



Causal effects of life-course obesity on sleep apnoea: a Mendelian randomization study

Jinyu Zhang^{1,5} · Jie Min^{2,5} · Haili Wang^{3,5} · Lei Zhong^{2,5} · Lu Xue^{4,5}

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Abstract

Sleep apnoea (SA) is a common condition associated with obesity, conferring significant cardiovascular and metabolic risks. This study investigates the causal effects of obesity phenotypes throughout the life course, from birth weight to adult obesity, on SA risk using Mendelian randomization (MR). A two-sample MR approach was utilized, employing genome-wide association study (GWAS) data from individuals of European ancestry. Exposures included birth weight, childhood obesity, adult obesity classifications (overweight and obesity classes 1–3), and fat distribution characteristics (waist/hip circumference and MRI-derived abdominal adipose tissue volumes). Outcome data were sourced from the FinnGen database. Analyses were conducted using inverse variance weighting (IVW), MR-Egger regression, and sensitivity analyses. A replication analysis using another GWAS dataset on SA was also performed. The analysis demonstrated a positive causal relationship between birth weight and SA risk (OR = 1.142, $P < 0.001$). Features of childhood obesity, including BMI (OR = 1.218, $P < 0.001$) and early life body size (OR = 1.533, $P < 0.001$), were associated with increased SA risk. In adulthood, BMI was strongly associated with SA risk (OR = 2.419, $P < 0.001$). Fat distribution measures, notably MRI-derived subcutaneous adipose tissue volume (OR = 1.119, $P = 0.003$) and waist circumference (OR = 1.953, $P < 0.001$), were also predictors of SA risk. Sensitivity analyses affirmed these findings, suggesting minimal horizontal pleiotropy. The replication analysis confirmed a positive correlation between obesity indicators and SA. This study supports the causal relationship of life-course obesity, including birth weight and obesity, in childhood and adulthood, on SA risk, highlighting the importance of fat distribution metrics in understanding SA determinants.

✉ Lu Xue
13735103696@163.com

Jinyu Zhang
m412079729@126.com

Jie Min
mj475121428@163.com

Haili Wang
whloggroup@163.com

Lei Zhong
perfecticu@163.com

² Department of Intensive Care Unit, Huzhou Central Hospital, Affiliated Central Hospital of Huzhou University, Huzhou 313000, China

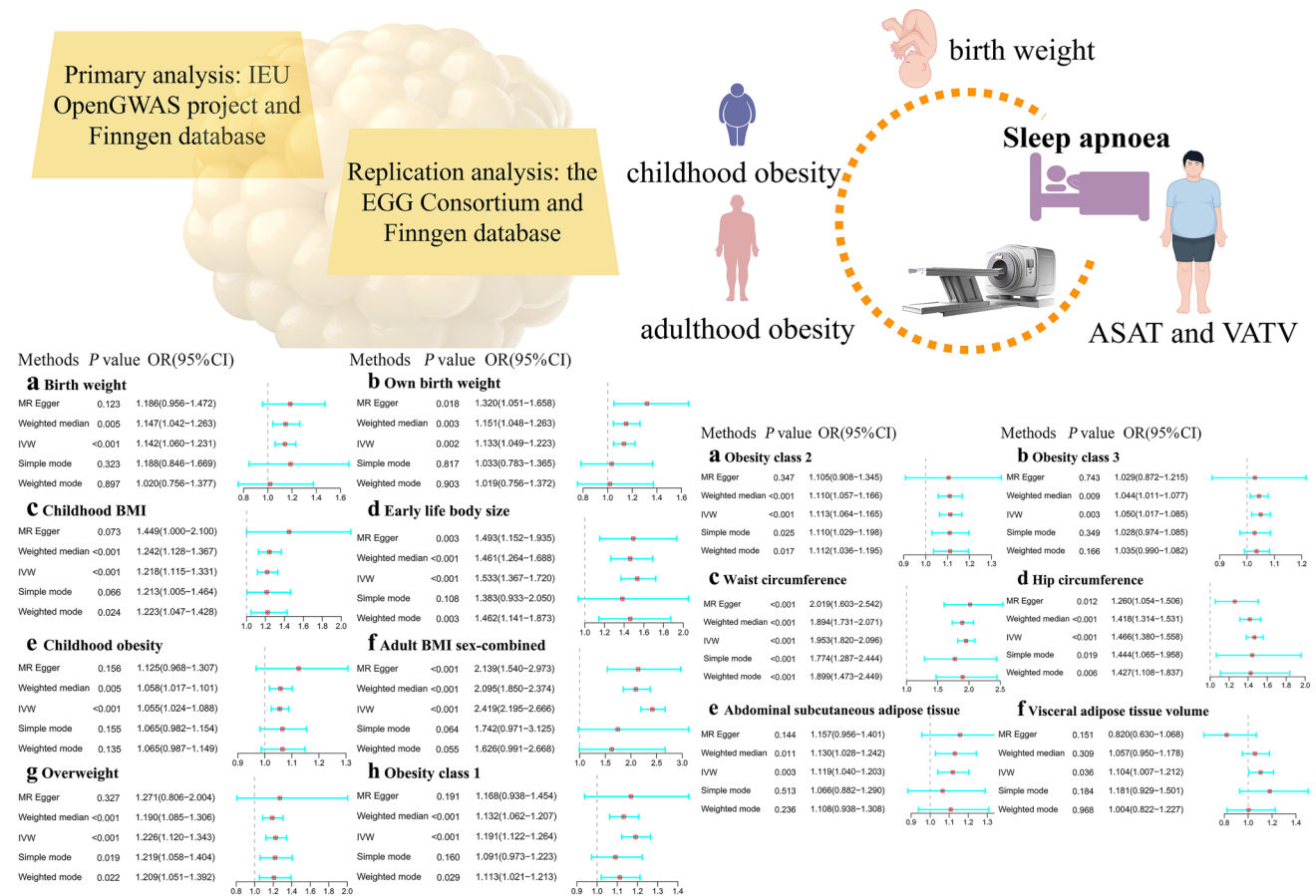
³ Department of Clinical Nutrition, Huzhou Central Hospital, Affiliated Central Hospital of Huzhou University, Huzhou 313000, China

⁴ Department of Radiology, Huzhou Central Hospital, Affiliated Central Hospital of Huzhou University, Huzhou 313000, China

⁵ Fifth School of Clinical Medicine of Zhejiang Chinese Medical University, Huzhou 313000, China

¹ Department of General Surgery, Huzhou Central Hospital, Affiliated Central Hospital of Huzhou University, Huzhou 313000, China

Graphical abstract



Keywords Life-course obesity · Sleep apnoea · Mendelian randomization · Body mass index · Fat distribution

Abbreviations

| | |
|-----------|--|
| SA | Sleep apnoea |
| MR | Mendelian randomization |
| GWAS | Genome-wide association study |
| IV | Instrumental variable |
| SNP | Single-nucleotide polymorphism |
| IVW | Inverse variance weighted |
| OR | Odds ratio |
| CI | Confidence interval |
| BMI | Body mass index |
| OSA | Obstructive sleep apnoea |
| STROBE-MR | Strengthening the reporting of observational studies in epidemiology using Mendelian randomization |
| EGG | Early growth genetics |
| MRI | Magnetic resonance imaging |
| AHI | Apnoea–hypopnoea index |
| VEGFA | Vascular endothelial growth factor A |

Introduction

Sleep apnoea (SA), defined by recurrent interruptions in breathing during sleep, has emerged as a significant global public health concern [1]. Evidence suggests that SA is linked not only to daytime functional impairment and neurocognitive deficits, but also to a marked elevation in the risk of cardiovascular and metabolic disorders, as well as overall mortality [2, 3]. Obesity, identified as a primary modifiable risk factor for SA, has experienced a dramatic increase in global prevalence over the past three decades. Specifically, from 1990 to 2022, the global prevalence of obesity more than doubled, reaching 16% in 2022, while the rate of adolescent obesity increased more than fourfold during the same period [4]. However, traditional observational studies are constrained by confounding biases, such as smoking and physical inactivity, and by reverse causation, which complicates the accurate quantification of the independent causal effects of obesity on SA [5].

