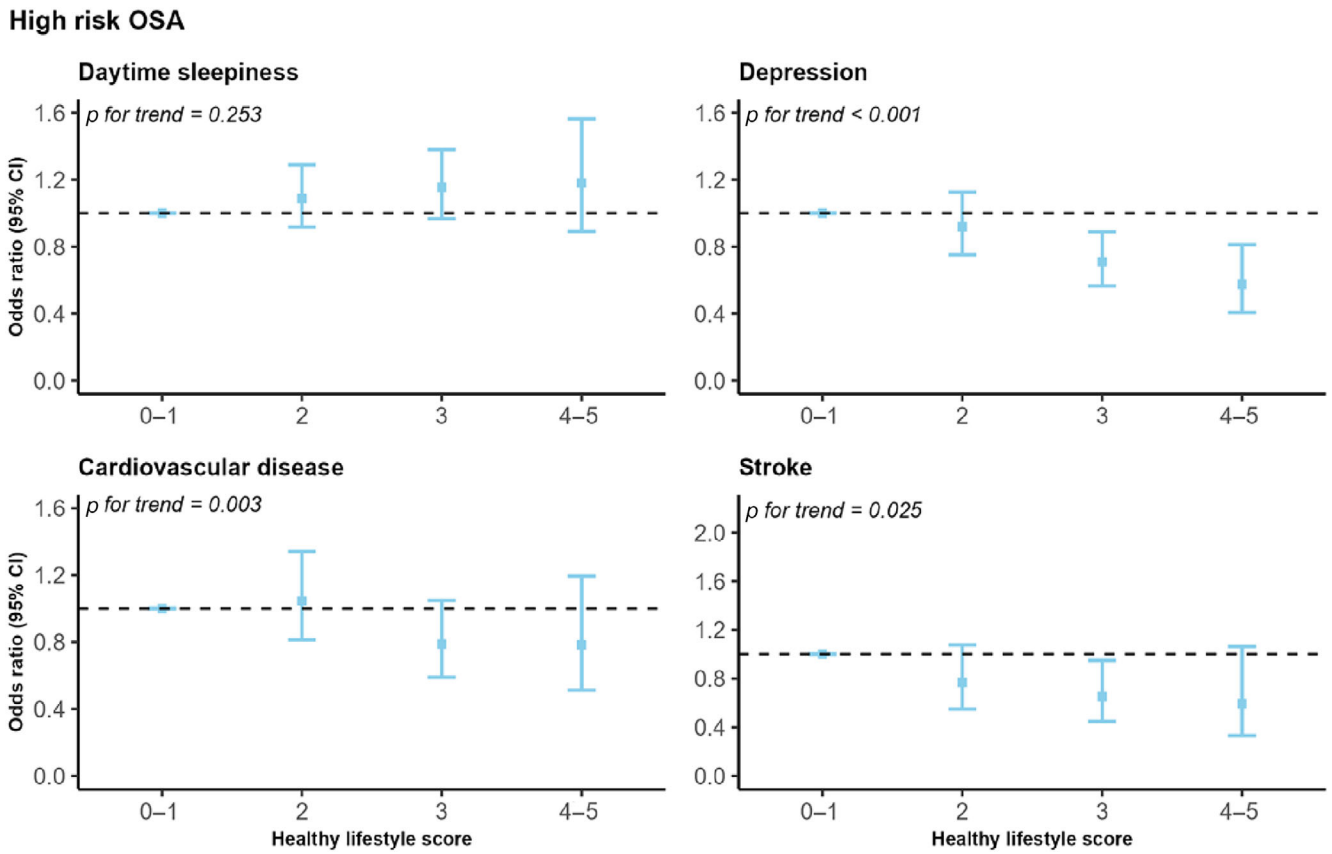

FIGURE 4 Association of healthy lifestyle score (0–1 [minimum] to 4/5 [maximum]) with excessive day time sleepiness (EDS), depression, cardiovascular disease (CVD) and stroke in those with high-risk obstructive sleep apnea (OSA). The model was adjusted for age, sex, race, marital status, education, income, cancer, diabetes, sleep duration and mutual adjustment of outcomes (EDS, depression, CVD and stroke). Reference group was lowest healthy lifestyle score (0).

