Am J Transl Res 2026;18(1):265-276
www.ajtr.org /ISSN:1943-8141/AJTR0170131

Original Article

The association between cardiovascular health, measured using Life's Essential 8, and obstructive sleep apnea: a cross-sectional and Mendelian randomization study

Hong Zhai[1*], Zhouyan Lin[1*], Minshu Ao[1*], Can Wang[1], Qingxuan Fan[1], Ziyan Yu[2], Feng Wen[2], Binxuan Zhang[2], Min Qian[2], Wei Zhang[1*], Yuchao Dong[1*], Meng Guo[2*], Chong Bai[1*]

[1]Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Naval Medical University, Shanghai, China; [2]National Key Laboratory of Immunity and Inflammation & Institute of Immunology, Navy Medical University, Shanghai, China. [*]Equal contributors.

Received November 20, 2025; Accepted December 6, 2025; Epub January 15, 2026; Published January 30, 2026

Abstract: Background: Cardiovascular health (CVH), operationalized using the Life's Essential 8 (LE8) construct, has been linked to a myriad of health outcomes. Although there is a link between CVH and Obstructive Sleep Apnea (OSA), which has become a significant public health issue, a thorough investigation of this relationships has not been undertaken. Methods: This study investigates the association between CVH, quantified according to the LE8 construct, and OSA using data from the National Health and Nutrition Examination Survey (NHANES). Based on data from the NHANES (2005-2008, 2015-2018), this study consisted of 9,350 adults aged 20-79 years. Logistic regression analysis is utilized to determine the association between LE8 scores and OSA. Two-sample Mendelian randomization (MR) is used to investigate the causal relationship between CVH and OSA with the inverse-variance weight (IVW) method being the primary source of analysis. Results: The connection between CVH and OSA risk was affirmed, with individuals who had better CVH (high LE8 vs. low LE8), being at significantly lower risk for OSA than those with worse CVH (Odds Ratio [OR]: 0.23, 95% confidence interval [CI]: 0.18-0.30). Additionally, patients with higher LE8 scores experienced a decreased risk of OSA in a manner that was dose-dependent. The MR analysis also provided evidence of a positive correlation between BMI (genetically determined) and increased risk for OSA (OR for 1 Standard Deviation [SD] increase = 2, 95% CI: 1.81-2.21). Additionally, individuals who smoked less and exercised more showed decreased risk of OSA with respect to smoking (OR = 0.5, 95% CI: 0.32-0.79) and exercise (OR = 0.73, 95% CI: 0.54-0.99). Conclusions: This study highlights the importance of keeping CVH in good shape (as measured by the LE8 score) to lower the risk of developing OSA.

Keywords: Obstructive sleep apnea, cardiovascular health, Life's Essential 8, NHANES, Mendelian randomization

Introduction

There are many ways to identify obstructive sleep apnea (OSA) which is complex in nature, yet a highly common condition, where a person will have repeated interruptions in their breathing or shallow breathing while they sleep [1, 2]. OSA can be diagnosed using multiple techniques and may be associated with a number of different cardiovascular diseases (CVD) [3]. Studies have shown that many people with OSA go undiagnosed, even though it affects a large number of people [4]. Approximately 13%-33% of adult men and approximately 6%-19% of adult women within the United States have OSA [5-7], which represents almost 1 billion people around the world [8]. Society also incurs significant costs associated with OSA, beginning from the time before an individual is diagnosed with OSA when they will lose out on potential earnings, to the time after they have been successfully treated for OSA. This is indicative of the need for improved awareness and early detection of OSA, as well as more effective management practices for improved health and reduced healthcare costs associated with OSA [9].

https://doi.org/10.62347/VVAT2613

There is strong evidence that OSA is an independent risk factor for hypertension [10], diabetes mellitus [11], and CVD [3]. In 2010, Life's Simple 7 (LS7) [12] introduced by the American Heart Association (AHA) identified seven important factors affecting heart health: Diet, Smoking, Body Weight (BMI), Physical Activity, Blood Pressure, Fasting Blood Sugar [13, 14] and Cholesterol Levels. Some of these factors, including Blood Pressure, Fasting Blood Glucose [15] and BMI [16], have a two-way relationship with OSA, demonstrating that the impact of one condition can affect another and vice versa. Subsequent studies have demonstrated the presence of a strong association between OSA and LS7 scores [17]. In 2022, the AHA expanded upon LS7 with Life's Essential 8 (LE8) [1] to promote further improvement in heart health. The higher one's LE8 scores, the better the health outcomes (e.g., Reduced CVD Rates, Reduced Rates of Other Major Illnesses, Reduced Rates of Total Mortality) [18-20]. Given the close link between OSA and cardiovascular health, strategies that improve components of the LE8 construct may play an important role in reducing OSA risk. However, the connection between LE8 scores and OSA needs to be thoroughly researched, which provides an opportunity for future study.

In the current research, we examined substantial datasets from the National Health and Nutrition Examination Surveys (NHANES) and Genome-Wide Association Studies (GWAS) performed by the United Kingdom Biobank (UKB). A primary focus was assessing how LE8 score levels at baseline (based on health behaviours and health risk factors, etc.) relate to the development of OSA. We also examined both linear and nonlinear associations of LE8 score levels with the incidence of OSA. Finally, we employed Mendelian Randomization (MR) to establish a cause-and-effect relationship between LE8 score levels and the development of OSA.

Method and materials

Study design and population in NHANES

For this investigation we utilized data from the National Health and NHANES, collected by the Centers for Disease Control and Prevention (CDC) and National Center for Health Statistics (NCHS) for the years 2005-2008 and 2015-2018. The NHANES methodology is based on a stratified, multistage method of sampling a representative population of the United States who are not currently institutionalized. In order to ensure that we provided a complete and comprehensive account of our research, we followed the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) guiding principles.

Adults aged 20 years or older were included from the NHANNES surveys (2005-2008 and 20152018). Our inclusion criteria were purposely broad to include as many people as possible. We excluded a large number of participants for a variety of reasons. For example, participants who were missing demographic information (age, gender, race/ethnic group, poverty income ratio (PIR), pregnant women (n=518), did not have data on Obstructive Sleep Apnea (2,047 individuals), missing LE8 data (7,408), and missing CVD data (2 individuals), etc. Exclusions a total of 30,372 individuals, providing us with 9,350 subjects for the analysis (**Figure 1**). This was done in order to have a quality dataset to work from.

Measurement of LE8 in HNANES

In this study, we measured LE8 based on the American Heart Association's Presidential Advisory guidelines [2], as shown in Table S1. The LE8 construct is used to operationalize cardiovascular health according to AHA guidance by considering four health behaviors - diet, physical activity, tobacco use, and sleep - and four health factors - BMI, non-HDL cholesterol, blood glucose, and blood pressure. Each of these indicators is scored from 0 to 100, with higher scores meaning better health [1]. To calculate the total LE8 score for an individual, we take the mean of the eight component scores; therefore, an individual can have a total LE8 score that has both a continuous and categorical value associated with it based on the AHA-defined cut-off values of 50 and 79 to determine CVH categories of low, moderate, or high CVH results based on the mean scoring of all eight components [1]. As an example, for assessing diet we used the 2015 Healthy Eating Index (HEI) [21], with scoring information in Table S2, and blood glucose control was assessed via glycated hemoglobin (HbA1c) levels as part of the LE8 score assessment process.

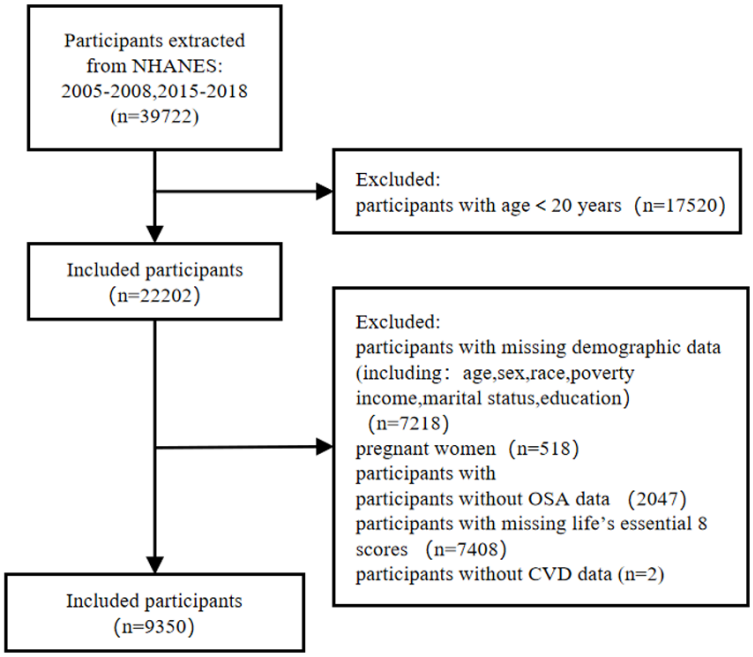

Figure 1. Selection of participants in the study. OSA, obstructive sleep apnea; NHANES, national health and nutrition examination survey; CVD, cardiovascular disease.

Measurements and definition of OSA in NHANES

This research was conducted using NHANES data, with the objective of clarifying what we meant by OSA and diagnosing it accurately. We determined whether or not individuals were diagnosed with OSA based on their answers to three distinct questions concerning common symptoms associated with OSA [22]. OSA was defined as meeting any of the following criteria: (1) Frequency of snoring - occurs at least 3 times per week; (2) Witnessed apneas - happening at least 3 times per week; (3) Excessive daytime sleepiness - experienced 16-30 times per month, when getting an average of 7 hours or more of sleep every night during the week and/or while working.

Mendelian randomization

Our analysis of the interplay of modifiable risk factors in Life's Essential 8 with OSA involved performing an extensive two-sample MR analysis [23]. Using SNPs as instruments and analyzing both genetic and environmental information, we tested the risk factors with the appropriate SNPs [24]. We established that our results were robust by following the three assumptions of MR: (1) SNPs must strongly associate with the risk factors, (2) SNPs must not be confounded by any external issues that would alter the exposure-outcome relationship, and (3) all manipulations from SNPs. We used selected genetic variants as instruments to perform our analyses, as previously performed by UKB, for this study.

Detailed descriptions of how these genetic instruments were created and applied can be reviewed in the Supplementary Information sections with complete lists shown in Tables S3, S4, S5, S6, S7, S8, S9, S10. The GWAS on which our analyses were based on OSA was obtained from the Finnish National Genome Project (FinnGen), following protocols established by the Global Alliance for Genomics and Health. This database includes a total of 217,955 people, with 16,761 OSA cases and 201,194 controls, for an available set of 16,380,465 SNPs for analysis. The diagnosis of OSA was made using ICD-10 code G47.3 and ICD-9 code 3472A and based on clinical diagnosis of symptoms and additionally confirmed using clinical exams and polysomnography [25].

Statistical analysis in a cross-sectional study

Using sample weights, clustering and stratification allowed us to make sure that our estimates were representative of the total U.S. population based on the complicated sampling designs used in NHANES. Categorical data presented as weighted percentages and continuous data presented as averages, with 95% CIs providing an indicator of the accuracy of our results. To compare the characteristics of NHANES participants, we used Rao-Scott chi-square testing and linear regression analysis without adjustment to provide a complete picture of the demographic and clinical factors related to CVH and to calculate unadjusted rates of CVH categories based on the overall population.

Using survey weighted logistic regression models allowed us to evaluate the relationship between OSA and LE8 Scores. Models 1-3 provide different levels of adjustment based on multiple covariates; Age, Gender, Race & Ethnicity in Model 1; Socioeconomic Variables (Poverty Ratio, Education and Marital Status) in Model 2; CVD and Obesity in Model 3. In addition, restricted cubic splines helped determine possible non-linear relationships between LE8 scores (and their individual components) and OSA, and we conducted likelihood ratio tests to evaluate those relationships for non-linearity.

Also notable is that we performed subgroup analyses concerning demographic characteristics of each study participant to assess if CVH has different effects on OSA in each of these subgroups, including exploration of interaction terms to assess how these groups interact collectively. Statistical tests were conducted bilaterally (two-sided) and were computed using R software, Version 4.2.1. All statistical results were thought to be statistically significant when *P* values were less than 0.05.

Statistical analysis in Mendelian randomization study

The main analysis was conducted using the IVW method with a random effects model to account for heterogeneity (or variances) among genetic tools used in the analyses [26]. To strengthen the findings from the IVW analysis further, we also performed additional analysis using both MR-Egger and weighted median methods [27]. To check that our genetic instruments were consistent, we tested for SNP variability using Cochran's Q tests [28]. In addition to these methods, we further verified by ruling out the effect of directional pleiotropy from genetic instruments, we conducted an MR-Egger regression where we examined the intercept value in order to assess potential confounding factors associated with genetic risk factors that might influence health through alternate pathways not assessed in this study. We utilized Cochran's Q statistic to estimate the degree of heterogeneity in the IVW MR framework and defined a statistically significant finding for each SNP to be any resultant Cochran's Q statistic with a *P* value less than 0.05.

Results

Baseline characteristics

The study sample consisted of 9,350 individuals aged 20 years and older who were separated by OSA status based on the demographic results presented in **Table 1**. The mean age of the participants was 47.75 years (Standard Error [SE]: 0.37), of which 52.11% were female (weighted percentage). The mean LE8 score across all participants was 67.81 (95% CI: 67.39-68.23), with the percentage of CVH levels classified as high being 34.84%, moderate being 50.48%, and low being 14.68%. Approximately 29.1% of individuals in the sample were diagnosed with OSA, resulting in a total of 2,993 participants with a diagnosis of OSA.

In comparing both groups together, we see that the individuals who had OSA were predominantly male, had a lower educational level than those without OSA, were more often in supportive relationships, and had a higher prevalence of cardiovascular disease and obesity when compared to those who did not suffer from OSA. However, despite these differences, there was no significant difference in physical activity between the two groups, as shown in **Table 1**.

Higher LE8 scores are associated with a lower prevalence of OSA

After adjusting for age, we found a clear negative relationship between OSA prevalence and CVH levels, as measured by the LE8 score. The results showed a big difference in OSA rates across the CVH categories: people with high CVH had a much lower OSA rate of 16.2% (95% CI: 14.6-17.8), compared to 31.1% (95% CI: 29.8-32.4) in the moderate CVH group and 48.4% (95% CI: 43.7-53.0) in the low CVH group (**Figure 2**).

Our analysis confirmed that people with better cardiovascular health (CVH) were much less likely to have OSA. Those with moderate CVH had an Odds Ratio (OR) of 0.52 (95% CI: 0.45-0.63), and those with high CVH had an OR of 0.23 (95% CI: 0.18-0.30), compared to people with low CVH (**Table 2**). When we looked at how the LE8 score impacted OSA, we found that for every 10-point increase in the LE8 score, the chances of having OSA went down significantly (OR: 0.72, 95% CI: 0.68-0.76), as shown in

Table 1. Baseline characteristics of the study population

	Overall (n = 10300)	Non OSA (n = 7307)	OSA (n = 2993)	*P* value
Age, years	47.75±0.37	47.47±0.40	48.40±0.45	0.03
Age strata				<0.0001
20-39	3291 (34.21)	2469 (36.22)	822 (29.48)	
40-59	3449 (40.36)	2253 (37.62)	1196 (46.83)	
≥60	3560 (25.43)	2585 (26.16)	975 (23.69)	
sex				<0.0001
Female	5249 (52.11)	3900 (55.41)	1349 (44.30)	
Male	5051 (47.89)	3407 (44.59)	1644 (55.70)	
Race/ethnicity				0.19
Black	2056 (9.79)	1464 (9.81)	592 (9.74)	
White	4926 (72.87)	3470 (72.49)	1456 (73.79)	
Mexican	1738 (7.27)	1268 (7.62)	470 (6.44)	
Others	1580 (10.06)	1105 (10.08)	475 (10.03)	
Poverty ratio				0.57
<1.3	4101 (36.48)	2889 (36.27)	1212 (36.98)	
1.3-3.5	2818 (17.30)	2038 (17.58)	780 (16.65)	
>3.5	3381 (46.22)	2380 (46.15)	1001 (46.37)	
Education levels				<0.0001
High school or less	4950 (38.44)	3488 (37.31)	1462 (41.12)	
Some college or associates degree	2952 (31.43)	2044 (30.85)	908 (32.77)	
College graduate or above	2398 (30.13)	1775 (31.84)	623 (26.10)	
Marital status				<0.0001
Coupled	7886 (80.28)	5472 (78.58)	2414 (84.31)	
Single or separated	2414 (19.72)	1835 (21.42)	579 (15.69)	
LE8 scores (out of 100 possible points)	67.81±0.42	69.71±0.41	63.31±0.51	<0.0001
HEI-2015 diet score	38.96±0.81	40.06±0.86	36.35±0.86	<0.0001
Physical activity score	68.74±0.79	69.39±0.92	67.18±1.17	0.11
Nicotine exposure score	70.16±0.79	72.25±0.80	65.23±1.14	<0.0001
Sleep health score	84.02±0.46	85.57±0.44	80.35±0.76	<0.0001
Body mass index score	61.25±0.66	66.13±0.66	49.72±0.91	<0.0001
Blood lipids score	63.49±0.37	64.98±0.44	59.99±0.68	<0.0001
Blood glucose score	86.91±0.40	88.34±0.44	83.54±0.62	<0.0001
Blood pressure score	68.93±0.45	70.95±0.48	64.14±0.68	<0.0001
CVH				<0.0001
High	3162 (34.84)	2559 (40.01)	603 (22.61)	
Moderate	5319 (50.48)	3661 (47.92)	1658 (56.54)	
Low	1819 (14.68)	1087 (12.07)	732 (20.85)	
Health behaviors score	65.47±0.59	66.82±0.59	62.28±0.74	<0.0001
Health factors score	70.15±0.33	72.60±0.34	64.35±0.44	<0.0001
CVD status				<0.001
No	9131 (91.71)	6547 (92.52)	2584 (89.79)	
Yes	1169 (8.29)	760 (7.48)	409 (10.21)	
Obesity status				<0.0001
No	6425 (63.78)	4947 (69.85)	1478 (49.43)	
Yes	3875 (36.22)	2360 (30.15)	1515 (50.57)	

Low CVH was defined as a LE8 score of 0 to 49, moderate CVH of 50-79, and high CVH of 80-100. LE8, Life's Essential 8; CVH, Cardiovascular health; CVD, cardiovascular disease.

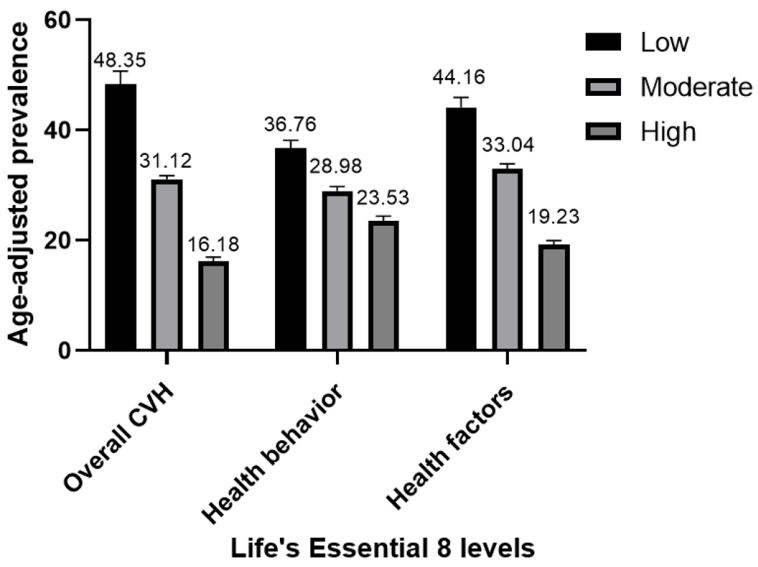

Figure 2. Age-adjusted prevalence of OSA in different levels of Life's Essential 8 scores. Numbers at the top of the bars represent the weighted percentage. Bar whiskers represent the 95% confidence level. Low CVH was defined as a LE8 score of 0 to 49, moderate CVH of 50-79, and high CVH of 80-100.

