# Joint Association of Modifiable Lifestyle and Metabolic Health Status with Incidence of Cardiovascular Diabetes and All-Cause mortality: A Perspective Cohort Study

**Yingting Zuo**
　Capital Medical University

**Haibin Li**
　Beijing Chaoyang Hospital

**Shuohua Chen**
　Kailuan General Hospital

**Xue Tian**
　Capital Medical University

**Dapeng Mo**
　Beijing Tiantan Hospital

**Shouling Wu**
　Kailuan General Hospital

**Anxin Wang** ( ✉ wanganxin@bjtth.org )
　Beijing Tiantan Hospital　https://orcid.org/0000-0003-4351-2877

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**Original investigation**

# Abstract

## Background

We investigated the joint associations of modifiable lifestyle and metabolic factors with incident cardiovascular disease (CVD) and all-cause mortality.

## Methods

This study included 94,831 participants (men, 79.76%; median age, 51.60 [43.47-58.87]) without a history of CVD at baseline from Kailuan study during 2006 to 2007 and followed them until new-onset CVD event, death or December 31, 2017. Baseline metabolic health status was assessed by Adult Treatment Panel-III (ATP-III) criteria and five lifestyle factors was collected using a self-reported questionnaire. We performed Cox proportional hazards models to evaluate the joint associations.

## Results

During a median follow-up of 11.03 years, we observed 6,590 CVD events and 9,218 all-cause mortality. Participants within more metabolic risk components and least healthy lifestyle had the highest CVD risk (hazard ratio [HR] 2.06 [95% CI 1.77-2.39]) and mortality risk (HR 1.53 [95% CI 1.31-1.78]), as compared with the less metabolic risk components and most healthy lifestyle group. Compared with the most healthy lifestyle, the HR of CVD for participants with least healthy lifestyle was 1.26 (95% CI 1.17−1.37) in the category with low metabolic risk, 1.16 (95% CI 1.03−1.31) and 1.07 (95% CI 0.90−1.27) for those with medium and high metabolic risk, respectively.

## Conclusions

We showed that healthy lifestyle and metabolic health were associated with a lower risk of CVD and all-cause mortality. The association between metabolic risk and the risk of CVD was not modified by healthy lifestyle. Our results indicated that healthy lifestyle should be promoted even for people with high metabolic risk.

# Background

Cardiovascular disease (CVD) is one of the leading causes of death worldwide and remains the great threat to public global health[1]. Clinical therapy has been proven to be beneficial, but may have adverse effects, and often making functional recovery incomplete[2]. Therefore, primary prevention is considered the most effective strategy in controlling CVD and its consequences[3]. Some previous studies have shown that both healthy lifestyle and metabolic health status could reduce the risk of CVD and all-cause mortality[4-8].

In most previous studies, lifestyle or metabolic factors have been consider individually, although those factors are typically correlated with one another. Recent studies and meta-analyses have consistently

reported that combined lifestyle factors were associated with a markedly lower incidence of cardiometabolic abnormalities[9-12]. While few studies described the relative relationship of lifestyle factors with risk of CVD, subtypes of CVD and all-cause mortality across a population at different degrees of metabolic risk, and whether different degrees of metabolic status affect the efficacy of lifestyle was inconclusive[7]. Whereas some studies have reported that the lifestyle modification is effective in reducing CVD risk factors and CVD, especially stroke, others indicate that the effectiveness of lifestyle interventions for reductions in long-term CVD has yet to be determined[13].

The relationship between lifestyle and metabolic health status with incident CVD has become an important public concern, which could improve our understanding of the composition of modifiable risk factors with different level of modifiable risks to prevent the occurrent of CVD. Therefore, the purpose of this study was to use data from a large-scale population-based prospective cohort to examine the jointed associations of lifestyle and metabolic health status with the risk of CVD and all-cause mortality.

# Methods

## Study Population

The Kailuan study is a prospective cohort study designed to identify the risk factors for common noncommunicable disease, especially CVD[14, 15]. The study protocol and informed consent were approved by Ethics Committees of both the Kailuan General Hospital and Beijing Tiantan Hospital. All participants signed the written informed consent.