The life-course epidemiology framework posits that the influence of obesity on SA is dynamic and cumulative. Developmental anomalies during the fetal stage may predispose individuals to central adiposity in adulthood through mechanisms of epigenetic reprogramming [6]. Both birth weight and childhood obesity have been linked to adult obesity [7]. The interplay between childhood obesity and SA may be attributed to anatomical alterations in the upper respiratory tract due to obesity, as well as metabolic disruptions induced by SA [8, 9]. Studies in adult populations demonstrate a strong correlation between general obesity and obstructive sleep apnoea (OSA), with findings indicating that each standard deviation increase in body mass index (BMI) elevates the risk of OSA by 2.21 times (95% Confidence Interval [CI] 1.62–3.02) [10, 11]. Nonetheless, the independent role of fat distribution patterns in contributing to SA remains a subject of debate. While some studies have established that abdominal visceral fat deposition and waist-to-height ratio are independent risk factors for SA in obese patients [12, 13], research conducted by Xiaolin Wu et al. suggests that, at the individual level, obesity itself has a causal relationship with OSA, rather than abdominal obesity specifically [10].

Mendelian randomization (MR) methods offer an innovative approach for causal inference by emulating natural randomized trials through the use of genetic variation. Unlike traditional observational studies, the MR approach employs genetic variants as instrumental variables, which are randomly assigned at conception and remain unaffected by lifestyle factors or disease status. This methodology enables a less biased estimation of the causal effects of obesity on SA. Recent MR studies have substantiated causal relationships between life-course obesity and various conditions, including atrial fibrillation [14], Alzheimer's disease [15], and severe liver disease [16]. Nonetheless, research examining the relationship between SA and obesity has frequently concentrated on singular obesity characteristics, lacking a comprehensive analysis of life-course obesity and often

restricting the focus to the OSA subtype, thereby neglecting the heterogeneity of SA.

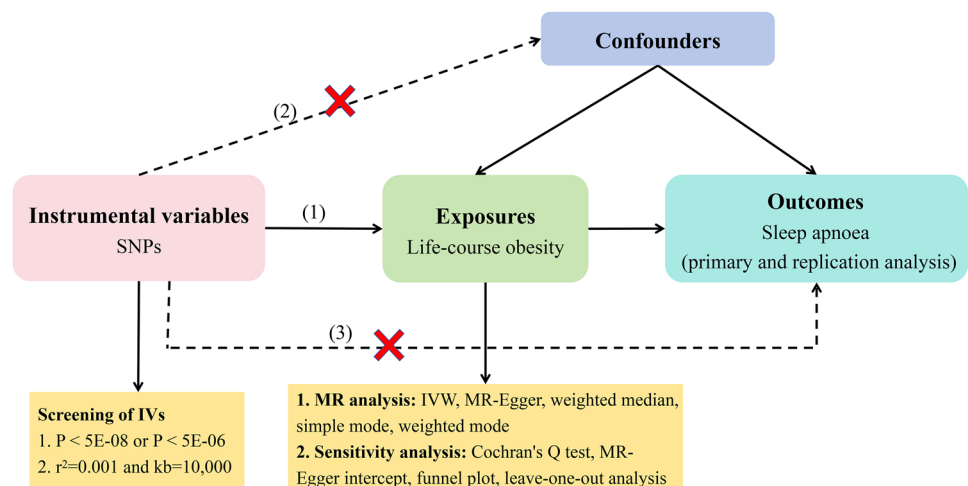
In light of this context, the present study synthesizes genome-wide association study (GWAS) data pertaining to multi-stage life-course obesity phenotypes, including birth weight, childhood BMI, adult obesity classification, and fat distribution characteristics. Utilizing a two-sample MR framework, this research systematically examines the causal relationships between life-course obesity traits and specific outcomes for the first time. This investigation provides an innovative analysis of obesity characteristics spanning from fetal development to adulthood, thereby contributing genetic epidemiological evidence to inform precision prevention strategies targeting specific outcomes across various life stages.

Materials and methods

Study design

This study utilizes a two-sample Mendelian Randomization (MR) analysis to investigate the potential causal relationship between life-course obesity and SA. To minimize the effects of population stratification, we restricted our analysis to individuals of European ancestry. We employed single nucleotide polymorphisms (SNPs) as instrumental variables (IVs), ensuring they meet the three core assumptions necessary for MR studies: (1) the relevance assumption, which requires that the IVs are strongly associated with the exposure variable, life-course obesity; (2) the independence assumption, which stipulates that the IVs must be independent of any confounding variables; and (3) the exclusivity assumption, which mandates that the IVs influence the outcome variable, SA, solely through the exposure variable, without alternative pathways. The comprehensive study design is depicted in Fig. 1.

Fig. 1 Overall design of the present study. *SNP* single nucleotide polymorphism



The study employed publicly accessible GWAS data, with all underlying studies having obtained ethical approval from the respective institutional review boards, and participants having provided informed consent. As this research does not involve the direct use of original data or human subjects, no additional ethical approval was required. The data utilized in this study were sourced from public repositories and complied rigorously with the 2021 strengthening the Reporting of Observational Studies in Epidemiology Using Mendelian Randomization: The STROBE-MR Statement [17].

Data sources of exposures

In this Mendelian analysis, the exposure variable, life-course obesity, is defined by several critical components, including birth weight, childhood body size and obesity, adult obesity, and fat distribution characteristics. The genome-wide association study (GWAS) data employed in this research primarily originates from the IEU OpenGWAS (<https://gwas.mrcieu.ac.uk>) and the Early Growth Genetics Consortium (EGG, <http://egg-consortium.org/>). The IEU OpenGWAS platform offers an extensive collection of datasets pertaining to human phenotypes and genome associations, distinguished by its large sample size and stringent analytical standards, thereby providing researchers with dependable information on genotype–phenotype associations. The Early Growth Genetics (EGG) Consortium is dedicated to genetic research concerning early growth and development.

Specifically, the early life data encompasses metrics, such as birth weight (ukb-b-13378) and own birth weight (<http://egg-consortium.org/birth-weight-2019.html>) [18], which illustrate the relationship between genetic factors and phenotypes. Measurement data related to childhood body size and obesity include Childhood BMI (ebi-a-GCST90002409) [19], early life body size (ieu-b-5107) [20], and childhood obesity (<http://egg-consortium.org/childhood-obesity.html>) [21], ensuring a comprehensive genetic representation of childhood obesity characteristics. The GWAS data pertaining to "childhood obesity" were obtained from a meta-analysis of case–control studies. In this context, cases were defined as individuals whose BMI was at or above the 95th percentile prior to the age of 18, while controls were characterized as those with a BMI below the 50th percentile throughout childhood [21]. The "early life body size" phenotype is generally represented as a questionnaire-based, ordered categorical variable, such as "comparative body size at age 10," which reflects individuals' recollections of their relative body size during childhood (e.g., thinner than average, about average, plumper than average) [20].