Table 2. We also saw a clear pattern where better CVH (higher LE8 scores) was linked to lower OSA rates, as shown in **Figure 3A**.

Higher health behavior scores are linked to reduced, but nonlinearly decreasing, OSA risk

After adjusting for age, we found that OSA rates were significantly lower in people with high health behavior scores (23.5%, 95% CI: 21.8-25.3%) compared to those with moderate (29.0%, 95% CI: 27.5-30.5%) and low health behavior scores (36.8%, 95% CI: 33.9-39.6%), as shown in **Figure 2**. The statistical analysis supports the concept that improved health behaviour choices directly correlate with decreased risk of developing OSA. Individuals with moderate and high health behaviour ratings were significantly less likely to have OSA than individuals with a poor health behaviour rating (OR: 0.73; 95% CI: 0.62-0.86 and OR: 0.59; 95% CI: 0.48-0.72, respectively) (**Table 2**). Every increase of 10 points in health behaviour rating was associated with a reduction in the chance of developing OSA. The odds of developing OSA decreased by 11% (OR: 0.89; 95% CI: 0.86-0.93) for every increase of 10 points in health behaviour rating (**Table 2**). We also found that the link between health behavior scores and OSA risk isn't linear (P for non-linearity <0.001) (**Figure 3B**), meaning the risk of OSA drops less as health behavior scores go up.

Improved health factor scores are linked to a non-linearly decreasing risk of OSA

After adjusting for age, we saw a significant drop in OSA rates among people with higher health factor scores. Those with high health factors had an OSA rate of 19.2% (95% CI: 17.8-20.7), compared to 33.0% (95% CI: 31.3-34.8) for those with moderate health factors and 44.2% (95% CI: 40.6-47.8) for those with low health factors, as shown in **Figure 2**. After adjusting for other factors, we found that people with moderate and high health factor scores had much lower odds of having OSA - OR = 0.66 (95% CI: 0.56-0.78) and OR = 0.33 (95% CI: 0.28-0.38), respectively - compared to those with low health factors. Additionally, every 10-point increase in the health factor score was linked to a lower odds of having OSA (OR = 0.79, 95% CI: 0.76-0.81) (**Table 2**). We also found that the relationship between health factor scores and OSA risk wasn't linear (non-linearity P = 0.002), meaning that as health factor scores improved, OSA risk kept dropping, but at a slower rate (**Figure 3C**).

Stronger LE8-OSA protective effect in younger and higher-educated groups. As shown in **Figure 4**, our subgroup analyses consistently found a negative relationship between the LE8 score and the likelihood of having OSA across different groups. A key finding was that there were significant interaction effects between the LE8 score and age as well as education levels in relation to OSA risk (interaction P < 0.05). Specifically, the link between higher LE8 scores and lower OSA risk was stronger in younger people (aged 20-39 years; OR per 10-point increase, 0.65; 95% CI: 0.59-0.71) and those with higher education, with some college or an associate degree (OR per 10-point increase, 0.68; 95% CI: 0.63-0.73).

Table 2. Association of the Life's Essential 8 scores with obstructive sleep apnea (OSA)

	Unadjusted model		Multivariable model 1*		Multivariable model 2†		Multivariable model 3‡	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
CVH								
Low (0-49)	ref		ref		ref		ref	
Moderate (50-79)	0.53 (0.46, 0.62)	<0.01	0.52 (0.44, 0.61)	<0.01	0.51 (0.43, 0.61)	<0.01	0.52 (0.44, 0.63)	<0.01
High (80-100)	0.22 (0.18, 0.27)	<0.01	0.22 (0.18, 0.28)	<0.01	0.23 (0.18, 0.29)	<0.01	0.23 (0.18, 0.30)	<0.01
Per 10 points increase	0.72 (0.69, 0.75)	<0.01	0.72 (0.69, 0.75)	<0.01	0.72 (0.68, 0.76)	<0.01	0.72 (0.68, 0.76)	<0.01
Health behaviors score								
Low (0-49)	ref		ref		ref		ref	
Moderate (50-79)	0.72 (0.62, 0.83)	<0.01	0.71 (0.61, 0.83)	<0.01	0.72 (0.61, 0.85)	<0.01	0.73 (0.62, 0.86)	<0.01
High (80-100)	0.55 (0.47, 0.65)	<0.01	0.55 (0.46, 0.65)	<0.01	0.58 (0.47, 0.71)	<0.01	0.59 (0.48, 0.72)	<0.01
Per 10 points increase	0.89 (0.86, 0.91)	<0.01	0.89 (0.86, 0.92)	<0.01	0.89 (0.86, 0.93)	<0.01	0.89 (0.86, 0.93)	<0.01
Health factors score								
Low (0-49)	ref		ref		ref		ref	
Moderate (50-79)	0.68 (0.58, 0.80)	<0.01	0.64 (0.55, 0.76)	<0.01	0.65 (0.55, 0.77)	<0.01	0.66 (0.56, 0.78)	<0.01
High (80-100)	0.33 (0.28, 0.38)	<0.01	0.31 (0.27, 0.36)	<0.01	0.32 (0.28, 0.37)	<0.01	0.33 (0.28, 0.38)	<0.01
Per 10 points increase	0.79 (0.77, 0.81)	<0.01	0.78 (0.76, 0.80)	<0.01	0.79 (0.76, 0.81)	<0.01	0.79 (0.76, 0.81)	<0.01

CVH, Cardiovascular health; OR, odds ratio; CI, confidence interval. *Adjusted for age, sex, race/ethnicity. †Additionally adjusted for poverty ratio, education levels, and marital status. ‡Additionally adjusted for CVD status, obesity status.

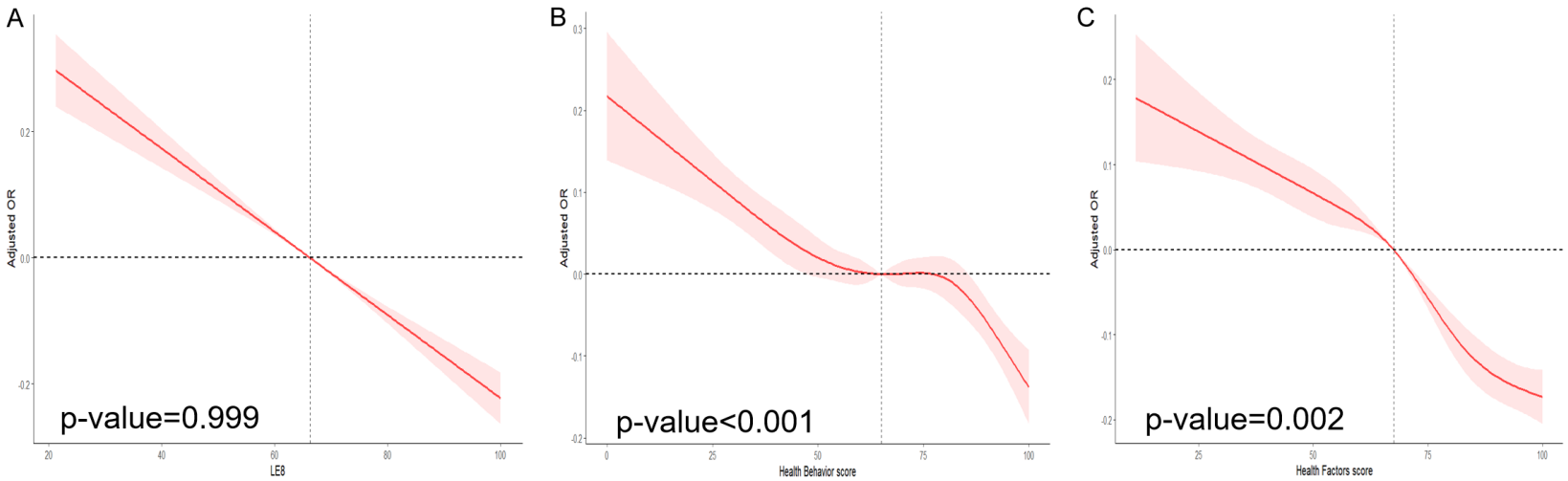

Figure 3. Dose-response relationships between Life's Essential 8 scores (A), Health Behavior score (B), Health Factors score (C), and OSA. ORs (solid lines) and 95% confidence levels (shaded areas) were adjusted for age, sex, race/ethnicity, obesity; poverty ratio (as a continuous variable), education level, marital status and CVD status. Vertical dotted lines indicate the minimal threshold for the beneficial association with estimated OR = 0. OR: odds ratio, LE8: Life's Essential 8.

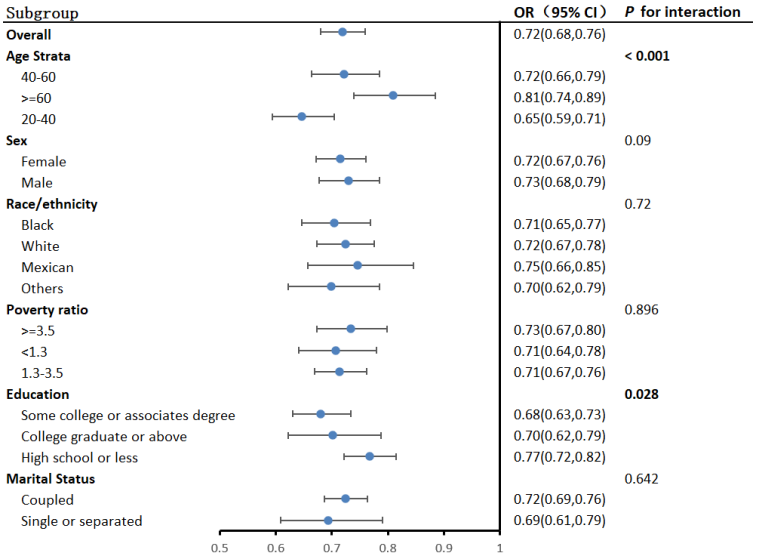

Figure 4. Subgroup analysis of the association of the Life's Essential 8 scores and the presence of OSA. ORs were calculated as per 10 scores increase in LE8 score. Each stratification was adjusted for age, sex, race/ethnicity, poverty ratio, education level, and marital status. An OR >1 indicates increased risk while <1 indicates decreased risk. OR odds ratio, CI confidence interval.

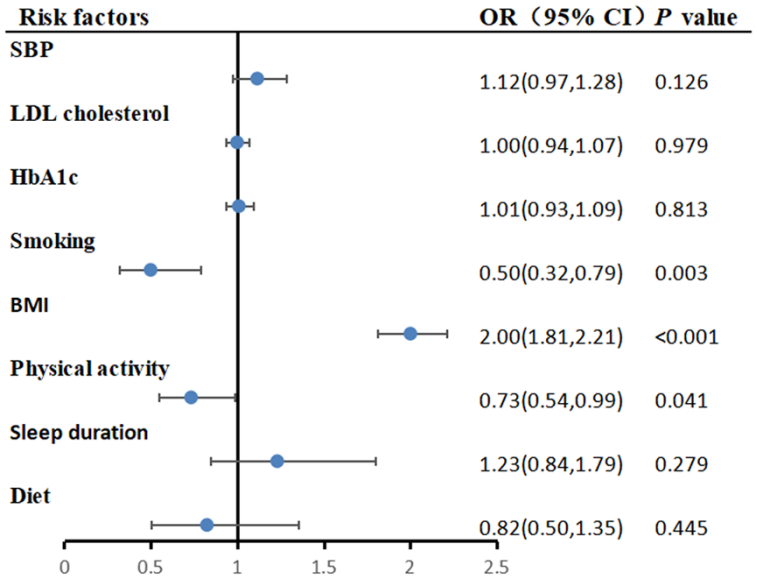

Figure 5. Forest plot of Mendelian randomization estimates between genetic predisposition to individual items of Life's Essential 8 (LE8) and risk of OSA. The figure showed the IVW estimates of significantly OSA-associated modifiable risk factor of LE8. The blue dots represent the IVW estimates, and the black bars represent the 95% confidence intervals of IVW estimates. The OR >1 indicates increased risk while <1 indicates decreased risk.

MR identifies causal roles of BMI, smoking, and physical activity in OSA risk

Using two independent datasets, we performed MR analyses to determine whether modification of eight risk factors has a causal relationship with OSA. We examined the effect of genetic variants associated with each of the eight factors (SBP, LDL-C, HbA1c, smoking behaviour, BMI, level of physical activity, sleep duration and dietary intake). Each of these genetic variants enabled us to establish independent causal relationships between each modifiable risk factor and OSA risk. Specifically, our main IVW MR analysis identified that there is a strong causal relationship between a genetic predisposition to having a higher BMI and developing OSA (OR for a 1 SD increase = 2, 95% CI: 1.81-2.21, P<0.001) (**Figure 5**). Conversely, a genetic predisposition to smoking less or engaging in more physical activity significantly decreased the risk of developing OSA (ORs = 0.50, 95% CI: 0.32-0.79, P = 0.003; OR = 0.73, 95% CI: 0.54-0.99, P = 0.041, **Figure 5**). All of these findings were subsequently confirmed using other MR analytic methods including MR-Egger and the weighted median method (**Table 3**). Conversely, there was no evidence of an independent causal relationship between genetically determined SBP, LDL-C, HbA1c, sleep duration or diet on the risk of developing OSA for either IVW or additional MR

Table 3. Mendelian randomization analysis estimates from each method of assessing the causal effect of modifiable risk factors on the risk of OSA

Exposure	Method	SNPs	ORs	95% CI	*P*	Heterogeneity		Pleiotropy		
						Q	*P*	Intercept	SE	*P*
SBP	IVW	233	1.12	(0.97, 1.28)	0.13	386.58	<0.01			
	MR-Egger	233	0.89	(0.58, 1.33)	0.54			0.004	0.004	0.23
	Weighted median	233	1.15	(0.97, 1.37)	0.10					
LDL cholesterol	IVW	151	0.10	(0.94, 1.07)	0.98	169.83	0.13			
	MR-Egger	151	0.98	(0.90, 1.07)	0.65			0.001	0.002	0.49
	Weighted median	151	0.98	(0.89, 1.08)	0.68					
HBA1C	IVW	316	1.01	(0.93, 1.09)	0.81	495.54	<0.01			
	MR-Egger	316	0.90	(0.78, 1.04)	0.15			0.004	0.002	0.06
	Weighted median	316	0.97	(0.87, 1.08)	0.56					
Smoking index	IVW	72	0.50	(0.32, 0.79)	0.00	98.42	0.02			
	MR-Egger	72	0.11	(0.02, 0.74)	0.03			0.014	0.008	0.11
	Weighted median	72	0.55	(0.31, 0.97)	0.04					
BMI	IVW	385	2.00	(1.81, 2.21)	<0.01	604.57	<0.01			
	MR-Egger	385	2.15	(1.63, 2.83)	<0.01			-0.001	0.003	0.58
	Weighted median	385	2.06	(1.80, 2.36)	<0.01					
Physical activity	IVW	11	0.73	(0.55, 0.99)	0.04	10.78	<0.01			
	MR-Egger	11	0.92	(0.08, 11.16)	0.95			-0.007	0.036	0.86
	Weighted median	11	0.65	(0.44, 0.96)	0.03					
Sleep duration	IVW	15	1.23	(0.84, 1.80)	0.28	32.63	<0.01			
	MR-Egger	15	2.40	(0.65, 8.96)	0.21			-0.019	0.018	0.32
	Weighted median	15	1.31	(0.89, 1.93)	0.16					
Diet score	IVW	68	0.83	(0.50, 1.35)	0.45	193.75	<0.01			
	MR-Egger	68	0.67	(0.10, 4.80)	0.70			0.002	0.012	0.84
	Weighted median	68	0.74	(0.47, 1.18)	0.20					

analyses (OR for a 1 SD increase = 2, 95% CI: 1.81-2.21).

Discussion

This large nationwide study demonstrates that as LE8 scores increase, the likelihood of having OSA decreases. It appears from the data that both the health behaviours as well as the health factors included in the LE8 score are inversely associated with the risk of OSA. These findings were also demonstrated by subgroup analyses and showed the same trend across multiple subgroupings. This is among the first studies to demonstrate a clear dose-response relationship between CVH, defined using the LE8 construct, and OSA. The data also indicates that improvement in CVH leads to a continual decline in OSA risk, making it likely that adopting the behaviours necessary to increase LE8 scores would decrease your risk of developing OSA. Additionally, the data indicates a genetic relationship between increased BMIs and decreased levels of physical activity, both of which influence increased risk for OSA; therefore, it is possible that higher BMI and less exercise, both of which can cause decreased levels of fitness, can potentially lead to the development of OSA.

Previous studies have shown that health behaviors and factors like physical activity, diet, and BMI are often linked to OSA [29, 30]. One study found an inverse relationship between OSA and the LS7 score [17], which is similar to our findings about the connection between LE8 scores and OSA. Therefore, early identification of high-risk OSA individuals is critical for their timely diagnosis and treatment. While obesity management has traditionally been listed among the recommendations to prevent OSA, our findings suggest a different focus for future prevention strategies [1, 2, 31, 32]. Physical activity, which is an integral part of both preventing and treating obesity, has also demonstrated positive effects on OSA risk [30, 33]. While the

presence of a concurrent association between OSA, elevated blood pressure, and HbA1c levels has been previously described [13, 15], our MR analysis did not reveal any evidence that increased risk of OSA from either elevated blood pressure or HbA1c levels could be attributed to a genetic component. This may indicate a possibility of reverse causality in observational studies. Another interesting outcome of our MR analysis is that there is a relationship between lower OSA risk and smoking. Further investigation into how smoking is related to both OSA and Sleep Health is required [34], more research is needed to better understand how smoking relates to sleep health.

Increasing evidence connects Lifestyle Environments 8 with Obstructive Sleep Apnea (OSA), primarily mediated by the lifestyle variables of Physical Activity (PA) and Body Mass Index (BMI) that are included in the definitions of LE8. Belly fat, in particular, contributes to an increased incidence, or severity, of OSA by collapsing the throat; thus, causing multiple instances of airway obstruction while sleeping. Mechanical pressure and nerve/muscle pathways are the two primary means via which belly fat can collapse the throat [35]. Furthermore, belly fat creates additional mechanical pressure in the airway and impairs the body's ability to respond to that pressure, potentially through the influence of fat-related hormones (e.g., adipokines) on the nervous system. In summary, while belly fat can lead to greater incidence or severity of OSA, physical activity improves weight loss and also supports improved cardiovascular and metabolic health across a wide variety of disorders [32].

Despite some limitations within the study's design, methodology, and reporting; the strengths of the research included various important components for each of the research objectives. First, this research used an extensive sample from the National Health and NHANES that included a diversity of individuals thus capturing representative information regarding the prevention and treatment of OSA. Second, the use of MR allowed researchers to determine if a causal relationship existed between the LE8 score and OSA. While researchers believe they have identified a statistically significant association between LE8 score and OSA, they must also consider that the results could be due in part to bias introduced from using self-reported health behaviours questionnaires (i.e., lifestyle choices). Lastly, since the majority of the NHANES study population was American, researchers cannot assume that the same findings would hold true for individuals of other ethnicities or demographics.

