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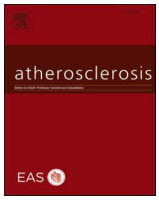

Daily stair climbing, disease susceptibility, and risk of atherosclerotic cardiovascular disease: A prospective cohort study

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ABSTRACT

Background and aims: The associations between intensity of stair climbing and atherosclerotic cardiovascular disease (ASCVD) and how these vary by underlying disease susceptibility are not fully understood. We aim to evaluate the intensity of stair climbing and risk of ASCVD types and whether these vary with the presence of ASCVD risk factors.

Methods: This prospective study used data of 458,860 adult participants from the UK Biobank. Information about stair climbing, sociodemographic, and lifestyle factors was collected at baseline and a resurvey 5 years after baseline. ASCVD was defined as coronary artery disease (CAD), ischemic stroke (IS), or acute complications. Associations between flights of stair climbing and ASCVD were examined as hazard ratios (HRs) from Cox proportional hazards models. The modification role of disease susceptibility on such associations was assessed by analyses stratified by levels of genetic risk score (GRS), 10-year risks of ASCVD, and self-reported family history of ASCVD.

Results: During a median of 12.5 years of follow-up, 39,043 ASCVD, 30,718 CAD, and 10,521 IS cases were recorded. Compared with the reference group (reported climbing stairs 0 times/day at baseline), the multivariable-adjusted HRs for ASCVD were 0.97 (95% CI, 0.93–1.01), 0.84 (0.82–0.87), 0.78 (0.75–0.81), 0.77 (0.73–0.80) and 0.81 (0.77–0.85) for stair climbing of 1–5, 6–10, 11–15, 16–20 and ≥21 times/day, respectively. Comparable results were obtained for CAD and IS. When stratified by different disease susceptibility based on the GRS for CAD/IS, 10-year risk, and family history of ASCVD, the protection association of stair climbing was attenuated by increasing levels of disease susceptibility. Furthermore, compared with people who reported no stair climbing (<5 times/d) at two examinations, those who climbed stairs at baseline and then stopped at resurvey experienced a 32% higher risk of ASCVD (HR 1.32, 95% CI:1.06–1.65).

Conclusions: Climbing more than five flights of stairs (approx 50 steps) daily was associated with a lower risk of ASCVD types independent of disease susceptibility. Participants who stopped stair climbing between baseline and resurvey had a higher risk of ASCVD compared with those who never climbed stairs.

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1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) and its clinical manifestations, including coronary artery disease (CAD) and ischaemic stroke (IS), are the leading causes of morbidity and mortality worldwide [1]. In addition to established risk factors, family history and genetic risk factors are associated with higher risks of ASCVD events [2]. Prevention of ASCVD through lifestyle modifications may have significant public health implications.

Regular physical activity (PA), including various types of sports, provides important protection against cardiovascular diseases [3,4]. Analysis of data collected from nearly 2 million participants reveals that in 2016, over a quarter of the adult population worldwide did not engage in sufficient physical activity [5]. Common self-reported barriers to engage in PA include health/physical impairments, a lack of resources, an inability to afford structured exercise [6] or a scarcity of time [7]. These barriers could be overcome in part by stair climbing, which promotes increased participation in daily PA (e.g., replacing elevators for short-to-medium distances without a substantial effect on time use). Furthermore, short bursts of high-intensity stair climbing are a time-efficient way to improve cardiorespiratory fitness and lipid profile, especially among those unable to achieve the current PA recommendations [8,9]. Previous work has mainly focused on a cluster of ASCVD risk factors, such as metabolic syndrome [10] and diabetes [11]; however, the long-term effects of stair climbing intensity or changes in stair climbing for the prevention of ASCVD are sparse.

Disease susceptibility plays a central role in the development of ASCVD [2]. For instance, the 10-year risk estimation of ASCVD is extensively employed in clinical practice for early prevention of CVD and its complications [12]. Genetic risk scores (GRS) of CAD [13] and IS [14], which are secondary genome-wide tools involving multiple genetic variants identified from genome-wide association studies (GWASs), have been utilized to aid in targeting disease prevention or treatment. Family history is another risk factor that reflects the inherited and shared environmental predisposition to ASCVD [15]. Thus, to achieve more precise prevention, efforts to reduce ASCVD risk must take an individual's environment and genetic makeup into account.

The objectives of the present study were to examine the associations of stair climbing, including changes over 12.5 years, and the risk of ASCVD. Further investigations were conducted to determine whether these associations vary by the presence or absence of different susceptibilities to ASCVD.

2. Patients and methods

2.1. Study design and setting

This study was a large-scale prospective cohort study that recruited about half a million adults aged 38–73 years [16]. Data on medical history, sociodemographic, and lifestyle information was assessed by questionnaires at baseline between 2006 and 2010 (baseline examination) and a resurvey in 2014. All participants underwent blood pressure, lung function, and anthropometry evaluation, as well as blood sample collection for the assessment of lipids and other related measurements. The study received ethical approval from the North-West Research Ethics Committee and all local participating centers. Details about UK Biobank (UKB) design and participant enrollment have been previously reported elsewhere [17].

2.2. Study population

After the exclusion of those with the hospital-documented diagnosis of ASCVD (n = 35,161), self-reported stroke (n = 7668) and heart disease (n = 22,943), or missing values of stair climbing (n = 8502) at baseline, 458,860 participants were included in the primary analysis. 50,657 of these participants were resurveyed in 2014 using a web questionnaire that contained the same questions from the baseline survey. Participants were then assigned to different groups based on their corresponding disease susceptibility, where missing values for a specific susceptibility item were removed from the analysis. Detailed information on the inclusion and exclusion criteria are shown in Supplementary eFig. 1.

2.3. Assessment of stair climbing

Information on the intensity of stair climbing was collected through self-report structured questionnaires using a 30-day recall method. The total number of times spent on stair climbing per day was determined by the following question: "At home, during the last four weeks, about how many times a day do you climb a flight of stairs? (approx ten steps)". Answers included six options that addressed the usual frequency. Changes in stair climbing between baseline and resurvey visits were classified according to the duration of time spent on stair climbing during both examinations: (1) no stair climbing: participants who reported ≤5 times/d of stair climbing at both examinations; (2) started stair climbing: participants who did not report stair climbing at baseline but did so (≥5 times/d) at the second examination; (3) stopped stair climbing: participants who reported stair climbing (≥5 times/d) at baseline but not at the second examination; or (4) maintained stair climbing: those reported stair climbing (≥5 times/d) at both examinations.