For adult obesity, analyses were conducted on adult BMI sex-combined (ieu-b-5118) [20], overweight (ieu-a-93) [22], and obesity classification, which includes obesity class 1, class 2, and class 3 (designated as ieu-a-90, ieu-a-91, and ieu-a-92, respectively) [22]. Clinical obesity classifications, as defined, include overweight (BMI ≥ 25 kg/m²), Class 1 obesity (BMI ≥ 30 kg/m²), Class 2 obesity (BMI ≥ 35 kg/m²), and Class 3 obesity (BMI ≥ 40 kg/m²). Furthermore, the dataset on body fat distribution encompasses traditional anthropometric measurements, specifically waist circumference (ukb-b-9405) and hip circumference (ukb-b-15590). In addition, it includes quantitative assessments of abdominal subcutaneous adipose tissue volume (ebi-a-GCST90016672) and visceral adipose tissue volume (ebi-a-GCST90016671), both derived from abdominal magnetic resonance imaging (MRI). These MRI-based metrics are the result of research employing deep learning methodologies to extract organ-specific features from abdominal MRI scans [23].

Data sources of outcomes

The primary outcome measure of this study is SA, a significant health condition linked to obesity and body composition characteristics. Our preliminary analysis of SA utilizes data from the 2024 FinnGen database (https://r11.finnngen.fi/pheno/G6_SLEEPAPNO_INCLAVO), which includes relevant information from 453,733 individuals of European descent. The FinnGen study is a comprehensive genomic initiative that has analyzed over 500,000 samples from the Finnish biobank, integrating genetic variations with health data to investigate disease mechanisms and susceptibility [24]. Additionally, we obtained SA data from various GWAS within the FinnGen database (https://r11.finnngen.fi/pheno/G6_SLEEPAPNO), encompassing 451,684 individuals of European ancestry, to conduct a replication analysis aimed at ensuring the consistency and reliability of our findings. Detailed information regarding all GWAS studies is presented in Table 1.

Screening of instrumental variables

To ensure the independence of each SNP and to mitigate the impact of genetic pleiotropy on the results, this study selected significant SNPs from the GWAS datasets. The initial selection criterion was set at $P < 5E-08$. In conducting MR studies, we required a minimum of 10 eligible IVs [25, 26]. If a dataset did not meet the IV quantity requirement, we relaxed the selection criterion to $P < 5E-06$ [27]. To minimize linkage disequilibrium, we employed a stringent clustering approach for SNPs, utilizing a clustering window with parameters of $r^2 = 0.001$ and $kb = 10,000$. We further quantified the genetic variation strength of each SNP by calculating the F -statistic, considering SNPs with an F -statistic

Table 1 A brief description of each GWAS summary statistics

| Traits | Consortium | Year | Sample size | Cases/controls | SNPs | Population | Web source |
|--|----------------|------|-------------|----------------|------------|------------|---|
| Exposures | | | | | | | |
| Birth weight | IEU OpenGWAS | 2018 | 261,932 | NA | 9,851,867 | European | https://gwas.mrcieu.ac.uk/datasets/ukb-b-13378/ |
| Own birth weight | EGG Consortium | 2019 | 298,142 | NA | 13,891,969 | European | http://egg-consortium.org/birth-weight-2019.html |
| Childhood BMI | IEU OpenGWAS | 2020 | 39,620 | NA | 8,173,382 | European | https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90002409/ |
| Early life body size | IEU OpenGWAS | 2020 | 453,169 | NA | 12,321,875 | European | https://gwas.mrcieu.ac.uk/datasets/ieu-b-5107/ |
| Childhood obesity | EGG Consortium | 2012 | 13,848 | 5,530/8,318 | 2,442,739 | European | http://egg-consortium.org/childhood-obesity.html |
| Adult BMI sex-combined | IEU OpenGWAS | 2020 | 453,169 | NA | | – European | https://gwas.mrcieu.ac.uk/datasets/ieu-b-5118/ |
| Overweight | IEU OpenGWAS | 2013 | 158,855 | 93,015/65,840 | 2,435,045 | European | https://gwas.mrcieu.ac.uk/datasets/ieu-a-93/ |
| Obesity class 1 | IEU OpenGWAS | 2013 | 98,697 | 32,858/65,839 | 2,380,428 | European | https://gwas.mrcieu.ac.uk/datasets/ieu-a-90/ |
| Obesity class 2 | IEU OpenGWAS | 2013 | 72,546 | 9,889/62,657 | 2,331,456 | European | https://gwas.mrcieu.ac.uk/datasets/ieu-a-91/ |
| Obesity class 3 | IEU OpenGWAS | 2013 | 50,364 | 2,896/47,468 | 2,250,779 | European | https://gwas.mrcieu.ac.uk/datasets/ieu-a-92/ |
| Waist circumference | IEU OpenGWAS | 2018 | 462,166 | NA | 9,851,867 | European | https://gwas.mrcieu.ac.uk/datasets/ukb-b-9405/ |
| Hip circumference | IEU OpenGWAS | 2018 | 462,117 | NA | 9,851,867 | European | https://gwas.mrcieu.ac.uk/datasets/ukb-b-15590/ |
| Abdominal subcutaneous adipose tissue volume | IEU OpenGWAS | 2021 | 32,860 | NA | 9,275,407 | European | https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90016672/ |
| Visceral adipose tissue volume | IEU OpenGWAS | 2021 | 32,860 | NA | 9,275,407 | European | https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST90016671/ |
| Outcomes | | | | | | | |
| Sleep apnea, including avohilmo (primary analysis) | Finngen | 2024 | 453,733 | 54,698/399,035 | 21,306,794 | European | https://r11.finnngen.fi/pheno/G6_SLEEPAPNO_INCLAVO |
| Sleep apnea (replication analysis) | Finngen | 2024 | 451,684 | 50,200/401,484 | 21,306,774 | European | https://r11.finnngen.fi/pheno/G6_SLEEPAPNO |

SNP single nucleotide polymorphism, GWAS genome-wide association study, BMI body mass index

exceeding 10 as robust instruments in MR analyses [28]. The F -statistic is computed using the formula: $F = R^2 \times (n - k - 1) / [k \times (1 - R^2)]$, where n represents the total sample size and k denotes the number of IVs. The R^2 value is derived from the equation: $R^2 = 2 \times (1 - \text{MAF}) \times \text{MAF} \times \beta^2$, where MAF stands for minor allele frequency and β signifies the effect size of the allele. We identified SNPs associated with life-course obesity from GWAS data on SA. For SNPs that were missing, we substituted them with highly correlated SNPs ($r > 0.8$), excluding those without suitable replacements. To maintain data integrity and reliability, SNPs directly associated with SA ($P < 5E-08$) were excluded. Prior to conducting analyses, we applied the MR-PRESSO method to address

potential outlier influences, thereby enhancing the reliability of the MR estimates. Following these procedures, the selected SNPs were employed as genetic instruments.

MR analysis

In this study, we investigated the causal relationship between life-course obesity and SA through the application of five MR analysis methods: inverse variance weighting (IVW), MR-Egger regression, weighted median, simple mode, and weighted mode. The IVW method was designated as the primary tool for effect estimation. To visually represent the causal relationship between these

variables, we utilized forest plots and scatter plots, supplemented by sensitivity analyses. Cochran's Q test was employed to assess heterogeneity within the IVW model, with a *P*-value of less than 0.05 indicating significant heterogeneity. The MR-Egger intercept test was applied to evaluate horizontal pleiotropy, where a *P*-value of less than 0.05 suggests the presence of potential horizontal pleiotropy. Additionally, funnel plots were used to visually inspect for evidence of horizontal pleiotropy. To evaluate the influence of individual SNPs, the leave-one-out analysis was conducted. All statistical analyses were performed using the "TwoSampleMR" package (version 0.6.22) and R software (version 4.2.3), with statistical significance defined as a two-tailed *P*-value of less than 0.05.