Conclusion

This research establishes an association between CVH, defined using the LE8 construct, and OSA. The findings highlight the importance of evaluating CVH among individuals with OSA, as lower levels of LE8-defined cardiovascular health were associated with a higher risk of OSA. The MR analysis demonstrated that weight management and physical activity are important strategies for managing OSA and to illustrate the importance of lifestyle changes in reducing the risk of OSA.

Acknowledgements

We extend our sincere gratitude to the authors and participants of the NHANES and GWAS studies, whose summary statistics data were invaluable to our research.

Disclosure of conflict of interest

None.

Abbreviations

CVH, Cardiovascular health; LE8, Life's Essential; OSA, Obstructive sleep apnea; NHANES, National Health and Nutrition Examination Surveys; MR, Mendelian Randomization; IVW, inverse variance weighted; CVD, Cardiovascular disease; LS7, Life's Simple 7; AHA, American Heart Association; BMI, Body mass index; GWAS, Genome-Wide Association Studies; UKB, United Kingdom Biobank; CDC, Centers for Disease Control and Prevention; NCHS, National Center for Health Statistics; HEI, Healthy Eating Index; HbA1c, glycated hemoglobin; SNP, Single Nucleotide Polymorphisms; FinnGen, Finnish National Genome Project; SE, Standard Error; SBP, Systolic blood pressure; OR, odds ratio; CI, confidence interval.

Address correspondence to: Wei Zhang, Yuchao Dong and Chong Bai, Department of Respiratory Medicine Changhai Hospital Affiliated to Naval Military Medical University, Shanghai, China. E-mail:

zhangweismmu@126.com (WZ); dongyc1020@aliyun.com (YCD); ChongBai@smmu.edu.cn (CB); Meng Guo, National Key Laboratory of Immunity and Inflammation & Institute of Immunology, Navy Medical University, Shanghai, China. E-mail: guo918meng@163.com

References

[1] Lloyd-Jones DM, Allen NB, Anderson CAM, Black T, Brewer LC, Foraker RE, Grandner MA, Lavretsky H, Marma Perak A, Sharma G and Rosamond W. Life's Essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a presidential advisory from the American Heart Association. Circulation 2022; 146: e18-e43.

[2] Lloyd-Jones DM, Ning H, Labarthe D, Brewer L, Sharma G, Rosamond W, Foraker RE, Black T, Grandner MA, Allen NB, Anderson C, Lavretsky H and Perak AM. Status of cardiovascular health in US adults and children using the American Heart Association's new "Life's Essential 8" metrics: prevalence estimates from the national health and nutrition examination survey (NHANES), 2013 through 2018. Circulation 2022; 146: 822-835.

[3] Redline S, Azarbarzin A and Peker Y. Obstructive sleep apnoea heterogeneity and cardiovascular disease. Nat Rev Cardiol 2023; 20: 560-573.

[4] Young T, Peppard PE and Gottlieb DJ. Epidemiology of obstructive sleep apnea. Am J Respir Crit Care Med 2002; 165: 1217-1239.

[5] Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS and Dharmage SC. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev 2017; 34: 70-81.

[6] Young T, Palta M, Dempsey J, Skatrud J, Weber S and Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328: 1230-1235.

[7] Quan SF, Howard BV, Iber C, Kiley JP, Nieto FJ, O'Connor GT, Rapoport DM, Redline S, Robbins J, Samet JM and Wahl PW. The sleep heart health study: design, rationale, and methods. Sleep 1997; 20: 1077-1085.

[8] Lyons MM, Bhatt NY, Pack AI and Magalang UJ. Global burden of sleep-disordered breathing and its implications. Respirology 2020; 25: 690-702.

[9] Alakörkkö I, Törmälehto S, Leppänen T, McNicholas WT, Arnardottir ES and Sund R. The economic cost of obstructive sleep apnea: a systematic review. Sleep Med Rev 2023; 72: 101854.

[10] Hou H, Zhao Y, Yu W, Dong H, Xue X, Ding J, Xing W and Wang W. Association of obstructive sleep apnea with hypertension: a systematic review and meta-analysis. J Glob Health 2018; 8: 010405.

[11] Reutrakul S and Mokhlesi B. Obstructive sleep apnea and diabetes. Chest 2017; 152: 1070-1086.

[12] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, Arnett DK, Fonarow GC, Ho PM, Lauer MS, Masoudi FA, Robertson RM, Roger V, Schwamm LH, Sorlie P, Yancy CW and Rosamond WD. Defining and setting national goals for cardiovascular health promotion and disease reduction. Circulation 2010; 121: 586-613.

[13] Lombardi C, Pengo MF and Parati G. Systemic hypertension in obstructive sleep apnea. J Thorac Dis 2018; 10: S4231-S4243.

[14] Khurshid K, Yabes J, Weiss PM, Dharia S, Brown L, Unruh M and Jhamb M. Effect of antihypertensive medications on the severity of obstructive sleep apnea: a systematic review and meta-analysis. J Clin Sleep Med 2016; 12: 1143-1151.

[15] Gleeson M and McNicholas WT. Bidirectional relationships of comorbidity with obstructive sleep apnoea. Eur Respir Rev 2022; 31: 210256.

[16] Chang JL, Goldberg AN, Alt JA, Alzoubaidi M, Ashbrook L, Auckley D, Ayappa I, Bakhtiar H, Barrera JE, Bartley BL, Billings ME, Boon MS, Bosschieter P, Braverman I, Brodie K, Cabrera-Muffly C, Caesar R, Cahali MB, Cai Y, Cao M, Capasso R, Caples SM, Chahine LM, Chang CP, Chang KW, Chaudhary N, Cheong CSJ, Chowdhuri S, Cistulli PA, Claman D, Collen J, Coughlin KC, Creamer J, Davis EM, Dupuy-McCauley KL, Durr ML, Dutt M, Ali ME, Elkassabany NM, Epstein LJ, Fiala JA, Freedman N, Gill K, Boyd Gillespie M, Golisch L, Gooneratne N, Gottlieb DJ, Green KK, Gulati A, Gurubhagavatula I, Hayward N, Hoff PT, Hoffmann OMG, Holfinger SJ, Hsia J, Huntley C, Huoh KC, Huyett P, Inala S, Ishman SL, Jella TK, Jobanputra AM, Johnson AP, Junna MR, Kado JT, Kaffenberger TM, Kapur VK, Kezirian EJ, Khan M, Kirsch DB, Kominsky A, Kryger M, Krystal AD, Kushida CA, Kuzniar TJ, Lam DJ, Lettieri CJ, Lim DC, Lin HC, Liu SYC, MacKay SG, Magalang UJ, Malhotra A, Mansukhani MP, Maurer JT, May AM, Mitchell RB, Mokhlesi B, Mullins AE, Nada EM, Naik S, Nokes B, Olson MD, Pack AI, Pang EB, Pang KP, Patil SP, Van de Perck E, Piccirillo JF, Pien GW, Piper AJ, Plawecki A, Quigg M, Ravesloot MJL, Redline S, Rotenberg BW, Ryden A, Sarmiento KF, Sbeih F, Schell AE, Schmickl CN, Schotland HM, Schwab RJ, Seo J, Shah N, Shelgikar AV, Shochat I, Soose RJ, Steele TO, Stephens E, Stepnowsky C, Strohl KP, Suther-

land K, Suurna MV, Thaler E, Thapa S, Vanderveken OM, de Vries N, Weaver EM, Weir ID, Wolfe LF, Tucker Woodson B, Won CHJ, Xu J, Yalamanchi P, Yaremchuk K, Yeghiazarians Y, Yu JL, Zeidler M and Rosen IM. International consensus statement on obstructive sleep apnea. Int Forum Allergy Rhinol 2023; 13: 1061-1482.

[17] Makarem N, St-Onge MP, Liao M, Lloyd-Jones DM and Aggarwal B. Association of sleep characteristics with cardiovascular health among women and differences by race/ethnicity and menopausal status: findings from the American Heart Association go red for women strategically focused research network. Sleep Health 2019; 5: 501-508.

[18] Wang X, Ma H, Li X, Heianza Y, Manson JE, Franco OH and Qi L. Association of cardiovascular health with life expectancy free of cardiovascular disease, diabetes, cancer, and dementia in UK adults. JAMA Intern Med 2023; 183: 340-349.

[19] Sun J, Li Y, Zhao M, Yu X, Zhang C, Magnussen CG and Xi B. Association of the American Heart Association's new "Life's Essential 8" with all-cause and cardiovascular disease-specific mortality: prospective cohort study. BMC Med 2023; 21: 116.

[20] Yu Y, Sun Y, Yu Y, Wang Y, Chen C, Tan X, Lu Y and Wang N. Life's Essential 8 and risk of noncommunicable chronic diseases: outcome-wide analyses. Chin Med J (Engl) 2024; 137: 1553-1562.

[21] Krebs-Smith SM, Pannucci TE, Subar AF, Kirkpatrick SI, Lerman JL, Tooze JA, Wilson MM and Reedy J. Update of the healthy eating index: HEI-2015. J Acad Nutr Diet 2018; 118: 1591-1602.

[22] Cavallino V, Rankin E, Popescu A, Gopang M, Hale L and Meliker JR. Antimony and sleep health outcomes: NHANES 2009-2016. Sleep Health J Natl Sleep Found 2022; 8: 373-379.

[23] Burgess S and Labrecque JA. Mendelian randomization with a binary exposure variable: interpretation and presentation of causal estimates. Eur J Epidemiol 2018; 33: 947-952.

[24] Little M. Mendelian randomization: methods for using genetic variants in causal estimation. J R Stat Soc Ser A Stat Soc 2018; 181: 549-550.

[25] Strausz S, Ruotsalainen S, Ollila HM, Karjalainen J, Kiiskinen T, Reeve M, Kurki M, Mars N, Havulinna AS, Luonsi E, Aly DM, Ahlqvist E, Teder-Laving M, Palta P, Groop L, Mägi R, Mäkitie A, Salomaa V, Bachour A, Tuomi T, FinnGen, Palotie A, Palotie T and Ripatti S. Genetic analysis of obstructive sleep apnoea discovers a strong association with cardiometabolic health. Eur Respir J 2021; 57: 2003091.

[26] Burgess S, Butterworth A and Thompson SG. Mendelian randomization analysis with multiple genetic variants using summarized data. Genet Epidemiol 2013; 37: 658-665.

[27] Burgess S, Bowden J, Fall T, Ingelsson E and Thompson SG. Sensitivity analyses for robust causal inference from Mendelian randomization analyses with multiple genetic variants. Epidemiol Camb Mass 2017; 28: 30-42.

[28] Bowden J, Hemani G and Davey Smith G. Invited commentary: detecting individual and global horizontal pleiotropy in Mendelian randomization-a job for the humble heterogeneity statistic? Am J Epidemiol 2018; 187: 2681-2685.

[29] Edwards BA, Bristow C, O'Driscoll DM, Wong AM, Ghazi L, Davidson ZE, Young A, Truby H, Haines TP and Hamilton GS. Assessing the impact of diet, exercise and the combination of the two as a treatment for OSA: a systematic review and meta-analysis. Respirology 2019; 24: 740-751.

[30] Liu Y, Yang L, Stampfer MJ, Redline S, Tworoger SS and Huang T. Physical activity, sedentary behavior, and incidence of obstructive sleep apnea in three prospective US cohorts. Eur Respir J 2022; 59: 2100606.

[31] Gunta SP, Jakulla RS, Ubaid A, Mohamed K, Bhat A, López-Candales A and Norgard N. Obstructive sleep apnea and cardiovascular diseases: sad realities and untold truths regarding care of patients in 2022. Cardiovasc Ther 2022; 2022: 6006127.

[32] Gottlieb DJ and Punjabi NM. Diagnosis and management of obstructive sleep apnea: a review. JAMA 2020; 323: 1389-1400.

[33] Elmaleh-Sachs A, Schwartz JL, Bramante CT, Nicklas JM, Gudzune KA and Jay M. Obesity management in adults: a review. JAMA 2023; 330: 2000-2015.

[34] Pataka A, Kotoulas S, Kalamaras G, Tzinas A, Grigoriou I, Kasnaki N, Argyropoulou P, Pataka A, Kotoulas S, Kalamaras G, Tzinas A, Grigoriou I, Kasnaki N and Argyropoulou P. Does smoking affect OSA? What about smoking cessation? J Clin Med 2022; 11: 5164.

[35] Schwartz AR, Patil SP, Laffan AM, Polotsky V, Schneider H and Smith PL. Obesity and obstructive sleep apnea. Proc Am Thorac Soc 2008; 5: 185-192.

Table S1. Definition and scoring approach for the American Heart Association's Life's Essential 8 score

Domain	CVH Metric	Measurement	Quantification and Scoring of CVH Metric
Health Behaviors	Diet	Healthy Eating Index-2015 diet score percentile	Quantiles of DASH-style diet adherence Scoring (Population): Points Quantile 100 ≥95th percentile (top/ideal diet) 80 75th - 94th percentile 50 50th - 74th percentile 25 25th - 49th percentile 0 1st - 24th percentile (bottom/least ideal quartile)
	Physical activity	Self-reported minutes of moderate or vigorous physical activity per week	Metric: Minutes of moderate (or greater) intensity activity per week Scoring: Points Minutes 100 ≥150 90 120 - 149 80 90 - 119 60 60 - 89 40 30 - 59 20 1 - 29 0 0
	Nicotine exposure	Self-reported use of cigarettes or inhaled nicotine- delivery system	Metric: Combustible tobacco use and/or inhaled NDS use; or secondhand smoke exposure Scoring: Points Status 100 Never smoker 75 Former smoker, quit ≥5 yrs 50 Former smoker, quit 1 - <5 yrs 25 Former smoker, quit <1 year, or currently using inhaled NDS 0 Current smoker Subtract 20 points (unless score is 0) for living with active indoor smoker in home
	Sleep health	Self-reported average hours of sleep per night	Metric: Average hours of sleep per night Scoring: Points Level 100 7 - <9 90 9 - <10 70 6 - <7 40 5 - <6 or ≥10 20 4 - <5 0 <4

Health Factors	Body mass index	Body weight (kg) divided by height squared (m^2)	Metric: Body mass index (kg/m^2) Scoring: Points Level 100 <25 70 25 - 29.9 30 30 - 34.9 15 35 - 39.9 0 ≥40.0
	Blood lipids	Plasma total and HDL-cholesterol with calculation of non-HDL-cholesterol	Metric: Non-HDL-cholesterol (mg/dL) Scoring: Points Level 100 <130 60 130 - 159 40 160 - 189 20 190 - 219 0 ≥220 If drug-treated level, subtract 20 points
	Blood glucose	Fasting blood glucose or casual hemoglobin A1c	Metric: Fasting blood glucose (mg/dL) or Hemoglobin A1c (%) Scoring: Points Level 100 No history of diabetes and FBG <100 (or HbA1c < 5.7) 60 No diabetes and FBG 100 - 125 (or HbA1c 5.7-6.4) (Pre-diabetes) 40 Diabetes with HbA1c <7.0 30 Diabetes with HbA1c 7.0 - 7.9 20 Diabetes with HbA1c 8.0 - 8.9 10 Diabetes with Hb A1c 9.0 - 9.9 0 Diabetes with HbA1c ≥10.0
	Blood pressure	Appropriately measured systolic and diastolic blood pressure	Metric: Systolic and diastolic blood pressure (mm Hg) Scoring: Points Level 100 <120/<80 (Optimal) 75 120-129/<80 (Elevated) 50 130-139 or 80-89 (Stage I HTN) 25 140-159 or 90-99 0 ≥160 or ≥100 Subtract 20 points if treated level

Table S2. Healthy Eating Index-2015 Components & Scoring Standards

Component	Maximum points	Standard for maximum score	Standard for minimum score of zero
Adequacy			
Total Fruits	5	≥0.8 cup equiv. per 1,000 kcal	No Fruit
Whole Fruits	5	≥0.4 cup equiv. per 1,000 kcal	No Whole Fruit
Total Vegetables	5	≥1.1 cup equiv. per 1,000 kcal	No Vegetables
Greens and Beans	5	≥0.2 cup equiv. per 1,000 kcal	No Dark Green Vegetables or Legumes
Whole Grains	10	≥1.5 oz equiv. per 1,000 kcal	No Whole Grains
Dairy	10	≥1.3 cup equiv. per 1,000 kcal	No Dairy
Total Protein Foods	5	≥2.5 oz equiv. per 1,000 kcal	No Protein Foods
Seafood and Plant Proteins	5	≥0.8 oz equiv. per 1,000 kcal	No Seafood or Plant Proteins
Fatty Acids	10	(PUFAs + MUFAs)/SFAs ≥2.5	(PUFAs+MUFAs)/SFAs ≤1.2
Moderation			
Refined Grains	10	≤1.8 oz equiv. per 1,000 kcal	≥4.3 oz equiv. per 1,000 kcal
Sodium	10	≤1.1 gram per 1,000 kcal	≥2.0 grams per 1,000 kcal
Added Sugars	10	≤6.5% of energy	≥26% of energy
Saturated Fats	10	≤8% of energy	≥16% of energy

(1) Intake between the minimum and maximum standards are scored proportionately. (2) Includes 100% fruit juice. (3) Includes all forms except juice. (4) Includes legumes (beans and peas). (5) Includes all milk products, such as fluid milk, yogurt, and cheese, and fortified soy beverages. (6) Includes legumes (beans and peas). (7) Includes seafood, nuts, seeds, soy products (other than beverages), and legumes (beans and peas). (8) Ratio of poly-and monounsaturated fatty acids (PUFAs and MUFAs) to saturated fatty acids (SFAs).