2.4. Ascertainment of ASCVD

Cases of ASCVD were documented by linking the records from the national death registry and Hospital Episode Statistics database, including diagnosis of coronary artery disease, ischemic stroke, or any associated acute complications, as well as coronary revascularization procedures. Additional details and ICD codes of ASCVD are provided in Supplementary eTable1. The hospital registry-based follow-up ended on 30th September 2021 in England, 31st July 2021 in Scotland, and 28th February 2018 in Wales, respectively. These individuals were followed until the occurrence of the ASCVD incident, loss to follow-up, or death, whichever came first.

2.5. Disease susceptibility to ASCVD

We assessed the susceptibility to ASCVD by utilizing a genetic risk score (GRS) of CAD and IS, 10-year ASCVD risk, or family history. Detailed descriptions of the genotyping process and arrays used in UKB have been described elsewhere [16]. The present study obtained 64 independent single nucleotide polymorphisms (SNPs) and 32 independent SNPs significantly associated with CAD [13] and IS [14] in recent genome-wide association studies (GWASs), respectively. A complete list of the selected SNPs is provided in Supplementary eTable 2 and eTable 3. The weighted genetic risk scores (GRS) of CAD and IS were calculated for each participant by multiplying the variant-specific weight (β-coefficient) with the imputed allelic dosage based on the GWAS and then summing across all variants, as previously reported [18]. Participants were categorized into low (quintile 1), intermediate (quintile 2–4), or high (quintile 5) GRS for CAD or IS based on their GRS. Data on the primary risk factors of ASCVD were utilized to estimate pooled cohort equations (PCEs) [12] for predicting the 10-year risk of ASCVD. In addition, the self-reported family history for ASCVD was defined as having ASCVD in a first-degree relative (parent, mother, or siblings).

2.6. Covariates collection

Standardized self-administered questionnaires (quantitative, semi-quantitative, or a combination) were used to collect information at baseline and resurveys on sociodemographic characteristics (age, sex, ethnicity, education, average annual household income), lifestyle factors (smoking status, physical activity, alcohol intake, and dietary pattern), and health status (family history, prevalent chronic diseases history, diabetes duration). The Townsend deprivation index (TDI) was used as an indicator of area-based socioeconomic deprivation, where higher values indicated elevated levels of poverty. Another physical activity-related energy expenditure was quantified as the metabolic equivalent of task (MET)-h/wk using data from the International Physical Activity Questionnaire (IPAQ) [19]. The information contained in MET did not overlap the daily frequency of stair climbing. Sedentary time was estimated by summing reported time spent watching TV, using a computer, and driving. Anthropometric measurements such as height, weight, and waist-hip ratio were measured during the initial visit to the assessment center by trained clinical staff following standardized protocols. Body mass index (BMI) was calculated by dividing weight by height in meters squared (kg/m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a digital blood pressure monitor. Further details of these measurements can be found in the UK Biobank online protocol (http://www.ukbiobank.ac.uk).

2.7. Statistical analyses

Baseline characteristics of participants were described as means ± standard deviations or proportions (%) in each category of stair climbing, with adjustment for age and sex using multiple linear regression (for continuous characteristics) or logistic regression (for binary characteristics). Poisson regression was used to derive adjusted incidence rates of ASCVD and ASCVD subtypes. Kaplan-Meier curves were constructed to estimate the 5 and 10-year cumulative incidence of ASCVD and compared using log-rank tests.

The associations between ASCVD and daily stair climbing at home or change (from baseline to the 2nd resurvey) were assessed using the Cox-proportional hazards model with time on study as the underlying time scale. For the primary analysis, participants were considered at risk based on their age at baseline, and for the analysis of change in stair climbing based on their age at resurvey. The proportional hazards assumption of the models was verified by visual inspection of log-log plots. The covariates were determined based on existing literature and the proposed mechanisms underlying the associations between stair climbing and clinical outcomes [11,20,21]. Restricted cubic splines were calculated using 4 knots at the 5th, 35th, 65th, and 95th percentiles to evaluate the dose-response association. A crude model (model 1) was fitted with categories of stair climbing as exposure (0 times/d [reference], 1–5 times/d, 6–10 times/d, 11–15 times/d, 16–20 times/d, and ≥20 times/d), adjusted for sex and age (years). Model 2 was further adjusted for ethnicity, educational attainment, household income, TDI, smoking, diet group, BMI, sedentary time, MET, family history of ASCVD, hypertension, hyperlipemia, and diabetes. The linear trend was performed by treating stair climbed as a continuous variable. Adjusted population-attributable fractions (PAFs) were calculated to evaluate the population-wide benefits of stair-climbing [22]. We conducted a range of preplanned sensitivity analyses for the primary model (model 2) to test the robustness of the findings and minimize the potential influence of reverse causality. Additionally, based on our estimated HR for ASCVD, the E-value was calculated to assess the impact of unmeasured confounding [23].

To explore whether the associations between stair climbing and ASCVD might be modified by disease susceptibility, we performed stratified analyses by family history of ASCVD (with or without), the 10-year risk of ASCVD (≤5%, 5%–10%, ≥10%), the GRS for CAD or IS (high, intermediate, low). Evidence for effect modification by these factors was assessed using likelihood ratio tests and multiplicative interaction terms. We have undertaken a comprehensive joint analysis to delve deeper into the impacts of stair climbing and susceptibility on ASCVD. All analyses were performed with R programming version 4.2.0 (http://www.R-project.org) and Stata 17 (StataCorp LP, College Station, TX, USA), with 2-sided a = 0.05 considered statistically significant.

3. Results

3.1. Baseline characteristics

Of the 502,530 adults enrolled in UKB, the present analyses were restricted to 458,860 participants, of whom 256,412 (55.9%) were female and 39,734 (8.7%) did not climb stairs at baseline (Table 1). The mean (SD) age of study participants was 56.2 (8.1) years. Table 1 shows the baseline characteristics of participants without any specific subtypes of ASCVD according to levels of stair climbing. Individuals with higher intensity of stair climbing were more likely to be younger, female, and non-regular smokers. Additionally, they exhibited a tendency towards higher levels of education and income, healthier dietary habits, and more prolonged exercise durations ($p < 0.001$).