Results

Instrumental variables

In this study, we selected SNPs associated with life-course obesity from GWAS data and matched them with SA to identify IVs. As detailed in Supplementary files 1 and 2, as well as Table 2, both preliminary and validation analyses identified SNPs linked to obesity at various life stages. These SNPs were subsequently included in MR analyses to evaluate their causal impact on the risk of SA.

Causal effect of birth weight on sleep apnoea

In the preliminary analysis, the IVW method was employed to evaluate the causal relationship of genetically predicted birth weight and own birth weight (both treated as

Table 2 Results of Cochran's Q test and pleiotropy test

| Outcomes | Exposures | Number of SNPs | Heterogeneity test | | Pleiotropy test | |
|---|--|----------------|--------------------|----------------|-----------------|----------------|
| | | | Cochran's Q | <i>P</i> value | SE | <i>P</i> value |
| Sleep apnoea, including avohilmo (primary analysis) | Birth weight | 137 | 251.915 | 5.921E-09 | 0.003 | 0.715 |
| | Own birth weight | 143 | 261.110 | 4.505E-09 | 0.003 | 0.163 |
| | Childhood BMI | 14 | 26.130 | 0.016 | 0.014 | 0.363 |
| | Early life body size | 196 | 400.799 | 2.472E-16 | 0.002 | 0.824 |
| | Childhood obesity | 12 | 14.531 | 0.205 | 0.012 | 0.414 |
| | Adult BMI sex-combined | 318 | 573.248 | 5.268E-17 | 0.002 | 0.444 |
| | Overweight | 12 | 25.815 | 0.007 | 0.017 | 0.879 |
| | Obesity class 1 | 14 | 29.696 | 0.005 | 0.011 | 0.857 |
| | Obesity class 2 | 10 | 18.542 | 0.029 | 0.015 | 0.943 |
| | Obesity class 3 | 9 | 16.195 | 0.040 | 0.018 | 0.812 |
| | Waist circumference | 340 | 599.344 | 1.018E-16 | 0.002 | 0.767 |
| | Hip circumference | 380 | 760.885 | 7.705E-28 | 0.002 | 0.078 |
| | Abdominal subcutaneous adipose tissue volume | 33 | 41.713 | 0.117 | 0.005 | 0.707 |
| | Visceral adipose tissue volume | 34 | 64.158 | 0.001 | 0.006 | 0.026 |
| Sleep apnoea (replication analysis) | Birth weight | 134 | 228.293 | 5.307E-07 | 0.003 | 0.636 |
| | Own birth weight | 144 | 249.605 | 8.538E-08 | 0.003 | 0.370 |
| | Childhood body mass index | 13 | 21.302 | 0.046 | 0.013 | 0.337 |
| | Early life body size | 195 | 368.459 | 6.066E-13 | 0.002 | 0.763 |
| | Childhood obesity | 12 | 18.400 | 0.073 | 0.602 | 0.602 |
| | Adult BMI sex-combined | 320 | 557.075 | 3.463E-15 | 0.002 | 0.255 |
| | Overweight | 12 | 30.790 | 0.001 | 0.019 | 0.900 |
| | Obesity class 1 | 14 | 31.666 | 0.003 | 0.012 | 0.770 |
| | Obesity class 2 | 9 | 11.748 | 0.163 | 0.014 | 0.388 |
| | Obesity class 3 | 9 | 15.167 | 0.056 | 0.018 | 0.855 |
| | Waist circumference | 343 | 616.126 | 5.790E-18 | 0.002 | 0.567 |
| | Hip circumference | 379 | 747.873 | 1.439E-26 | 0.002 | 0.022 |
| | Abdominal subcutaneous adipose tissue volume | 33 | 45.126 | 0.062 | 0.005 | 0.513 |
| | Visceral adipose tissue volume | 34 | 58.134 | 0.004 | 0.006 | 0.023 |

SNP single-nucleotide polymorphism, BMI body mass index

continuous variables) with the risk of SA. The findings indicated that each one standard deviation increase in genetically predicted birth weight was significantly associated with an elevated risk of SA, with an Odds Ratio (OR) of 1.142 (95% CI= 1.060–1.231, $P < 0.001$). Similarly, a significant positive causal effect was identified for own birth weight, yielding an OR of 1.133 (95% CI= 1.049–1.223, $P = 0.002$) (see Fig. 2 and Table 3). The scatter plots of SNP effects are provided in Supplementary file 3: Supplementary Figs. 1–2. Cochran's Q test indicated potential heterogeneity among the SNPs ($P < 0.05$), while the MR-Egger intercept test did not reveal significant horizontal pleiotropy ($P > 0.05$) (see Table 2). The funnel plots demonstrated an approximately

symmetrical distribution, indicating a low probability of bias (see Supplementary file 3: Supplementary Figs. 15–16). The leave-one-out analysis revealed minimal changes in the overall results upon the exclusion of any single SNP, thereby suggesting a robust association between birth weight and SA (see Supplementary file 3: Supplementary Figs. 29–30).

Causal effect of childhood obesity on sleep apnoea

We conducted a comprehensive evaluation of the causal effects of genetic traits associated with childhood obesity on the risk of SA. Through IVW analyses, we determined that a one standard deviation increase in genetically