Table S3. Instruments used in the Mendelian randomization analysis of SBP derived from a GWAS performed in UK Biobank and the Biobank Japan

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs10009202	C	T	0.45801	-0.0176	0.0023	<0.0001
rs10032729	A	G	0.60798	0.0115	0.002	<0.0001
rs10048404	T	C	0.33133	-0.0148	0.002	<0.0001
rs10069690	T	C	0.25258	0.0133	0.0022	<0.0001
rs1009358	C	T	0.35909	-0.0158	0.0019	<0.0001
rs10177584	T	C	0.18528	-0.0153	0.0024	<0.0001
rs10197864	C	T	0.21849	-0.0155	0.0023	<0.0001
rs10212058	G	A	0.15347	-0.0147	0.0027	<0.0001
rs10269774	A	G	0.25716	-0.0193	0.0022	<0.0001
rs10409243	T	C	0.49552	-0.0151	0.002	<0.0001
rs1044822	T	C	0.12907	-0.0155	0.0028	<0.0001
rs10477646	T	C	0.26628	-0.012	0.0022	<0.0001
rs10735823	C	T	0.42442	-0.015	0.0022	<0.0001
rs10737683	A	G	0.34704	0.0139	0.0022	<0.0001
rs10817007	G	T	0.20558	0.0145	0.0024	<0.0001
rs10883543	T	G	0.88854	0.0297	0.0036	<0.0001
rs10891480	G	T	0.45222	-0.0142	0.0019	<0.0001
rs10958099	A	G	0.20387	0.0177	0.0023	<0.0001
rs10995311	G	C	0.36945	-0.0173	0.002	<0.0001
rs11067762	A	G	0.16129	-0.0152	0.0026	<0.0001
rs11105352	A	G	0.22999	-0.0361	0.0023	<0.0001
rs11153071	A	G	0.16638	0.0192	0.0025	<0.0001
rs11170390	A	G	0.08695	-0.0194	0.0033	<0.0001

rs11187838	A	G	0.43806	-0.0219	0.0019	<0.0001
rs11208903	C	T	0.74793	0.0129	0.0023	<0.0001
rs11252321	C	T	0.06344	-0.0211	0.0038	<0.0001
rs112537273	C	T	0.25873	0.0117	0.0021	<0.0001
rs112641450	A	G	0.13275	-0.0168	0.0029	<0.0001
rs113221086	C	A	0.13936	0.0178	0.0033	<0.0001
rs113614541	C	A	0.01521	-0.0513	0.0093	<0.0001
rs11641308	C	T	0.62124	0.016	0.002	<0.0001
rs11649091	G	T	0.36655	0.0117	0.002	<0.0001
rs116734066	T	C	0.09236	-0.0252	0.0039	<0.0001
rs11710813	T	C	0.22127	0.0156	0.0023	<0.0001
rs11721984	T	C	0.32952	-0.0141	0.0022	<0.0001
rs11722924	C	G	0.47962	-0.0113	0.0019	<0.0001
rs11727343	G	A	0.46858	0.0123	0.0019	<0.0001
rs117472357	T	C	0.04166	0.0317	0.0058	<0.0001
rs1177764	G	C	0.59728	0.0301	0.0019	<0.0001
rs117908583	T	C	0.04021	0.0297	0.005	<0.0001
rs11874	A	G	0.13676	0.0302	0.0033	<0.0001
rs11928547	C	T	0.47404	-0.0147	0.0019	<0.0001
rs11970688	C	G	0.57601	-0.0127	0.0023	<0.0001
rs12035750	C	T	0.38601	0.0175	0.0023	<0.0001
rs12147852	A	G	0.24784	0.0161	0.0026	<0.0001
rs12147852	A	G	0.24784	0.0161	0.0026	<0.0001
rs12258967	G	C	0.21275	-0.0312	0.0024	<0.0001
rs1234988	A	G	0.64293	0.0292	0.002	<0.0001
rs12363520	A	T	0.22912	0.0149	0.0027	<0.0001
rs12421055	C	A	0.19781	0.0134	0.0024	<0.0001
rs1250259	A	T	0.79663	-0.0183	0.0024	<0.0001
rs12509595	C	T	0.2951	0.0374	0.002	<0.0001
rs12530912	G	T	0.23423	0.0124	0.0022	<0.0001
rs12546319	T	A	0.38266	-0.0157	0.0019	<0.0001
rs12609950	G	T	0.25864	-0.0138	0.0022	<0.0001
rs12638862	G	A	0.37626	-0.0137	0.0021	<0.0001
rs12714414	C	T	0.13575	-0.0186	0.0028	<0.0001
rs12746365	A	G	0.30128	-0.019	0.0025	<0.0001
rs1275980	T	C	0.49862	-0.0273	0.002	<0.0001
rs12801636	A	G	0.30703	-0.0163	0.0021	<0.0001
rs12906125	A	G	0.26041	0.0282	0.0022	<0.0001
rs12911255	T	A	0.13615	0.0155	0.0027	<0.0001
rs13017511	G	A	0.22508	0.0142	0.0024	<0.0001
rs13112725	C	G	0.72542	0.0181	0.0021	<0.0001
rs13129779	T	C	0.60304	-0.0116	0.002	<0.0001
rs13131350	G	A	0.16656	0.0151	0.0025	<0.0001
rs13276026	A	G	0.57084	-0.0186	0.0023	<0.0001
rs1371597	A	C	0.46196	0.013	0.0023	<0.0001
rs138110118	G	T	0.11424	-0.0228	0.0036	<0.0001
rs138443500	G	T	0.01589	0.0611	0.009	<0.0001
rs1407256	G	A	0.26802	0.0128	0.0023	<0.0001
rs141206533	A	G	0.15536	0.0183	0.0027	<0.0001

rs1422279	T	C	0.45197	0.015	0.0019	<0.0001
rs143167197	G	A	0.07517	0.0212	0.0036	<0.0001
rs1435514	T	C	0.37375	0.015	0.0019	<0.0001
rs1436138	G	A	0.38655	-0.0146	0.0019	<0.0001
rs1448919	A	G	0.24113	0.013	0.0022	<0.0001
rs1458727	T	C	0.29822	0.0125	0.0021	<0.0001
rs1465406	C	A	0.25556	-0.0122	0.0021	<0.0001
rs1475130	C	T	0.6834	0.0122	0.002	<0.0001
rs148321568	T	A	0.14092	0.0225	0.0032	<0.0001
rs148351986	G	A	0.15788	-0.0177	0.0031	<0.0001
rs148753960	T	C	0.01013	-0.0679	0.0119	<0.0001
rs148862242	T	C	0.09144	0.024	0.0039	<0.0001
rs149764880	T	G	0.16378	-0.0455	0.003	<0.0001
rs1543270	T	C	0.54071	-0.0151	0.0019	<0.0001
rs166912	C	T	0.75775	-0.0163	0.0023	<0.0001
rs167479	T	G	0.47998	-0.0268	0.0019	<0.0001
rs16939338	A	G	0.24366	-0.0128	0.0023	<0.0001
rs17010961	A	T	0.16228	0.0229	0.0025	<0.0001
rs17173238	G	A	0.28639	0.0171	0.0025	<0.0001
rs17245822	C	A	0.33025	0.0114	0.002	<0.0001
rs17389148	A	C	0.3782	-0.0138	0.002	<0.0001
rs17410535	C	T	0.2767	0.0135	0.0021	<0.0001
rs17694791	T	C	0.24129	-0.0157	0.0022	<0.0001
rs17715065	T	C	0.45736	0.0161	0.0019	<0.0001
rs17722107	C	A	0.20165	-0.0168	0.0023	<0.0001
rs17759661	A	C	0.39601	0.0129	0.002	<0.0001
rs1813006	T	G	0.06008	-0.0303	0.0049	<0.0001
rs1848510	A	G	0.44469	0.0119	0.0019	<0.0001
rs200528	G	A	0.84063	0.0244	0.0026	<0.0001
rs200584255	C	T	0.21923	-0.0154	0.0027	<0.0001
rs2048240	T	C	0.53171	0.0107	0.0019	<0.0001
rs2055726	A	G	0.46172	0.0119	0.002	<0.0001
rs2062316	G	A	0.33185	0.0173	0.0021	<0.0001
rs2071303	C	T	0.47203	0.0142	0.002	<0.0001
rs2074633	C	T	0.25567	0.0172	0.0022	<0.0001
rs2206815	A	C	0.47854	-0.0144	0.0019	<0.0001
rs2238786	G	A	0.25773	0.0142	0.0021	<0.0001
rs2242296	G	C	0.37079	-0.0142	0.0019	<0.0001
rs2254240	A	G	0.30189	-0.0194	0.0022	<0.0001
rs2288276	C	G	0.88457	0.0218	0.0029	<0.0001
rs2289125	C	A	0.70224	0.0146	0.0021	<0.0001
rs2301597	C	T	0.47351	-0.0223	0.002	<0.0001
rs2306526	T	C	0.52394	-0.0156	0.0023	<0.0001
rs2314650	A	G	0.27961	-0.0128	0.0023	<0.0001
rs2382818	T	A	0.40471	0.0104	0.0019	<0.0001
rs2447607	T	C	0.62997	0.0126	0.0019	<0.0001
rs2478539	T	G	0.52482	0.0152	0.002	<0.0001
rs2493292	T	C	0.09856	0.0232	0.0032	<0.0001
rs2569880	A	C	0.55785	-0.0121	0.002	<0.0001

rs2571445	G	A	0.58781	-0.0115	0.0019	<0.0001
rs2578655	G	T	0.38601	0.0135	0.0019	<0.0001
rs2580315	C	T	0.1097	-0.0175	0.003	<0.0001
rs263012	C	A	0.55581	-0.0107	0.0019	<0.0001
rs2638432	T	G	0.26186	-0.0137	0.0022	<0.0001
rs2643826	T	C	0.42839	0.0186	0.002	<0.0001
rs267513	T	G	0.64737	-0.0121	0.002	<0.0001
rs268263	A	T	0.70949	0.0272	0.0021	<0.0001
rs2721796	T	C	0.15152	-0.0151	0.0027	<0.0001
rs28478118	G	T	0.33523	-0.0114	0.002	<0.0001
rs28534747	C	T	0.331	-0.0141	0.0024	<0.0001
rs2935545	A	G	0.26708	-0.0121	0.0021	<0.0001
rs3110057	A	G	0.60227	-0.0116	0.0019	<0.0001
rs3211995	A	G	0.15903	-0.0219	0.0031	<0.0001
rs34325	C	T	0.52195	0.0106	0.0019	<0.0001
rs35183011	G	C	0.06637	0.029	0.0045	<0.0001
rs35300112	C	A	0.19902	-0.0191	0.0024	<0.0001
rs35427	G	T	0.34555	-0.0214	0.002	<0.0001
rs35479618	A	G	0.01735	0.0649	0.0086	<0.0001
rs35680304	T	C	0.58127	0.0143	0.0019	<0.0001
rs35704455	A	T	0.66105	0.0119	0.0021	<0.0001
rs36002174	T	C	0.18996	-0.0156	0.0024	<0.0001
rs360158	A	G	0.60201	0.0178	0.0019	<0.0001
rs36144291	C	T	0.23468	-0.0147	0.0022	<0.0001
rs3774620	A	G	0.55772	0.0129	0.002	<0.0001
rs3786516	A	T	0.82123	0.014	0.0025	<0.0001
rs3790604	A	C	0.14037	0.0309	0.0028	<0.0001
rs3817198	C	T	0.26955	-0.0135	0.0021	<0.0001
rs3821843	A	G	0.61017	0.0186	0.002	<0.0001
rs389546	C	T	0.90286	-0.0206	0.0032	<0.0001
rs419076	C	T	0.62784	-0.016	0.002	<0.0001
rs4245599	G	A	0.52427	0.0126	0.0019	<0.0001
rs440466	C	T	0.28245	-0.0135	0.0022	<0.0001
rs4411554	G	C	0.69216	0.0123	0.002	<0.0001
rs460718	G	A	0.60808	0.0165	0.002	<0.0001
rs4690774	T	A	0.56635	-0.0114	0.002	<0.0001
rs4767321	C	T	0.41096	0.012	0.002	<0.0001
rs4842266	A	G	0.57825	-0.0129	0.002	<0.0001
rs4936098	G	A	0.71272	-0.0183	0.0022	<0.0001
rs494264	G	A	0.49407	-0.0129	0.0019	<0.0001
rs4968716	T	C	0.59034	0.0127	0.002	<0.0001
rs507506	G	A	0.53848	0.0124	0.0019	<0.0001
rs55940342	C	G	0.18007	-0.0175	0.0029	<0.0001
rs56083149	G	C	0.36929	0.0121	0.002	<0.0001
rs56092448	T	C	0.14207	0.0187	0.0027	<0.0001
rs56180741	C	T	0.57153	-0.0129	0.0023	<0.0001
rs56743174	A	G	0.0755	-0.0235	0.0035	<0.0001
rs574794	T	A	0.03979	0.0304	0.0048	<0.0001
rs57946343	C	T	0.15129	-0.0291	0.0031	<0.0001

rs6017281	G	A	0.17762	0.019	0.0025	<0.0001
rs6026739	T	A	0.10831	0.0278	0.003	<0.0001
rs605410	G	A	0.5007	-0.0117	0.0019	<0.0001
rs60691990	C	T	0.24776	-0.0185	0.0023	<0.0001
rs6077991	T	C	0.27529	0.0187	0.0021	<0.0001
rs6122049	T	C	0.23075	0.0179	0.0027	<0.0001
rs615567	T	A	0.34583	-0.0128	0.002	<0.0001
rs62189012	A	G	0.09502	-0.0234	0.0032	<0.0001
rs62368019	C	T	0.32366	0.0141	0.002	<0.0001
rs62430713	C	T	0.17698	-0.0175	0.003	<0.0001
rs62434129	T	A	0.05768	-0.0296	0.004	<0.0001
rs62481856	A	G	0.17093	0.0357	0.0025	<0.0001
rs62524579	A	G	0.48801	-0.0155	0.0019	<0.0001
rs62536879	T	A	0.35482	-0.0139	0.0024	<0.0001
rs6271	T	C	0.07393	-0.0256	0.0043	<0.0001
rs6460542	T	C	0.26589	0.0142	0.0021	<0.0001
rs6490061	C	T	0.34236	-0.0242	0.0022	<0.0001
rs6540125	G	T	0.63042	-0.011	0.0019	<0.0001
rs66563455	C	T	0.22379	-0.0176	0.0023	<0.0001
rs6708660	C	T	0.29392	-0.0134	0.0022	<0.0001
rs6789614	A	G	0.43404	-0.0148	0.002	<0.0001
rs6815273	A	G	0.40936	-0.0136	0.0019	<0.0001
rs6912683	A	C	0.53432	0.014	0.0019	<0.0001
rs7020491	T	C	0.47039	-0.0119	0.0019	<0.0001
rs704	A	G	0.56164	-0.0108	0.002	<0.0001
rs708164	A	C	0.34675	0.0125	0.0022	<0.0001
rs7099026	T	C	0.57795	-0.0126	0.0023	<0.0001
rs7131442	T	A	0.2155	0.0163	0.0023	<0.0001
rs7134677	T	C	0.3293	-0.0151	0.002	<0.0001
rs71654213	T	C	0.38374	-0.0174	0.0023	<0.0001
rs7236548	A	C	0.22131	0.0128	0.0023	<0.0001
rs72677850	A	G	0.01896	-0.0507	0.0084	<0.0001
rs72730503	A	G	0.68301	-0.0188	0.002	<0.0001
rs72834437	G	A	0.11436	0.0201	0.0035	<0.0001
rs73033340	G	A	0.03166	-0.0388	0.0064	<0.0001
rs73046792	A	G	0.16476	-0.0241	0.003	<0.0001
rs73077157	C	A	0.08947	-0.0192	0.0034	<0.0001
rs7315980	A	G	0.06704	0.0217	0.0038	<0.0001
rs73563812	T	G	0.2778	-0.0169	0.0021	<0.0001
rs7404616	A	G	0.61697	-0.0108	0.0019	<0.0001
rs740698	T	C	0.59767	-0.0144	0.0019	<0.0001
rs74826317	G	A	0.02807	-0.0479	0.0068	<0.0001
rs751984	C	T	0.24282	-0.0169	0.0024	<0.0001
rs7575103	A	G	0.37098	0.0113	0.0019	<0.0001
rs75989961	G	T	0.08155	0.024	0.0041	<0.0001
rs76785323	A	C	0.43271	0.0209	0.0019	<0.0001
rs7687234	T	C	0.43339	0.0117	0.0019	<0.0001
rs7772739	A	G	0.52798	0.0114	0.0019	<0.0001
rs77870048	T	C	0.05304	0.0495	0.005	<0.0001

rs78089855	T	C	0.05167	0.0294	0.0042	<0.0001
rs78744936	A	G	0.18798	0.0153	0.0026	<0.0001
rs7911644	T	C	0.34521	0.0135	0.002	<0.0001
rs7926602	A	G	0.48462	0.0138	0.0019	<0.0001
rs79349366	T	C	0.03253	-0.04	0.0064	<0.0001
rs7938342	A	T	0.64949	0.0245	0.002	<0.0001
rs79680647	A	G	0.12903	-0.0408	0.0028	<0.0001
rs8076897	C	T	0.74468	-0.0177	0.0023	<0.0001
rs8123890	G	A	0.41222	0.0109	0.0019	<0.0001
rs861581	T	G	0.55381	0.0114	0.0019	<0.0001
rs8904	A	G	0.34363	0.0113	0.002	<0.0001
rs891511	A	G	0.40295	-0.0178	0.002	<0.0001
rs896693	A	G	0.35363	-0.012	0.002	<0.0001
rs9294987	C	T	0.36081	0.0148	0.0022	<0.0001
rs9330353	A	T	0.41329	0.0114	0.0019	<0.0001
rs9349379	G	A	0.47891	-0.0132	0.002	<0.0001
rs9401013	A	T	0.52206	0.0145	0.0023	<0.0001
rs9442841	A	G	0.11908	-0.0163	0.003	<0.0001
rs9472040	G	A	0.32845	0.0176	0.002	<0.0001
rs9549328	T	C	0.24667	0.0143	0.0022	<0.0001
rs9899357	C	T	0.32924	0.0116	0.0021	<0.0001
rs9907379	C	T	0.75513	0.0188	0.0022	<0.0001

Table S4. Instruments used in the Mendelian randomization analysis of LDL

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs1010759	A	G	0.13298	-0.025	0.0031	<0.0001
rs10201242	A	G	0.09955	-0.0226	0.0036	<0.0001
rs10260606	C	G	0.1824	0.0353	0.003	<0.0001
rs10448340	G	T	0.30318	-0.0145	0.0023	<0.0001
rs10794579	C	T	0.5726	0.0162	0.0021	<0.0001
rs1081105	C	A	0.02788	0.1736	0.0072	<0.0001
rs10910476	T	C	0.50471	0.0136	0.0022	<0.0001
rs10953298	T	C	0.21183	-0.0188	0.0026	<0.0001
rs11024735	T	C	0.69253	0.0145	0.0023	<0.0001
rs11099097	T	C	0.2976	-0.0183	0.0023	<0.0001
rs11149612	T	C	0.51153	-0.0166	0.0022	<0.0001
rs113177823	A	G	0.05441	-0.037	0.0053	<0.0001
rs11591147	T	G	0.0177	-0.3485	0.0089	<0.0001
rs11601507	A	C	0.06588	0.0335	0.0042	<0.0001
rs11621792	T	C	0.38435	0.0185	0.0023	<0.0001
rs11641811	A	C	0.55042	0.0181	0.0021	<0.0001
rs116734477	T	C	0.03425	-0.0514	0.0059	<0.0001
rs1169288	C	A	0.34453	0.024	0.0022	<0.0001
rs11709868	T	G	0.25439	-0.0159	0.0025	<0.0001
rs117139027	A	G	0.01722	-0.0598	0.009	<0.0001
rs11789603	T	C	0.09935	0.021	0.0036	<0.0001
rs118039278	A	G	0.0806	0.0819	0.0043	<0.0001
rs11911615	G	T	0.32304	-0.0125	0.0023	<0.0001