Differences regarding disease susceptibility (except GRS of IS) were noted between individuals with different stair climbing intensities. Those who did not climb stairs or climbed fewer stairs were more likely to have a positive family history of ASCVD, a higher 10-year risk of ASCVD, and a higher GRS of CAD ($p < 0.001$). The GRS of CAD followed a normal distribution, with a higher GRS statistically related to a greater age- and sex-adjusted ASCVD incidence density (Supplementary eFig. 2).

3.2. Associations of baseline stair climbed with subsequent ASCVD and its subtypes

During the median follow-up of 12.5 years (IQR 11.7–13.2 years; 5,486,210 person-years), we identified 39,043 ASCVD cases, 30,718 CAD cases, and 10,521 IS cases. The 10-year cumulative incidence rates of ASCVD were 8.95 (95% CI: 8.67–9.24), 6.42 (6.30–6.54), 5.64 (5.42–5.88) per 100 person-years for participants who climbed stairs 0 times/d, 6–10 times/d, and 16–20 times/d respectively (Supplementary eFig. 3).

Table 2 shows the HRs and 95% CIs for subtypes of ASCVD by different levels of stair climbing, using the 0 times/d group as the reference. In the multivariable-adjusted models, the risk of ASCVD associated with stair climbs was significantly decreased above 5 times per day (HR, 0.93; 95% CI, 0.90–0.96 for 6–10 times/d; 0.90 (0.86–0.93) for 11–15 times/d; 0.90 (0.85–0.94) for 16–20 times/d, 0.94 (0.89–0.99) for ≥21 times/d; p for trend <0.001). The intensity of stair climbing had a U-shaped relationship with the adjusted risk of ASCVD. Each five times increment in stair climbing was associated with a 2% lower incidence of total ASCVD. For comparison, the dose-response relationship for ASCVD was provided using baseline MET as a continuous variable (excluding stair climbing, Supplementary eFig. 4). If all participants climbed stairs 16–20 times/d, the PAR% would have been 4.65% (95% CI: 1.33%–7.86%) compared with 0 times/d, indicating that approximately 5% of ASCVD events would not have occurred in this cohort. The beneficial effects of stair climbing were consistent irrespective of ASCVD subtypes. In sensitivity analysis, additional adjustment for walking pace did not materially change the risk estimates. No appreciable differences were observed when excluding: (1) participants whose ASCVD outcomes occurred in the first 2 years; (2) participants with poor health conditions (cancer/diabetes) at baseline; (3) participants who reported sedentary time>24 h/d or missing, or walking time 0 min/d; (4) those who lived in mobile or temporary structures, sheltered accommodation, or care homes; (5) participants reporting poor self-perceived health, or required attendance, disability, or mobility allowance; (6) underweight participants (BMI <18.5 kg/m^2)

Table 1
Baseline characteristics of the total cohort and stratified by groups of stairs climbed per day.

Characteristic		Time spent on stairs climbed at baseline, times/day						*p* trend
	Total	0	1–5	6–10	11–15	16–20	≥21	
No. of participants	458860	39734	92038	167610	86376	40230	32872	
Demographic factors								
Age, mean (SD), y	56.2 ± 8.1	58.8 ± 7.7	55.7 ± 8.0	56.1 ± 8.0	56.0 ± 8.2	56.0 ± 8.2	55.4 ± 8.2	<0.001
Female (%)	256,412 (55.9)	22,414 (56.4)	48,764 (53.0)	92,043 (54.9)	49,651 (57.5)	23,687 (58.9)	19,853 (60.4)	<0.001
White race (%)	433,085 (94.4)	37,754 (94.3)	84,514 (92.0)	159,367 (95.1)	82,591 (95.7)	38,380 (95.4)	30,479 (93.0)	<0.001
Socioeconomic factors								
College/University (%)	153,282 (33.4)	9075 (25.7)	27,928 (31.1)	56,565 (34.5)	32,132 (38.0)	15,535 (39.6)	12,047 (37.7)	<0.001
Household income≥31,000 $/year (%)	210,756 (45.9)	10731 (49.1)	38,864 (55.8)	81,866 (61.7)	43,540 (63.3)	20,089 (63.9)	15,666 (62.8)	<0.001
TDI (most deprived %)	87,818 (19.1)	9936 (26.4)	24,976 (27.1)	27,637 (16.6)	12,932 (15.0)	6213 (15.5)	6124 (18.5)	<0.001
Lifestyle factors								
Non-regular smoker (%)	409,865 (89.3)	34,382 (86.0)	79,800 (87.4)	150,847 (90.4)	78,601 (91.3)	36,599 (91.2)	29,636 (90.6)	<0.001
Not excessive drinking (%)	226,053 (49.3)	17,818 (44.6)	43,221 (47.0)	84,902 (50.7)	44,133 (51.3)	20,246 (50.7)	15,733 (48.5)	<0.001
Healthy diet (%)	212,186 (46.2)	17,931 (45.3)	38,101 (43.3)	76,049 (46.3)	42,567 (49.8)	20,517 (51.3)	17,021 (52.4)	<0.001
Healthy physical activity (%)	236,559 (51.6)	18,974 (50.2)	40,808 (47.0)	85,313 (52.6)	47,702 (56.7)	23,613 (60.2)	20,149 (63.6)	<0.001
Physical measurements								
MET (h/wk)	44.4 ± 45.2	43.5 ± 46.2	38.8 ± 43.7	42.4 ± 43.3	46.1 ± 44.4	50.4 ± 46.4	60.0 ± 53.4	<0.001
Sedentary time (h/d)	4.8 ± 2.4	5.0 ± 2.5	4.9 ± 2.6	4.8 ± 2.3	4.7 ± 2.3	4.7 ± 2.3	4.7 ± 2.5	<0.001
BMI (kg/m^2)	27.3 ± 4.7	27.8 ± 5.0	28.2 ± 5.3	27.3 ± 4.6	26.7 ± 4.3	26.4 ± 4.2	26.3 ± 4.2	<0.001
Waist-hip ratio (SD)	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	<0.001
Medical history								
Baseline hypertension (%)	245,264 (53.5)	24,162 (56.5)	50,787 (55.8)	89,377 (53.5)	44,143 (51.7)	20,378 (51.3)	16,417 (52.0)	<0.001
Baseline dyslipidemia (%)	215,826 (47.0)	19,901 (48.8)	44,503 (48.3)	79,090 (47.1)	39,633 (46.2)	18,299 (45.9)	14,400 (44.7)	<0.001
Baseline diabetes (%)	23,550 (5.1)	2875 (6.6)	6304 (6.9)	8137 (4.8)	3446 (4.0)	1539 (3.9)	1249 (4.0)	<0.001
Diabetes duration, mean (SD), y	8.6 ± 10.5	8.6 ± 10.7	8.4 ± 10.1	8.5 ± 10.3	8.8 ± 11.0	8.8 ± 11.0	9.2 ± 11.2	0.083
ASCVD susceptibility								
Family history of ASCVD (%)	253,916 (55.3)	22,845 (55.5)	50,705 (55.5)	92,636 (55.3)	47,825 (55.5)	22,137 (55.1)	17,768 (54.6)	0.011
The 10-year risk of ASCVD (SD)	4.4 ± 5.6	4.6 ± 6.4	4.5 ± 5.9	4.4 ± 5.6	4.3 ± 5.3	4.3 ± 5.3	4.4 ± 5.1	<0.001
Genetic risk score of CAD (SD)	61.2 ± 4.6	61.2 ± 4.6	61.3 ± 4.6	61.1 ± 4.6	61.1 ± 4.6	61.1 ± 4.6	61.2 ± 4.6	<0.001
Genetic risk score of IS (SD)	25.1 ± 4.1	25.1 ± 4.2	25.1 ± 4.1	25.1 ± 4.2	25.1 ± 4.1	25.1 ± 4.1	25.1 ± 4.1	0.7