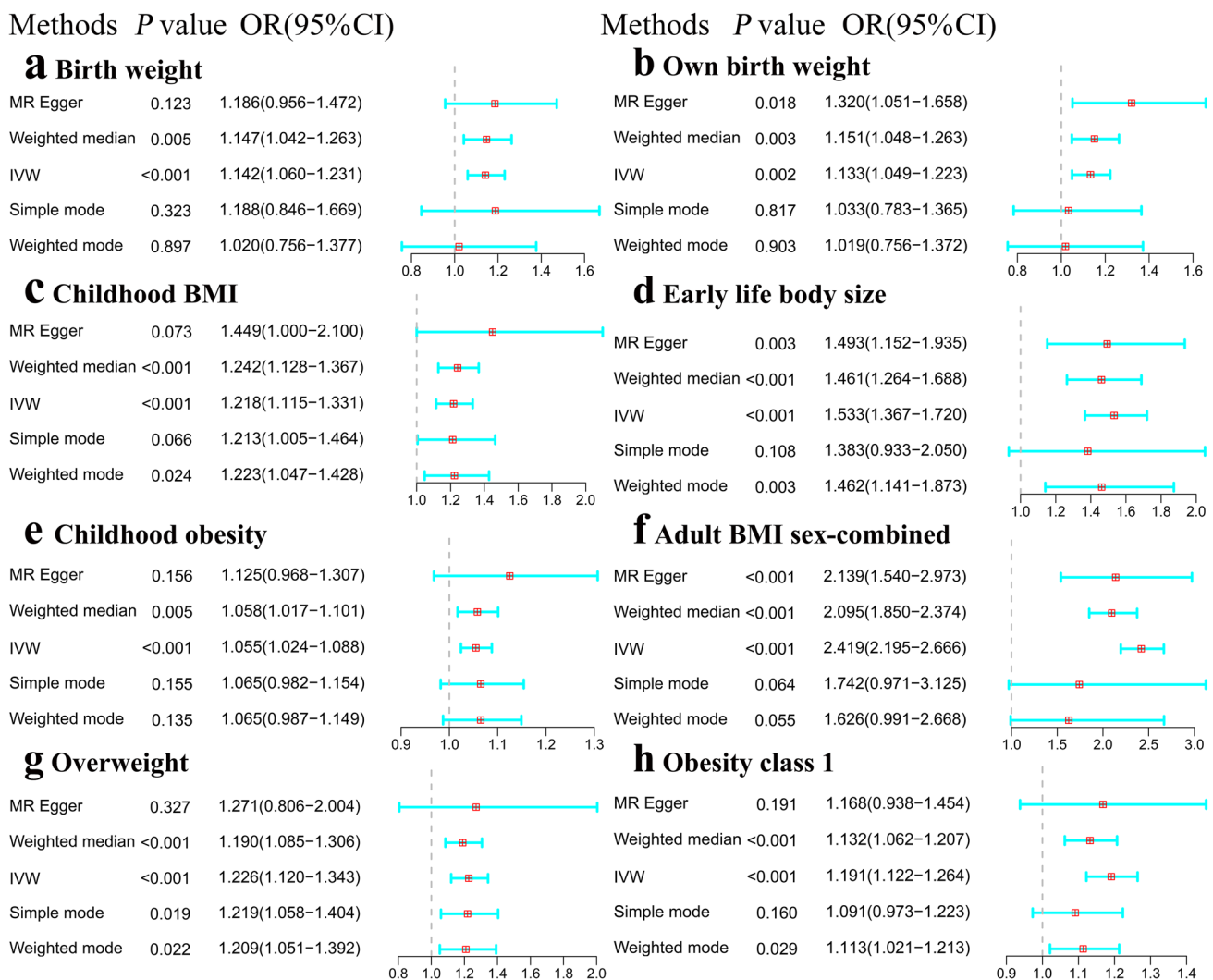


Fig. 2 Forest plot of Mendelian randomization estimates for the causal effects of birth weight (a), own birth weight (b), childhood BMI (c), early life body size (d), childhood obesity (e), adult BMI sex-combined (f), overweight (g), obesity class 1 (h) on sleep apnoea risk. The plot displays odds ratios (squares) with 95% CIs (horizontal lines) for each exposure estimated using five MR methods: IVW, MR-Egger, weighted median, simple mode, and weighted mode. The IVW

method serves as the primary analysis. The odds ratios represent the effect per one-standard-deviation increase in genetically predicted continuous exposures (birth weight, childhood BMI, adult BMI) or per one-category increase in ordered categorical exposures (early life body size, childhood obesity, overweight, obesity class 1). *MR* mendelian randomization, *BMI* body mass index, *OR* odds ratio, *CI* confidence interval, *IVW* inverse variance weighted

Table 3 Summary of causal estimates for life-course obesity phenotypes on sleep apnoea risk

| Exposures | OR (95% CI) | P value |
|--|---------------------|---------|
| Birth weight | 1.142 (1.060–1.231) | <0.001 |
| Own birth weight | 1.133 (1.049–1.223) | 0.002 |
| Childhood BMI | 1.218 (1.115–1.331) | <0.001 |
| Early life body size | 1.533 (1.367–1.720) | <0.001 |
| Childhood obesity | 1.055 (1.024–1.088) | <0.001 |
| Adult BMI sex-combined | 2.419 (2.195–2.666) | <0.001 |
| Overweight | 1.226 (1.120–1.343) | <0.001 |
| Obesity class 1 | 1.191 (1.122–1.264) | <0.001 |
| Obesity class 2 | 1.113 (1.064–1.165) | <0.001 |
| Obesity class 3 | 1.050 (1.017–1.085) | 0.003 |
| Waist circumference | 1.953 (1.820–2.096) | <0.001 |
| Hip circumference | 1.466 (1.380–1.588) | <0.001 |
| Abdominal subcutaneous adipose tissue volume | 1.119 (1.040–1.203) | 0.003 |
| Visceral adipose tissue | 1.104 (1.007–1.212) | 0.036 |

All estimates are from the primary IVW analysis using the FinnGen dataset. For continuous exposures (birth weight, own birth weight, childhood BMI, adult BMI, waist circumference, hip circumference, abdominal subcutaneous adipose tissue volume, visceral adipose tissue volume), odds ratios represent the effect per one-standard-deviation increase. For ordered categorical exposures (early life body size, childhood obesity, overweight, obesity class 1–3), odds ratios represent the effect per category increase. *OR* odds ratio, *CI* confidence interval

predicted childhood BMI was significantly correlated with an elevated risk of SA (OR = 1.218, 95% CI = 1.115–1.331, $P < 0.001$). Regarding early life body size, which is categorized ordinally, each incremental increase toward a larger body size category was significantly linked to a heightened risk of SA (OR = 1.533, 95% CI = 1.367–1.720, $P < 0.001$). Furthermore, a unit increase in the genetic predisposition to childhood obesity, measured on a log-odds scale, was modestly yet significantly associated with an increased risk of SA (OR = 1.055, 95% CI = 1.024–1.088, $P < 0.001$) (see Fig. 2 and Table 3). The scatter plots of SNP effects are provided in Supplementary file 3: Supplementary Figs. 3–5. Cochran's Q test identified significant heterogeneity among the genetic IVs for childhood BMI and early life body size ($P < 0.05$), while no significant heterogeneity was detected for the SNPs associated with childhood obesity ($P = 0.205$). The MR-Egger intercept test did not reveal significant horizontal pleiotropy ($P > 0.05$) (see Table 2). The funnel plots exhibited a symmetrical distribution, and the leave-one-out analysis corroborated the robustness of the findings (see Supplementary file 3: Supplementary Figs. 17–19 and Supplementary Figs. 31–33).

Causal effect of adult obesity on sleep apnoea

The findings derived from the IVW method revealed that a one standard deviation increase in genetically predicted adult BMI sex-combined is significantly correlated with an increased risk of SA (OR = 2.419, 95% CI = 2.195–2.666, $P < 0.001$). Furthermore, significant positive causal associations were observed for overweight (OR = 1.226, 95% CI = 1.120–1.343, $P < 0.001$), obesity class 1 (OR = 1.191, 95% CI = 1.122–1.264, $P < 0.001$), obesity class 2 (OR = 1.113, 95% CI = 1.064–1.165, $P < 0.001$), and obesity class 3 (OR = 1.050, 95% CI = 1.017–1.085, $P = 0.003$) (see Figs. 2, 3 and Table 3). The SNPs associated with these metrics exhibited consistent effect trends in the scatter plots (see Supplementary file 3: Supplementary Figs. 6–10). Despite the presence of heterogeneity as indicated by Cochran's Q test ($P < 0.05$), the MR-Egger intercept test did not reveal significant pleiotropy ($P > 0.05$), thereby reinforcing the validity of the causal inference (see Table 2). The funnel plots displayed a symmetrical distribution, indicating a minimal likelihood of publication bias (see Supplementary file 3: Supplementary Figs. 20–24), and the leave-one-out analysis corroborated the robustness of the results (see Supplementary file 3: Supplementary Figs. 34–38).

Causal effect of fat distribution characteristics on sleep apnoea

The IVW analysis identified positive associations between waist circumference (OR = 1.953, 95% CI = 1.820–2.096, $P < 0.001$), hip circumference (OR = 1.466, 95% CI = 1.380–1.588, $P < 0.001$), abdominal subcutaneous adipose tissue volume (OR = 1.119, 95% CI = 1.040–1.203, $P = 0.003$), and visceral adipose tissue volume (OR = 1.104, 95% CI = 1.007–1.212, $P = 0.036$) with the risk of SA (see Fig. 3 and Table 3). Certain SNPs in the scatter plots exhibited strong signals (see Supplementary file 3: Supplementary Figs. 11–14). For abdominal subcutaneous adipose tissue volume, sensitivity analyses consistently indicated an association, suggesting a robust causal relationship between this indicator and SA. However, the Cochran's Q test for waist circumference, hip circumference, and visceral adipose tissue volume suggested potential heterogeneity ($P < 0.05$), indicating that the genetic instrumental variables for these indicators may contribute differentially to the observed effects. Further MR-Egger intercept tests revealed that only visceral adipose tissue volume exhibited significant horizontal pleiotropy ($P < 0.05$), suggesting that the genetic IVs for visceral adipose tissue volume may influence SA through pathways other than solely through visceral adipose tissue volume itself; therefore, the causal evidence for this exposure should be interpreted with caution (see Table 2).