rs12151108	A	G	0.11874	-0.1777	0.0036	<0.0001
rs12208357	T	C	0.06989	0.0569	0.0046	<0.0001
rs12445804	A	G	0.13419	0.0249	0.0033	<0.0001
rs12473839	T	C	0.40591	0.0147	0.0022	<0.0001
rs12478841	G	A	0.30976	0.0234	0.0024	<0.0001
rs12533280	T	C	0.19929	0.0154	0.0026	<0.0001
rs12588332	C	T	0.86209	0.0189	0.0031	<0.0001
rs12657266	T	C	0.6695	0.0345	0.0023	<0.0001
rs12740374	T	G	0.1953	-0.1173	0.0027	<0.0001
rs12905203	G	A	0.37036	-0.0123	0.0023	<0.0001
rs12916	C	T	0.42208	0.0602	0.0021	<0.0001
rs12989783	A	T	0.62707	-0.0197	0.0022	<0.0001
rs13098031	T	G	0.22316	-0.0204	0.0026	<0.0001
rs1350559	G	C	0.45792	0.0139	0.0022	<0.0001
rs1367117	A	G	0.2931	0.0803	0.0024	<0.0001
rs141973904	T	C	0.00999	-0.0758	0.0119	<0.0001
rs144078421	A	G	0.01649	0.0515	0.0093	<0.0001
rs144439590	T	C	0.0304	-0.1448	0.007	<0.0001
rs144861591	T	C	0.0776	-0.0554	0.0044	<0.0001
rs145184406	A	T	0.19109	-0.019	0.003	<0.0001
rs145730801	C	T	0.04545	0.0344	0.0058	<0.0001
rs146534110	T	G	0.01338	0.0627	0.0103	<0.0001
rs147540853	A	G	0.06463	-0.071	0.0044	<0.0001
rs147711004	A	G	0.03701	0.1486	0.0064	<0.0001
rs148601586	G	C	0.01354	0.1345	0.0104	<0.0001
rs150474434	A	G	0.08422	-0.0355	0.0039	<0.0001
rs16926246	T	C	0.13069	-0.0221	0.0035	<0.0001
rs17029617	A	G	0.07924	-0.0339	0.0039	<0.0001
rs17050272	A	G	0.42241	-0.0207	0.0021	<0.0001
rs17185536	T	C	0.24437	-0.0176	0.0027	<0.0001
rs174553	G	A	0.35307	-0.0306	0.0022	<0.0001
rs1800961	T	C	0.0277	-0.0634	0.0065	<0.0001
rs1801689	C	A	0.02989	0.0649	0.0069	<0.0001
rs1883711	C	G	0.03108	0.108	0.0069	<0.0001
rs2066714	C	T	0.21569	0.0197	0.0029	<0.0001
rs2068888	A	G	0.4786	-0.0185	0.0021	<0.0001
rs2160994	C	T	0.7036	0.018	0.0024	<0.0001
rs2179050	G	A	0.67099	-0.0152	0.0023	<0.0001
rs2253736	A	C	0.87713	-0.0197	0.0033	<0.0001
rs2291217	G	A	0.29391	-0.0143	0.0023	<0.0001
rs2302429	A	G	0.20721	0.0149	0.0026	<0.0001
rs2306363	T	G	0.21853	0.0146	0.0026	<0.0001
rs2414577	C	T	0.47168	0.0158	0.0023	<0.0001
rs247617	A	C	0.30481	-0.0312	0.0023	<0.0001
rs2519093	T	C	0.20048	0.0562	0.0026	<0.0001
rs2618566	T	G	0.66495	-0.0219	0.0023	<0.0001
rs2642438	G	A	0.72266	0.0248	0.0024	<0.0001
rs2706383	A	G	0.21704	-0.0162	0.0026	<0.0001
rs2710644	C	A	0.71233	0.0212	0.0023	<0.0001

rs2737245	T	G	0.27935	-0.0229	0.0024	<0.0001
rs2740488	C	A	0.26726	-0.0213	0.0024	<0.0001
rs28601761	G	C	0.37526	-0.0553	0.0023	<0.0001
rs28615248	C	T	0.19854	0.023	0.0027	<0.0001
rs334558	G	A	0.39057	0.0155	0.0022	<0.0001
rs33997707	A	G	0.11628	0.0422	0.0033	<0.0001
rs34019521	C	G	0.22206	0.0152	0.0026	<0.0001
rs34042070	G	C	0.22273	0.0465	0.0026	<0.0001
rs34071855	G	C	0.4173	-0.0134	0.0023	<0.0001
rs34568880	T	C	0.01176	0.054	0.0099	<0.0001
rs34927723	T	C	0.16271	-0.0159	0.0029	<0.0001
rs35081008	T	C	0.14661	-0.0349	0.0033	<0.0001
rs35203651	C	T	0.11374	0.0191	0.0033	<0.0001
rs35206901	G	A	0.18214	-0.0384	0.003	<0.0001
rs3756772	T	C	0.45324	0.017	0.0022	<0.0001
rs3780181	G	A	0.07118	-0.0298	0.0041	<0.0001
rs4044515	A	G	0.0532	-0.0282	0.005	<0.0001
rs41280378	G	T	0.07946	-0.0315	0.0041	<0.0001
rs438568	G	A	0.60398	0.0124	0.0022	<0.0001
rs45537841	T	C	0.1964	-0.0152	0.0027	<0.0001
rs4678192	G	A	0.40882	0.0137	0.0022	<0.0001
rs4714638	G	A	0.47597	-0.013	0.0022	<0.0001
rs472495	T	G	0.67191	0.0438	0.0023	<0.0001
rs4738684	G	A	0.69463	-0.0294	0.0023	<0.0001
rs4751996	G	A	0.4792	0.0122	0.0022	<0.0001
rs4850047	C	T	0.76686	-0.0183	0.0029	<0.0001
rs486142	A	G	0.55159	0.0353	0.0022	<0.0001
rs4939883	C	T	0.81436	0.0157	0.0027	<0.0001
rs542049	C	T	0.28298	-0.0149	0.0024	<0.0001
rs55714927	T	C	0.20899	-0.0258	0.0027	<0.0001
rs55831924	T	C	0.32512	0.0157	0.0023	<0.0001
rs55921103	T	G	0.63174	0.0129	0.0023	<0.0001
rs56248798	T	C	0.03423	0.0396	0.006	<0.0001
rs5758128	T	C	0.47375	0.0136	0.0024	<0.0001
rs57667647	A	G	0.04556	-0.0789	0.0056	<0.0001
rs58699591	T	C	0.18541	-0.0164	0.0027	<0.0001
rs59509802	C	A	0.25074	0.028	0.0024	<0.0001
rs597808	G	A	0.51664	0.0264	0.0024	<0.0001
rs59784135	G	A	0.64023	-0.0268	0.0024	<0.0001
rs60073330	G	A	0.29234	0.0132	0.0023	<0.0001
rs60403956	G	A	0.02584	-0.0492	0.0071	<0.0001
rs6090101	A	G	0.19903	0.0182	0.003	<0.0001
rs62006565	C	T	0.73275	0.0186	0.0027	<0.0001
rs62118464	A	G	0.1183	0.0316	0.0037	<0.0001
rs62275880	T	A	0.26033	0.02	0.0027	<0.0001
rs6475606	T	C	0.51613	-0.0195	0.0021	<0.0001
rs6602911	T	C	0.37222	0.0203	0.0022	<0.0001
rs6667939	T	C	0.73621	0.0145	0.0024	<0.0001
rs67431680	G	A	0.34841	0.013	0.0022	<0.0001

rs6920309	T	C	0.54453	-0.0215	0.0023	<0.0001
rs704	A	G	0.52631	0.0182	0.0022	<0.0001
rs7096937	C	T	0.73889	-0.021	0.0024	<0.0001
rs71628040	C	T	0.05571	-0.0306	0.0051	<0.0001
rs72631343	G	C	0.19054	-0.027	0.0029	<0.0001
rs72750932	C	G	0.13997	0.0197	0.0034	<0.0001
rs73013176	C	T	0.01162	-0.1811	0.0112	<0.0001
rs73034893	T	C	0.06938	0.0273	0.0047	<0.0001
rs7412	T	C	0.07312	-0.477	0.004	<0.0001
rs75331444	A	G	0.05496	-0.0978	0.0047	<0.0001
rs75460349	C	A	0.02368	0.058	0.0079	<0.0001
rs7551451	G	A	0.20224	-0.0167	0.0026	<0.0001
rs7569317	C	T	0.57058	0.0178	0.0022	<0.0001
rs7601939	T	G	0.1774	0.0188	0.0028	<0.0001
rs7709540	C	T	0.50592	0.0187	0.0021	<0.0001
rs77542162	G	A	0.023	0.1306	0.0079	<0.0001
rs77960347	G	A	0.01348	0.0711	0.0102	<0.0001
rs79120103	G	A	0.03129	-0.0379	0.0068	<0.0001
rs7952602	C	G	0.17473	0.0356	0.0028	<0.0001
rs80276949	A	G	0.0231	0.0456	0.0079	<0.0001
rs836550	G	A	0.4079	0.0137	0.0024	<0.0001
rs907867	G	T	0.44166	-0.0173	0.0021	<0.0001
rs9376090	C	T	0.27411	-0.0144	0.0024	<0.0001
rs9411465	A	G	0.05685	0.0346	0.0049	<0.0001
rs9438909	C	T	0.51742	0.0237	0.0021	<0.0001
rs964184	C	G	0.84202	-0.0381	0.0029	<0.0001
rs9844432	G	C	0.08231	-0.0313	0.0043	<0.0001
rs9884390	C	T	0.2365	0.0252	0.0028	<0.0001
rs9894946	G	A	0.86616	-0.0185	0.0032	<0.0001
rs9982111	A	G	0.55439	0.0118	0.0021	<0.0001
rs9987289	G	A	0.92252	0.0437	0.004	<0.0001
rs998974	C	T	0.37043	0.0127	0.0022	<0.0001

Table S5. Instruments used in the Mendelian randomization analysis of HbA1c

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs10053046	G	A	NA	0.01702	0.00217	<0.0001
rs1005752	A	C	NA	0.03053	0.00224	<0.0001
rs10228066	T	C	NA	0.02662	0.00202	<0.0001
rs10401969	C	T	NA	0.02085	0.00379	<0.0001
rs10407429	A	G	NA	-0.0254	0.00203	<0.0001
rs10492373	A	G	NA	-0.0253	0.00253	<0.0001
rs10501320	C	G	NA	-0.0265	0.00228	<0.0001
rs10752943	T	C	NA	-0.017	0.00204	<0.0001
rs10758593	A	G	NA	0.01615	0.00205	<0.0001
rs10811660	A	G	NA	-0.0544	0.00265	<0.0001
rs10830963	G	C	NA	0.06241	0.00225	<0.0001
rs10841518	G	C	NA	0.01366	0.00241	<0.0001
rs10841891	G	T	NA	-0.0147	0.00238	<0.0001

rs10886280	T	C	NA	-0.0132	0.00219	<0.0001
rs10888260	C	T	NA	0.02049	0.00329	<0.0001
rs10890181	T	C	NA	0.01194	0.00202	<0.0001
rs10910045	G	A	NA	-0.0124	0.00206	<0.0001
rs10916610	T	C	NA	-0.0121	0.00222	<0.0001
rs10998673	C	G	NA	0.05745	0.00455	<0.0001
rs11042852	G	A	NA	0.0407	0.0036	<0.0001
rs11065979	T	C	NA	-0.029	0.00204	<0.0001
rs11070339	G	A	NA	0.01564	0.00205	<0.0001
rs1108646	G	A	NA	-0.0328	0.00219	<0.0001
rs11120149	T	G	NA	-0.017	0.00227	<0.0001
rs111333451	A	G	NA	0.02921	0.00345	<0.0001
rs11149059	C	T	NA	-0.014	0.0024	<0.0001
rs111492193	T	C	NA	-0.0353	0.00273	<0.0001
rs111559769	C	T	NA	0.0206	0.00262	<0.0001
rs111631066	A	G	NA	-0.076	0.00842	<0.0001
rs11166447	C	T	NA	-0.0128	0.00211	<0.0001
rs111754661	C	T	NA	-0.047	0.00372	<0.0001
rs1121980	A	G	NA	0.0221	0.00204	<0.0001
rs112270735	G	A	NA	0.02042	0.00288	<0.0001
rs112381655	A	T	NA	0.03162	0.00576	<0.0001
rs11257655	T	C	NA	0.03857	0.00251	<0.0001
rs11258437	T	C	NA	0.01167	0.00204	<0.0001
rs112750178	C	T	NA	0.01639	0.00238	<0.0001
rs112784971	T	C	NA	0.03032	0.00486	<0.0001
rs113582976	T	G	NA	-0.0147	0.0026	<0.0001
rs113902512	A	G	NA	-0.0155	0.00271	<0.0001
rs11512059	T	C	NA	0.02883	0.00367	<0.0001
rs115340137	C	T	NA	-0.1453	0.01072	<0.0001
rs1154514	T	C	NA	0.01434	0.00201	<0.0001
rs11564725	T	C	NA	0.02511	0.00239	<0.0001
rs115730158	A	G	NA	0.02497	0.00425	<0.0001
rs1159619	A	C	NA	0.01939	0.00202	<0.0001
rs11598987	G	C	NA	0.01294	0.00205	<0.0001
rs11602873	T	A	NA	-0.0366	0.00276	<0.0001
rs11616380	T	G	NA	-0.0195	0.00223	<0.0001
rs1166698	A	G	NA	-0.0179	0.00246	<0.0001
rs11708067	G	A	NA	-0.0533	0.00234	<0.0001
rs117276569	T	C	NA	-0.0425	0.00748	<0.0001
rs117370443	C	T	NA	0.05444	0.0052	<0.0001
rs117447349	A	G	NA	-0.2193	0.00879	<0.0001
rs1175550	G	A	NA	-0.0423	0.00243	<0.0001
rs11762803	G	A	NA	-0.0143	0.00241	<0.0001
rs117709065	T	C	NA	-0.0827	0.00799	<0.0001
rs117783723	C	T	NA	0.02373	0.00433	<0.0001
rs117861560	T	G	NA	0.01284	0.00213	<0.0001
rs11917973	T	C	NA	-0.0132	0.00203	<0.0001
rs11926854	C	T	NA	-0.0369	0.00541	<0.0001
rs1193851	G	C	NA	0.01261	0.00211	<0.0001

rs12035330	G	A	NA	0.02273	0.00231	<0.0001
rs12040433	G	A	NA	-0.0126	0.00213	<0.0001
rs12365580	A	G	NA	-0.0363	0.00283	<0.0001
rs12459419	T	C	NA	-0.0257	0.00214	<0.0001
rs12466687	C	A	NA	-0.0215	0.00317	<0.0001
rs12493136	A	G	NA	0.02581	0.00273	<0.0001
rs1259180	C	T	NA	-0.0121	0.00206	<0.0001
rs12607898	G	A	NA	0.02536	0.00231	<0.0001
rs12645001	A	G	NA	-0.0138	0.00211	<0.0001
rs12650788	A	G	NA	0.0122	0.00207	<0.0001
rs12712928	C	G	NA	0.0294	0.00271	<0.0001
rs12813389	T	A	NA	0.01255	0.00202	<0.0001
rs12876143	C	T	NA	0.07752	0.00353	<0.0001
rs12943904	C	G	NA	-0.0147	0.0022	<0.0001
rs13019832	A	G	NA	-0.0225	0.00205	<0.0001
rs13059110	T	G	NA	0.0201	0.00299	<0.0001
rs13167071	C	G	NA	0.01993	0.0021	<0.0001
rs13170854	C	A	NA	-0.0129	0.00213	<0.0001
rs13192435	C	T	NA	0.04735	0.00642	<0.0001
rs13233631	G	A	NA	-0.0163	0.00203	<0.0001
rs13248311	A	C	NA	-0.0114	0.00208	<0.0001
rs13266634	T	C	NA	-0.0544	0.00218	<0.0001
rs13272050	T	C	NA	-0.0207	0.00268	<0.0001
rs13383320	A	C	NA	-0.0121	0.00206	<0.0001
rs138409370	T	A	NA	0.02853	0.00316	<0.0001
rs138599549	T	G	NA	-0.0597	0.00944	<0.0001
rs1399627	G	A	NA	0.02213	0.00212	<0.0001
rs141192775	T	C	NA	-0.0386	0.00609	<0.0001
rs142235947	A	G	NA	-0.0623	0.00935	<0.0001
rs142394825	C	G	NA	-0.0892	0.00897	<0.0001
rs1427297	T	C	NA	-0.0137	0.00216	<0.0001
rs144155527	T	C	NA	-0.0476	0.00754	<0.0001
rs144489757	G	C	NA	-0.0169	0.00223	<0.0001
rs144993543	C	T	NA	0.07327	0.0108	<0.0001
rs145173553	T	G	NA	0.01273	0.00207	<0.0001
rs145381182	A	G	NA	0.01973	0.00355	<0.0001
rs145496147	T	C	NA	-0.074	0.00935	<0.0001
rs147208676	T	C	NA	0.02381	0.0037	<0.0001
rs147558893	C	T	NA	0.04301	0.0067	<0.0001
rs147730268	T	G	NA	-0.0268	0.00363	<0.0001
rs148407308	T	C	NA	0.02867	0.00472	<0.0001
rs148570357	T	C	NA	-0.0233	0.00222	<0.0001
rs1496653	G	A	NA	-0.0206	0.00249	<0.0001
rs150025254	T	C	NA	-0.1557	0.00606	<0.0001
rs1531583	T	G	NA	0.03504	0.0052	<0.0001
rs1535464	A	G	NA	-0.0222	0.00233	<0.0001
rs1550026	T	A	NA	0.02095	0.00205	<0.0001
rs1562397	A	G	NA	0.01397	0.00217	<0.0001
rs156265	G	C	NA	-0.0164	0.00287	<0.0001

rs1569780	C	A	NA	-0.0185	0.00207	<0.0001
rs1570360	G	A	NA	0.01785	0.00214	<0.0001
rs1579238	G	A	NA	-0.0212	0.00236	<0.0001
rs1604038	T	C	NA	-0.0412	0.00223	<0.0001
rs1641523	T	C	NA	-0.0276	0.00205	<0.0001
rs16856859	G	A	NA	0.02906	0.00205	<0.0001
rs16873415	G	A	NA	-0.0115	0.00206	<0.0001
rs1705263	A	C	NA	-0.0137	0.00203	<0.0001
rs1707731	C	T	NA	-0.0129	0.00214	<0.0001
rs17168486	T	C	NA	0.02948	0.00267	<0.0001
rs17419291	C	T	NA	-0.0199	0.00357	<0.0001
rs17430251	G	A	NA	0.02416	0.00308	<0.0001
rs17447545	G	A	NA	-0.0205	0.00253	<0.0001
rs174559	A	G	NA	-0.0267	0.00224	<0.0001
rs17561351	G	A	NA	0.03212	0.00414	<0.0001
rs17698176	G	T	NA	0.0213	0.00242	<0.0001
rs1774217	G	A	NA	0.01191	0.00203	<0.0001
rs17850433	C	T	NA	0.09651	0.00917	<0.0001
rs1800562	A	G	NA	-0.1254	0.00375	<0.0001
rs1822534	G	A	NA	-0.0408	0.00207	<0.0001
rs184458383	T	C	NA	-0.0245	0.00377	<0.0001
rs1866476	C	T	NA	-0.0193	0.00227	<0.0001
rs1891058	A	G	NA	0.0174	0.00207	<0.0001
rs190003288	G	A	NA	0.05578	0.00687	<0.0001
rs191358944	T	C	NA	-0.338	0.00881	<0.0001
rs1965794	T	G	NA	-0.0209	0.0035	<0.0001
rs1967604	G	A	NA	-0.0292	0.00223	<0.0001
rs1975283	C	A	NA	-0.0231	0.00218	<0.0001
rs1981767	A	G	NA	0.01962	0.00226	<0.0001
rs2044960	T	C	NA	-0.0138	0.00239	<0.0001
rs2060779	A	G	NA	-0.0275	0.00244	<0.0001
rs2060985	G	A	NA	-0.015	0.00202	<0.0001
rs2068888	A	G	NA	-0.0178	0.00205	<0.0001
rs2073040	G	A	NA	0.01442	0.00211	<0.0001
rs2143918	C	A	NA	-0.0275	0.00202	<0.0001
rs216195	G	T	NA	0.01792	0.0022	<0.0001
rs2175756	C	G	NA	0.0146	0.00212	<0.0001
rs2236497	C	T	NA	-0.0249	0.00248	<0.0001
rs2237895	C	A	NA	0.02708	0.00204	<0.0001
rs2248369	A	G	NA	0.02004	0.00212	<0.0001
rs2258238	T	A	NA	0.03346	0.00329	<0.0001
rs2267716	C	T	NA	-0.0148	0.00238	<0.0001
rs2270927	G	C	NA	0.02937	0.00344	<0.0001
rs2285005	A	G	NA	0.02604	0.00212	<0.0001
rs2292662	T	C	NA	-0.0168	0.00284	<0.0001
rs246232	G	C	NA	0.01678	0.00218	<0.0001
rs2478025	C	G	NA	0.02648	0.00268	<0.0001
rs247826	T	C	NA	0.02611	0.00242	<0.0001
rs2512539	T	G	NA	-0.0212	0.00292	<0.0001