2.6 | Sensitivity analysis

To evaluate the robustness of our results, we additionally used the STOP criteria (≥ 2; Chung et al., 2016) and scores from the OSA-50 (≥ 5; Chai-Coetzer et al., 2011) to define increased risk of OSA for both cross-sectional and survival analyses. In the main survival analysis, we removed participants who died in the first 2 years to limit potential reverse causation. In another sensitivity analysis, we excluded participants with chronic disease at baseline (cancer, diabetes, CVD and depression).

All analyses were conducted in R (version 4.2.1, R Foundation for Statistical Computing, Vienna, Austria). All *p*-values in this study refer to *p* for trend unless specified.

3 | RESULTS

3.1 | Characteristics of participants

Female participants comprised 50% of the sample. The median age of participants was 46 (IQR = 33, 59) years. More than a quarter (25.8%) of the participants had high OSA risk based on STOP-BANG. Based on STOP and OSA-50 criteria, 26.6% and 42.6% had high OSA risk, respectively. While 15.9% of participants had a lifestyle score of zero (most unhealthy) or 1, 18.9% had a score of 4 or 5 (most healthy). A third (32.7%) had a lifestyle score of 2. The prevalence of EDS, depression, CVD and stroke were 22.9%, 17.1%, 6.1% and 2.5%, respectively (Table 1).

3.2 | Association of OSA and healthy lifestyle with health outcomes

While EDS, depression, CVD and stroke prevalence tended to increase with increasing OSA risk, the prevalence of these chronic conditions/symptoms decreased with increasing healthy lifestyle score categories (linear trend test [M^2] for all, $p < 0.001$; Figure 2).

The OSA risk was positively associated with all chronic conditions, and demonstrated dose–response relationships ($p < 0.001$) in both Model 1 and Model 2 (Table 2). Healthy lifestyle score was inversely associated with all chronic conditions in Model 1 ($p < 0.001$). In Model 2, the results were similar to Model 1 ($p < 0.005$), except for EDS where there was no evidence of association ($p = 0.379$).