Mean ± SD for continuous variables and percentage for categorical variables. The significance level α was adjusted by the Bonferroni correction (α corrected = 0.05/20 = 0.0025).
All variables were adjusted for age and sex except for the number of participants, age, and female (%).
TDI, Townsend deprivation index; MET-h/week, metabolic equivalents of task per hour per week; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ASCVD, atherosclerotic cardiovascular disease.

Table 2
Associations between flight of stairs climbed at the baseline and total or specific subtypes of ASCVD.

	Stairs climbed at baseline, HR (95% CI), times/day						Continuous per 5 times/day	PAR%	*p* trend
	0	1–5	6–10	11–15	16–20	≥21			
Atherosclerotic cardiovascular disease									
Cases/1000 PY	9.59	7.83	6.96	6.31	6.24	6.25			
Model 1	Ref	0.97 (0.93–1.01)	0.84 (0.82–0.87)	0.78 (0.75–0.81)	0.77 (0.73–0.80)	0.81 (0.77–0.85)	0.94 (0.93–0.95)	11.09% (8.02–14.05)	<0.001
Model 2	Ref	0.97 (0.94–1.01)	0.93 (0.90–0.96)	0.90 (0.86–0.93)	0.90 (0.85–0.94)	0.94 (0.89–0.99)	0.98 (0.97–0.99)	4.65% (1.33–7.86)	<0.001
Coronary artery disease									
Cases/1000 PY	7.38	6.19	5.46	4.86	4.84	4.85			
Model 1	Ref	0.98 (0.94–1.02)	0.85 (0.82–0.88)	0.77 (0.74–0.80)	0.77 (0.73–0.81)	0.81 (0.77–0.86)	0.94 (0.93–0.94)	11.50% (8.04–14.83)	<0.001
Model 2	Ref	0.98 (0.94–1.03)	0.94 (0.91–0.98)	0.89 (0.86–0.93)	0.90 (0.86–0.95)	0.95 (0.90–1.00)	0.98 (0.97–0.99)	4.62% (0.85–8.24)	<0.001
Ischemic stroke									
Cases/1000 PY	2.63	2	1.79	1.68	1.67	1.68			
Model 1	Ref	0.95 (0.89–1.02)	0.82 (0.77–0.88)	0.78 (0.73–0.84)	0.77 (0.71–0.84)	0.82 (0.75–0.90)	0.94 (0.93–0.96)	9.52% (3.47–15.19)	<0.001
Model 2	Ref	0.96 (0.89–1.02)	0.91 (0.85–0.97)	0.89 (0.83–0.96)	0.89 (0.81–0.97)	0.93 (0.85–1.03)	0.98 (0.96–0.99)	3.93% (−2.55-10.01)	0.006

Model 1 was adjusted for age and sex. Model 2 was adjusted for model 1+race, education, household income, Townsend deprived index, smoking, diet group, BMI, sedentary time, MET, family history of ASCVD, hypertension, hyperlipidemia, and diabetes.
HR, hazard ratio; CI, confidence interval; PAR%, population-attributable risk percent; Ref, reference.

(Supplementary eTable 4). The E-value analysis showed that only a confounder with a risk factor of 1.15–1.37 above and beyond the measured confounders could alter the observed association, suggesting that weak unmeasured confounding could not explain the observed HRs (Supplementary eTable 5).

When stratified by socioeconomic and lifestyle factors, the associations between each five-times increment in stair climbing and ASCVD were more pronounced in females (HR, 0.97; 95% CI, 0.96–0.99), current smokers (HR, 0.96; 95% CI, 0.94–0.98), participants with BMI <25 kg/m^2 (HR, 0.98; 95% CI, 0.96–0.99) or with prevalent hypertension (HR, 0.98; 95% CI, 0.97–0.99). Among these subgroups, all *p* for interaction <0.004 (Supplementary eTable 6 and eTable 7).

3.3. The modification role of disease susceptibility to ASCVD on the phenotypic associations

When stratified by family history of ASCVD, the relationship between stair climbing and ASCVD displayed similar patterns to the primary analysis (Fig. 1A; and Supplementary eTable 8). Among participants with a family history of ASCVD, the most significant benefit was observed when they climbed stairs 16–20 times/d (HR, 0.88; 95% CI: 0.83–0.93). In contrast, participants without a family history of

ASCVD experienced the greatest benefit when they climbed stairs 11–15 times/d (HR, 0.90; 95% CI: 0.84–0.96). Although the ASCVD risk was reduced with increased stair climbed intensity, the benefit of climbing more flights of stairs was gradually diminished beyond 20 times/d.