The details of the Kailuan study design have been described previously[16]. At baseline, active and retired employees aged ≥18 years of the Kailuan Group, Tangshan, China, were invited to participate in this study. Generally, 101,510 participants (81,110 men and 20,400 women) with an age ranging between 18 years and 98 years, were enrolled and completed survey at baseline between June 2006 and October 2007. All participants underwent face-to-face questionnaire measurements, physical examinations, and laboratory assessments in the 11 local health care hospitals. We performed re-examinations biennially to the end of the follow-up on December 31,2017.

In the current study, we excluded 3,238 participants without data for any metabolic component at baseline, 3,358 participants with missing data on lifestyle risk factors, 83 participants with a history of myocardial infarction (MI) or stroke at baseline, finally, a total of 94,831 participants was selected for the current analysis (Figure S1 in Supplemental file).

## Metabolic Health Status

Metabolic health status at baseline was determined based on the physical examinations and laboratory assessment by trained nurses and physicians. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured 3 times with the participants in the seated position at least 5 minutes using a mercury sphygmomanometer, and the average of 3 readings was used for further analysis[17]. Blood

samples were collected after an overnight fast (8-h to 12-h) and measured the fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol levels by an automatic analyzer (Hitachi 747; Hitachi, Tokyo, Japan) at local hospitals.

We used Adult Treatment Panel-III (ATP-III) criteria to define metabolic health status in the current study, which has been widely used to determine metabolic syndrome in adults worldwide. In the ATP-III criteria is based on the five CVD risk factors[18]: 1) central obesity: waist circumference ≥90 cm in men and ≥80 cm in women; 2) elevated TG: TG level ≥1.69 mmol/L; 3) low HDL cholesterol: HDL cholesterol level <1.03 mmol/L in men and <1.29 mmol/L in women; 4) elevated BP: SBP/DBP ≥130/85 mmHg or taking antihypertensive drugs or self-reported history of hypertension; 5) elevated FPG: FPG level ≥5.6 mmol/L or taking hypoglycemic medications or self-reported history of diabetes. The metabolic health status ranged from 0 to 5, with lower scores indicating normal healthy metabolic, and were subsequently classified into three categories based on the distribution in this population: low risk (0-2 components), medium risk (3 components), and high risk (4-5 components) (Table S1 in Supplement file).

## Lifestyle Health Status

Lifestyle health status at baseline was collected by trained nurses and physicians using a standardized questionnaire interview. Current smoking was defined as smoking at least the previous year. Current alcohol consumption was defined as the average daily strong spirit (alcohol content >50%) consumption of 100 ml or more than 100 ml for at least the previous year. Physical activity level was categorized as 1) ideally active: ≥80 minutes/week moderate and vigorous intensity; 2) moderately active: <80 minutes/week; 3) inactive: none. Sedentary behavior was classified into three categories: 1) < 4 hour/day; 2) 4-8 hour/day; 3) ≥8 hour/day. Considering salt intake plays an important role in the prevention of CVD in previous reports[19, 20], salt intake was used as a surrogate of health diet. The healthy diet was categorized as 1) ideal: < 6 g/day; 2) intermediate: 6-10 g/day; 3) poor: ≥10 g/day.

We estimated lifestyle health status in the current study according to five lifestyle risk factors: 1) current smoking; 2) current alcohol consumption; 3) physical inactivity: <80 minutes/week or none; 4) sedentary behavior: sedentary time ≥4 hour/day; 5) unhealth diet: salt intake ≥6 g/day. The lifestyle health status ranged from 0 to 5, with higher scores indicating unhealthy lifestyle, and were recorded as three categories: most healthy lifestyle (0–1 risk factor), moderately healthy lifestyle (2 risk factors), and least healthy lifestyle (3–5 risk factors) (Table S2 in Supplement file).