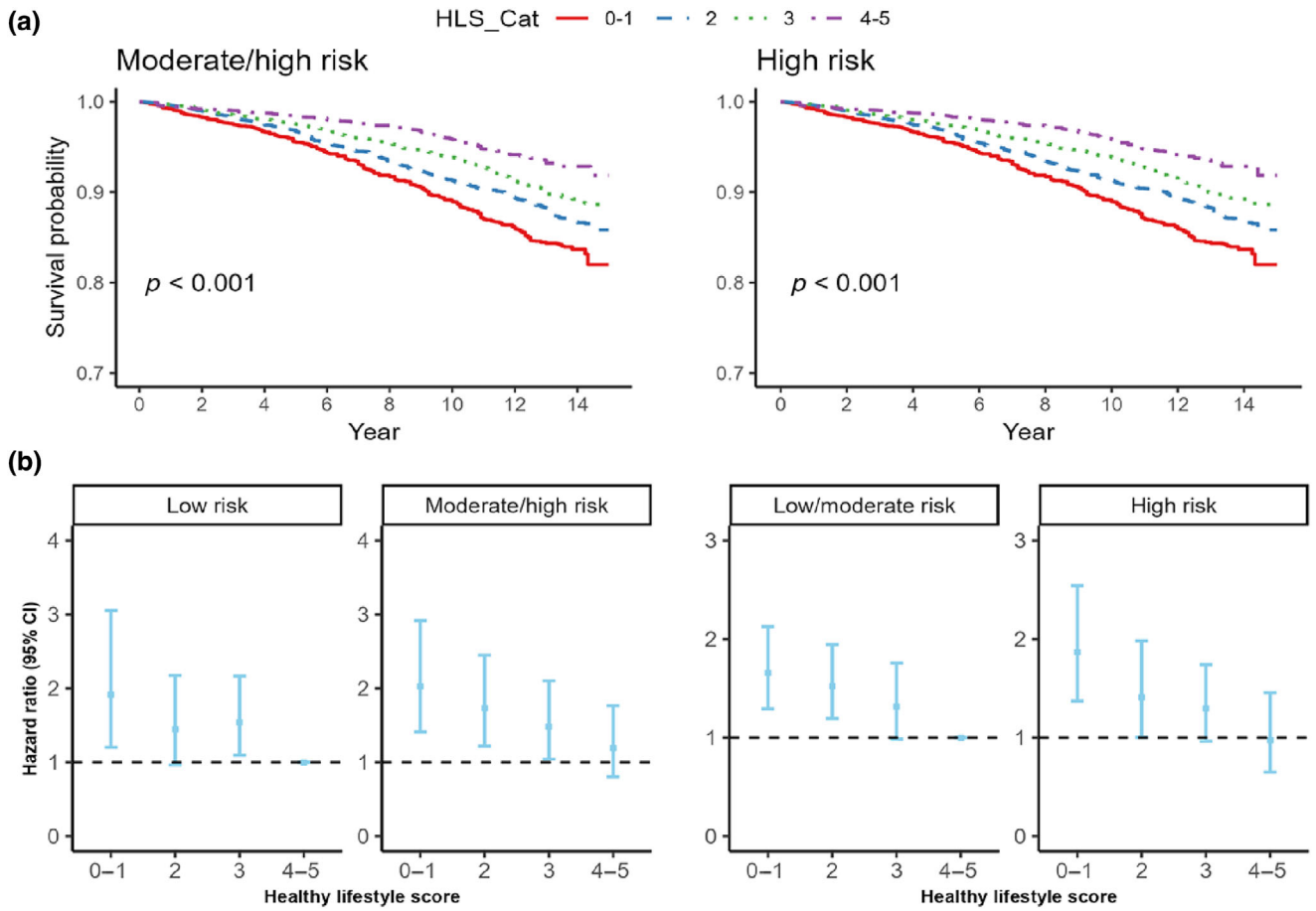

FIGURE 5 Kaplan–Meier figure depicting survival probability by healthy lifestyle score in moderate/high and high sleep apnea risk participants (a), and joint association of obstructive sleep apnea (OSA) risk (low versus high/moderate and low/moderate versus high risk) and healthy lifestyle score (0/1, the most unhealthy lifestyle to 4/5, most healthy) with all-cause mortality (b). HLS_Cat, healthy lifestyle score; OSA, obstructive sleep apnea. The model was adjusted for age, sex, race, marital status, education, income, cancer, diabetes, depression, cardiovascular disease (CVD; including stroke) and sleep duration.

3.3 | Joint association of OSA risk and healthy lifestyle with chronic conditions and EDS

When combining OSA risk with healthy lifestyle score (reference group: low/moderate OSA risk and 4 to 5 score of healthy lifestyles), we observed attenuated odds of depression and CVD with increased score of healthy lifestyle in the high OSA group (Figure 3; Table S5 for numerical results). This pattern of association was also found when we classified OSA risk into low and moderate/high risk (Figure S4). Restricting our analysis only for those who had moderate to high OSA risk, we found a reduction in odds of depression ($p < 0.001$), CVD ($p = 0.003$) and stroke ($p = 0.025$) with increased healthy lifestyle score (Figures 4 and S5; Table S6 for numerical results). We found that all components of healthy lifestyle except optimal alcohol intake were independently and inversely associated with chronic conditions and EDS (Table S7).