rs2540156	G	C	NA	0.0205	0.00354	<0.0001
rs2546197	G	T	NA	0.02183	0.00377	<0.0001
rs255154	C	T	NA	0.01243	0.00204	<0.0001
rs2595701	G	A	NA	-0.0209	0.00217	<0.0001
rs2658747	G	A	NA	0.0171	0.00207	<0.0001
rs2665357	C	A	NA	0.01709	0.00202	<0.0001
rs267738	G	T	NA	-0.0249	0.00243	<0.0001
rs2726032	C	T	NA	0.01389	0.00203	<0.0001
rs2737263	T	G	NA	-0.0239	0.00223	<0.0001
rs2771425	G	A	NA	-0.0126	0.00208	<0.0001
rs2793003	C	T	NA	0.02028	0.00286	<0.0001
rs2796441	A	G	NA	-0.0131	0.00204	<0.0001
rs28421305	A	G	NA	0.02325	0.00226	<0.0001
rs2858010	C	T	NA	-0.0256	0.00213	<0.0001
rs28641468	C	T	NA	0.03536	0.00234	<0.0001
rs28690107	C	G	NA	-0.0195	0.00243	<0.0001
rs28794650	A	C	NA	0.01827	0.00205	<0.0001
rs2920880	T	C	NA	0.01186	0.00206	<0.0001
rs2927328	C	T	NA	-0.0133	0.00213	<0.0001
rs2954031	T	G	NA	0.02005	0.00203	<0.0001
rs2959356	G	A	NA	0.01339	0.0022	<0.0001
rs2978457	C	T	NA	0.01678	0.00202	<0.0001
rs332123	G	C	NA	0.01114	0.00204	<0.0001
rs34079969	A	C	NA	0.01729	0.00312	<0.0001
rs340882	G	C	NA	0.03483	0.00209	<0.0001
rs34165383	G	C	NA	-0.021	0.00343	<0.0001
rs34831382	G	A	NA	-0.0188	0.00341	<0.0001
rs348330	A	G	NA	-0.0219	0.0021	<0.0001
rs351978	G	A	NA	-0.0151	0.00207	<0.0001
rs35303761	G	A	NA	0.0195	0.00235	<0.0001
rs35365035	C	T	NA	0.04661	0.00206	<0.0001
rs35678857	A	C	NA	-0.013	0.00211	<0.0001
rs35824917	T	A	NA	-0.0196	0.00339	<0.0001
rs35889227	T	G	NA	-0.0201	0.00209	<0.0001
rs35895680	A	C	NA	-0.0139	0.00217	<0.0001
rs35958372	C	T	NA	-0.014	0.00249	<0.0001
rs368865	G	A	NA	0.03027	0.00225	<0.0001
rs3731197	T	C	NA	0.01322	0.00208	<0.0001
rs3741414	T	C	NA	-0.0184	0.00234	<0.0001
rs3748059	G	A	NA	-0.0225	0.00252	<0.0001
rs3757970	G	A	NA	0.01841	0.00207	<0.0001
rs3758725	G	C	NA	0.01405	0.0023	<0.0001
rs3793342	A	G	NA	-0.0165	0.00288	<0.0001
rs3810027	G	C	NA	0.01428	0.00213	<0.0001
rs3811444	T	C	NA	0.02454	0.00214	<0.0001
rs3827181	T	C	NA	0.01767	0.00211	<0.0001
rs3845724	G	A	NA	0.01911	0.00205	<0.0001
rs3847378	G	A	NA	-0.0179	0.00231	<0.0001
rs3918296	G	C	NA	-0.0471	0.00634	<0.0001

rs41273438	G	A	NA	0.04178	0.00505	<0.0001
rs41295942	T	C	NA	-0.0375	0.00585	<0.0001
rs4234731	G	A	NA	0.01761	0.00206	<0.0001
rs4238013	T	C	NA	-0.0187	0.00253	<0.0001
rs4239217	A	G	NA	-0.0196	0.00207	<0.0001
rs4261754	T	C	NA	-0.015	0.00224	<0.0001
rs4368494	A	G	NA	-0.018	0.00223	<0.0001
rs4382717	T	C	NA	-0.0115	0.00211	<0.0001
rs4485355	T	C	NA	0.02642	0.00223	<0.0001
rs4499344	A	G	NA	-0.0295	0.00221	<0.0001
rs4509	A	G	NA	-0.0132	0.0021	<0.0001
rs4516170	C	T	NA	-0.0489	0.00459	<0.0001
rs45607834	T	C	NA	0.02118	0.00332	<0.0001
rs4660342	G	T	NA	0.01908	0.0022	<0.0001
rs4687680	A	G	NA	0.01355	0.00211	<0.0001
rs4713573	C	A	NA	0.01887	0.00223	<0.0001
rs4737010	A	G	NA	0.0793	0.00241	<0.0001
rs4760682	A	C	NA	0.07713	0.00258	<0.0001
rs4804023	A	T	NA	0.01616	0.00223	<0.0001
rs4808072	C	T	NA	0.01391	0.00204	<0.0001
rs4809330	G	A	NA	0.01561	0.00213	<0.0001
rs4809556	A	G	NA	-0.0158	0.00205	<0.0001
rs4837345	T	C	NA	-0.0197	0.00218	<0.0001
rs4910498	T	A	NA	-0.0323	0.0021	<0.0001
rs4911256	G	A	NA	0.01376	0.00203	<0.0001
rs4945829	C	T	NA	0.01297	0.00213	<0.0001
rs4947490	G	A	NA	0.01538	0.00216	<0.0001
rs4985996	T	C	NA	-0.0204	0.00212	<0.0001
rs504348	G	C	NA	0.01716	0.00269	<0.0001
rs521048	G	A	NA	-0.019	0.00229	<0.0001
rs550057	T	C	NA	0.04661	0.00231	<0.0001
rs551118	G	C	NA	0.05683	0.00207	<0.0001
rs55770587	T	C	NA	-0.0454	0.00502	<0.0001
rs55881843	A	G	NA	-0.0312	0.00292	<0.0001
rs56395926	A	G	NA	-0.0149	0.0024	<0.0001
rs56777435	G	A	NA	0.03552	0.00598	<0.0001
rs57060554	G	A	NA	-0.0147	0.0023	<0.0001
rs57625745	C	T	NA	0.01922	0.00284	<0.0001
rs57696714	C	T	NA	-0.0624	0.00327	<0.0001
rs57787629	C	T	NA	0.01483	0.00222	<0.0001
rs57891429	C	T	NA	0.01763	0.00299	<0.0001
rs58310247	T	G	NA	0.01344	0.00246	<0.0001
rs59034241	T	G	NA	0.01467	0.00204	<0.0001
rs592423	C	A	NA	-0.021	0.00202	<0.0001
rs59791349	T	C	NA	-0.0186	0.00224	<0.0001
rs6014993	G	A	NA	0.02767	0.00202	<0.0001
rs603923	A	G	NA	0.02155	0.00318	<0.0001
rs60426421	A	G	NA	-0.0174	0.00271	<0.0001
rs6045615	C	A	NA	-0.0158	0.00216	<0.0001

rs6077396	A	G	NA	-0.0199	0.00201	<0.0001
rs60833263	A	G	NA	0.01878	0.00203	<0.0001
rs61138219	T	C	NA	-0.0205	0.0028	<0.0001
rs61750929	T	C	NA	-0.1037	0.00442	<0.0001
rs61850681	A	G	NA	-0.0342	0.0024	<0.0001
rs61944004	A	G	NA	0.03383	0.00244	<0.0001
rs61963209	A	G	NA	-0.0139	0.00251	<0.0001
rs62036942	C	T	NA	0.01684	0.00292	<0.0001
rs62132522	C	T	NA	-0.0131	0.00205	<0.0001
rs62246446	G	C	NA	-0.0199	0.00264	<0.0001
rs62466318	T	C	NA	0.01381	0.00251	<0.0001
rs62585575	T	C	NA	0.02403	0.00433	<0.0001
rs636089	C	T	NA	0.01551	0.00207	<0.0001
rs6445826	C	T	NA	0.01177	0.00206	<0.0001
rs6518681	G	A	NA	0.03641	0.00349	<0.0001
rs6583177	G	T	NA	0.01117	0.00201	<0.0001
rs6584535	C	T	NA	0.01397	0.00248	<0.0001
rs6589939	G	A	NA	0.01775	0.00208	<0.0001
rs66593272	T	A	NA	-0.133	0.00529	<0.0001
rs67131976	T	C	NA	0.04753	0.00266	<0.0001
rs6720896	C	T	NA	-0.013	0.00227	<0.0001
rs6726007	T	A	NA	-0.0145	0.00203	<0.0001
rs6736362	T	C	NA	0.01795	0.00204	<0.0001
rs6777684	G	A	NA	0.02461	0.00207	<0.0001
rs6780171	A	T	NA	0.02199	0.00218	<0.0001
rs6785881	T	C	NA	-0.0201	0.00202	<0.0001
rs67882627	T	A	NA	0.0386	0.00268	<0.0001
rs6804686	C	G	NA	0.01364	0.00203	<0.0001
rs6840504	T	C	NA	0.01619	0.00203	<0.0001
rs6844176	C	T	NA	0.01147	0.00203	<0.0001
rs6885132	G	C	NA	-0.0338	0.00341	<0.0001
rs6893283	T	C	NA	-0.0607	0.00839	<0.0001
rs7025532	C	T	NA	0.03618	0.00252	<0.0001
rs7124355	G	A	NA	-0.0198	0.00216	<0.0001
rs7126413	G	A	NA	0.01164	0.00208	<0.0001
rs71313931	G	C	NA	0.01573	0.00223	<0.0001
rs7151822	C	T	NA	-0.0222	0.00234	<0.0001
rs71603867	T	C	NA	0.02255	0.00313	<0.0001
rs7195055	T	C	NA	-0.0535	0.00844	<0.0001
rs72683923	C	T	NA	-0.0489	0.00719	<0.0001
rs72698718	A	G	NA	0.02484	0.00295	<0.0001
rs72753548	T	C	NA	0.01285	0.00229	<0.0001
rs72765381	C	T	NA	-0.0157	0.00286	<0.0001
rs72805701	T	G	NA	0.05808	0.00695	<0.0001
rs72811487	A	G	NA	-0.0559	0.00545	<0.0001
rs72814215	A	G	NA	-0.0598	0.00972	<0.0001
rs72900998	C	T	NA	-0.0346	0.00354	<0.0001
rs72939920	T	A	NA	-0.0256	0.00238	<0.0001
rs72973028	C	A	NA	0.01705	0.00268	<0.0001

rs72986458	T	A	NA	0.01705	0.00245	<0.0001
rs7306544	C	T	NA	0.02168	0.00331	<0.0001
rs7327432	A	T	NA	0.02019	0.00368	<0.0001
rs73564493	A	G	NA	-0.0303	0.00389	<0.0001
rs73856768	C	T	NA	-0.0264	0.00375	<0.0001
rs7400121	G	A	NA	0.0416	0.00276	<0.0001
rs74857652	T	C	NA	0.0335	0.00547	<0.0001
rs75367758	A	G	NA	-0.0446	0.0047	<0.0001
rs7546390	C	T	NA	0.02847	0.00349	<0.0001
rs75629141	A	T	NA	-0.0291	0.00268	<0.0001
rs7572278	A	T	NA	0.02663	0.00251	<0.0001
rs76413056	A	G	NA	0.02836	0.00495	<0.0001
rs76505278	C	T	NA	-0.0261	0.0033	<0.0001
rs76701589	T	G	NA	0.01586	0.00279	<0.0001
rs7679687	T	G	NA	0.05566	0.00217	<0.0001
rs76827930	C	T	NA	0.02572	0.00443	<0.0001
rs76895963	G	T	NA	-0.1863	0.0078	<0.0001
rs7720275	C	T	NA	0.02454	0.00267	<0.0001
rs7732130	A	G	NA	-0.0265	0.00216	<0.0001
rs7798364	A	G	NA	-0.0147	0.00248	<0.0001
rs7844805	G	C	NA	-0.0237	0.00218	<0.0001
rs78588343	A	G	NA	-0.0342	0.00262	<0.0001
rs7903146	T	C	NA	0.07402	0.00224	<0.0001
rs79121130	T	C	NA	0.03793	0.00275	<0.0001
rs79221399	A	C	NA	-0.0314	0.00368	<0.0001
rs7923837	A	G	NA	-0.0288	0.0021	<0.0001
rs79514927	G	A	NA	0.0275	0.00496	<0.0001
rs797399	G	A	NA	-0.0151	0.00228	<0.0001
rs79755767	A	G	NA	-0.0339	0.00339	<0.0001
rs8006908	G	A	NA	0.01243	0.00202	<0.0001
rs8013143	G	A	NA	0.01952	0.00224	<0.0001
rs8050500	C	T	NA	-0.0262	0.00202	<0.0001
rs8069197	T	C	NA	-0.0183	0.00235	<0.0001
rs8078338	G	A	NA	-0.0215	0.00202	<0.0001
rs8110787	T	C	NA	-0.0231	0.00206	<0.0001
rs8176059	A	G	NA	-0.0683	0.00955	<0.0001
rs838717	A	G	NA	0.01568	0.00204	<0.0001
rs849142	C	T	NA	-0.0266	0.00201	<0.0001
rs853773	G	A	NA	0.07029	0.00206	<0.0001
rs855791	G	A	NA	-0.0633	0.00203	<0.0001
rs857725	G	T	NA	0.07782	0.00228	<0.0001
rs878521	A	G	NA	0.08542	0.00232	<0.0001
rs8887	C	T	NA	-0.0119	0.00205	<0.0001
rs918739	T	G	NA	-0.0221	0.00215	<0.0001
rs9273368	A	G	NA	0.03025	0.00219	<0.0001
rs9302377	T	C	NA	0.0158	0.00213	<0.0001
rs9303620	C	T	NA	-0.028	0.00225	<0.0001
rs9314323	G	A	NA	0.01255	0.00221	<0.0001
rs9320429	G	T	NA	0.01331	0.00207	<0.0001

rs9323450	G	A	NA	0.01333	0.00212	<0.0001
rs9376091	T	C	NA	-0.0395	0.0023	<0.0001
rs9398642	T	C	NA	-0.0179	0.00286	<0.0001
rs9423289	T	C	NA	0.01533	0.00206	<0.0001
rs9479509	A	G	NA	0.01387	0.00223	<0.0001
rs9494600	C	T	NA	-0.0117	0.00211	<0.0001
rs9892222	C	T	NA	0.0299	0.00378	<0.0001
rs998584	A	C	NA	0.0219	0.00202	<0.0001
rs9994509	G	A	NA	-0.0199	0.00207	<0.0001

Table S6. Instruments used in the Mendelian randomization analysis of the smoking index

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs10173733	C	G	0.40302	-0.0065	0.00118	<0.0001
rs10193706	C	A	0.52527	-0.0118	0.00117	<0.0001
rs10233018	G	A	0.50419	-0.0077	0.00116	<0.0001
rs10274594	G	T	0.49589	0.00783	0.00117	<0.0001
rs1029986	T	C	0.58492	-0.007	0.0012	<0.0001
rs10774625	G	A	0.50415	0.00749	0.00116	<0.0001
rs10813628	C	T	0.51513	-0.0069	0.00117	<0.0001
rs10897561	C	T	0.35646	-0.0067	0.00122	<0.0001
rs10905461	C	T	0.74419	0.00727	0.00133	<0.0001
rs10914684	A	G	0.32398	0.00774	0.00124	<0.0001
rs10956808	G	T	0.42225	0.00762	0.00118	<0.0001
rs11103667	T	C	0.19203	-0.0086	0.00149	<0.0001
rs11127913	C	T	0.39018	0.00818	0.00119	<0.0001
rs11611651	A	G	0.08771	-0.012	0.00205	<0.0001
rs11631530	T	C	0.11806	-0.01	0.0018	<0.0001
rs11646575	A	G	0.43874	-0.0082	0.00117	<0.0001
rs11693702	A	T	0.46635	-0.008	0.00117	<0.0001
rs117435980	C	G	0.16339	-0.0092	0.00157	<0.0001
rs12042107	C	T	0.54986	0.00718	0.00117	<0.0001
rs12244388	A	G	0.3363	-0.0104	0.00123	<0.0001
rs12450028	T	C	0.34473	-0.0071	0.00122	<0.0001
rs12479064	T	C	0.2083	-0.008	0.00147	<0.0001
rs12487411	A	G	0.47206	0.0075	0.00117	<0.0001
rs12608052	T	C	0.51967	0.00675	0.00116	<0.0001
rs12725407	C	G	0.19104	0.00814	0.00148	<0.0001
rs12886628	C	G	0.66462	-0.0071	0.00123	<0.0001
rs12910916	T	C	0.21213	-0.009	0.00142	<0.0001
rs1492546	G	C	0.55039	-0.0069	0.00117	<0.0001
rs1499982	T	C	0.85128	-0.0115	0.00164	<0.0001
rs1549213	C	G	0.64145	0.00853	0.00121	<0.0001
rs1561195	A	C	0.52267	-0.0079	0.00119	<0.0001
rs1565735	A	T	0.20157	0.01159	0.00146	<0.0001
rs16951001	T	G	0.4186	-0.0066	0.00118	<0.0001
rs17003752	G	A	0.13869	0.00986	0.0017	<0.0001
rs17151637	T	C	0.28124	0.00751	0.00129	<0.0001
rs1899896	T	C	0.29758	-0.008	0.00127	<0.0001

rs2240294	A	T	0.44369	0.00696	0.00117	<0.0001
rs2416770	T	C	0.53106	-0.0065	0.00117	<0.0001
rs264974	A	T	0.48628	0.00931	0.00116	<0.0001
rs2675609	C	T	0.62749	0.00816	0.00121	<0.0001
rs2797116	C	T	0.2672	0.00791	0.00131	<0.0001
rs2867749	A	C	0.31885	0.00694	0.00125	<0.0001
rs299688	T	G	0.71584	-0.0073	0.00131	<0.0001
rs326341	A	G	0.47601	0.00658	0.00117	<0.0001
rs35891966	A	G	0.07211	0.01478	0.00224	<0.0001
rs379525	T	C	0.48132	-0.0065	0.00119	<0.0001
rs42417	T	C	0.69019	-0.007	0.00126	<0.0001
rs4566215	C	A	0.53263	0.00662	0.00117	<0.0001
rs4910656	C	T	0.34157	0.00684	0.00123	<0.0001
rs4957528	C	A	0.79196	-0.0085	0.00145	<0.0001
rs523528	T	C	0.58572	0.00807	0.00119	<0.0001
rs528301	A	G	0.55203	-0.0086	0.00117	<0.0001
rs55921136	C	T	0.20309	0.0086	0.00145	<0.0001
rs568599	C	G	0.5428	-0.0067	0.00116	<0.0001
rs6141314	A	G	0.24247	-0.0081	0.00136	<0.0001
rs6265	T	C	0.18869	0.01016	0.00148	<0.0001
rs6433897	C	T	0.73667	-0.0072	0.00132	<0.0001
rs6676022	T	C	0.12162	0.01159	0.00178	<0.0001
rs6690680	C	T	0.15777	0.00884	0.0016	<0.0001
rs6828849	T	A	0.41741	0.00671	0.00118	<0.0001
rs72505558	G	A	0.39864	0.00674	0.00119	<0.0001
rs72678864	A	G	0.17383	0.00975	0.00153	<0.0001
rs7333559	A	G	0.79032	0.00805	0.00144	<0.0001
rs7451586	G	C	0.4048	-0.0067	0.0012	<0.0001
rs748828	T	C	0.2831	0.00862	0.00129	<0.0001
rs7528604	A	G	0.43329	0.00687	0.00118	<0.0001
rs7567570	C	T	0.82691	-0.0091	0.00153	<0.0001
rs763053	C	T	0.22457	0.00806	0.0014	<0.0001
rs76608582	A	C	0.04771	0.01829	0.00286	<0.0001
rs772921	T	C	0.34311	0.00727	0.00122	<0.0001
rs77878475	A	T	0.08583	0.0126	0.00215	<0.0001
rs7870475	C	T	0.47429	-0.0072	0.00116	<0.0001
rs7948789	G	A	0.38609	-0.0162	0.0012	<0.0001
rs883403	C	T	0.15412	0.00942	0.00161	<0.0001
rs9375371	A	G	0.26887	-0.0074	0.00131	<0.0001
rs9381917	A	G	0.10209	0.01126	0.00192	<0.0001
rs9423279	G	C	0.65667	0.00767	0.00125	<0.0001
rs9487626	T	C	0.81778	0.0131	0.0015	<0.0001