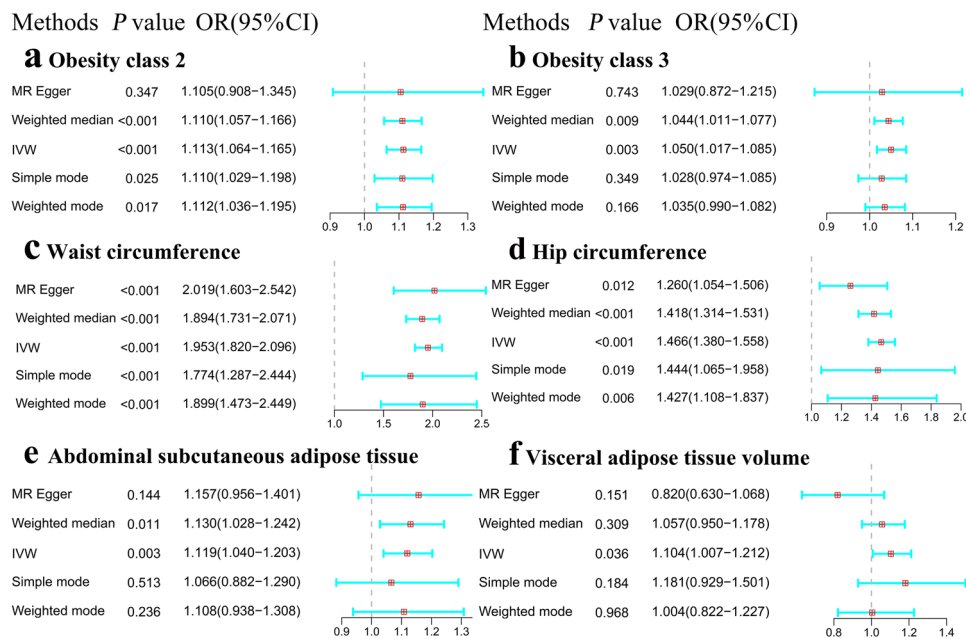


Fig. 3 Forest plot of Mendelian randomization estimates for the causal effects of obesity class 2 (**a**), obesity class 3 (**b**), waist circumference (**c**), hip circumference (**d**), abdominal subcutaneous adipose tissue volume (**e**), and visceral adipose tissue volume (**f**) on sleep apnoea risk. The plot displays odds ratios (squares) with 95% CIs (horizontal lines) for each exposure estimated using five MR methods: IVW, MR-Egger, weighted median, simple mode, and weighted

mode. The IVW method serves as the primary analysis. For continuous exposures (waist circumference, hip circumference, and adipose tissue volumes), the odds ratios represent the effect per one-standard-deviation increase in the genetically predicted value. For categorical exposures (obesity classes 2 and 3), odds ratios represent the effect per category increase. *MR* mendelian randomization, *OR* odds ratio, *CI* confidence interval, *IVW* inverse variance weighted

The funnel plots demonstrated a symmetrical distribution, indicating a low likelihood of bias, and the leave-one-out analysis confirmed the robustness of the overall findings against the exclusion of individual SNPs (see Supplementary file 3: Supplementary Figs. 25–28 and Supplementary Figs. 39–42).

Replication analysis

In the replication analysis, a positive correlation between various obesity indicators throughout the life course and SA was substantiated (see Supplementary file 4: Supplementary Table 29). The Cochran's Q test revealed significant heterogeneity among the genetic IVs for waist circumference, hip circumference, and adult BMI sex-combined, whereas no significant heterogeneity was detected for childhood obesity and abdominal subcutaneous adipose tissue volume. The MR-Egger intercept test indicated potential pleiotropy in the genetic instruments for hip circumference and visceral adipose tissue volume, while no significant pleiotropy was observed for other indicators, aligning with the results of the main analysis (see Supplementary files 4 and 5). Funnel plot analysis suggested a low probability of publication bias, and the leave-one-out analysis confirmed robustness, thereby

supporting the robustness of the associations between obesity indicators and SA.

Discussion

This study represents a pioneering effort in systematically elucidating the dynamic accumulation and anatomical specificity of the causal effects of obesity on SA by integrating genetic data of obesity phenotypes across multiple life stages. Mendelian randomization analysis revealed that abnormal body weight at each life stage, ranging from fetal birth weight ($OR = 1.14$) to obesity class 3 in adulthood ($OR = 1.05$), independently elevates the risk of SA, with the effect size varying across different life stages. In addition, each standard deviation increase in adult BMI corresponds to a 141.9% higher risk of SA. These findings highlight potential intervention targets throughout the life course for the prevention of obesity-related SA.

Beginning from the earliest stages of life, the study identified a significant positive association between higher birth weight and SA risk ($OR = 1.142$), thereby supporting the developmental overnutrition hypothesis. From a fetal perspective, exposure to hyperglycemia or excessive fat accumulation in utero may influence genes associated with

metabolism and craniofacial development through epigenetic mechanisms, such as DNA methylation and histone modification. This can lead to lifelong metabolic dysregulation and structural abnormalities of the airway, such as retrognathia or airway narrowing. [29, 30] This interpretation aligns with evidence indicating that maternal overweight or obesity exhibits a dose–response relationship with the risk of SA in offspring [31]. Furthermore, the MR-Egger analysis excluded the possibility of horizontal pleiotropy ($P > 0.05$), thereby reinforcing the notion of a direct causal effect. However, birth weight is a multifaceted trait influenced by both fetal and maternal genetics, encompassing intrauterine growth and the prenatal environment [32]. Traditional two-sample MR is limited in its ability to disentangle these maternal–fetal pathways, as genetic instruments may simultaneously capture fetal effects and indirect maternal effects mediated through the intrauterine environment [33]. Although our findings are consistent with the developmental overnutrition hypothesis, we cannot rule out the possibility of residual confounding by maternal factors, such as maternal BMI or gestational diabetes, which affect both offspring birth weight and subsequent metabolic health [34, 35]. Consequently, future research utilizing maternal-specific genetic instruments or multivariable MR is necessary to elucidate the independent contributions of fetal and maternal effects.

Beyond the fetal period, our findings highlight childhood as an equally critical window for intervention. Importantly, the effect size for early life body phenotype (OR = 1.533) surpasses that of adult obesity classification, indicating that childhood is a critical period for SA intervention. Research on children and adolescents has shown a significant positive correlation between BMI and the apnea–hypopnea index (AHI), with AHI severity increasing alongside BMI [36]. From an anatomical standpoint, the ages of 6 to 12 are vital for mandibular development; obesity during this period may result in craniofacial structural abnormalities, such as brachycephaly and a high-arched palate, thereby elevating the risk of airway collapse [37]. Animal studies have demonstrated that obesity during childhood, induced by a high-fat diet, can result in fat accumulation in the tongue and impaired respiratory drive function, a pathological process closely mirroring the abnormal tongue-pharyngeal fat distribution observed in human patients with SA [38, 39]. Genetic evidence indicates that genes associated with childhood obesity, such as FTO rs9939609, may influence fat distribution by regulating the hypothalamic centers responsible for energy metabolism, underscoring the critical role of gene–environment interactions in the pathogenesis of SA [40]. Collectively, these findings align with the significant effects observed for childhood indicators in the results, underscoring the clinical imperative for obesity screening during school age. Consequently, assessments of craniofacial development and monitoring of

respiratory function in obese children are of considerable clinical importance.

