Aging Clinical and Experimental Research (2025) 37:285
https://doi.org/10.1007/s40520-025-03193-3

RESEARCH

# Synergistic effects of diabetes and sarcopenic obesity on cardiovascular disease risk in middle-aged and elderly Chinese adults: a large-scale prospective cohort study

**Fang Wan[1,2] · Ruonan Lian[1] · Jing Huang[3] · Jianling Du[1]**

Received: 16 June 2025 / Revised: 1 September 2025 / Accepted: 2 September 2025


## Abstract

**Background** Diabetes mellitus and sarcopenic obesity are increasingly prevalent conditions in aging populations, both independently associated with elevated cardiovascular disease risk. However, their synergistic effects on cardiovascular outcomes in Asian populations remain poorly understood. This study aimed to evaluate the individual and combined impacts of diabetes and sarcopenic obesity on cardiovascular disease risk in middle-aged and elderly Chinese adults.

**Methods** We conducted a prospective cohort analysis using data from the China Health and Retirement Longitudinal Study (CHARLS). A total of 10,478 participants without baseline cardiovascular disease (5,122 men and 5,356 women; mean age 58.77 ± 9.24 years) were followed for 9 years (2011–2020). Participants were categorized into four groups: neither condition, diabetes alone, sarcopenic obesity alone, and both conditions. Cardiovascular disease events were identified through physician-diagnosed reports. Cox proportional hazards models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs), adjusting for demographic, lifestyle, and clinical covariates.

**Results** During 9 years of follow-up, 2,443 participants (23.3%) developed cardiovascular disease. Compared to participants with neither condition, the multivariable-adjusted HRs for cardiovascular disease were 1.11 (95% CI: 0.96–1.29) for diabetes alone, 1.05 (95% CI: 0.94–1.17) for sarcopenic obesity alone, and 1.34 (95% CI: 1.10–1.63, $P = 0.004$) for both conditions combined. The cumulative incidence of cardiovascular disease was significantly higher in the combined group (39.0%) compared to the control group (24.4%), diabetes alone (31.6%), and sarcopenic obesity alone (27.3%). Similar patterns were observed for stroke and cardiac events separately.

**Conclusions** The coexistence of diabetes and sarcopenic obesity synergistically increases cardiovascular disease risk beyond the effects of either condition alone in Chinese adults. These findings highlight the importance of comprehensive screening and integrated management strategies for individuals with both conditions to prevent cardiovascular complications.

**Keywords** Diabetes mellitus · Sarcopenic obesity · Cardiovascular disease · Cohort study · Risk factors · Chinese population · Synergistic effects

## Introduction

Cardiovascular disease remains the leading cause of mortality worldwide, accounting for approximately 20 million deaths annually and representing a substantial global health burden [1]. The prevalence of cardiovascular disease continues to rise, particularly in developing countries experiencing rapid demographic and epidemiological transitions [2]. China, as the world's most populous nation, faces an unprecedented challenge with cardiovascular disease, which has become the primary cause of death and disability, affecting over 330 million individuals [3]. This epidemic is

✉ Fang Wan
wfang_0904@163.com

✉ Jianling Du
dujianlingcn@163.com

[1] Department of Endocrinology, The First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning, China

[2] Department of Endocrinology, Jiujiang No. 1 People's Hospital, Jiujiang, Jiangxi, China

[3] School of Public Health, Jiangxi Provincial Key Laboratory of Disease Prevention and Public Health, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi, China

Published online: 07 October 2025

further compounded by the concurrent rise in diabetes mellitus, with China now harboring the world's largest diabetic population, exceeding 233 million individuals and projected to reach 291 million by 2050 [4]. Diabetes mellitus represents a well-established and potent risk factor for cardiovascular disease, with diabetic individuals demonstrating a two to four-fold increased risk of cardiovascular events compared to their non-diabetic counterparts [5]. Diabetic patients exhibit accelerated cardiovascular risk trajectories, entering high-risk categories 5–15 years earlier than non-diabetic individuals [6]. The pathophysiological mechanisms underlying this association are multifaceted, involving chronic hyperglycemia, insulin resistance, oxidative stress, chronic inflammation, and endothelial dysfunction, which collectively accelerate atherosclerosis and vascular aging [7]. These metabolic disturbances create a pro-atherogenic environment that significantly amplifies cardiovascular risk beyond traditional risk factors.

Concurrent with the diabetes epidemic, aging populations worldwide are experiencing an increasing prevalence of sarcopenia, characterized by progressive loss of skeletal muscle mass, strength, and function [8]. Sarcopenic obesity, defined as the coexistence of sarcopenia with obesity, represents a particularly concerning phenotype that combines the adverse effects of muscle loss with excess adiposity [9].

This condition affects approximately 11% of older adults globally, with significantly higher prevalence rates observed in individuals with type 2 diabetes, reaching nearly 20% [10]. Sarcopenic obesity is associated with increased insulin resistance, chronic inflammation, and metabolic dysfunction, creating a pathophysiological milieu that substantially elevates cardiovascular disease risk [11]. Sarcopenic obesity is associated with worse glycemic control and a 2.1-fold higher risk of diabetes-related complications compared to obesity alone, while also increasing cardiovascular event risk by 1.8-fold independent of traditional risk factor [12].

The relationship between diabetes mellitus and sarcopenic obesity is bidirectional and complex. Diabetes contributes to muscle loss through multiple mechanisms, including chronic inflammation, oxidative stress, mitochondrial dysfunction, and altered protein metabolism [13]. Conversely, sarcopenic obesity exacerbates insulin resistance and glucose dysregulation through reduced muscle glucose uptake capacity and increased inflammatory cytokine production from visceral adipose tissue [14]. This creates a vicious cycle where each condition potentiates the other, potentially leading to synergistic effects on cardiovascular disease risk that exceed the sum of their individual contributions.

Despite the growing recognition of both diabetes and sarcopenic obesity as significant cardiovascular risk factors, the combined effects of these conditions on cardiovascular outcomes remain poorly understood, particularly in Asian populations. Most existing research has focused on Western populations, with limited data available from Asian countries where genetic, environmental, and lifestyle factors may influence disease patterns differently. Furthermore, previous studies have typically examined diabetes and sarcopenic obesity as separate entities, with few investigations specifically designed to evaluate their synergistic effects on cardiovascular disease risk. This represents a critical knowledge gap, given the increasing prevalence of both conditions in aging Asian populations and their potential synergistic effect for cardiovascular risk.

The China Health and Retirement Longitudinal Study (CHARLS) provides a unique opportunity to address this research gap through its large-scale, nationally representative cohort of middle-aged and elderly Chinese adults with comprehensive longitudinal follow-up data [15]. This study design enables robust evaluation of the individual and combined effects of diabetes and sarcopenic obesity on cardiovascular disease incidence over an extended follow-up period. Understanding these relationships is crucial for developing targeted prevention strategies, optimizing clinical management approaches, and informing public health policies aimed at reducing cardiovascular disease burden in rapidly aging populations.

Therefore, this study aimed to investigate the individual and synergistic effects of diabetes mellitus and sarcopenic obesity on cardiovascular disease risk in a large-scale prospective cohort of Chinese adults. We hypothesized that the coexistence of diabetes and sarcopenic obesity would demonstrate synergistic effects on cardiovascular disease risk, resulting in substantially higher risk than either condition alone. Secondary objectives included examining the effects on specific cardiovascular outcomes (stroke and cardiac events) and evaluating potential sex-specific differences in these associations.

## Methods

### Study design and participants

This prospective cohort study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal survey of Chinese adults aged 45 years and older [16]. CHARLS employs a multistage stratified probability sampling design to ensure national representativeness, with participants recruited from 450 villages and urban communities across 28 provinces in mainland China. The baseline survey was conducted in 2011, enrolling 17,705 individuals, with subsequent biennial follow-up surveys conducted in 2013, 2015, 2018, and 2020.

The CHARLS study protocol was approved by the Biomedical Ethics Review Board of Peking University (IRB00001052-11015), and all participants provided written informed consent. Additional ethical approval for the current analysis was obtained from the Human Research Ethics Committee of Newcastle University (H-2015-0290). The study was conducted in accordance with the Declaration of Helsinki and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.

For the present retrospective analysis, we analyzed 9-year follow-up data from 2011 to 2020. Participants were selected according to the following criteria (Fig. 1). Inclusion criteria were: (1) age≥45 years at baseline; and (2) complete baseline data without missing values. Exclusion criteria included: (1) age<45 years; (2) missing baseline diabetes diagnosis; (3) baseline cardiovascular disease; (4) missing baseline waist circumference; (5) missing appendicular skeletal muscle mass (ASM); (6) missing grip strength; (7) missing chair stand test; and (8) loss to follow-up. The final analytical cohort comprised participants who met all inclusion criteria and had complete follow-up data for cardiovascular disease outcomes.

## Assessment of diabetes mellitus

Diabetes mellitus was defined according to the American Diabetes Association (ADA) diagnostic criteria, incorporating multiple diagnostic approaches to ensure comprehensive case identification [17]. Participants were classified as having diabetes if they met any of the following criteria: (1) fasting plasma glucose≥126 mg/dL (7.0 mmol/L); (2) glycated hemoglobin (HbA1c)≥6.5%; (3) self-reported physician diagnosis of diabetes mellitus; or (4) current use of glucose-lowering medications, including insulin or oral antidiabetic agents. Meeting any one of these criteria was considered indicative of diabetes mellitus.