When stratified by 10-year risk of ASCVD, the association between stair climbing and ASCVD was more significant in participants with a 10-year risk ≤5% (11–15 times/d: HR, 0.80; 95% CI, 0.76–0.85) compared to those with a 10-year risk of ≥10% (HR, 0.90; 95% CI, 0.83–0.98; *p* for interaction <0.001, Fig. 1B). We also discovered a significant positive association for ASCVD subtypes (Supplementary eTable 9).

When stratified by genetic risk of CAD, we found directionally consistent results across different genetic risk strata (low genetic risk: HR, 0.88; 95% CI, 0.82–0.94 for 11–15 times/d of stair climbed; *p* for trend = 0.001; moderate genetic risk: HR, 0.92; 95% CI, 0.86–0.98; *p* for trend = 0.107; high genetic risk: HR, 0.90; 95% CI, 0.84–0.96; *p* for trend<0.001) and no statistical evidence of heterogeneity (*p* for interaction = 0.895) (Fig. 1C and Supplementary eTable 10). The results also revealed slight disparities across different genetic risks of IS, but the higher intensity in stair climbing was consistently correlated with reduced risks of ASCVD (*p* for interaction = 0.255) (Fig. 1D and Supplementary eTable 11).

The joint analysis revealed a significantly heightened risk of ASCVD in groups with higher disease susceptibility (excluding GRS for IS), regardless of their intensity of stair climbing. The risk of ASCVD was reduced by 8%–32% among those who climbed stairs 10–20 times/d, whether they had a family history of ASCVD or not (Fig. 2A and Supplementary eTable 12). Additionally, participants at different 10-year risk of ASCVD levels experienced a 29%–47% reduction in risk by engaging in stair climbing 10–20 times/d (Fig. 2B and Supplementary eTable 13). However, the ASCVD risk of participants who had a high genetic risk of CAD but regularly engaged in moderate-high intensity stair climbing (16–20 times/d) was comparable to that of participants with a moderate genetic risk who did not regularly climb stairs (HR, 0.89; 95% CI, 0.83–0.95 VS HR, 0.89; 95% CI, 0.85–0.93; Fig. 2C and Supplementary eTable 14). The benefits of stair climbing were similar for people with different genetic risks of IS. For instance, the HR for stair climbed 11–15 times/d was both 0.90 (95% CI: 0.86–0.95) in individuals with low and high genetic risk of IS (*p* for trend = 0.268; Fig. 2D and Supplementary eTable 15).

3.4. Associations of change in stair climbed with subsequent ASCVD and its subtypes

A subset of participants (n = 50,657) also completed the second examination and was included in the analysis of changes in stair climbing. The number of stairs climbed in the study population slightly decreased from the baseline to the second resurvey (Fig. 3A). Additionally, a sizable portion of participants altered their stair climbing pattern throughout the study, either becoming more or less active. Participants who rarely climbed stairs were more likely to be older, less educated, reside in more deprived areas, be heavy drinkers, and follow unhealthful diets (Supplementary eTable 16, $p < 0.001$). After excluding

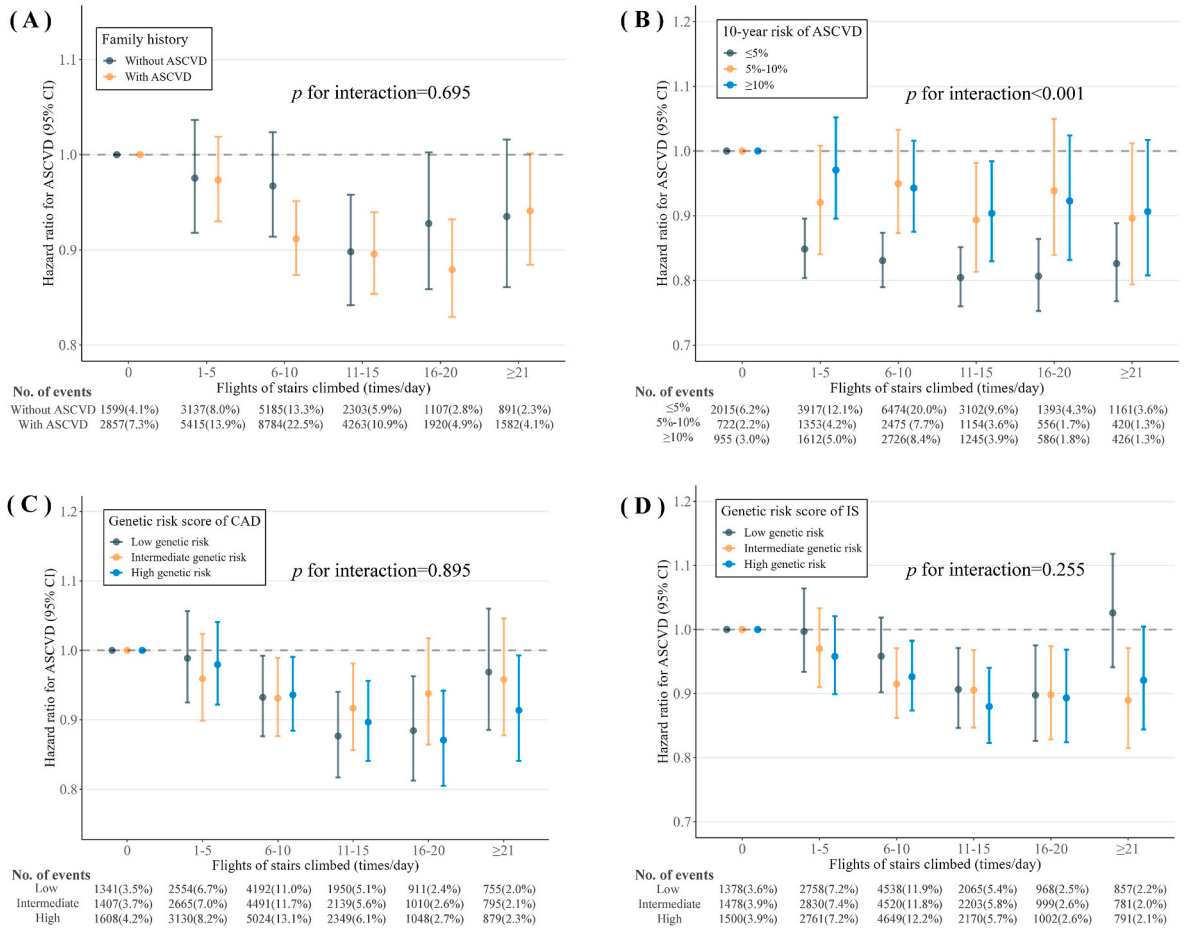


Fig. 1. Stratified associations of the intensity of stair climbing and risk of ASCVD.
(A) Stratified association with family history of ASCVD; (B) stratified association with 10-year risk of ASCVD; (C) stratified association with genetic risk score of CAD; (D) stratified association with genetic risk score of IS. Adjusted for age, sex, race, education, household income, Townsend deprived index, smoking, diet group, BMI, sedentary time, MET, and family histories of ASCVD, hypertension, hyperlipemia, and diabetes. ASCVD, atherosclerotic cardiovascular diseases; HR, hazard ratio; high, genetic risk score (quintile 5); intermediate (quintile 2–4); low (quintile 1).