3.4 | Joint association of OSA risk and healthy lifestyle with all-cause mortality

There were a total of 1291 deaths (3 per 1000 person-years), of which 225 (1 per 1000 person-years) and 1066 (5.0 deaths per 1000 person-years), in the moderate to high OSA risk; and 513 (5.0 deaths per 1000 person-years) in the high OSA risk participants. In moderate/high and high OSA risk groups, there was a difference in crude survival probability by healthy lifestyle score (Figure 5a). No evidence of association with all-cause mortality was observed for moderate (HR = 1.08; 95% CI: 0.90, 1.30) or high (HR = 1.05; 95% CI: 0.87, 1.27) OSA risk relative to low OSA risk (data not shown). We did not observe a significant interaction between OSA risk and healthy lifestyle score in predicting all-cause mortality. We observed reduced risk of mortality with increased score of healthy lifestyle overall and for each of the categories of OSA risk, including the high

TABLE 2 Association of sleep apnea risk and healthy lifestyle score with EDS, depression, CVD and stroke

Outcome/Exposure	Model 1 OR	95% CI	Model 2 OR	95% CI
Daytime sleepiness				
OSA risk				
Low	1.00		1.00	
Moderate	2.62	2.20, 3.13	2.41	2.02, 2.88
High	12.6	10.9, 14.5	11.0	9.45, 12.8
p for trend	*< 0.001*		*< 0.001*	
Healthy lifestyle				
0–1	1.00		1.00	
2	0.95	0.84, 1.07	1.13	0.98, 1.30
3	0.75	0.67, 0.85	1.15	0.99, 1.34
4–5	0.57	0.49, 0.66	1.19	0.97, 1.47
p for trend	*< 0.001*		*0.376*	
Depression				
OSA risk				
Low	1.00		1.00	
Moderate	1.84	1.58, 2.14	1.43	1.21, 1.69
High	5.24	4.59, 5.99	3.32	2.74, 4.04
p for trend	*< 0.001*		*< 0.001*	
Healthy lifestyle				
0–1	1.00		1.00	
2	0.77	0.66, 0.89	0.80	0.69, 0.93
3	0.56	0.49, 0.64	0.67	0.59, 0.76
4–5	0.40	0.34, 0.47	0.58	0.46, 0.73
p for trend	*< 0.001*		*< 0.001*	
CVD				
OSA risk				
Low	1.00		1.00	
Moderate	1.88	1.42, 2.48	1.62	1.15, 2.30
High	3.79	2.90, 4.94	2.55	1.83, 3.56
p for trend	*< 0.001*		*< 0.001*	
Healthy lifestyle				
0–1	1.00		1.00	
2	0.86	0.71, 1.05	0.97	0.79, 1.19
3	0.61	0.50, 0.74	0.74	0.60, 0.92
4–5	0.40	0.31, 0.52	0.69	0.53, 0.89
p for trend	*< 0.001*		*< 0.001*	
Stroke				
OSA risk				
Low	1.00		1.00	
Moderate	1.73	1.15, 2.60	1.08	0.63, 1.83
High	3.45	2.33, 5.10	1.55	0.90, 2.66
p for trend	*< 0.001*		*0.093*	
Healthy lifestyle				
0–1	1.00		1.00	
2	0.75	0.59, 0.95	0.86	0.67, 1.11

(Continues)

TABLE 2 (Continued)

Outcome/Exposure	Model 1 OR	95% CI	Model 2 OR	95% CI
3	0.61	0.48, 0.77	0.78	0.60, 1.02
4–5	0.38	0.26, 0.56	0.70	0.47, 1.04
p for trend	*< 0.001*		*0.025*	

Note: Model 1: adjusted for age, sex, race, marital status, education and income. Model 2: additionally adjusted for cancer, diabetes, sleep duration and mutual adjustment of the exposures (sleep apnea risk and healthy lifestyle score) and outcomes (EDS, depression, CVD and stroke).
Abbreviation: CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio; OSA, obstructive sleep apnea.