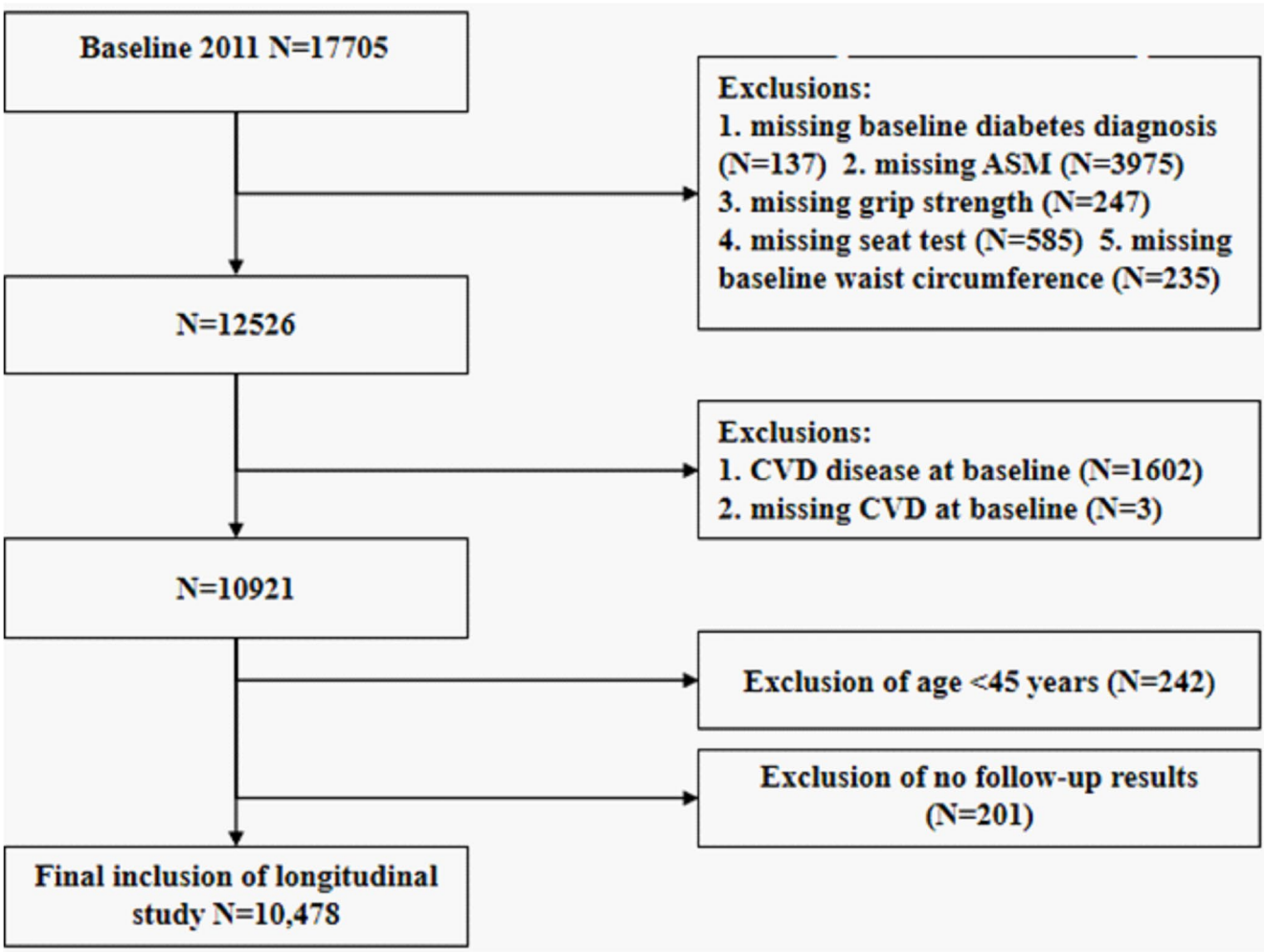



**Fig. 1** Subjects selection flowchart

## Assessment of obesity and sarcopenic status

Sarcopenic obesity was defined as the coexistence of sarcopenia and obesity, with each component assessed using internationally recognized criteria adapted for the Asian population [18]. Obesity was defined according to the 2024 Chinese Guidelines for Obesity Diagnosis and Treatment. Participants were classified as obese if they had both a body mass index (BMI)≥24 kg/m² and waist circumference≥90 cm in men or ≥85 cm in women [19]. These criteria reflect the lower BMI thresholds appropriate for Asian populations while incorporating central obesity measures that better capture metabolic risk in this population.

Sarcopenia was diagnosed using the 2019 consensus criteria from the Asian Working Group for Sarcopenia (AWGS), which incorporates three key components: muscle strength, physical performance, and muscle mass [20]. The diagnostic criteria included: (1) reduced grip strength: <28 kg in men and <18 kg in women; (2) poor physical performance: five-repetition chair stand test≥12 s; and (3) low muscle mass: height-adjusted muscle mass (ASM/height²)<7.0 kg/m² in men and <5.4 kg/m² in women.

Probable sarcopenia was diagnosed when participants had either criterion (1) or (2), while confirmed sarcopenia required the presence of criterion (3) combined with either criterion (1) or (2). Sarcopenic obesity was defined as the coexistence of sarcopenia (probable or confirmed) and obesity as defined above. This approach aligns with current international consensus recommendations and has been validated in Asian populations.

## Assessment of cardiovascular disease events

The primary outcome was incident cardiovascular disease, defined as the first occurrence of either heart disease or stroke during the follow-up period. Cardiovascular disease events were identified through self-reported physician diagnoses obtained during biennial follow-up interviews. Participants were asked standardized questions including: "Have you been diagnosed by a physician with heart disease, angina, coronary artery disease, heart failure, or other heart problems?" and "Have you been diagnosed with a stroke by a doctor?" The main endpoint was new-onset cardiovascular disease events occurring between study entry in 2011 and 2020.

Secondary outcomes included stroke and cardiac events analyzed separately. The validity of self-reported cardiovascular disease in CHARLS has been previously demonstrated through comparison with medical records and shows good agreement with clinical diagnoses. Follow-up time was calculated from the baseline interview date to the date of first cardiovascular disease event, loss to follow-up, or end of study period, whichever occurred first.

## Covariate assessment

Comprehensive covariate data were collected through standardized questionnaires and physical examinations. Demographic variables included age, sex, place of residence (rural or urban), education level (illiterate, primary school, secondary school, high school or above), and marital status (married, unmarried, separated/divorced/widowed). Lifestyle factors included smoking status (never smoker, former smoker, current smoker) and alcohol consumption (never, occasional, regular).

Physical measurements included height, weight, waist circumference, and blood pressure measured using standardized protocols. Blood pressure measurements included systolic blood pressure (SBP) and diastolic blood pressure (DBP), measured three times after a 5-minute rest period, with the average of the second and third measurements used for analysis.

Laboratory assessments included comprehensive lipid profiles: high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC), and glycated hemoglobin (HbA1c). All blood samples were collected after an overnight fast of at least 8 h and analyzed using standardized laboratory procedures.

Comorbidity assessment included self-reported physician-diagnosed conditions such as diabetes mellitus, cancer, chronic lung disease, dyslipidemia, kidney disease, and liver disease. Medication use was documented for glucose-lowering medications, antihypertensive agents, and lipid-lowering drugs. All measurements were performed by trained research staff following standardized protocols to ensure data quality and consistency across study sites.

## Statistical analysis

Continuous quantitative variables with normal distribution were described using means±standard deviations, with between-group comparisons performed using t-tests for two groups and one-way analysis of variance (ANOVA) for multiple groups. Non-normally distributed data were described using quartiles [P25, P75] and compared using rank-sum tests. Categorical variables were described using frequencies and percentages, with between-group comparisons performed using chi-square tests or Fisher's exact probability method as appropriate.

Missing values among covariates were handled using multiple imputation with the random forest algorithm implemented in R software. The imputation model included

all variables used in the main analysis plus auxiliary variables associated with missingness patterns to ensure robust imputation.

For cardiovascular disease incidence risk differences among different groups, Kaplan-Meier (KM) survival curves were constructed to plot cumulative incidence curves, with log-rank tests performed to explore between-group differences. Subsequently, univariate and multivariable Cox regression analyses were conducted to explore the association between different groupings and cardiovascular disease incidence risk.

Three sequential Cox regression models were constructed: Model 1 included no adjustment for confounding factors; Model 2 adjusted for age and sex; Model 3 adjusted for variables in Model 2 plus residence, education level, smoking, alcohol consumption, lipid profiles (total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein), comorbidities (hypertension, chronic lung disease, cancer, kidney disease, liver disease), and medication use (insulin, glucose-lowering medications, antihypertensive medications, lipid-lowering medications).

Subsequently, the cardiovascular disease incidence risk associated with diabetes mellitus was examined separately in participants with and without sarcopenic obesity, with heterogeneity testing performed to analyze differences. Both multiplicative and additive interaction effects were analyzed to assess potential synergistic effects between diabetes and sarcopenic obesity.