The impact of adult obesity phenotypes on SA demonstrates significant variation: the effect sizes for BMI (OR = 2.419) and waist circumference (OR = 1.953) are notably higher than those for obesity classification tiers (Class 1 to Class 3: OR = 1.191–1.050). This non-linear relationship likely reflects the dynamic interplay between metabolic compensation and pathological damage. Visceral fat accumulation, for instance, induces leptin resistance via pro-inflammatory factors such as IL-6 and TNF- α , which impair neuromuscular control of the upper airway [41]. Conversely, individuals with severe obesity may partially mitigate the risk of airway collapse through compensatory mechanisms, including cervical muscle thickening or an enhanced respiratory drive. Notably, the strong associations of waist circumference and abdominal subcutaneous fat volume with SA, with OR of 1.953 and 1.119, respectively, lend support to the mechanical compression hypothesis. This hypothesis posits that abdominal fat accumulation may elevate the diaphragm, reduce thoracic cavity volume, and consequently lower the threshold for airway closing pressure [42]. However, the relatively small effect size for visceral fat volume (OR = 1.104) suggests a modest association, while the evidence of pleiotropy (MR-Egger intercept $P = 0.023$), raises concerns about the validity of the causal estimate. From a methodological perspective, this may be attributed to the limited number of SNPs and the adoption of a more lenient threshold ($P < 5 \times 10^{-6}$) to acquire adequate instruments, which could elevate the likelihood of incorporating pleiotropic variants. From a pathophysiological standpoint, the metabolic activity of visceral fat may influence SA risk through various pathways, such as vascular endothelial growth factor A (VEGFA) gene-mediated vascular proliferation in the tongue [43] or systemic inflammation, suggesting that the observed pleiotropy may partly arise from inherent biological complexity. Consequently, these findings should be interpreted with caution, and further studies involving larger GWAS of visceral fat are necessary to elucidate the underlying mechanisms.

The findings of this study partially contradict the conclusions of Xiaolin Wu et al. [10], whose MR study suggested that overall obesity, rather than abdominal obesity, is the primary driver of the risk for OSA. In contrast, our study identified independent effects of waist circumference and abdominal subcutaneous fat volume. This discrepancy may be attributed to: 1) Differences in metric definitions, as Wu's study employed the waist-to-hip ratio, whereas our study utilized direct measurements of waist circumference and quantitative assessments of fat volume; and 2) Population heterogeneity, given that Wu's study focused on patients with OSA, while our study targeted a broader SA population. Nonetheless, both studies underscore the central role

of obesity intervention in SA prevention, providing complementary evidence for clinical practice. From a translational perspective, the quantitative relationships identified in this study provide quantitative tools for stratifying the risk of SA. We advocate for the inclusion of a BMI of ≥ 25 kg/m² (associated with a 1.226-fold increase in SA risk) in the management of high-risk populations, with weight reduction as a potential strategy to mitigate this risk. We propose a three-tier prevention strategy across different life stages: (1) During the fetal period, efforts should focus on reducing the incidence of macrosomia through gestational diabetes screening and personalized nutritional interventions, such as controlling gestational weight gain and optimizing dietary composition; (2) In childhood, assessments of craniofacial development and monitoring for sleep-disordered breathing should be conducted for individuals with a BMI at or above the 85th percentile to identify high-risk phenotypes; (3) In adulthood, the integration of waist circumference metrics into the STOP-Bang questionnaire is recommended to enhance screening sensitivity. Furthermore, evidence from metabolic surgery underscores the long-term benefits of obesity management, with sustained reductions in SA events observed for over five years in patients with a BMI of ≥ 35 kg/m² following surgical intervention [44].

This study exhibits several notable strengths. First, it pioneers the elucidation of the cumulative and stage-specific effects of obesity across the lifespan, particularly during critical periods, such as pregnancy and childhood. This research not only uncovers the long-term consequences of obesity, but also provides compelling evidence for the necessity of implementing weight management interventions early in life, thereby underscoring the urgency of advancing preventive strategies. Second, the study includes a diverse cohort of SA patients, rather than focusing solely on a single subtype, such as OSA, thereby significantly enhancing the generalizability of the findings. Methodologically, this study utilized a two-sample Mendelian randomization (MR) design, supplemented by independent validation analyses, to robustly enhance the causal inferences derived from the research. Notably, the study innovatively incorporated precise metrics of adipose distribution obtained from abdominal MRI, including subcutaneous and visceral fat volumes. The objective and precise quantitative measurements afforded by MRI technology allow these metrics to more accurately and reliably elucidate visceral fat distribution characteristics that are closely linked to SA risk, compared to traditional anthropometric indices. This augments the biological relevance and translational potential of the findings.

Nonetheless, several limitations merit consideration. First, the study predominantly relies on data from individuals of European ancestry, which constrains the generalizability of the results. This is particularly pertinent given the ethnic variations in fat distribution that may influence

the risk of obesity-related SA through distinct mechanisms. Second, the application of standard two-sample MR does not fully disentangle maternal and fetal influences on birth weight, and residual confounding by maternal factors, such as maternal BMI or gestational diabetes, cannot be ruled out. Third, for certain phenotypes, notably visceral adipose tissue, the limited availability of SNPs necessitated the use of a more relaxed significance threshold ($P < 5 \times 10^{-6}$), which may increase the likelihood of incorporating pleiotropic variants. Finally, the broad definition of SA in the outcome GWAS, which lacks stratification by subtype (obstructive versus central) and severity (AHI), may have resulted in misclassification bias. This is particularly relevant regarding the inclusion of undiagnosed mild cases in the control group, which would typically bias our estimates towards the null. Future studies incorporating diverse ancestries, larger-scale visceral fat GWAS, polysomnography-defined SA, and maternal-specific genetic instruments are needed to validate and extend our findings.

Conclusion

This study corroborates the causal effects of life-course obesity, including the birth weight, childhood and adulthood obesity, on SA. Furthermore, the integration of MRI-derived fat distribution metrics provides novel anatomical insights into SA risk determinants, revealing stage-specific associations.

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Data availability All the GWAS data involved in our manuscript is publicly available. The main relevant data is included in the manuscript and supplemental files, further inquiries can be directed to the corresponding authors.

Declarations

Conflict of interest The authors declare no competing interests.