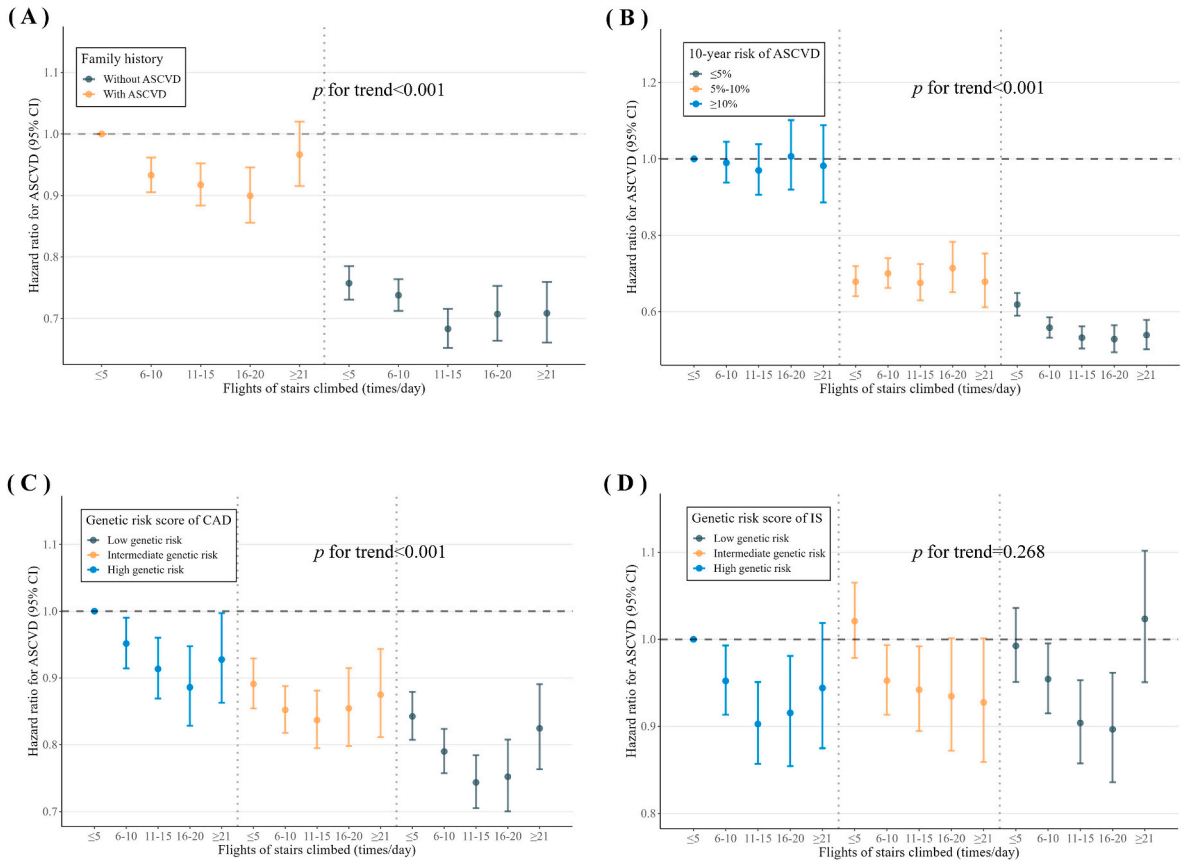


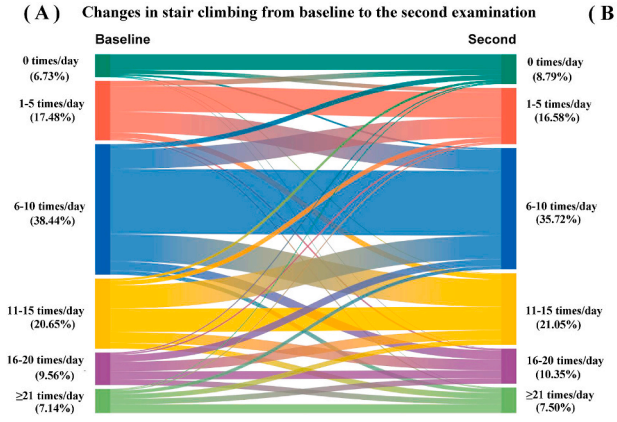
Fig. 2. Joint associations of the intensity of stair climbing and risk of ASCVD stratified by disease susceptibility.
(A) Joint association with family history of ASCVD; (B) joint association with 10-year risk of ASCVD; (C) joint association with genetic risk score of CAD; (D) joint association with genetic risk score of IS. Adjusted for age, sex, race, education, household income, Townsend deprived index, smoking, diet group, BMI, sedentary time, MET, and family histories of ASCVD, hypertension, hyperlipemia, and diabetes. ASCVD, atherosclerotic cardiovascular diseases; HR, hazard ratio; High, genetic risk score (quintile 5); intermediate (quintile 2–4); low (quintile 1).

ASCVD that occurred between the baseline and second examination, we accumulated a total of 1,641,235 person-years with 1152 ASCVD cases. During a mean (SD) of 3.70 (1.6) years of follow-up, HRs were 1.31 (95% CI, 1.05–1.64, $p = 0.02$) among participants who stopped climbing stairs (Fig. 3B) relative to those who did not climb stairs. However, further adjustment for several potential confounders (model 2 in the primary analysis) did not yield significant changes in the results (HR, 1.32, 95% CI, 1.06–1.65, $p = 0.01$).