Finally, cardiovascular disease incidence risk differences among different groups were analyzed separately in men and women to test for potential sex-specific interaction effects.

All statistical analyses and related graphical presentations were performed using R software (version 4.4.1). Two-sided $P$-values $< 0.05$ were considered statistically significant.

## Results

### Baseline characteristics

A total of 10,478 participants from the China Health and Retirement Longitudinal Study (CHARLS) were included in this analysis, with data collection spanning from 2011 to 2020. The mean age of participants was $58.77 \pm 9.24$ years, and 5,122 (48.9%) were male. At baseline, participants were categorized into four distinct groups based on their diabetes mellitus (DM) and sarcopenic obesity (SO) status: 7,416 individuals had neither condition (reference group), 944 had diabetes alone, 1,742 had sarcopenic obesity alone, and 376 had both conditions combined.

Significant differences were observed across the four groups in demographic characteristics, laboratory parameters, comorbidities, and medication use, with the exception of cancer and liver disease prevalence (Table 1). Participants with both diabetes and sarcopenic obesity demonstrated the most adverse metabolic profile, exhibiting significantly higher systolic and diastolic blood pressure, elevated lipid parameters including low-density lipoprotein cholesterol (LDL), total cholesterol (TC), and triglycerides (TG), as well as higher glycated hemoglobin (HbA1c) levels compared to the other three groups. These findings underscore the complex metabolic derangements present in individuals with the combined phenotype, providing biological plausibility for their potentially elevated cardiovascular disease risk.

### Cumulative incidence of cardiovascular outcomes

Figure 2 presents the Kaplan-Meier survival curves illustrating the cumulative incidence of cardiovascular disease, stroke, and cardiac events across the four study groups over the 9-year follow-up period from 2011 to 2020. The curves demonstrate a clear hierarchical pattern of risk, with participants having both diabetes and sarcopenic obesity consistently exhibiting the highest cumulative incidence rates for all cardiovascular outcomes examined.

For overall cardiovascular disease, the combined diabetes and sarcopenic obesity group demonstrated a markedly elevated cumulative incidence of 39.0%, representing substantial increases compared to the reference group (24.4%), diabetes alone group (31.6%), and sarcopenic obesity alone group (27.3%). This pattern indicates that the presence of both conditions confers cardiovascular risk that exceeds either condition in isolation, with the combined group showing a 60% relative increase in cumulative incidence compared to the reference population.

When stroke events were analyzed separately, even more pronounced differences emerged across the groups. The combined diabetes and sarcopenic obesity group exhibited a cumulative stroke incidence of 18.5%, which was more than double that observed in the reference group (8.3%). Compared to participants with diabetes alone (10.7%) or sarcopenic obesity alone (8.4%), the combined group demonstrated substantially higher stroke risk, suggesting particularly strong synergistic effects for cerebrovascular outcomes.

For cardiac events, the cumulative incidence in the combined group reached 28.9%, compared to 19.3% in the reference group, 25.3% in the diabetes alone group, and 21.8% in the sarcopenic obesity alone group. While the relative differences were less pronounced than for stroke, the combined

**Table 1** Baseline characteristics of groups classified according to diabetes and sarcopenic obesity

| Variables | All participants ($n$=10478) | Neither SO nor DM ($n$=7416) | DM alone ($n$=944) | SO alone ($n$=1742) | Both DM and SO ($n$=376) | $p$ |
|---|---|---|---|---|---|---|
| Age, years, Mean±SD | 58.77±9.24 | 59.27±9.42 | 61.33±9.35 | 55.62±7.78 | 57.18±7.88 | <0.001 |
| Gender, n (%) | | | | | | <0.001 |
| Male | 5122 (48.9) | 3777 (50.9) | 464 (49.2) | 715 (41.0) | 166 (44.1) | |
| Female | 5356 (51.1) | 3639 (49.1) | 480 (50.8) | 1027 (59.0) | 210 (55.9) | |
| Living place, n (%) | | | | | | <0.001 |
| Rural | 6859 (65.5) | 5081 (68.5) | 620 (65.7) | 959 (55.1) | 199 (52.9) | |
| Urban | 3619 (34.5) | 2335 (31.5) | 324 (34.3) | 783 (44.9) | 177 (47.1) | |
| Education level, n (%) | | | | | | <0.001 |
| Illiteracy | 4835 (46.1) | 3582 (48.3) | 489 (51.8) | 631 (36.2) | 133 (35.4) | |
| Primary school | 2355 (22.5) | 1685 (22.7) | 209 (22.1) | 383 (22.0) | 78 (20.7) | |
| Middle school | 2181 (20.8) | 1440 (19.4) | 157 (16.6) | 469 (26.9) | 115 (30.6) | |
| High school or above | 1107 (10.6) | 709 (9.6) | 89 (9.4) | 259 (14.9) | 50 (13.3) | |
| Marital status, n (%) | | | | | | <0.001 |
| Married | 9232 (88.1) | 6445 (86.9) | 813 (86.1) | 1627 (93.4) | 347 (92.3) | |
| Separated/Divorced/Widowed | 1158 (11.1) | 890 (12.0) | 125 (13.2) | 115 (6.6) | 28 (7.4) | |
| Never married | 88 (0.8) | 81 (1.1) | 6 (0.6) | 0 (0.0) | 1 (0.3) | |
| Smoking status, n (%) | | | | | | <0.001 |
| Never | 6228 (59.4) | 4250 (57.3) | 552 (58.5) | 1179 (67.7) | 247 (65.7) | |
| Former | 891 (8.5) | 603 (8.1) | 92 (9.7) | 155 (8.9) | 41 (10.9) | |
| Current | 3359 (32.1) | 2563 (34.6) | 300 (31.8) | 408 (23.4) | 88 (23.4) | |
| Drinking status, n (%) | | | | | | 0.004 |
| Never | 7009 (66.9) | 4919 (66.3) | 614 (65.0) | 1221 (70.1) | 255 (67.8) | |
| Seldom | 1287 (12.3) | 922 (12.4) | 128 (13.6) | 206 (11.8) | 31 (8.2) | |
| Regular | 2182 (20.8) | 1575 (21.2) | 202 (21.4) | 315 (18.1) | 90 (23.9) | |
| SBP, mmHg, Mean±SD | 129.96±21.19 | 128.44±21.35 | 133.94±21.32 | 132.77±19.80 | 136.99±20.01 | <0.001 |
| DBP, mmHg, Mean±SD | 75.76±12.06 | 74.66±12.02 | 76.21±11.40 | 79.23±11.88 | 80.37±11.08 | <0.001 |
| HDL, mg/dl, Mean±SD | 52.79±14.99 | 54.93±14.94 | 48.66±16.21 | 47.95±12.18 | 43.43±13.80 | <0.001 |
| LDL, mg/dl, Mean±SD | 113.75±33.66 | 112.51±32.63 | 114.21±39.01 | 118.31±33.19 | 115.85±39.03 | <0.001 |
| TC, mg/dl, Mean±SD | 190.29±37.47 | 187.89±36.15 | 198.29±43.84 | 192.83±35.73 | 205.93±45.56 | <0.001 |
| TG, mg/dl, Mean±SD | 119.81±85.07 | 106.18±62.66 | 166.47±139.14 | 132.51±81.32 | 212.74±163.05 | <0.001 |
| HbAlc,%, Mean±SD | 5.24±0.79 | 5.11±0.48 | 6.04±1.56 | 5.17±0.54 | 6.26±1.51 | <0.001 |
| Comorbidity | | | | | | |
| Diabetes, n (%) | 1320 (12.6) | 0 (0.0) | 944 (100.0) | 0 (0.0) | 376 (100.0) | <0.001 |
| Hypertension, n (%) | 3915 (37.4) | 2445 (33.0) | 447 (47.4) | 806 (46.3) | 217 (57.7) | |
| Cancer, n (%) | 90 (0.9) | 60 (0.8) | 11 (1.2) | 16 (0.9) | 3 (0.8) | 0.658 |
| Chronic Lung Diseases, n (%) | 928 (8.9) | 691 (9.3) | 98 (10.4) | 105 (6.0) | 34 (9.0) | <0.001 |
| Dyslipidemia, n (%) | 3746 (35.8) | 2156 (29.1) | 543 (57.5) | 781 (44.8) | 266 (70.7) | <0.001 |
| Kidney Diease, n (%) | 571 (5.4) | 428 (5.8) | 58 (6.1) | 67 (3.8) | 18 (4.8) | 0.010 |
| Liver Disease, n (%) | 366 (3.5) | 252 (3.4) | 33 (3.5) | 64 (3.7) | 17 (4.5) | 0.671 |
| Medication use | | | | | | |
| Insulin injections, n (%) | 49 (0.5) | 0 (0.0) | 34 (3.6) | 0 (0.0) | 15 (4.0) | <0.001 |
| Hypoglycemic, n (%) | 264 (2.5) | 2 (0.0) | 174 (18.4) | 0 (0.0) | 88 (23.4) | <0.001 |
| Antihypertensive, n (%) | 1494 (14.3) | 832 (11.2) | 218 (23.1) | 325 (18.7) | 119 (31.6) | <0.001 |
| Lipidlowering, n (%) | 328 (3.1) | 147 (2.0) | 69 (7.3) | 68 (3.9) | 44 (11.7) | <0.001 |

group still demonstrated a 50% relative increase in cardiac event incidence compared to the reference population.