Table S7. Instruments used in the Mendelian randomization analysis of BMI

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs10018743	A	G	0.4855	0.0154	0.002	<0.0001
rs1002226	T	C	0.62158	0.0135	0.0019	<0.0001
rs10084743	G	A	0.39663	0.0122	0.002	<0.0001

rs10091265	G	C	0.55212	-0.0159	0.002	<0.0001
rs10139547	A	G	0.26847	0.0127	0.0022	<0.0001
rs10172070	T	C	0.15119	0.0168	0.0026	<0.0001
rs10206023	C	G	0.27988	-0.0136	0.0022	<0.0001
rs10236214	T	C	0.74885	0.0153	0.0024	<0.0001
rs1026534	C	G	0.53686	0.0204	0.0019	<0.0001
rs1030049	G	A	0.30758	0.0131	0.0021	<0.0001
rs10403370	A	G	0.15603	-0.0156	0.0027	<0.0001
rs10404726	T	C	0.61072	-0.0189	0.0022	<0.0001
rs10464757	C	G	0.46535	0.0115	0.0019	<0.0001
rs1048932	A	C	0.45991	-0.0165	0.0019	<0.0001
rs10492229	T	C	0.16714	0.0149	0.0027	<0.0001
rs10507483	C	T	0.11863	0.0184	0.003	<0.0001
rs10752651	T	C	0.47071	0.0129	0.0019	<0.0001
rs10769931	C	T	0.56439	0.0174	0.002	<0.0001
rs10771041	T	C	0.30166	0.0168	0.0025	<0.0001
rs10798886	G	A	0.53045	0.0135	0.002	<0.0001
rs10811662	A	G	0.25482	0.0201	0.0022	<0.0001
rs10824211	T	C	0.12394	0.0168	0.0029	<0.0001
rs10835488	A	C	0.11985	-0.0171	0.0029	<0.0001
rs10852374	C	G	0.76696	-0.0143	0.0023	<0.0001
rs10865612	C	T	0.46899	-0.0173	0.002	<0.0001
rs10883553	A	C	0.33249	0.0143	0.0022	<0.0001
rs10887578	C	G	0.44789	0.0106	0.0019	<0.0001
rs10894670	A	C	0.63143	-0.0114	0.002	<0.0001
rs10938397	G	A	0.39221	0.0289	0.0019	<0.0001
rs10941611	C	T	0.67467	0.0162	0.0025	<0.0001
rs10954772	C	T	0.76168	-0.0187	0.0023	<0.0001
rs10962552	T	C	0.21178	0.0223	0.0023	<0.0001
rs11001963	T	C	0.50991	0.0121	0.0019	<0.0001
rs1100237	C	T	0.67475	-0.0118	0.0022	<0.0001
rs11012732	G	A	0.22863	0.0227	0.0025	<0.0001
rs11055888	G	A	0.20047	-0.0161	0.0029	<0.0001
rs11076153	C	T	0.16668	0.0153	0.0025	<0.0001
rs11137826	T	G	0.50855	-0.0112	0.0019	<0.0001
rs11150745	G	A	0.32415	-0.0161	0.002	<0.0001
rs11164849	C	A	0.55771	-0.0113	0.002	<0.0001
rs111909661	C	G	0.17295	0.0179	0.0026	<0.0001
rs11264489	G	A	0.45403	0.0114	0.002	<0.0001
rs113728099	A	G	0.01747	-0.0706	0.0075	<0.0001
rs11525873	C	T	0.17969	-0.0165	0.0025	<0.0001
rs1154988	A	T	0.78797	0.0173	0.0023	<0.0001
rs11639144	A	G	0.18406	-0.0151	0.0025	<0.0001
rs116394958	T	C	0.20857	0.0159	0.0024	<0.0001
rs11642015	T	C	0.3399	0.074	0.002	<0.0001
rs11652025	G	T	0.42995	0.0125	0.0021	<0.0001
rs11653258	T	G	0.23154	-0.0155	0.0028	<0.0001
rs11655587	T	C	0.29935	-0.0185	0.0021	<0.0001
rs117342986	T	C	0.02667	0.0424	0.0076	<0.0001

rs11741307	G	T	0.14905	-0.0189	0.003	<0.0001
rs11757278	C	T	0.37015	-0.0121	0.002	<0.0001
rs11782074	T	G	0.30871	0.017	0.0022	<0.0001
rs11851122	G	A	0.61086	0.0188	0.002	<0.0001
rs11857221	A	C	0.41556	0.0143	0.0019	<0.0001
rs11907932	G	A	0.35139	-0.0193	0.002	<0.0001
rs11979174	C	G	0.19709	-0.0166	0.0024	<0.0001
rs11986009	T	G	0.34698	-0.0172	0.002	<0.0001
rs12024554	T	C	0.36653	-0.0122	0.0021	<0.0001
rs12042959	G	A	0.12206	-0.0186	0.0029	<0.0001
rs12044012	A	G	0.27786	-0.0122	0.0021	<0.0001
rs12121950	T	G	0.42865	0.0184	0.002	<0.0001
rs12140153	T	G	0.09599	-0.0328	0.0041	<0.0001
rs12144626	C	T	0.40834	-0.0171	0.0023	<0.0001
rs12195582	T	C	0.45601	-0.0202	0.0032	<0.0001
rs12290350	T	C	0.16272	-0.0156	0.0027	<0.0001
rs1229984	C	T	0.74811	0.0292	0.0035	<0.0001
rs12331784	A	G	0.51991	0.0107	0.0019	<0.0001
rs12357890	G	A	0.55887	0.021	0.0024	<0.0001
rs12364470	G	T	0.1653	0.0208	0.0031	<0.0001
rs12435171	A	G	0.53973	-0.0137	0.0022	<0.0001
rs12440879	A	G	0.49506	-0.0123	0.0019	<0.0001
rs12444338	T	G	0.43197	-0.0117	0.0019	<0.0001
rs12448257	A	G	0.24553	0.0173	0.0022	<0.0001
rs12474491	T	A	0.50428	-0.0113	0.0019	<0.0001
rs12479357	G	A	0.65847	0.0176	0.002	<0.0001
rs12495519	C	T	0.31288	0.0136	0.0021	<0.0001
rs12508307	T	C	0.42597	-0.0129	0.002	<0.0001
rs12537134	G	A	0.50669	-0.0125	0.0019	<0.0001
rs12553508	T	C	0.36712	0.0161	0.002	<0.0001
rs1269175	G	A	0.37791	-0.0114	0.002	<0.0001
rs12697021	A	G	0.31279	-0.0149	0.002	<0.0001
rs12714415	C	T	0.14265	-0.0525	0.0027	<0.0001
rs12888955	A	G	0.62111	-0.016	0.0019	<0.0001
rs12920259	A	G	0.70603	-0.0135	0.0022	<0.0001
rs12926311	C	G	0.2824	-0.0147	0.0022	<0.0001
rs12926311	C	G	0.2824	-0.0147	0.0022	<0.0001
rs12937411	T	C	0.40998	-0.0176	0.0019	<0.0001
rs12964145	G	C	0.72605	-0.0119	0.0021	<0.0001
rs12974458	T	C	0.54366	0.0187	0.0023	<0.0001
rs12995314	C	T	0.31484	0.0184	0.0025	<0.0001
rs13000361	C	T	0.57694	0.0139	0.002	<0.0001
rs13047416	G	C	0.48391	-0.0143	0.002	<0.0001
rs13073568	T	G	0.57492	-0.019	0.0019	<0.0001
rs13107325	T	C	0.07483	0.0493	0.0044	<0.0001
rs13132853	G	A	0.36524	-0.0139	0.0024	<0.0001
rs13156484	A	G	0.48746	-0.0163	0.0019	<0.0001
rs13182474	C	G	0.2654	-0.0165	0.0022	<0.0001
rs13210756	A	T	0.12887	-0.0207	0.0035	<0.0001

rs13306780	C	A	0.57861	-0.0113	0.0021	<0.0001
rs13403962	T	C	0.54092	-0.0147	0.0021	<0.0001
rs13419498	A	G	0.31746	0.0127	0.0021	<0.0001
rs13427822	G	A	0.19838	-0.0198	0.0025	<0.0001
rs1349414	C	A	0.20068	0.0164	0.0024	<0.0001
rs1356505	C	A	0.446	-0.0148	0.0019	<0.0001
rs138395	T	C	0.49207	-0.0108	0.0019	<0.0001
rs138685654	C	T	0.13664	0.0248	0.0028	<0.0001
rs1389067	G	A	0.71326	0.0136	0.0023	<0.0001
rs142592509	C	G	0.0812	-0.0261	0.0044	<0.0001
rs1458913	T	A	0.41286	-0.0128	0.0019	<0.0001
rs1470687	G	C	0.23473	-0.0147	0.0024	<0.0001
rs147678035	G	A	0.15314	0.03	0.0034	<0.0001
rs147730268	T	G	0.08865	-0.0357	0.0042	<0.0001
rs1481012	G	A	0.16959	-0.0148	0.0025	<0.0001
rs148636479	T	A	0.02896	-0.0405	0.0074	<0.0001
rs1544690	C	T	0.31397	-0.0155	0.0022	<0.0001
rs1557329	A	C	0.82393	-0.0168	0.0025	<0.0001
rs1561073	A	T	0.62427	-0.0139	0.0021	<0.0001
rs1576655	C	A	0.57286	0.0135	0.0019	<0.0001
rs1599539	A	G	0.49053	0.0122	0.0022	<0.0001
rs168083	T	G	0.69457	-0.0121	0.0021	<0.0001
rs16846140	G	A	0.38248	0.0139	0.0019	<0.0001
rs16906845	A	G	0.08527	-0.0184	0.0034	<0.0001
rs1691101	C	T	0.47842	0.0103	0.0019	<0.0001
rs17024393	C	T	0.02584	0.0635	0.0074	<0.0001
rs1717776	G	A	0.35468	-0.0145	0.002	<0.0001
rs17201143	T	C	0.35916	-0.0121	0.002	<0.0001
rs17399739	G	A	0.07032	0.0236	0.0037	<0.0001
rs17724992	G	A	0.32606	-0.0166	0.002	<0.0001
rs17731998	T	C	0.21025	0.0142	0.0024	<0.0001
rs17767765	T	C	0.47131	-0.0143	0.0019	<0.0001
rs17770336	T	C	0.28326	0.0201	0.0021	<0.0001
rs1788808	G	A	0.62516	-0.0193	0.0021	<0.0001
rs1799992	C	T	0.31564	0.0141	0.0021	<0.0001
rs1861410	T	C	0.56678	-0.0203	0.0019	<0.0001
rs1877139	A	G	0.06056	-0.0281	0.0049	<0.0001
rs1905505	A	G	0.26243	0.0171	0.0021	<0.0001
rs1933437	A	G	0.66867	-0.0124	0.002	<0.0001
rs1936433	T	C	0.18443	-0.014	0.0024	<0.0001
rs1937433	G	C	0.42131	0.0127	0.0021	<0.0001
rs1950436	G	A	0.71786	0.0208	0.0021	<0.0001
rs1973993	C	T	0.67704	0.0162	0.0021	<0.0001
rs199750218	G	T	0.34845	0.0156	0.0024	<0.0001
rs2032912	T	G	0.32279	-0.0197	0.0021	<0.0001
rs2046002	C	T	0.6635	-0.0119	0.002	<0.0001
rs2048523	A	G	0.3609	-0.0125	0.0021	<0.0001
rs2147905	C	T	0.50912	0.0136	0.0019	<0.0001
rs215669	A	G	0.52317	-0.0142	0.002	<0.0001

rs2237579	G	T	0.44246	0.0115	0.0019	<0.0001
rs2237897	T	C	0.37613	0.0422	0.0033	<0.0001
rs2247859	A	G	0.37256	0.0139	0.002	<0.0001
rs2254992	T	C	0.19349	-0.0141	0.0024	<0.0001
rs227200	C	G	0.47818	-0.0135	0.0019	<0.0001
rs2289379	T	C	0.32114	-0.0165	0.0021	<0.0001
rs2307111	C	T	0.44562	-0.0268	0.0019	<0.0001
rs2322459	G	T	0.45277	-0.0132	0.0021	<0.0001
rs236660	C	T	0.57107	0.0262	0.0024	<0.0001
rs2413611	A	T	0.50866	-0.0122	0.002	<0.0001
rs2429148	G	A	0.53993	0.0131	0.0021	<0.0001
rs2450139	A	G	0.2486	-0.0126	0.0022	<0.0001
rs2453763	A	T	0.52102	0.0118	0.002	<0.0001
rs2454812	T	C	0.68152	0.0115	0.0021	<0.0001
rs2455821	A	C	0.26819	0.0131	0.0021	<0.0001
rs245775	G	A	0.79062	0.0195	0.0024	<0.0001
rs2465054	A	G	0.40184	-0.0151	0.0019	<0.0001
rs2482395	A	G	0.52321	-0.014	0.0023	<0.0001
rs2489219	A	G	0.72911	0.014	0.0021	<0.0001
rs2491864	A	G	0.30378	0.0125	0.0021	<0.0001
rs2528787	T	C	0.31608	-0.0152	0.0021	<0.0001
rs2579040	A	T	0.79689	-0.0153	0.0025	<0.0001
rs2608984	T	A	0.21771	0.0136	0.0023	<0.0001
rs2618039	T	A	0.39915	0.0131	0.0019	<0.0001
rs2637650	T	C	0.17313	0.0162	0.0026	<0.0001
rs2693838	A	C	0.49674	-0.0124	0.0019	<0.0001
rs2733289	C	T	0.45628	0.0128	0.0019	<0.0001
rs273503	C	T	0.42149	0.018	0.0024	<0.0001
rs2759700	C	T	0.66669	-0.0114	0.0021	<0.0001
rs2802295	G	A	0.66365	0.0175	0.002	<0.0001
rs2820295	A	G	0.26593	0.0248	0.0022	<0.0001
rs28350	G	A	0.85132	-0.0181	0.0027	<0.0001
rs2861685	C	T	0.47955	-0.0144	0.0019	<0.0001
rs28836792	C	T	0.15146	0.0179	0.0026	<0.0001
rs2933223	C	T	0.47673	0.015	0.0019	<0.0001
rs2952863	G	T	0.6141	-0.0137	0.002	<0.0001
rs2977321	T	C	0.66751	0.0209	0.002	<0.0001
rs3003614	A	G	0.56164	-0.0129	0.0019	<0.0001
rs3098843	G	A	0.58542	-0.0186	0.0019	<0.0001
rs329118	T	C	0.40385	-0.0176	0.0019	<0.0001
rs329651	T	G	0.80357	0.0166	0.0029	<0.0001
rs34298980	C	T	0.46748	-0.0214	0.002	<0.0001
rs34361149	A	G	0.13656	-0.0309	0.0029	<0.0001
rs34379767	A	G	0.26835	-0.036	0.0021	<0.0001
rs34421088	G	A	0.35942	-0.0202	0.0022	<0.0001
rs34433316	G	A	0.23827	-0.0176	0.0023	<0.0001
rs34607423	C	A	0.33798	-0.011	0.002	<0.0001
rs34811474	A	G	0.23204	-0.0323	0.0028	<0.0001
rs34916533	A	C	0.29674	-0.0167	0.0021	<0.0001

rs35198068	C	T	0.21392	-0.0187	0.0024	<0.0001
rs35364449	T	C	0.11145	0.0259	0.0037	<0.0001
rs35537311	T	C	0.35391	-0.0118	0.002	<0.0001
rs35851183	G	A	0.40746	0.0141	0.0019	<0.0001
rs35957544	T	G	0.45972	-0.0166	0.002	<0.0001
rs35991856	A	C	0.24046	0.0285	0.0023	<0.0001
rs3732359	A	G	0.68808	0.0143	0.0021	<0.0001
rs3740397	C	G	0.37642	0.0139	0.0019	<0.0001
rs3784710	C	T	0.34831	-0.0233	0.0021	<0.0001
rs3798519	C	A	0.21262	0.035	0.0023	<0.0001
rs3808477	T	C	0.27871	-0.0172	0.0021	<0.0001
rs3810505	G	C	0.35217	0.0119	0.002	<0.0001
rs3853475	C	A	0.43749	-0.012	0.0019	<0.0001
rs3931548	A	C	0.37786	0.0175	0.0024	<0.0001
rs39330	T	A	0.45166	-0.0152	0.0019	<0.0001
rs3943933	A	T	0.59687	0.0134	0.0021	<0.0001
rs394608	C	T	0.53973	0.0142	0.0019	<0.0001
rs3955162	T	C	0.54495	-0.0173	0.002	<0.0001
rs3966782	C	T	0.44411	0.0126	0.002	<0.0001
rs4017425	T	C	0.53844	-0.012	0.0019	<0.0001
rs408067	G	C	0.66538	-0.0139	0.002	<0.0001
rs41129	G	T	0.23841	-0.0185	0.0022	<0.0001
rs412378	A	G	0.81454	-0.0161	0.0025	<0.0001
rs4261944	G	T	0.50373	0.0151	0.0021	<0.0001
rs4402589	G	T	0.47852	0.0236	0.0019	<0.0001
rs4405740	C	T	0.66326	-0.0181	0.0023	<0.0001
rs4477562	T	C	0.15819	0.0279	0.0026	<0.0001
rs452154	G	A	0.26287	0.0141	0.0022	<0.0001
rs4543518	G	C	0.68066	0.013	0.002	<0.0001
rs45486197	A	G	0.06617	0.0267	0.0047	<0.0001
rs4595495	G	A	0.30679	0.013	0.0022	<0.0001
rs4657793	A	T	0.32326	-0.0149	0.002	<0.0001
rs4670627	T	C	0.6474	0.0112	0.0021	<0.0001
rs4710941	T	C	0.24917	-0.0253	0.0022	<0.0001
rs4718964	T	G	0.50709	0.0134	0.002	<0.0001
rs4790296	C	T	0.18941	-0.0242	0.003	<0.0001
rs4795608	G	A	0.34864	0.0122	0.002	<0.0001
rs4813800	G	A	0.70457	0.0185	0.0021	<0.0001
rs4839716	C	T	0.39986	-0.0187	0.0024	<0.0001
rs4851254	G	C	0.2358	-0.021	0.0027	<0.0001
rs4860804	C	T	0.78458	-0.0169	0.0028	<0.0001
rs4889898	A	C	0.35639	-0.0144	0.002	<0.0001
rs4911399	A	C	0.60529	0.0128	0.0019	<0.0001
rs4986044	T	C	0.51587	-0.0163	0.0019	<0.0001
rs513249	A	T	0.20897	0.013	0.0024	<0.0001
rs539515	C	A	0.21209	0.0468	0.0023	<0.0001
rs55938344	C	A	0.16723	-0.0176	0.0027	<0.0001
rs56161855	T	A	0.18112	0.0179	0.0025	<0.0001
rs56211164	A	G	0.21295	-0.0132	0.0024	<0.0001