4. Discussion

4.1. Principal findings

This large cohort of UK adults demonstrated that climbing more than five flights of stairs daily was associated with over a 20% lower risk of ASCVD (Fig. 4). The associations were broadly concordant in populations with varying susceptibilities to ASCVD. Moreover, it seemed



(B) Association Between ASCVD and Changes in Stairs Climbed from Baseline to the Second Examination

Source	Incidence/per 1000 PY	Hazard ratio (95% CI)	P value
Model 1			
No stair climbed	7.34	1.00 (ref)	
Started	7.03	1.07 (0.84-1.37)	0.57
Stopped	8.78	1.31 (1.05-1.64)	0.02
Maintained	6.69	0.99 (0.84-1.17)	0.89
Model 2			
No stair climbed	7.34	1.00 (ref)	
Started	7.03	1.10 (0.87-1.41)	0.43
Stopped	8.78	1.32 (1.06-1.65)	0.01
Maintained	6.69	1.05 (0.89-1.24)	0.55

Fig. 3. Associations of changes in stair climbing between baseline and resurvey and risk of ASCVD.
(A) Changes in stair climbing between baseline and resurvey at 5 years. (B) Model 1 was adjusted for sex and age (second examination). Model 2 was adjusted for model 1+ race, education, household income, Townsend deprived index, smoking, diet group, BMI, sedentary time, MET, and family histories of ASCVD, hypertension, hyperlipemia, and diabetes.

that there was a threshold beyond which the number of stairs climbed did not result in any additional decrease in the risk of ASCVD. Participants who discontinued stair climbing between baseline and resurvey exhibited a higher risk of ASCVD in comparison to those who never engaged in stair climbing. Therefore, promoting the act of climbing stairs could be considered an additional primary prevention strategy for ASCVD.

4.2. Comparison with other studies

The importance of physical activity for ASCVD protection has been well demonstrated in various studies [3]. Our observations were in line with existing evidence that supports the positive effects of stair climbing on ASCVD risk factors such as atrial fibrillation, metabolic syndrome, diabetes, hypertension, and all-cause mortality [10,11,20,24]. In a Japanese prospective cohort study, people who used stairs more frequently than escalators or elevators (≥60% of the time) had a lower risk of developing atrial fibrillation (HR: 0.69, 95% CI: 0.49–0.98) [24]. According to a UK Biobank study, taking 110–150 steps of stairs per day at home can lower type 2 diabetes by 14% (HR:0.86, 95% CI: 0.80–0.91), especially in individuals with low genetic susceptibility to the disease [11]. Another cohort study from UKB also reported long-term effects of stair climbing and suggested a modest beneficial effect on all-cause mortality but not CVD mortality [20]. Uncertainty exists regarding the causes of the associations being present only for all-cause mortality rather than ASCVD mortality. The Dutch Famine Birth Cohort Study revealed that not climbing stairs daily was linked to a higher incidence of metabolic syndrome (OR:1.90, 95% CI:1.23–2.92, $p = 0.004$) [10]. Several clinical trials focusing on the immediate effects of stair climbing intervention found that brief stair climbing exercise effectively lowered postprandial insulin and total nonesterified fatty acid in adults with overweight/obesity and increased peak oxygen uptake in sedentary young adults [25,26].

The present study extended available evidence on this topic by documenting the positive effects of stair climbing on ASCVD. The study also highlighted that climbing stairs may offer specific ASCVD benefits for individuals with different disease tendencies, regardless of their engagement in other physical activities. Interestingly, we discovered that the greatest benefits were observed when stair climbing occurred 11–15 times/d for individuals less susceptible to ASCVD, whereas predisposed individuals required approximately 16–20 times/d. Consequently, if individuals with a predisposition to ASCVD engaged in a high level of stair climbing, their adjusted risk of ASCVD was equivalent to, if not lower than, that of individuals without a predisposition. Therefore, the promotion of stair climbing is a promising physical activity initiative for the primary prevention of ASCVD, particularly in individuals with more ASCVD risk factors.

According to the findings of this study, the intensity of stair climbing varied from baseline to follow-up for many participants. For individuals who rarely climbed stairs in both surveys, not only were they older and had multiple comorbidities (hypertension, hyperlipidemia, and diabetes), but they also had a higher 10-year risk of ASCVD. It is important to note that the observed higher risks of ASCVD among those who stopped climbing stairs may be attributed to comorbidities or other risk factors that compelled them to reduce stair climbing between baseline and second resurveys. Therefore, we are cautious about interpreting our data as evidence of the risk effect of stopping stair climbing (reduction in physical activity) on ASCVD.

Overall, across strata of disease susceptibility, the relation between stair climbing and ASCVD risk followed a curvilinear trend. One possible explanation for the uptick could be attributed to the potential adverse impact of excessive amounts of other physical activity, as we found a weak correlation between stair climbing and MET (Spearman r = 0.121; $p < 0.001$). Previous studies also reported the existence of a "sweet spot" beyond which excessive amounts of stair climbing [11,20] or physical activity [27,28] could be detrimental. Although some findings might not support the adverse effects of high physical activity [29], we believe that it would be prudent to advocate moderate levels of stair climbing for primary prevention of ASCVD.

The biological mechanisms underpinning the cardiometabolic benefits of stair climbing are not fully understood. Stair climbing has been shown to reduce a variety of ASCVD risk factors, including improved maximal aerobic capacity [30], lower low-density lipoprotein cholesterol (LDL) [9], reductions in blood pressure, and muscle strengthening