Statistical testing confirmed significant differences in cumulative incidence rates across all four groups for cardiovascular disease ($P$<0.001), stroke ($P$<0.001), and cardiac events ($P$<0.001), providing strong evidence for differential risk patterns based on the presence and combination of diabetes and sarcopenic obesity.

## Cox proportional hazards regression analysis

To quantify the associations between diabetes, sarcopenic obesity, and cardiovascular outcomes, we constructed three sequential Cox proportional hazards regression models with progressively comprehensive covariate adjustment (Fig. 3). This analytical approach allowed for systematic evaluation

of how confounding factors influenced the observed associations and provided robust estimates of the independent effects of each exposure combination.

## Cardiovascular disease risk

In the unadjusted Model 1, all three exposure groups demonstrated significantly elevated cardiovascular disease risk compared to the reference group. However, the magnitude of associations varied considerably across groups, with the combined diabetes and sarcopenic obesity group showing the strongest association. After adjustment for age and sex in Model 2, the associations remained statistically significant but were attenuated, suggesting that demographic factors partially explained the observed relationships.

The fully adjusted Model 3, which incorporated comprehensive adjustment for demographic factors (residence, education), lifestyle variables (smoking, alcohol consumption), lipid parameters (total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein), comorbidities (hypertension, chronic lung disease, cancer, kidney disease, liver disease), and medication use (glucose-lowering, antihypertensive, and lipid-lowering medications), revealed important distinctions in the independent effects of different exposure combinations.

In this fully adjusted model, neither diabetes alone nor sarcopenic obesity alone demonstrated statistically significant associations with cardiovascular disease risk. Specifically, participants with diabetes alone showed a hazard ratio of 1.11 (95% CI: 0.96–1.29, $P=0.154$), while those with sarcopenic obesity alone had a hazard ratio of 1.05 (95% CI: 0.94–1.17, $P=0.385$). These findings suggest that when comprehensive confounding adjustment is applied, the individual effects of either condition alone are largely explained by associated risk factors.

In striking contrast, participants with both diabetes and sarcopenic obesity maintained a statistically significant and clinically meaningful elevation in cardiovascular disease risk, with a hazard ratio of 1.34 (95% CI: 1.10–1.63, $P=0.004$). This represents a 34% increased risk of cardiovascular disease that persists after extensive adjustment for potential confounding factors, providing strong evidence for synergistic effects between these two conditions.

## Stroke risk analysis

When stroke events were analyzed as a separate outcome, the pattern of associations was even more pronounced, with the combined diabetes and sarcopenic obesity group demonstrating particularly elevated risk. In the fully adjusted Model 3, participants with diabetes alone showed a hazard ratio of 0.93 (95% CI: 0.72–1.19, $P=0.549$), while those with sarcopenic obesity alone had a hazard ratio of 0.94 (95% CI: 0.77–1.15, $P=0.560$), neither of which reached statistical significance.

However, participants with both conditions combined exhibited a substantial 56% increased risk of stroke, with a hazard ratio of 1.56 (95% CI: 1.14–2.12, $P=0.005$). This finding indicates that the synergistic effects of diabetes and sarcopenic obesity are particularly pronounced for cerebrovascular outcomes, potentially reflecting the combined impact of metabolic dysfunction and altered body composition on stroke pathophysiology.

## Cardiac events risk analysis

For cardiac events, the fully adjusted analysis revealed a more modest but still significant association for the combined group. Participants with diabetes alone demonstrated a hazard ratio of 1.15 (95% CI: 0.98–1.35, $P=0.091$), while those with sarcopenic obesity alone showed a hazard ratio of 1.06 (95% CI: 0.93–1.20, $P=0.383$), neither reaching statistical significance.

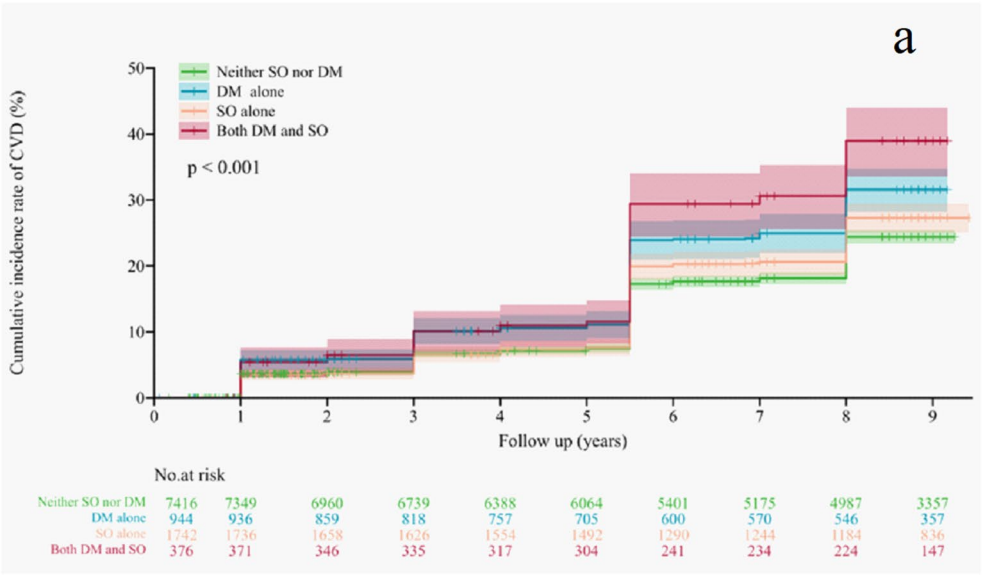
The combined diabetes and sarcopenic obesity group exhibited a 27% increased risk of cardiac events, with a hazard ratio of 1.27 (95% CI: 1.01–1.59, $P=0.041$). While this effect was less pronounced than that observed for stroke, it nonetheless represents a clinically significant elevation in risk that persists after comprehensive adjustment for confounding factors.

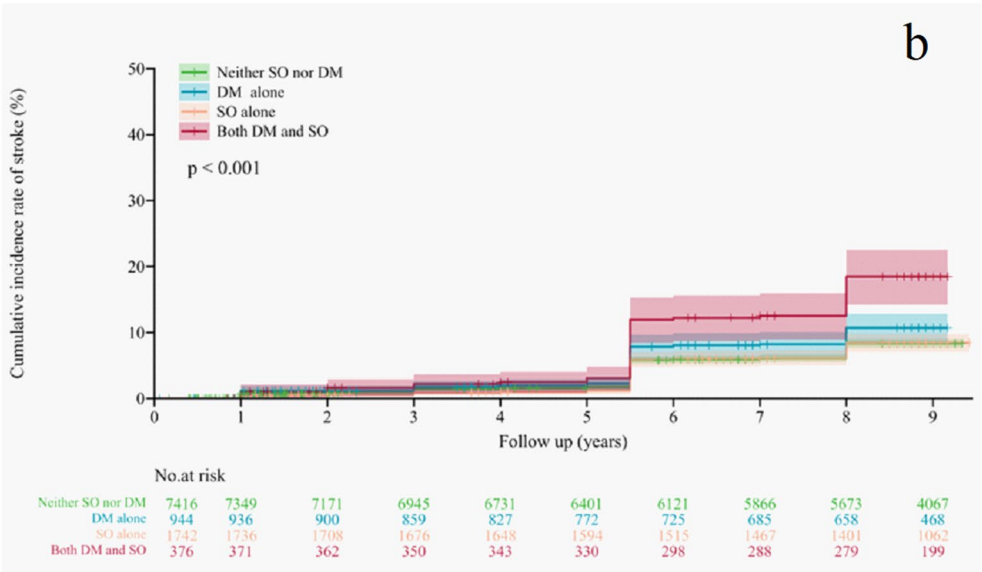
## Interaction analysis

To formally evaluate whether the combined effects of diabetes and sarcopenic obesity exceeded what would be expected from their individual contributions, we conducted comprehensive interaction analyses using both additive and multiplicative scales (Table 2). These analyses provide crucial insights into the mechanistic relationships between these conditions and their collective impact on cardiovascular outcomes.