rs56212061	T	C	0.15047	-0.022	0.0033	<0.0001
rs56773984	T	A	0.16762	-0.0188	0.0031	<0.0001
rs56803094	G	A	0.22633	-0.0159	0.0023	<0.0001
rs57010886	G	T	0.13012	0.0247	0.0035	<0.0001
rs57307148	A	C	0.21453	0.0236	0.0028	<0.0001
rs57371116	T	G	0.19228	0.0225	0.003	<0.0001
rs57590313	A	C	0.29048	0.0136	0.0022	<0.0001
rs58243462	C	T	0.23131	-0.0161	0.0028	<0.0001
rs58895838	G	A	0.20044	-0.0138	0.0024	<0.0001
rs58948644	A	G	0.51085	0.012	0.0019	<0.0001
rs59299413	C	G	0.21904	-0.0141	0.0023	<0.0001
rs59525802	G	A	0.09183	0.019	0.0034	<0.0001
rs6001877	A	G	0.38191	-0.0191	0.0019	<0.0001
rs6029180	G	A	0.39523	0.0111	0.002	<0.0001
rs6030803	C	T	0.1491	-0.0172	0.0026	<0.0001
rs6050446	G	A	0.96692	0.0404	0.0066	<0.0001
rs607824	A	G	0.53952	-0.0109	0.002	<0.0001
rs61743745	A	G	0.03028	-0.042	0.0068	<0.0001
rs61746970	A	G	0.03964	0.0345	0.0061	<0.0001
rs61813324	T	C	0.13559	0.028	0.0035	<0.0001
rs61826865	A	T	0.13924	0.0229	0.0027	<0.0001
rs61876744	C	T	0.58645	0.0112	0.0019	<0.0001
rs61903695	G	A	0.21143	0.0157	0.0024	<0.0001
rs61991650	G	A	0.73272	0.0119	0.0021	<0.0001
rs62009152	C	T	0.18066	-0.0185	0.0026	<0.0001
rs62086046	T	C	0.36298	0.0195	0.0022	<0.0001
rs62104483	A	G	0.25333	0.0202	0.0023	<0.0001
rs62147189	G	T	0.62114	-0.016	0.0024	<0.0001
rs62223042	G	A	0.33406	0.0117	0.002	<0.0001
rs62242105	A	G	0.23729	-0.014	0.0024	<0.0001
rs62290352	A	G	0.26544	-0.0127	0.0022	<0.0001
rs6235	G	C	0.25268	0.0171	0.0022	<0.0001
rs625652	A	T	0.63962	-0.0211	0.0024	<0.0001
rs6441086	A	T	0.25998	-0.0136	0.0022	<0.0001
rs6444082	T	G	0.27672	-0.0149	0.0021	<0.0001
rs6445264	A	G	0.57828	0.0123	0.002	<0.0001
rs6471352	T	C	0.56722	0.0124	0.0019	<0.0001
rs6476613	G	A	0.33877	-0.0124	0.002	<0.0001
rs6530737	G	A	0.7106	-0.015	0.0021	<0.0001
rs6539064	G	C	0.28557	-0.0157	0.0021	<0.0001
rs6567160	C	T	0.22812	0.0518	0.0022	<0.0001
rs66637616	A	T	0.34339	0.0112	0.002	<0.0001
rs6710091	G	C	0.3078	-0.0144	0.0021	<0.0001
rs6716898	A	G	0.41761	0.0167	0.0019	<0.0001
rs6730142	T	C	0.23827	-0.0126	0.0022	<0.0001
rs6741157	T	C	0.31312	0.0152	0.0023	<0.0001
rs6749422	G	C	0.46756	0.0308	0.0019	<0.0001
rs6754968	A	G	0.46719	0.0146	0.002	<0.0001
rs67609008	C	T	0.20113	0.0149	0.0025	<0.0001

rs680071	C	T	0.86775	0.016	0.0028	<0.0001
rs6804181	T	A	0.19007	-0.0139	0.0024	<0.0001
rs6831020	A	C	0.22075	-0.0164	0.0024	<0.0001
rs6905321	A	G	0.33243	0.0122	0.0022	<0.0001
rs6909685	T	C	0.33155	-0.0126	0.002	<0.0001
rs6915002	C	T	0.53041	-0.0109	0.0019	<0.0001
rs6926186	A	G	0.77684	-0.0131	0.0024	<0.0001
rs6950442	G	A	0.62074	0.015	0.0023	<0.0001
rs699330	T	G	0.37997	0.0109	0.0019	<0.0001
rs6993870	C	T	0.28206	-0.0124	0.0021	<0.0001
rs7024334	G	T	0.66763	-0.0154	0.0021	<0.0001
rs7027304	T	C	0.62148	0.0134	0.0019	<0.0001
rs7029718	A	G	0.43239	0.0114	0.0019	<0.0001
rs7038943	C	T	0.36914	-0.0134	0.002	<0.0001
rs704078	G	T	0.08511	0.0219	0.0035	<0.0001
rs705139	A	G	0.4569	0.0159	0.0019	<0.0001
rs705705	C	G	0.34134	-0.0178	0.0025	<0.0001
rs7085659	T	C	0.75213	0.0148	0.0023	<0.0001
rs708921	G	C	0.27399	-0.012	0.0021	<0.0001
rs7132908	A	G	0.35385	0.0261	0.002	<0.0001
rs7141420	T	C	0.46345	0.0172	0.0019	<0.0001
rs71495049	A	G	0.11249	0.0193	0.003	<0.0001
rs7161194	G	A	0.70601	-0.0143	0.0022	<0.0001
rs7170907	T	C	0.37091	-0.0135	0.002	<0.0001
rs7189149	G	C	0.11064	0.0167	0.003	<0.0001
rs7219913	G	A	0.10583	0.0228	0.0038	<0.0001
rs7238896	G	A	0.09833	0.024	0.0033	<0.0001
rs7239114	A	G	0.40846	0.0129	0.0021	<0.0001
rs72618637	A	T	0.28597	-0.0159	0.0022	<0.0001
rs72634822	T	C	0.25438	-0.0214	0.0027	<0.0001
rs72749744	A	G	0.07986	-0.0253	0.0035	<0.0001
rs72793818	A	G	0.31933	0.0272	0.0021	<0.0001
rs72838588	A	G	0.40888	0.0145	0.0019	<0.0001
rs72948836	G	A	0.10694	-0.0176	0.0031	<0.0001
rs72976986	A	G	0.18974	-0.0237	0.003	<0.0001
rs73026721	T	C	0.15661	-0.0216	0.0032	<0.0001
rs7313220	G	A	0.56941	-0.0134	0.0019	<0.0001
rs7375701	A	G	0.72103	0.0119	0.0021	<0.0001
rs740157	G	A	0.58768	-0.0119	0.0019	<0.0001
rs74625348	C	G	0.26708	0.0137	0.0022	<0.0001
rs74944897	G	T	0.27576	-0.0126	0.0022	<0.0001
rs7498044	A	G	0.2192	-0.0179	0.0028	<0.0001
rs750090	C	T	0.49092	-0.0138	0.0021	<0.0001
rs7525548	T	A	0.41341	-0.0201	0.0022	<0.0001
rs7536458	G	T	0.3391	0.0129	0.002	<0.0001
rs754635	G	C	0.83146	0.0203	0.0025	<0.0001
rs75500572	A	G	0.38631	0.0128	0.0019	<0.0001
rs75557510	G	A	0.06064	-0.0344	0.0049	<0.0001
rs7560871	A	G	0.0696	0.0278	0.0046	<0.0001

rs7563480	T	C	0.45302	-0.0116	0.002	<0.0001
rs75641275	C	A	0.10741	0.0177	0.0031	<0.0001
rs756717	A	G	0.36966	-0.0155	0.002	<0.0001
rs7613261	T	A	0.17557	0.0225	0.0025	<0.0001
rs76179989	G	T	0.1573	0.0168	0.0026	<0.0001
rs7634084	T	A	0.40606	0.0271	0.002	<0.0001
rs76632630	G	A	0.18532	-0.0145	0.0024	<0.0001
rs7690222	T	C	0.16622	-0.0147	0.0026	<0.0001
rs7715256	T	G	0.40245	-0.0156	0.0023	<0.0001
rs77165542	T	C	0.03544	-0.096	0.0064	<0.0001
rs7720050	G	A	0.20506	-0.0159	0.0025	<0.0001
rs7728095	G	A	0.32264	0.0152	0.0021	<0.0001
rs7755574	T	G	0.37062	0.0172	0.002	<0.0001
rs778100	C	A	0.48046	-0.0145	0.0021	<0.0001
rs778433	A	G	0.41764	-0.013	0.0019	<0.0001
rs77936594	A	G	0.26537	0.0124	0.0022	<0.0001
rs7827419	A	G	0.30949	-0.012	0.002	<0.0001
rs7870970	T	G	0.46552	0.0112	0.0019	<0.0001
rs78967725	A	G	0.13671	0.0186	0.0028	<0.0001
rs7928842	C	T	0.37806	0.0243	0.0019	<0.0001
rs79348488	G	A	0.27761	-0.0133	0.0021	<0.0001
rs79430301	G	C	0.11717	-0.0164	0.003	<0.0001
rs7949071	C	T	0.48106	0.0136	0.0019	<0.0001
rs7973540	G	A	0.70223	0.0147	0.0026	<0.0001
rs7975187	G	A	0.26388	0.0132	0.0021	<0.0001
rs7978353	G	A	0.39826	-0.0111	0.0019	<0.0001
rs7990098	G	T	0.41369	0.0141	0.0019	<0.0001
rs7992832	T	C	0.19997	-0.0196	0.0025	<0.0001
rs8007832	C	T	0.36346	-0.0118	0.002	<0.0001
rs80082351	G	A	0.06148	-0.0295	0.0049	<0.0001
rs8072058	A	T	0.72936	-0.0124	0.0021	<0.0001
rs814697	C	G	0.47586	0.011	0.002	<0.0001
rs852042	G	A	0.59279	-0.0143	0.0022	<0.0001
rs869400	G	T	0.86781	0.0303	0.0029	<0.0001
rs879620	T	C	0.52673	0.0242	0.002	<0.0001
rs892761	T	G	0.54205	-0.0116	0.0019	<0.0001
rs893006	A	C	0.54885	0.0139	0.0022	<0.0001
rs902700	A	C	0.14666	0.0153	0.0028	<0.0001
rs9257157	T	C	0.25062	-0.0154	0.0022	<0.0001
rs9277988	C	T	0.19607	0.0228	0.0029	<0.0001
rs9287838	C	G	0.75765	-0.0136	0.0023	<0.0001
rs935166	A	G	0.4111	-0.0162	0.002	<0.0001
rs9366639	G	C	0.14067	-0.0169	0.0028	<0.0001
rs9368828	T	A	0.66163	-0.0308	0.0025	<0.0001
rs94398	C	G	0.48823	0.0105	0.0019	<0.0001
rs9463175	T	C	0.28657	-0.013	0.0021	<0.0001
rs947612	A	G	0.58082	-0.014	0.0022	<0.0001
rs9489620	C	G	0.42874	0.0122	0.0021	<0.0001
rs9522173	T	A	0.27877	-0.0133	0.0023	<0.0001

rs9633835	A	G	0.40733	-0.0128	0.0019	<0.0001
rs9651614	T	C	0.67716	-0.0198	0.0021	<0.0001
rs9688977	C	T	0.11125	0.0204	0.0031	<0.0001
rs980183	A	G	0.68035	-0.0184	0.0021	<0.0001
rs9860241	A	G	0.45713	-0.0133	0.0019	<0.0001
rs9861443	C	A	0.75241	0.0133	0.0022	<0.0001
rs9908480	T	G	0.44569	0.0138	0.0019	<0.0001
rs9919429	G	A	0.43495	0.0132	0.0019	<0.0001
rs994596	T	C	0.30296	0.0145	0.002	<0.0001

Table S8. Instruments used in the Mendelian randomization analysis of physical activity

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs1491872	T	C	0.34678	0.02538	0.00437	<0.0001
rs2005617	C	T	0.62535	0.02503	0.00427	<0.0001
rs2189464	T	C	0.2477	-0.0268	0.00482	<0.0001
rs2764261	G	A	0.62572	-0.0279	0.00428	<0.0001
rs328900	T	C	0.31465	0.02914	0.00446	<0.0001
rs382210	A	G	0.65481	0.0282	0.00435	<0.0001
rs429358	C	T	0.15418	0.03887	0.00573	<0.0001
rs6533635	A	G	0.62379	0.02573	0.00429	<0.0001
rs6955240	A	G	0.39014	-0.0321	0.00425	<0.0001
rs7072776	G	A	0.72155	0.02735	0.00463	<0.0001
rs7749823	C	A	0.1488	-0.0348	0.00581	<0.0001

Table S9. Instruments used in the Mendelian randomization analysis of diet score

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs1260326	C	T	NA	0.0224538	0.00356612	<0.0001
rs16843603	C	T	NA	-0.0237617	0.00388046	<0.0001
rs2136355	A	G	NA	-0.025412	0.00353205	<0.0001
rs2472297	T	C	NA	0.0506132	0.00394053	<0.0001
rs2533273	A	C	NA	0.0223024	0.00349992	<0.0001
rs2815753	A	G	NA	-0.0267262	0.0035614	<0.0001
rs4410790	C	T	NA	0.0390576	0.00362449	<0.0001
rs477813	T	C	NA	-0.0204243	0.00353631	<0.0001
rs6594014	G	A	NA	0.0206764	0.0034889	<0.0001
rs66721590	A	G	NA	-0.0217767	0.00367216	<0.0001
rs72783115	A	G	NA	0.0231814	0.00394475	<0.0001
rs898751	T	C	NA	0.0194018	0.00349099	<0.0001
rs9379829	T	C	NA	-0.0304962	0.00420701	<0.0001
rs9411419	T	C	NA	-0.0210062	0.00365064	<0.0001
rs9607805	T	C	NA	0.025946	0.00393124	<0.0001

Table S10. Instruments used in the Mendelian randomization analysis of sleep duration

MarkerName	effect_allele	other_allele	eaf	beta	standard error	*p* value
rs10510128	A	G	0.20795	0.0114	0.00197	<0.0001
rs11039216	T	C	0.53294	-0.0103	0.0016	<0.0001
rs112100783	A	G	0.03344	-0.0253	0.00455	<0.0001

rs113021516	C	G	0.3359	0.01148	0.0017	<0.0001
rs113113059	C	T	0.21983	-0.0111	0.00193	<0.0001
rs11621908	T	C	0.08281	-0.02	0.00294	<0.0001
rs11643715	G	C	0.29263	0.01095	0.00176	<0.0001
rs11650677	A	G	0.33919	0.01117	0.00169	<0.0001
rs11982852	T	C	0.24386	-0.0117	0.00186	<0.0001
rs12518468	C	T	0.32869	-0.0106	0.0017	<0.0001
rs12567114	A	G	0.27637	0.01234	0.00179	<0.0001
rs13107325	T	C	0.07491	-0.0243	0.00304	<0.0001
rs1348047	T	G	0.26725	-0.0126	0.00182	<0.0001
rs1463053	A	G	0.63969	0.00927	0.00166	<0.0001
rs151014368	A	G	0.20734	0.01138	0.00199	<0.0001
rs1517572	C	A	0.58126	0.01166	0.00162	<0.0001
rs1553132	G	A	0.25864	0.01053	0.00183	<0.0001
rs17391944	G	T	0.04986	0.02185	0.00372	<0.0001
rs174564	G	A	0.3486	0.00975	0.00168	<0.0001
rs17732997	G	C	0.42968	-0.0088	0.00162	<0.0001
rs1939455	T	G	0.12029	-0.0158	0.00252	<0.0001
rs1972712	C	T	0.24946	0.0118	0.00185	<0.0001
rs2072727	C	T	0.56459	-0.0093	0.00161	<0.0001
rs2079070	G	C	0.73458	-0.0134	0.00181	<0.0001
rs2186122	T	A	0.55991	-0.0108	0.00162	<0.0001
rs2192528	G	A	0.52249	-0.0098	0.0016	<0.0001
rs2236295	T	G	0.40304	-0.0091	0.00164	<0.0001
rs2279681	G	C	0.34179	0.0093	0.00168	<0.0001
rs2683630	G	C	0.62908	0.01495	0.00166	<0.0001
rs2734831	G	T	0.60688	-0.0098	0.00164	<0.0001
rs2748809	C	T	0.42926	-0.0093	0.00165	<0.0001
rs2839753	C	T	0.26535	-0.0106	0.00181	<0.0001
rs2863957	A	C	0.22054	0.0289	0.00193	<0.0001
rs34354917	A	C	0.28863	-0.01	0.00177	<0.0001
rs34556183	G	A	0.27989	-0.0134	0.00178	<0.0001
rs34786000	T	G	0.55336	0.01096	0.00163	<0.0001
rs35126035	C	A	0.55833	-0.0092	0.00164	<0.0001
rs35662245	A	T	0.33871	0.01016	0.00169	<0.0001
rs365663	G	A	0.45495	-0.0093	0.00161	<0.0001
rs374153	T	C	0.84257	-0.0131	0.0022	<0.0001
rs4767550	G	A	0.41317	0.01087	0.00163	<0.0001
rs55658675	T	C	0.35291	-0.0097	0.00167	<0.0001
rs56367859	G	A	0.39759	0.01162	0.00164	<0.0001
rs62444917	C	A	0.22232	0.01296	0.00193	<0.0001
rs6561715	A	T	0.63064	0.00978	0.00166	<0.0001
rs6681755	A	G	0.19978	0.01153	0.002	<0.0001
rs6783516	T	G	0.58382	-0.0098	0.00163	<0.0001
rs6889592	A	G	0.33261	0.01177	0.0017	<0.0001
rs7016314	C	T	0.65593	0.01	0.00169	<0.0001
rs7115856	C	A	0.46127	0.01082	0.0016	<0.0001
rs72771082	G	A	0.21783	0.01097	0.00194	<0.0001
rs72831782	A	T	0.26941	-0.0102	0.00184	<0.0001

rs7517981	C	T	0.6015	-0.01	0.00163	<0.0001
rs75539574	C	A	0.08577	0.02366	0.00287	<0.0001
rs76258078	G	A	0.04999	-0.0217	0.00368	<0.0001
rs7644809	C	T	0.57603	-0.0102	0.00162	<0.0001
rs7711696	T	G	0.30499	-0.0099	0.00174	<0.0001
rs7740402	G	T	0.3061	-0.0095	0.00173	<0.0001
rs7831557	A	G	0.51744	-0.0106	0.0016	<0.0001
rs8038326	G	A	0.27317	-0.0134	0.00179	<0.0001
rs8047587	T	G	0.43951	-0.011	0.00161	<0.0001
rs8072993	G	T	0.63568	0.01092	0.00199	<0.0001
rs8074498	A	T	0.58095	-0.0093	0.00163	<0.0001
rs915416	G	C	0.70906	-0.0127	0.00176	<0.0001
rs9302680	A	G	0.43927	0.01204	0.00161	<0.0001
rs9345234	C	A	0.57786	0.00919	0.00162	<0.0001
rs9382445	C	T	0.37517	-0.0095	0.00165	<0.0001
rs9611007	T	C	0.14167	-0.0136	0.0023	<0.0001
rs9810474	T	C	0.23218	-0.0112	0.00189	<0.0001
rs9903898	T	C	0.48888	-0.0094	0.0016	<0.0001