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References

- Zhang Y, Wang H, Yang J, Wang S, Tong W, Teng B (2024) Obstructive sleep apnea syndrome and obesity indicators, circulating blood lipid levels, and adipokines levels: a bidirectional two-sample Mendelian randomization study. *Nat Sci Sleep* 16:573–583
- Henning RJ, Anderson WM (2025) Sleep apnea is a common and dangerous cardiovascular risk factor. *Curr Probl Cardiol* 50(1):102838
- Pennings N, Golden L, Yashi K, Tondt J, Bays HE (2022) Sleep-disordered breathing, sleep apnea, and other obesity-related sleep disorders: an obesity medicine association (OMA) clinical practice statement (CPS) 2022. *Obes Pillars* 4:100043
- Harris E (2023) US obesity prevalence surged over the past decade. *JAMA* 330(16):1515
- Deng H, Duan X, Huang J et al (2023) Association of adiposity with risk of obstructive sleep apnea: a population-based study. *BMC Public Health* 23(1):1835
- Sarr O, Thompson JA, Zhao L, Lee TY, Regnault TR (2014) Low birth weight male guinea pig offspring display increased visceral adiposity in early adulthood. *PLoS ONE* 9(6):e98433
- Khera AV, Chaffin M, Wade KH et al (2019) Polygenic prediction of weight and obesity trajectories from birth to adulthood. *Cell* 177(3):587–596.e9
- Bhatt SP, Guleria R, Kabra SK (2021) Metabolic alterations and systemic inflammation in overweight/obese children with obstructive sleep apnea. *PLoS ONE* 16(6):e0252353
- Wang P, Liu S, Kong LM, Qi N (2024) Causal relationship between childhood obesity and sleep apnea syndrome: bidirectional two-sample Mendelian randomization analysis. *Nat Sci Sleep* 16:1713–1723
- Li X, Wang T, Jin L et al (2023) Overall obesity not abdominal obesity has a causal relationship with obstructive sleep apnea in individual level data. *Nat Sci Sleep* 15:785–797
- Strausz S, Ruotsalainen S, Ollila HM et al (2021) Genetic analysis of obstructive sleep apnoea discovers a strong association with cardiometabolic health. *Eur Respir J* 57(5):2003091
- Ma B, Li Y, Wang X et al (2022) Association between abdominal adipose tissue distribution and obstructive sleep apnea in Chinese obese patients. *Front Endocrinol (Lausanne)* 13:847324
- Wang H, Yang B, Zeng X et al (2024) Association between the weight-adjusted waist index and OSA risk: insights from the NHANES 2017–2020 and Mendelian randomization analyses. *Nat Sci Sleep* 16:1779–1795
- Zhou Y, Zha L, Pan S (2022) The risk of atrial fibrillation increases with earlier onset of obesity: a Mendelian randomization study. *Int J Med Sci* 19(9):1388–1398
- Li X, Tian Y, Yang YX et al (2021) Life course adiposity and Alzheimer's disease: a Mendelian randomization study. *J Alzheimers Dis* 82(2):503–512
- Wang X, Wu Z, Lv J et al (2023) Life-course adiposity and severe liver disease: a Mendelian randomization analysis. *Obesity Silver Spring* 31(12):3077–3085
- Skrivankova VW, Richmond RC, Woolf B et al (2021) Strengthening the reporting of observational studies in epidemiology using Mendelian randomization: the STROBE-MR statement. *JAMA* 326(16):1614–1621
- Warrington NM, Beaumont RN, Horikoshi M et al (2019) Maternal and fetal genetic effects on birth weight and their relevance to cardio-metabolic risk factors. *Nat Genet* 51(5):804–814
- Vogelezang S, Bradfield JP, Ahluwalia TS et al (2020) Novel loci for childhood body mass index and shared heritability with adult cardiometabolic traits. *PLoS Genet* 16(10):e1008718
- Richardson TG, Sanderson E, Elsworth B, Tilling K, Davey Smith G (2020) Use of genetic variation to separate the effects of early and later life adiposity on disease risk: Mendelian randomisation study. *BMJ* 369:m1203
- Bradfield JP, Taal HR, Timpson NJ et al (2012) A genome-wide association meta-analysis identifies new childhood obesity loci. *Nat Genet* 44(5):526–531
- Berndt SI, Gustafsson S, Mägi R et al (2013) Genome-wide meta-analysis identifies 11 new loci for anthropometric traits and provides insights into genetic architecture. *Nat Genet* 45(5):501–512
- Liu Y, Bastly N, Whitcher B et al (2021) Genetic architecture of 11 organ traits derived from abdominal MRI using deep learning. *Elife* 10:e65554
- Kurki MI, Karjalainen J, Palta P et al (2023) FinnGen provides genetic insights from a well-phenotyped isolated population. *Nature* 613(7944):508–518
- Gao X, Meng LX, Ma KL et al (2019) The bidirectional causal relationships of insomnia with five major psychiatric disorders: a Mendelian randomization study. *Eur Psychiatry* 60:79–85
- Savage JE, Jansen PR, Stringer S et al (2018) Genome-wide association meta-analysis in 269,867 individuals identifies new genetic and functional links to intelligence. *Nat Genet* 50(7):912–919
- Zou XL, Wang S, Wang LY et al (2021) Childhood obesity and risk of stroke: a Mendelian randomisation analysis. *Front Genet* 12:727475
- Pierce BL, Ahsan H, Vanderweele TJ (2011) Power and instrument strength requirements for Mendelian randomization studies using multiple genetic variants. *Int J Epidemiol* 40(3):740–752
- Page KA, Luo S, Wang X et al (2019) Children exposed to maternal obesity or gestational diabetes mellitus during early fetal development have hypothalamic alterations that predict future weight gain. *Diabetes Care* 42(8):1473–1480
- Zhou P, Li L, Lin Z et al (2024) Exploring the shared genetic architecture between obstructive sleep apnea and body mass index. *Nat Sci Sleep* 16:711–723
- Zhu MQ, Cnattingius S, O'Brien LM, Villamor E (2024) Maternal early pregnancy body mass index and risk of sleep apnea in the offspring. *J Clin Sleep Med* 20(10):1675–1684
- Chatterjee S, Ouidir M, Tekola-Ayele F (2021) Pleiotropic genetic influence on birth weight and childhood obesity. *Sci Rep* 11(1):48
- Hou N, Jiao Y, Zhang R et al (2026) Impact of fetal and maternal genetically predicted birth weight on cardiometabolic risk: a Mendelian randomization study of cytokine mediation in Europeans. *J Matern Fetal Neonatal Med* 39(1):2629082
- Cristian A, Tarry-Adkins JL, Aiken CE (2023) The uterine environment and childhood obesity risk: mechanisms and predictions. *Curr Nutr Rep* 12(3):416–425
- Bond TA, Karhunen V, Wielscher M et al (2020) Exploring the role of genetic confounding in the association between maternal

- and offspring body mass index: evidence from three birth cohorts. *Int J Epidemiol* 49(1):233–243
36. Caliendo C, Femiano R, Umamo GR et al (2023) Effect of obesity on the respiratory parameters in children with obstructive sleep apnea syndrome. *Children* 10(12):1874
 37. Vora SR, Tam S, Katsube M, Pliska B, Heda K (2022) Craniofacial form differences between obese and nonobese children. *Am J Orthod Dentofacial Orthop* 162(5):744–752.e3
 38. Chen Q, Han X, Chen M et al (2021) High-fat diet-induced mitochondrial dysfunction promotes genioglossus injury—a potential mechanism for obstructive sleep apnea with obesity. *Nat Sci Sleep* 13:2203–2219
 39. Saito T, Yamane A, Kaneko S et al (2010) Changes in the lingual muscles of obese rats induced by high-fat diet feeding. *Arch Oral Biol* 55(10):803–808
 40. Rinkwitz S, Geng FS, Manning E, Suster M, Kawakami K, Becker TS (2015) BAC transgenic zebrafish reveal hypothalamic enhancer activity around obesity associated SNP rs9939609 within the human FTO gene. *Genesis* 53(10):640–651
 41. Li X, He J (2021) The association between serum/plasma leptin levels and obstructive sleep apnea syndrome: a meta-analysis and meta-regression. *Front Endocrinol (Lausanne)* 12:696418
 42. Lee S, Ryu S, Lee GE, Redline S, Morey BN (2024) Risk of sleep apnea is associated with abdominal obesity among Asian Americans: comparing waist-to-hip ratio and body mass index. *J Racial Ethn Health Disparities* 11(1):157–167
 43. Bujaldon E, Cornide-Petronio ME, Gulfo J et al (2019) Relevance of VEGFA in rat livers subjected to partial hepatectomy under ischemia-reperfusion. *J Mol Med (Berl)* 97(9):1299–1314
 44. Eisenberg D, Shikora SA, Aarts E et al (2023) 2022 American society of metabolic and bariatric surgery (ASMBS) and International federation for the surgery of obesity and metabolic disorders (IFSO) indications for metabolic and bariatric surgery. *Obes Surg* 33(1):3–14

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