## Additive interaction assessment

Additive interaction analysis, which examines whether the combined effect exceeds the sum of individual effects, revealed differential patterns across cardiovascular outcomes. For overall cardiovascular disease, the RERI (relative excess risk of interaction) was 0.17, suggesting that the cardiovascular disease risk in individuals with both diabetes and sarcopenic obesity imposes an additional 17%. However, this additive interaction did not reach statistical significance, indicating that while there may be some synergistic


a
Neither SO nor DM
DM alone
SO alone
Both DM and SO
p < 0.001
Cumulative incidence rate of CVD (%)
Follow up (years)
No.at risk
Neither SO nor DM 7416 7349 6960 6739 6388 6064 5401 5175 4987 3357
DM alone 944 936 859 818 757 705 600 570 546 357
SO alone 1742 1736 1658 1626 1554 1492 1290 1244 1184 836
Both DM and SO 376 371 346 335 317 304 241 234 224 147


b
Neither SO nor DM
DM alone
SO alone
Both DM and SO
p < 0.001
Cumulative incidence rate of stroke (%)
Follow up (years)
No.at risk
Neither SO nor DM 7416 7349 7171 6945 6731 6401 6121 5866 5673 4067
DM alone 944 936 900 859 827 772 725 685 658 468
SO alone 1742 1736 1708 1676 1648 1594 1515 1467 1401 1062
Both DM and SO 376 371 362 350 343 330 298 288 279 199

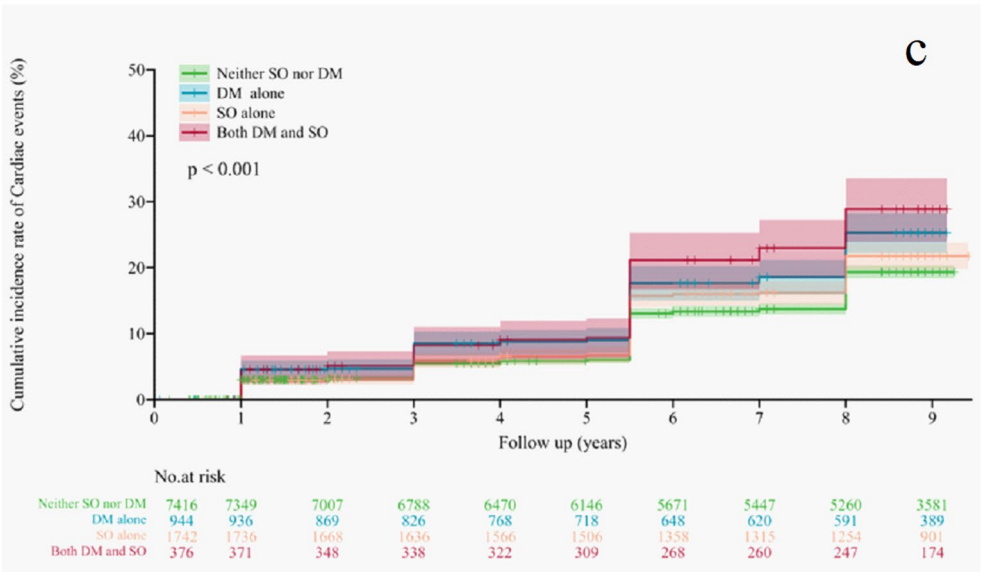

c
Neither SO nor DM
DM alone
SO alone
Both DM and SO
p < 0.001
Cumulative incidence rate of Cardiac events (%)
Follow up (years)
No.at risk
Neither SO nor DM 7416 7349 7007 6788 6470 6146 5671 5447 5260 3581
DM alone 944 936 869 826 768 718 648 620 591 389
SO alone 1742 1736 1668 1636 1566 1506 1358 1315 1254 901
Both DM and SO 376 371 348 338 322 309 268 260 247 174

**Fig. 2** Kaplan-Meier curves of cumulative incidence of CVD (**a**) Stroke (**b**) and risk of cardiac events (**c**) for the four groups over 9 years from CHARLES 2011 to 2020. The difference in cumulative incidence of CVD by groups without DM without SO, DM, SO, and DM with SO were statistically significant ($P<0.001$). The difference in cumulative incidence of Stroke by the grouping of no DM without SO, DM, SO, and DM with SO was statistically significant ($P<0.001$). The difference in cumulative incidence of heart problems grouped by no DM without SO, DM, SO, and DM with SO was statistically significant ($P<0.001$)

effect, it was not definitively established for the composite cardiovascular outcome.

For cardiac events, the RERI was 0.06, representing a modest 6% excess risk attributable to interaction effects. Similar to cardiovascular disease overall, this additive interaction was not statistically significant, suggesting that the combined effect for cardiac events approximates the sum of individual effects rather than demonstrating clear synergy.

In contrast, stroke demonstrated compelling evidence of significant additive interaction. The RERI for stroke was 0.69 ($P=0.003$), indicating that the stroke risk in individuals with both diabetes and sarcopenic obesity imposes an additional 69%. The AP (attribution proportion) for stroke was 0.44 ($P<0.001$), further indicating that 44% of all stroke events occurring in these individuals with both diabetes can be attributed to this synergistic effect, rather than the simple summation of the two risk factors. This substantial and statistically significant additive interaction suggests that the biological mechanisms underlying stroke risk are particularly susceptible to the combined effects of metabolic dysfunction and altered body composition.

## Multiplicative interaction assessment

Multiplicative interaction analysis, which examines whether the combined effect exceeds the product of individual effects, provided additional insights into the nature of these relationships. For overall cardiovascular disease, there was no evidence of multiplicative interaction ($P=0.261$), suggesting that the combined effect approximates what would be expected from the product of individual risk ratios. Similarly, for cardiac events, multiplicative interaction was not statistically significant ($P=0.766$).

However, consistent with the additive interaction findings, stroke demonstrated significant multiplicative interaction between diabetes and sarcopenic obesity ($P=0.003$). This finding reinforces the conclusion that cerebrovascular outcomes are particularly susceptible to synergistic effects between these conditions, with the combined impact exceeding both additive and multiplicative expectations based on individual effects.

The convergent evidence from both additive and multiplicative interaction analyses for stroke outcomes provides robust support for true biological synergy between diabetes and sarcopenic obesity in cerebrovascular disease pathogenesis, distinguishing stroke from other cardiovascular outcomes in terms of interaction patterns.

## Stratified analysis by sarcopenic obesity status

To better understand the modifying effect of sarcopenic obesity on the relationship between diabetes and cardiovascular disease, we conducted a stratified analysis examining diabetes effects within subgroups defined by sarcopenic obesity status (Fig. 4). This approach provides insights into whether the presence of sarcopenic obesity fundamentally alters the cardiovascular risk profile associated with diabetes.

Among participants without sarcopenic obesity, the presence of diabetes was not associated with significantly increased cardiovascular disease risk, with a hazard ratio of 1.05 (95% CI: 0.90–1.22, $P=0.563$). This finding suggests that in individuals with preserved muscle mass and function, diabetes alone may not confer substantial cardiovascular risk after adjustment for other risk factors, or that the risk is effectively mitigated by the absence of sarcopenic obesity.

In striking contrast, among participants with sarcopenic obesity, the presence of diabetes was associated with a substantial 47% increased risk of cardiovascular disease, with a hazard ratio of 1.47 (95% CI: 1.17–1.86, $P<0.001$). This finding indicates that sarcopenic obesity creates a biological milieu in which diabetes exerts much more pronounced cardiovascular effects.

The heterogeneity test confirmed that these differences between strata were statistically significant ($P=0.016$), providing formal evidence that sarcopenic obesity significantly modifies the relationship between diabetes and cardiovascular disease risk. This interaction suggests that the metabolic and inflammatory consequences of sarcopenic obesity may amplify the cardiovascular toxicity of diabetes through shared or synergistic pathophysiological pathways.

## Subgroup analysis by age and sex

Comprehensive subgroup analyses were conducted to evaluate potential effect modification by demographic factors, with particular attention to age and sex differences in the associations between diabetes, sarcopenic obesity, and cardiovascular outcomes (Fig. 5).

## Age-stratified analysis

Age-stratified analysis did not reveal significant interaction effects for cardiovascular disease risk, suggesting that the synergistic effects of diabetes and sarcopenic obesity

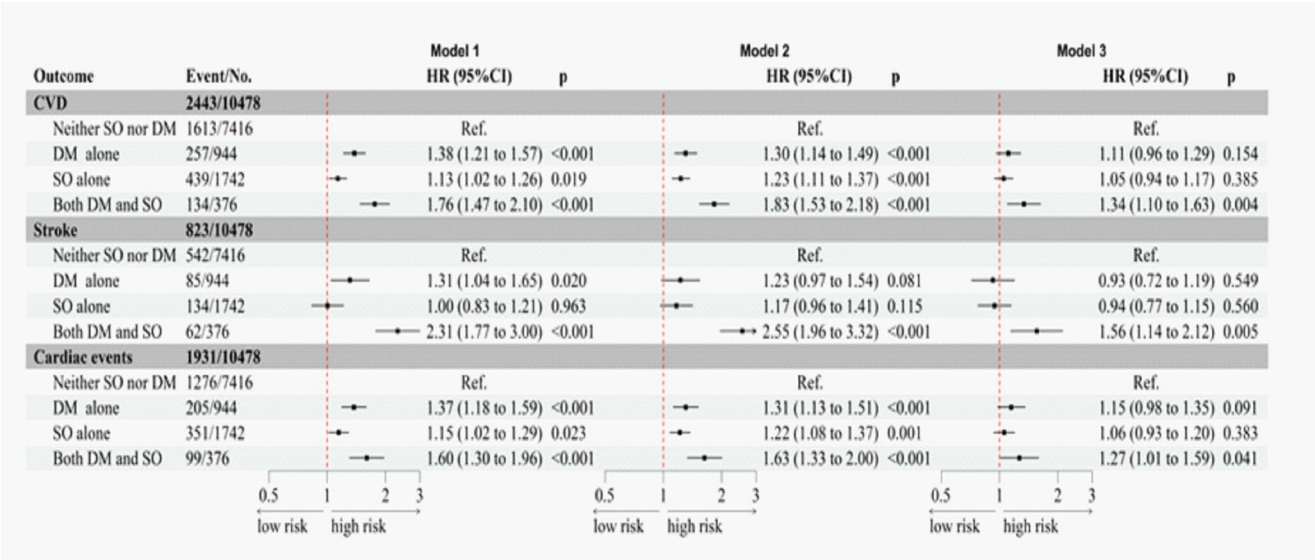



**Fig. 3** Joint association of DM, SO and risk of CVD, stroke and cardiovascular disease development. Model 1 Unadjusted model. Model 2 Adjusted for age and sex Model 3 Adjusted for residence, education, smoking, alcohol consumption, lipids (total cholesterol, triglycerides, HDL, LDL), comorbidities (hypertension, chronic lung disease, cancer, kidney disease, liver disease), medication use (hypoglycaemic, antihypertensive, lipid-lowering)