TABLE 3 Associations of healthy lifestyle score with all-cause mortality in participants with moderate/high and high OSA risk

Exposure	Rate of death/1000 person-years	Model 1 HR	95% CI	Model 2 HR	95% CI
Overall	3.0				
Healthy lifestyle score[a]					
0–1	4.4	1.00		1.00	
2	3.3	0.82	0.71, 0.95	0.84	0.74, 0.95
3	2.6	0.71	0.60, 0.84	0.75	0.63, 0.88
4–5	1.8	0.49	0.39, 0.62	0.57	0.45, 0.72
p for trend		*< 0.001*		*< 0.001*	
Low OSA risk	1.00				
Healthy lifestyle score					
0–1	1.8	1.00		1.00	
2	1.2	0.82	0.52, 1.29	0.78	0.50, 1.22
3	1.1	0.74	0.42, 1.30	0.80	0.47, 1.34
4–5	0.7	0.53	0.29, 0.95	0.57	0.33, 0.98
p for trend		*< 0.001*		*< 0.001*	
Moderate/high OSA risk	5.0				
Healthy lifestyle score					
0–1	5.9	1.00		1.00	
2	4.9	0.83	0.71, 0.96	0.85	0.74, 0.98
3	4.6	0.70	0.59, 0.83	0.72	0.62, 0.85
4–5	4.8	0.52	0.40, 0.69	0.60	0.46, 0.78
p for trend		*< 0.001*		*< 0.001*	
High OSA risk	5.0				
Healthy lifestyle score					
0–1	6.2	1.00		1.00	
2	4.5	0.77	0.65, 0.92	0.77	0.64, 0.91
3	4.8	0.70	0.57, 0.85	0.70	0.57, 0.86
4–5	4.4	0.48	0.33, 0.70	0.56	0.39, 0.82
p for trend		*< 0.001*		*< 0.001*	

Note: Model 1: adjusted for age, sex, race, marital status, education and income. Model 2: additionally adjusted for cancer, diabetes, cardiovascular disease (including stroke), depression and sleep duration.
Abbreviation: CI, confidence interval; HR, hazard ratio; OSA, obstructive sleep apnea.
[a]Model 2 was additionally adjusted for OSA risk (low, moderate and high).

and high OSA groups (Figure 5b; Table S8 for numerical results). While physical activity and not smoking were independently and inversely associated with all-cause mortality in moderate/high and high OSA risk groups, normal BMI was positively associated with mortality risk in both groups (Tables 3 and S9).

All sensitivity analyses (using Model 2) made little or no difference to estimated associations of OSA risk/healthy lifestyle score with chronic conditions, EDS and all-cause mortality (Figures S6–S9 and Tables S10–S13).

4 | DISCUSSION

The findings of this study indicate that adherence to a healthier lifestyle (healthy diet, limited alcohol intake, adequate physical activity, not smoking and healthy BMI) is associated with reduced odds of chronic conditions, overall and in people at moderate and high risk of OSA. Similarly, a higher healthy lifestyle score is associated with lower risk of all-cause mortality in people at moderate and high risk of OSA. Sensitivity analyses confirmed that these results are consistent across multiple indicators of OSA risk.

4.1 | Strengths and limitations

Strengths of our study include a relatively large cohort of adults with comprehensive data collected on a wide range of lifestyle factors, linked mortality data and several sensitivity analyses that confirmed the main findings. However, there are several limitations. First, the potential for reverse causation must be acknowledged, as those with chronic conditions may be more likely to engage in less or more healthy behaviour in the cross-sectional analysis. We attempted to address this for morality with our sensitivity analysis excluding deaths in the first 2 years. Nonetheless, we acknowledge that this may not capture all reverse causation. Secondly, chronic conditions were self-reported; no objective assessment of these was performed, although participants reported that they were doctor-diagnosed. Third, OSA was not assessed using objective approaches; rather, risk of OSA was assessed based on a modified version of a widely used and standardised tool, the STOP-BANG. To confirm the primary findings, we used alternative definitions of OSA using two defined tools, STOP and OSA-50, which did not change the main findings. Fourth, the study used self-reported questionnaires to assess lifestyle factors (diet, height and weight, smoking, physical activity and alcohol intake), which could result in recall bias. Fifth, diet and alcohol intake were assessed based on using 24-hr recall method. Although this method is used widely in the literature, it may not reflect usual intake. Sixth, the study only investigated all-cause mortality, and there was no analysis of cause-specific mortality that may be more specific to OSA, for example, CVD mortality.