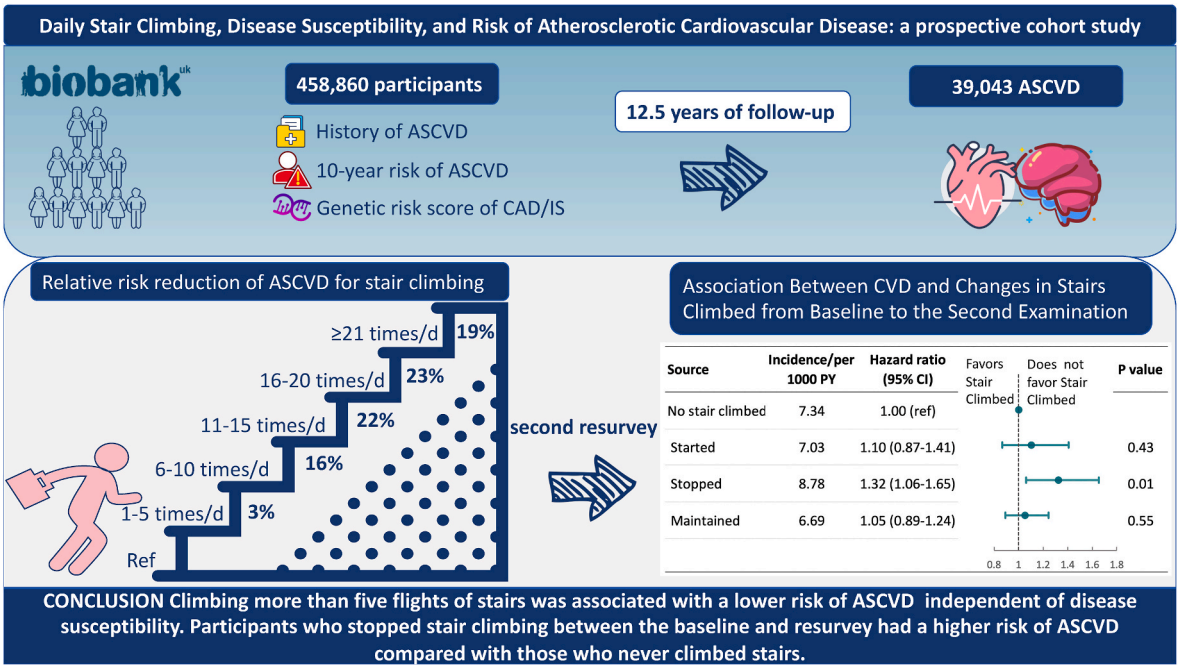


Fig. 4. Graphical abstract.
Daily stair climbing, disease susceptibility, and risk of atherosclerotic cardiovascular disease. ASCVD, atherosclerotic cardiovascular diseases; CAD, coronary artery disease. IS, ischemic strokes. PY, person year. Ref, reference.

[31]. Studies have also reported that stair climbing, as a form of vigorous-intensity physical activity, had a beneficial effect on cardiorespiratory fitness (CRF) [8], a strong indicator of a 15–20% reduction in the risk of ASCVD [32].

4.3. Implications for public practice

Unlike structured exercise and sports, stair climbing is a minimal-equipment, low-cost option that can be easily incorporated into one's daily routine. It addresses common barriers to exercise, such as access to facilities, gym fees, and lack of time due to work and home obligations. Evidence from the previous review supports the effectiveness of interventions to increase stair use, especially in public settings [33]. The current study provides novel evidence for the protective effects of stair climbing on the risk of ASCVD, particularly for individuals with multiple ASCVD risk factors. These individuals should be encouraged to incorporate stair climbing into their daily routine. Clinicians could nudge the importance of a physically active lifestyle for people with ASCVD susceptibility. The government or health-related departments can implement policies that encourage people to use stairs instead of elevators, or they can increase the appeal of stairwells to encourage people to climb stairs. We believe this finding might be of great motivation to ASCVD risk groups who are not enthusiastic about exercise per se.

4.4. Strengths and limitations

Our study had several strengths, including using a prospective design with a long follow-up period, documenting changes in baseline variables over time, and applying standardized approaches to ascertain ASCVD. This study should be interpreted in light of several limitations. First, observational design limits causal inferences in this study. Secondly, recall bias was identified as one of the major potential limitations due to the collection of information through self-administered questionnaires. Such bias might be overcome by prospective studies that make use of diaries and, if possible, record the times of stair climbing. Third, the UK Biobank participants do not represent the entire population of the country, with a healthy volunteer selection bias previously reported [34]. Nevertheless, it should be acknowledged that despite this bias, studies on risk factors based on UK Biobank data have shown satisfactory levels of reproducibility [35]. Fourth, stairs may be climbed on different occasions throughout the day, while this study only analyzed at-home stair-climbing activities. Thus, if someone was climbing stairs at work, they might have been appointed to no stair climbing group, which could have resulted in a probable differential misclassification that underestimated the protective effect of stair climbing. Fifth, due to a lack of quantitative stair climbing data, our study had limited utility for dose-response analysis. The magnitude of the association between stair climbing and ASCVD was likely underestimated as a result of imprecision in stair climbing measurements. Electronic device-based measures of stair climbing might help to address these concerns. Sixth, refraining from climbing stairs could be a sign of preclinical conditions related to the increased risk of ASCVD. For example, participants who climbed fewer stairs may have exhibited a higher disease burden (as found in our study) and worse cardiac function. However, both possibilities seem unlikely because adjusting for potential confounders and removing people with short follow-up periods did not materially affect the results. Calculations of the E-values indicated that an unmeasured confounder would have to have an HR of 1.15 with ASCVD to explain away the estimated associations of baseline stair climbing with ASCVD when adjusting for the measured covariates.

4.5. Conclusions

Overall, higher intensity of stair climbing was significantly associated with a lower risk of ASCVD in disease susceptibilities diverse settings, especially in those with lower susceptibility. Moreover, the increased risk of ASCVD in susceptible individuals could be effectively offset by engaging in more stair climbing. These findings highlight the potential advantages of stair climbing as a primary preventative measure for ASCVD in the general population.

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Data availability

Details of how to access UK Biobank data and the data release schedule are available from https://www.ukbiobank.ac.uk/. This research has been conducted using the UK Biobank Resource under Application Number 44430. Statistical codes are available from the corresponding author.

CRediT authorship contribution statement

Zimin Song: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. **Li Wan:** Conceptualization, Data curation, Writing – review & editing. **Wenxiu Wang:** Data curation, Investigation, Writing – original draft, Writing – review & editing. **Yueying Li:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Yimin Zhao:** Investigation, Methodology, Writing – review & editing. **Zhenhuang Zhuang:** Data curation, Writing – review & editing. **Xue Dong:** Data curation, Writing – review & editing. **Wendi Xiao:** Data curation, Writing – review & editing. **Ninghao Huang:** Data curation, Writing – review & editing. **Ming Xu:** Methodology, Writing – review & editing. **Robert Clarke:** Conceptualization, Methodology, Writing – review & editing. **Lu Qi:** Conceptualization, Methodology, Writing – review & editing. **Tao Huang:** Conceptualization, Funding acquisition, Investigation, Methodology, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2023.117300.

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