**Table 2** Cumulative and multiplicative interactions of DM and SO on risk of CVD, stroke and cardiac eve

| Measures | Estimate | *p* |
|---|---|---|
| CVD | | |
| Additive interaction | | |
| RERI | 0.17(-0.11to 0.46) | 0.118 |
| AP | 0.13 (-0.07 to 0.33) | 0.099 |
| SI | 2.08 (0.55 to 7.88) | 0.141 |
| Multiplicative scale | 1.14 (0.90 to 1.45) | 0.261 |
| Stroke | | |
| Additive interaction | | |
| RERI | 0.69 (0.20 to 1.17) | 0.003 |
| AP | 0.44(0.22 to 0.66) | <0.001 |
| SI | —— | |
| Multiplicative scale | 1.78(1.22 to 2.61) | 0.003 |
| Cardiac events | | |
| Additive interaction | | |
| RERI | 0.06 (-0.26 to 0.38) | 0.359 |
| AP | 0.05 (-0.20 to 0.29) | 0.355 |
| SI | 1.29 (0.33 to 5.03) | 0.359 |
| Multiplicative scale | 1.04 (0.80 to 1.36) | 0.766 |

AP: attribution proportion;

RERI: relative excess risk of interaction;

SI: synergy index

Corrective variables in the model are consistent with model 3

are consistent across different age groups within our study population. This finding indicates that the biological mechanisms underlying the observed synergy are not substantially modified by aging processes within the age range examined (45 years and older), and that the combined effects of these conditions remain clinically relevant across the spectrum of middle-aged and older adults.

## Sex-stratified analysis

Sex-stratified analysis revealed evidence of potential effect modification, with a statistically significant interaction term ($P=0.017$). The analysis suggested that male participants may experience stronger cardiovascular risk effects from the combination of diabetes and sarcopenic obesity compared to female participants. This sex difference may reflect differential patterns of muscle loss, fat distribution, hormonal influences, or cardiovascular disease pathophysiology between men and women.

The observed sex interaction has important clinical implications, suggesting that male patients with both diabetes and sarcopenic obesity may represent a particularly high-risk subgroup requiring intensified cardiovascular prevention strategies. However, it is important to note that while the interaction was statistically significant, both sexes demonstrated elevated risk in the combined exposure group, indicating that the synergistic effects are relevant for both men and women, albeit potentially with different magnitudes.

These subgroup findings contribute to a more nuanced understanding of the populations most susceptible to the combined effects of diabetes and sarcopenic obesity, providing guidance for targeted clinical interventions and risk stratification approaches.

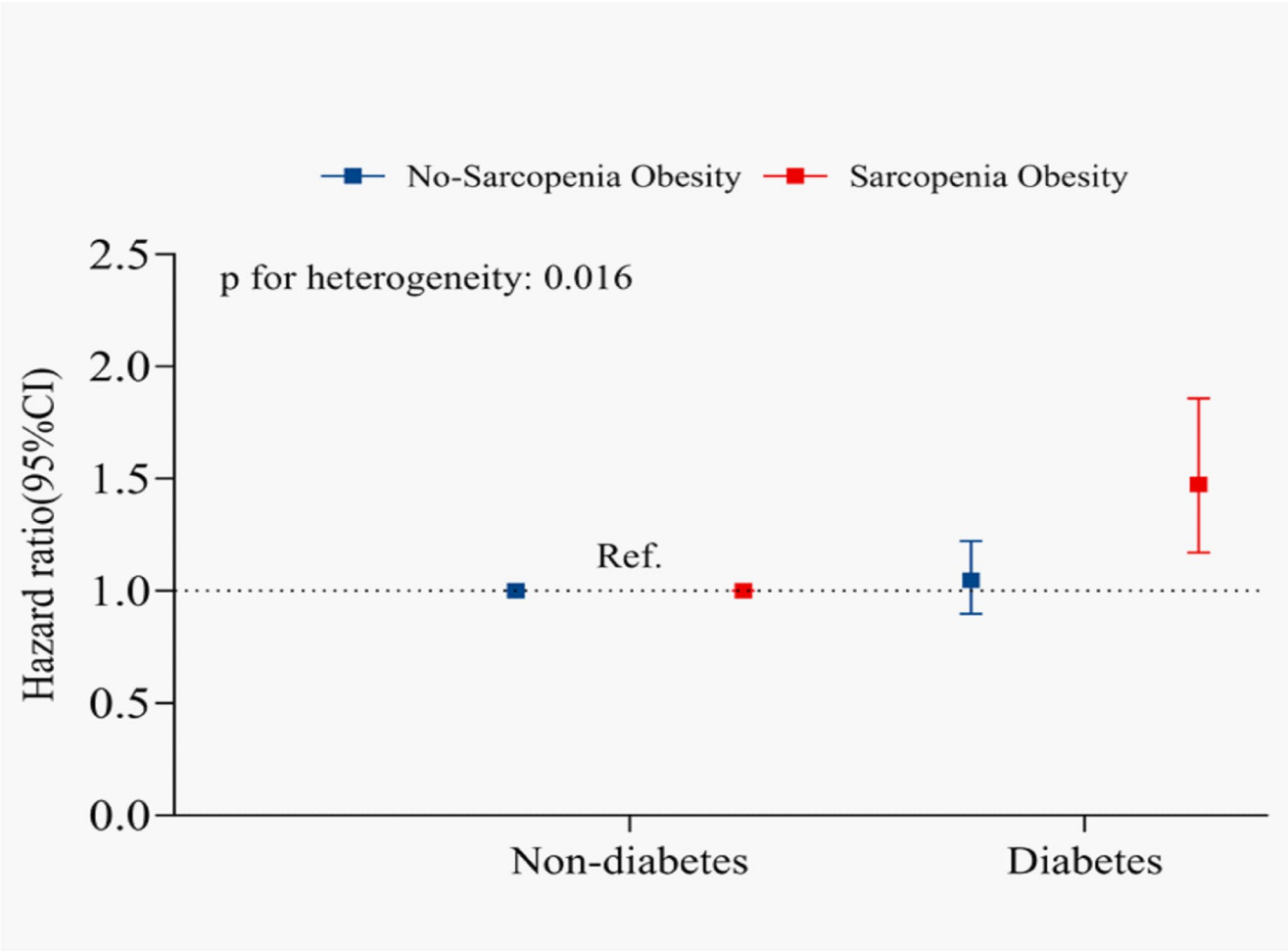



**Fig. 4** Association between baseline DM and CVD onset after SO stratification. Corrective variables in the model were consistent with model 3

## Discussion

This large-scale prospective cohort study provides the first comprehensive evidence of synergistic effects between diabetes mellitus and sarcopenic obesity on cardiovascular disease risk in a Chinese adult population. Our findings demonstrate that individuals with both conditions face a 34% increased risk of cardiovascular disease compared to those with neither condition, representing a risk elevation that exceeds the individual effects of either diabetes or sarcopenic obesity alone. These results have important implications for cardiovascular risk stratification, clinical management, and public health policy in aging populations worldwide.

### Principal findings and clinical significance

The identification of synergistic effects between diabetes and sarcopenic obesity has several important clinical implications. First, it suggests the need for comprehensive screening approaches that assess both metabolic and body composition parameters in middle-aged and older adults. Current clinical practice guidelines typically address diabetes and sarcopenia as separate entities, but our findings suggest that their combination represents a distinct high-risk phenotype requiring integrated management strategies.

Healthcare providers should consider implementing routine sarcopenia screening in diabetic patients, particularly those over 50 years of age. This could include simple assessments such as handgrip strength measurement and chair stand tests, which are feasible in most clinical settings and have been validated as predictors of adverse outcomes [21]. Similarly, diabetic patients identified with sarcopenic obesity should receive intensified cardiovascular risk assessment and prevention strategies [22].