4.2 | Comparison with previous studies

The findings of the current study suggest that individuals with moderate to high risk of OSA have higher odds of chronic conditions. Additionally, there was a dose–response association between OSA risk and prevalent chronic conditions (depression, CVD and stroke) and EDS. The finding that individuals with moderate to high risk of OSA were more likely than those with low OSA risk to have chronic conditions is consistent with previous research (Dong et al., 2013; Jehan et al., 2018; Povitz et al., 2014). In parallel, the current study highlights low prevalence of chronic conditions associated with higher adherence to healthy lifestyle. Although there is limited prior evidence, several studies (Dissanayake et al., 2021; Dobrosielski et al., 2017; Mitra et al., 2021) have indicated that adopting a healthy lifestyle can help reduce chronic conditions linked with OSA. The lack of association between healthy lifestyle score and EDS in our study may suggest that other factors, such as OSA severity, may play a more prominent role in the development of EDS.

The current study also found that all components of healthy lifestyle, except alcohol intake ≤ 1 drink for females and ≤ 2 drinks for males per day, were independently associated with reduced odds of chronic conditions and EDS, overall, and for moderate to high OSA risk participants. Studies that have attempted to investigate the individual role of these five components of healthy lifestyle on chronic conditions are scarce. One study reported a correlation between protein and vitamin B6 consumption and metabolic markers, including fasting glucose levels, in people with OSA (Stelmach-Mardas et al., 2016). However, the study did not examine other factors like overall dietary quality, exercise, smoking, BMI or alcohol consumption. In another study, a synergistic effect was observed between smoking and OSA on metabolic disorder parameters (Zhu et al., 2017). The lack of association between alcohol consumption and chronic health conditions in participants with high to moderate OSA risk in our study could be attributed to measurement error. Our study utilised alcohol intake data derived from a 24-hr recall method, which may not accurately reflect individuals' typical drinking habits.

While we found that healthy lifestyle may reduce all-cause mortality overall, and in individuals with moderate/high and high OSA risk, there was no significant association between moderate and high OSA risk and all-cause mortality. These findings are consistent with previous studies that have shown the beneficial effects of a healthy lifestyle to reduce mortality risk in the general population (Sun et al., 2021). Our study also found that all components of a healthy lifestyle, except normal BMI, were independently and inversely associated with all-cause mortality in moderate/high and high OSA risk groups. BMI within the normal range was positively associated with mortality risk in both groups. This might be due to reverse causation whereby participants who were already sick had lost weight and were in the normal BMI category rather than overweight or obese (Flegal et al., 2011). The findings underscore the potential importance of maintaining a healthy lifestyle, including regular physical activity, a healthy diet, non-smoking and moderate alcohol consumption, to reduce mortality risk in individuals with moderate and high OSA risk.

4.3 | Potential mechanisms

Adopting a healthy lifestyle that includes regular exercise and a balanced diet can help reduce the risk of chronic conditions and mortality

in patients with OSA through different physiological mechanisms, including reduced adiposity, inflammation and increased muscle strength (Kaleelullah & Nagarajan, 2021; Piovezan et al., 2022). Exercise and healthy diet can improve cardiovascular health by reducing blood pressure, improving blood glucose control and reducing inflammation, while a healthy diet can reduce inflammation and improve metabolic function, both of which can reduce the risk of CVD (Georgoulis et al., 2021; Yacoub et al., 2017) in patients at high risk of OSA. Furthermore, smoking and high alcohol intake can exacerbate the effects of OSA on the cardiovascular system and increase the risk of depression and stroke through increased upper airway collapsibility (Kim et al., 2012; Mitler et al., 1988), highlighting the potential importance for people with OSA to quit smoking and limit alcohol intake.