The management of individuals with both conditions should adopt a multidisciplinary approach addressing metabolic control, body composition optimization, and cardiovascular risk reduction simultaneously. This might include structured exercise programs combining resistance training

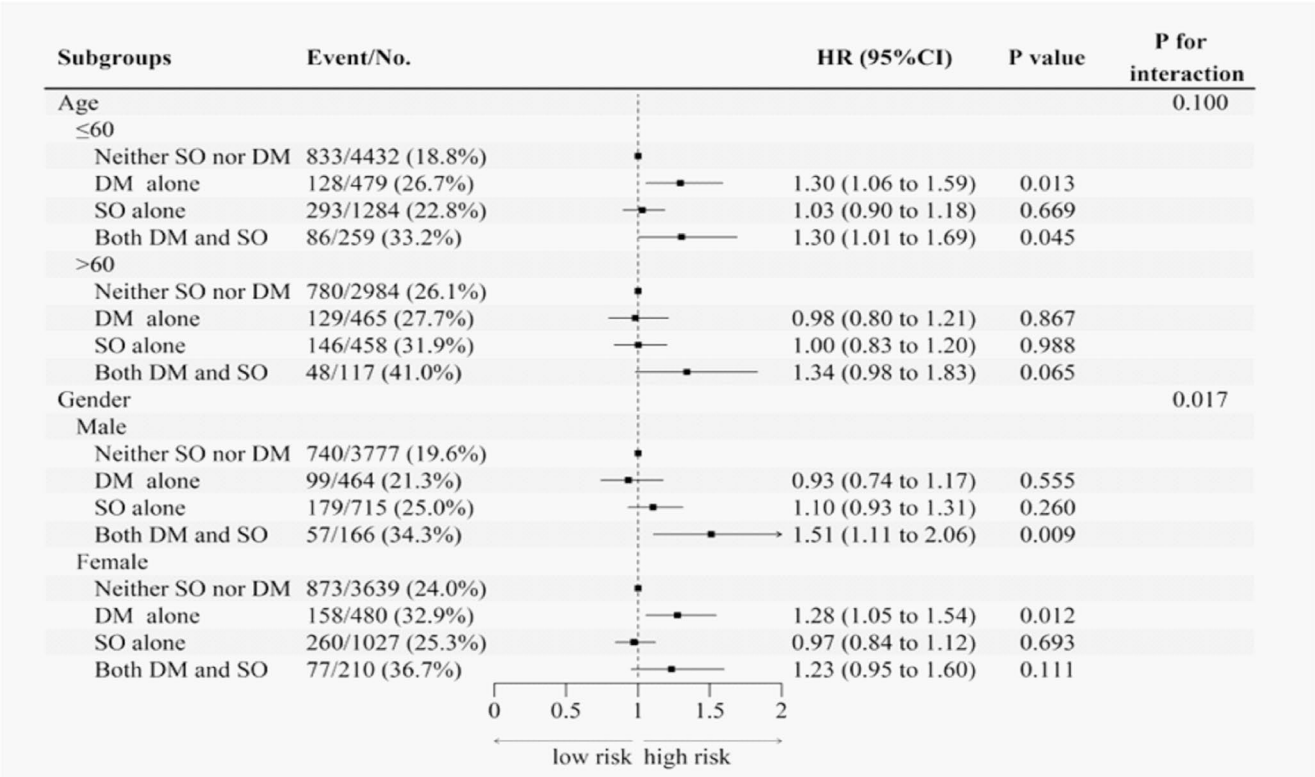



**Fig. 5** Subgroup analyses of age- and sex-stratified CVD risk. Corrective variables in the model were consistent with model 3

to preserve muscle mass with aerobic exercise for cardiovascular benefits [23]. Nutritional interventions should focus on adequate protein intake to support muscle protein synthesis [24], and while maintaining glycemic control through appropriate carbohydrate management [25].

## Mechanistic insights and biological plausibility

The observed synergistic effects between diabetes and sarcopenic obesity are biologically plausible and supported by several mechanistic pathways. Skeletal muscle, the largest insulin-sensitive organ, loses mass and function, directly impairing glucose tolerance and promoting diabetes [26]. Conversely, diabetes triggers muscle loss through chronic inflammation, oxidative stress, mitochondrial dysfunction, and altered protein metabolism [13]. Free fatty acids, inflammatory mediators, and adipokines released from excess visceral adipose tissue exacerbate insulin resistance and accelerate cardiovascular disease via myocardial lipid deposition and endothelial dysfunction [27]. Hyperglycemia and microvascular complications damage muscle fibers, while cardiovascular disease–induced hypoperfusion and chronic inflammation suppress protein synthesis, establishing a vicious cycle among muscle, metabolism, and cardiovascular function [28].

Sarcopenic obesity and diabetes present a synergistic risk for stroke, whereas no such synergy is observed for overall cardiovascular events. The mechanism lies in the fact that their combined presence amplifies cerebral microvascular endothelial dysfunction, pro-inflammatory and pro-thrombotic states, and insulin resistance, significantly elevating the probability of ischaemic stroke [29]. Cardiovascular endpoints such as coronary heart disease and heart failure have already reached a plateau by the classic pathways of diabetes and obesity (hypertension, dyslipidaemia) [30]. Sarcopenia contributes only marginally to this plateau [31], and the ‘obesity paradox’—where moderate fat reserves may actually buffer against heart failure—dilutes the synergistic effects [32]. The significant additive and multiplicative interactions observed for stroke provide strong evidence for true biological synergy in cerebrovascular disease pathogenesis.

Naturally, we must acknowledge that although CHARLS has validated several self-reported outcomes, the question ‘Have you been diagnosed with a stroke by a doctor?’ remains fundamentally a patient-reported physician diagnosis (PPD), carrying inherent potential for classification bias. The core risk of classification bias stems from the combined effect of variations in reporting accuracy and disease characteristics. Firstly, the specialised nature of stroke diagnosis conflicts with patient cognitive biases: some patients may

misinterpret mild symptoms (such as lacunar infarction) or express non-specific symptoms (like transient dizziness or limb numbness due to cognitive decline in the elderly) as stroke, leading to false negative classifications. Conversely, anxious patients with underlying conditions like hypertension or diabetes may over-report other cerebrovascular discomforts (e.g., migraines, transient ischaemic attacks) as strokes, triggering false positive classifications.

### Comparison with previous literature

Our results are consistent with findings from the Korean Longitudinal Study on Health and Aging, which reported increased cardiovascular mortality in individuals with sarcopenic obesity, though that study did not examine diabetes interactions [33]. The Health, Aging and Body Composition Study in the United States found similar associations between muscle loss and cardiovascular events in older adults, but again did not specifically investigate diabetes interactions [34].

The magnitude of cardiovascular risk elevation observed in our study (34% for overall cardiovascular disease, 56% for stroke) is clinically significant and comparable to that associated with other established cardiovascular risk factors. This positions the combination of diabetes and sarcopenic obesity as a major modifiable risk factor that warrants recognition in cardiovascular risk prediction models and clinical guidelines.

### Public health implications

From a public health perspective, our findings highlight the importance of integrated prevention strategies addressing both diabetes and sarcopenic obesity in aging populations. Traditional diabetes prevention programs focus primarily on weight loss and glycemic control [35], while sarcopenia prevention emphasizes physical activity and nutrition [36]. Our results suggest that combined approaches targeting both conditions simultaneously may be more effective for cardiovascular disease prevention.

Population-level interventions should consider the synergistic nature of these conditions when designing screening and prevention programs. This might include community-based exercise programs that combine resistance training with diabetes education, or integrated health assessments that evaluate both metabolic and physical function parameters. Given the aging demographics in China and other developing countries, such integrated approaches could have substantial population health benefits.

### Strengths and limitations

This study has several notable strengths. The large sample size of over 10,000 participants provides adequate statistical power to detect clinically meaningful associations and examine interaction effects. The prospective design with nine years of follow-up enables robust assessment of temporal relationships and reduces the risk of reverse causation. The use of standardized, internationally recognized criteria for diabetes and sarcopenic obesity enhances the generalizability of findings to other populations.

However, several limitations should be acknowledged. The reliance on self-reported cardiovascular disease outcomes may introduce misclassification bias, though previous validation studies in CHARLS have demonstrated good agreement with medical records.

The observational study design precludes definitive causal inferences, and residual confounding from unmeasured variables remains possible. The study population was limited to Chinese adults, which may limit generalizability to other ethnic groups, though the biological mechanisms underlying the observed associations are likely to be similar across populations.

## Conclusions

This large-scale prospective cohort study demonstrates that diabetes mellitus and sarcopenic obesity exert synergistic effects on cardiovascular disease risk in Chinese adults, with individuals having both conditions facing substantially higher risk than those with either condition alone. The 34% increased cardiovascular disease risk and 56% increased stroke risk in the combined group represent clinically significant elevations that warrant recognition as a distinct high-risk phenotype.

These findings have important implications for clinical practice, suggesting the need for integrated screening and management approaches that address both metabolic and body composition abnormalities simultaneously. From a public health perspective, the results highlight the importance of comprehensive prevention strategies targeting both diabetes and sarcopenic obesity in aging populations.

The identification of synergistic effects between these increasingly prevalent conditions provides new insights into cardiovascular risk stratification and offers opportunities for more targeted and effective prevention strategies. As populations continue to age globally, understanding and addressing the combined effects of diabetes and sarcopenic obesity will become increasingly important for reducing the burden of cardiovascular disease and improving health outcomes in older adults.

**Acknowledgements** We thank all participants in the China Health and Retirement Longitudinal Study (CHARLS) for their valuable contributions to this research. We acknowledge the CHARLS research team for their efforts in data collection and management. We also thank the staff at participating hospitals and community health centers for their support in participant recruitment and follow-up.