Depression is also a common condition in people with OSA, as the repeated episodes of breathing cessation can lead to fragmented sleep, daytime fatigue and cognitive impairment (Ejaz et al., 2011). Regular exercise has been shown to improve mood and reduce symptoms of depression (Heissel et al., 2023), while a healthy diet can improve brain function and support mental health (Gutierrez et al., 2021; Quirk et al., 2013). Moreover, stroke is a potential complication of OSA, as the repeated drops in oxygen levels during sleep can damage blood vessels in the brain due to repetitive oxidative stress and inflammation (Jehan et al., 2018). By adopting a healthy lifestyle that includes regular exercise, a balanced diet and smoking cessation, people with OSA may reduce the risk of stroke and increase their chances of survival. The mechanism behind this is that healthy lifestyle choices can maintain normal weight, improve oxygenation, reduce inflammation, and support cardiovascular and metabolic health, all of which can reduce the risk of complications in people with OSA (Dobrosielski et al., 2017).

4.4 | Significance

The findings of this study may have important implications for the management and prevention of chronic conditions among individuals with moderate to high risk of OSA. Clinicians should support people with moderate to high OSA risk to adopt a healthy lifestyle, including healthy diet, limited alcohol intake, physical activity, not smoking, and maintaining a healthy BMI to reduce the risk of chronic conditions and all-cause mortality. Treatment plans for people with OSA should include lifestyle interventions beyond typical reliance on weight loss advice as an important component to improve health outcomes and improve survival rates.

5 | CONCLUSIONS

In these relatively large cross-sectional and survival analyses of US adults, while higher OSA risk was associated with increased odds of chronic conditions (depression, CVD and stroke), adhering to more healthy lifestyle behaviours was associated with decreased prevalence of these conditions. A higher number of healthy behaviours was associated with lower mortality risk in those with moderate and high risk of OSA. These findings have implications for clinical practice and public health, and emphasise the importance of promoting healthy lifestyles in individuals with OSA. Emerging evidence (Dobrosielski et al., 2017; Melaku et al., 2022) suggests that the incorporation of a healthy dietary pattern and regular physical exercise may offer promising avenues for the management of OSA and associated adverse health outcomes. Further investigation that includes objective assessment of OSA and prospective investigation of chronic conditions is warranted to confirm our findings.

Given the potential benefits of lifestyle interventions in the management of OSA and other chronic conditions (Carneiro-Barrera et al., 2019; Dobrosielski et al., 2017; Heissel et al., 2023; Kaleelullah & Nagarajan, 2021; Melaku et al., 2022), there is a need for large-scale randomised controlled trials to investigate their efficacy and inform clinical practice. Trials could explore the optimal type, frequency and duration of lifestyle interventions, as well as their effects on OSA-related outcomes, such as sleep quality, daytime function and quality of life. Additionally, investigating the potential mechanisms underlying the beneficial effects of lifestyle interventions could aid in the development of targeted interventions, and enhance our understanding of the pathophysiology of OSA and related conditions.

AUTHOR CONTRIBUTIONS

Yohannes Adama Melaku: Conceptualization; methodology; software; data curation; formal analysis; visualization; writing – review and editing; writing – original draft. **Sarah Appleton:** Conceptualization; writing – review and editing; methodology; supervision. **Amy Reynolds:** Conceptualization; writing – review and editing; methodology; supervision. **Roger Milne L:** Writing – review and editing; methodology; supervision. **Brigid Lynch M:** Methodology; writing – review and editing; supervision. **Danny Eckert J:** Methodology; conceptualization; writing – review and editing; supervision. **Robert Adams:** Conceptualization; methodology; writing – review and editing; supervision.

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CONFLICT OF INTEREST STATEMENT

Other authors declare no conflicts of interest. Outside the submitted work, DJE has had research grants from Bayer, Takeda, Invicta Medical, Apnimed, Eli Lilly and Withings and has served on Scientific

Advisory Boards or as a consultant for Apnimed, Invicta, Mosanna, Takeda and Bayer

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in NHANES at https://www.cdc.gov/nchs/nhanes/index.htm. These data were derived from the following resources available in the public domain: CDC/NHANES, https://www.cdc.gov/nchs/nhanes/index.htm.

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SUPPORTING INFORMATION

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

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