**Author contributions** F.W. and J.D. conceived and designed the study. F.W., R.L., and J.H. performed the statistical analysis. F.W. drafted the manuscript. J.D. supervised the study and provided critical revision of the manuscript. All authors contributed to data interpretation and approved the final version of the manuscript.

**Funding** This work was supported by the Science Fund of Jiangxi Provincial Health Commission (#202410643).

**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate** The Ethical Review Committee of Peking University approved the human studies, which adhered to local laws and institutional guidelines. Participants gave written informed consent.

**Competing interests** The authors declare no competing interests.



## References

1. Lindstrom M, DeCleene N, Dorsey H et al (2022) Global burden of cardiovascular diseases and risks collaboration, 1990–2021. J Am Coll Cardiol 80(25):2372–2425. https://doi.org/10.1016/j.jacc.2022.11.001
2. Mocumbi AO (2024) Cardiovascular health care in Low- and Middle-Income countries. Circulation 149(8):557–559. https://doi.org/10.1161/CIRCULATIONAHA.123.065717
3. Zhang X, Lu J, Yang Y et al (2022) Cardiovascular disease prevention and mortality across 1 million urban populations in china: data from a nationwide population-based study. Lancet Public Health 7(12):e1041–e1050. https://doi.org/10.1016/S2468-2667(22)00170-0
4. Zhou YC, Liu JM, Zhao ZP et al (2025) The National and provincial prevalence and non-fatal burdens of diabetes in China from 2005 to 2023 with projections of prevalence to 2050. Mil Med Res 12(1):28. https://doi.org/10.1186/s40779-025-00615-1
5. Wong ND Sattar N (2023) Cardiovascular risk in diabetes mellitus: epidemiology, assessment, and prevention. Nat Reviews Cardiol 20(10):685–695. https://doi.org/10.1038/s41569-023-00877-z
6. Ke C, Lipscombe LL, Weisman A et al (2023) Change in the relation between age and cardiovascular events among men and women with diabetes compared with those without diabetes in 1994–1999 and 2014–2019: A Population-Based cohort study. Diabetes Care 46(10):e200–e202. https://doi.org/10.2337/dc23-0952
7. Beckman JA, Creager MA, Libby P (2002) Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA 287(19):2570–2581. https://doi.org/10.1001/jama.287.19.2570
8. Sayer AA, Cruz-Jentoft A (2022) Sarcopenia definition, diagnosis, and treatment: consensus is growing. Age Ageing 51(10):afac220. https://doi.org/10.1093/ageing/afac220
9. Batsis JA, Villareal DT (2018) Sarcopenic obesity in older adults: aetiology, epidemiology, and treatment strategies. Nat Reviews Endocrinol 14(9):513–537. https://doi.org/10.1038/s41574-018-0062-9
10. Prado CM, Batsis JA, Donini LM et al (2024) Sarcopenic obesity in older adults: A clinical overview. Nat Reviews Endocrinol 20(5):261–277. https://doi.org/10.1038/s41574-023-00943-z
11. Wei S, Nguyen TT, Zhang Y et al (2023) Sarcopenic obesity: epidemiology, pathophysiology, cardiovascular disease, mortality, and management. Front Endocrinol 14:1185221. https://doi.org/10.3389/fendo.2023.1185221
12. Chuan F, Chen S, Ye X et al (2022) Sarcopenic obesity predicts negative health outcomes among older patients with type 2 diabetes: the ageing and body composition of diabetes (ABCD) cohort study. Clin Nutr 41(12):2740–2748. https://doi.org/10.1016/j.clnu.2022.10.023
13. Mesinovic J, Zengin A, De Courten B et al (2019) Sarcopenia and type 2 diabetes mellitus: A bidirectional relationship. Diabetes Metab Syndr Obes 12:1057–1072. https://doi.org/10.2147/DMSO.S186600
14. Kalinkovich A, Livshits G (2017) Sarcopenic obesity or obese sarcopenia: A cross talk between age-associated adipose tissue and skeletal muscle inflammation as a main mechanism of the pathogenesis. Ageing Res Rev 35:200–221. https://doi.org/10.1016/j.arr.2016.09.008
15. Zhao Y, Hu Y, Smith JP et al (2014) Cohort profile: the China health and retirement longitudinal study (CHARLS). Int J Epidemiol 43(1):61–68. https://doi.org/10.1093/ije/dys203
16. Chen X, Crimmins E, Hu PP et al (2019) Venous Blood-Based biomarkers in the China health and retirement longitudinal study: rationale, design, and results from the 2015 wave. Am J Epidemiol 188(11):18711877. https://doi.org/10.1093/aje/kwz170
17. American Diabetes Association (2021) Classification and diagnosis of diabetes: standards of medical care in diabetes-2021. Diabetes Care 44(Suppl 1):S15–S33. https://doi.org/10.2337/dc21-S002
18. Donini LM, Busetto L, Bischoff SC et al (2022) Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement. Obes Facts 15(3):321–335. https://doi.org/10.1159/000521241
19. Chinese Medical Association (2024) Chinese guidelines for the prevention and treatment of obesity (2024 edition). Chin J Endocrinol Metabolism 40(1):1–28
20. Chen LK, Woo J, Assantachai P et al (2020) Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. J Am Med Dir Assoc 21(3):300–307e2. https://doi.org/10.1016/j.jamda.2019.12.012
21. Johansson J, Grimsgaard S, Strand BH et al (2023) Comparing associations of handgrip strength and chair stand performance

with all-cause mortality-implications for defining probable sarcopenia: the Tromsø study 2015–2020. BMC Med 21(1):451. https://doi.org/10.1186/s12916-023-03172-3
22. Dent E, Morley JE, Cruz-Jentoft AJ et al (2018) International clinical practice guidelines for sarcopenia (ICFSR): screening, diagnosis and management. J Nutr Health Aging 22(10):1148–1161https://doi.org/10.1007/s12603-018-1139-9
23. Brellenthin AG, Lanningham-Foster LM, Kohut ML et al (2019) Comparison of the cardiovascular benefits of resistance, aerobic, and combined exercise (CardioRACE): rationale, design, and methods. Am Heart J 217:101–111. https://doi.org/10.1016/j.ahj.2019.08.008
24. Nunes EA, Colenso-Semple L, McKellar SR et al (2022) Systematic review and meta-analysis of protein intake to support muscle mass and function in healthy adults. J Cachexia Sarcopenia Muscle 13(2):795–810. https://doi.org/10.1002/jcsm.1292
25. Jing T, Zhang S, Bai M et al (2023) Effect of dietary approaches on glycemic control in patients with type 2 diabetes: A systematic review with network Meta-Analysis of randomized trials. Nutrients 15(14):3156. https://doi.org/10.3390/nu15143156
26. DeFronzo RA, Tripathy D (2009) Skeletal muscle insulin resistance is the primary defect in type 2 diabetes. Diabetes Care 32(Suppl 2):S157–S163. https://doi.org/10.2337/dc09-S302
27. Cesaro A, De Michele G, Fimiani F et al (2023) Visceral adipose tissue and residual cardiovascular risk: a pathological link and new therapeutic options. Front Cardiovasc Med 10:1187735. https://doi.org/10.3389/fcvm.2023.1187735
28. Barrett EJ, Liu Z, Khamaisi M et al (2017) Diabetic microvascular disease: an endocrine society scientific statement. J Clin Endocrinol Metab 102(12):4343–4410. https://doi.org/10.1210/jc.2017-01922
29. Wang M, Tan Y, Shi Y et al (2020) Diabetes and sarcopenic obesity:pathogenesis, diagnosis, and treatments. Front Endocrinol 11:568. https://doi.org/10.3389/fendo.2020.00568
30. Artola Arita V, Beigrezaei S, Franco OH (2024) Risk factors for cardiovascular disease: the known unknown. Eur J Prev Cardiol 31(14):e106–e107. https://doi.org/10.1093/eurjpc/zwad392
31. Zuo X, Li X, Tang K et al (2023) Sarcopenia and cardiovascular diseases: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle 14(3):1183–1198. https://doi.org/10.1002/jcsm.13221
32. Tutor AW, Lavie CJ, Kachur S et al (2023) Updates on obesity and the obesity paradox in cardiovascular diseases. Prog Cardiovasc Dis 78:2–10. https://doi.org/10.1016/j.pcad.2022.11.013
33. Kim JH, Cho JJ, Park YS (2015) Relationship between sarcopenic obesity and cardiovascular disease risk as estimated by the Framingham risk score. J Korean Med Sci 30(3):264–271. https://doi.org/10.3346/jkms.2015.30.3.264
34. Kim D, Lee J, Park R et al (2024) Association of low muscle mass and obesity with increased all-cause and cardiovascular disease mortality in US adults. J Cachexia Sarcopenia Muscle 15(1):240–254. https://doi.org/10.1002/jcsm.13397
35. ElSayed NA, Aleppo G, Aroda VR et al (2023) Glycemic targets: standards of care in diabetes. Diabetes Care 46(Suppl 1):S97–S110. https://doi.org/10.2337/dc23-S006
36. Cruz-Jentoft AJ, Bahat G, Bauer J et al (2019) Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 48(1):16–31. https://doi.org/10.1093/ageing/afy169