## Outcome Ascertainment

The present study participants were followed-up from the baseline examination at 2006 or 2007 up to December 31, 2017 as the end of the follow-up period, or to the date of a CVD event, or death, whichever came first. CVD events were defined as a composite of nonfatal MI and stroke during follow-up[21, 22]. To retrieve potential CVD events, the subjects were linked to the Municipal Social Insurance and Hospital Discharge Register. All medical records including emergency department or hospitalized in local hospital

were collected and adjudicated centrally. Stroke was defined according to the World Health Organization criteria on the basis of clinical symptoms, images obtained by computed tomography or magnetic resonance imaging, and other diagnostic reports[23]. MI was defined based on cardiac enzymes levels, symptoms, electrocardiogram (ECG) signs and necropsy[24]. Additionally, information on mortality was collected from vital statistics offices, with the death certificate reviewed by the study clinicians[21].

## Statistical Analyses

The baseline characteristics were presented as mean ± standard deviation (SD) or median with inter-quartile range (IQR), or frequencies with percentages. Baseline characteristics across metabolic and lifestyle health status were compared using the ANOVA or Kruskal-Wallis tests for continuous variables and chi-square test for categorical variables.

The incidence rate of CVD, stroke, MI and all-cause mortality were reported as per 1,000 person-years (PY) with 95% confidence intervals (CIs). The Kaplan-Meier curves and the log-rank test was used to visual and test the significance of differences in the cumulative-incidence of clinical outcomes by metabolic and lifestyle health status. The multivariable adjusted hazard ratios (HRs) and 95% CIs for CVD, stroke, MI and all-cause mortality were calculated using Cox proportional hazards regression analysis after adjustments for covariates. These included age (continuous, years), sex (categorical, male or female), the family average monthly income (categorical, <¥800" or "≥ ¥800"), body mass index (BMI, calculated as continuous) and education (categorical, literacy/primary or middle school, high school or college/university). We first separately explored the association between lifestyle and metabolic risk and each clinical outcome. Moreover, an interaction between lifestyle and metabolic risk was tested by the likelihood-ratio test, and analyses were stratified by different metabolic risk category. Lastly, we assessed the joint association by creating a product-term between lifestyle and metabolic health status, with most healthy lifestyle and low metabolic risk group as reference.

All analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). All reported $P$ values were based on two-sided test of significance, and $P < 0.05$ was consider statistically significant in the current study.

# Results

## Baseline Characteristics

A total of 94,831 participants (men, 79.76%; median age, 51.60 [43.47-58.87]) were eventually analyzed in our study. Baseline characteristics of the participants in different baseline metabolic health status are presented in Table 1. Compared with participants with low metabolic risk, the other two groups with more metabolic risk components were older, were more likely to be women, had a lower self-reported education, and had a higher level of BMI, waist circumference, SBP, DBP, FBG and adverse lipid profile. The proportion of participants with unhealthy salt intake habits or sedentary behavior increased markedly

with the more metabolic risk components, whereas the proportion of current smokers and those with physical inactivity decreased (Table 1).

## Individual Associations of Lifestyle and Metabolic Health Status with Clinical Outcomes

During a median follow-up of 11.03 years (IQR: 10.74-11.22 years), we observed 6,590 CVD events (rate 6.74 per 1000 person-year, [95% CI 6.58-6.91]), including 5,233 non-fatal strokes and 1,519 non-fatal MIs, and 9,218 participants died (9.17 per 1000 person-year, [95% CI 8.99-9.36]).

The risk of incident CVD increased significantly as the number of metabolic components increased (*P* for trend <0.001, Figure 2A). The same pattern of results was observed when categories were used instead of the number of metabolic risk components. CVD risk increased monotonically across metabolic health status categories (Figure 2B). In the multivariable model, the HRs for CVD were 1.47 (95% CI 1.39-1.56) for participants with medium metabolic risk, and 1.85 (95% CI 1.72-2.00) for those with high metabolic risk, compared with low metabolic risk (*P* for trend <0.001, Table 2). With regards to all-cause mortality, the adjusted HR for the participants with medium metabolic risk was 1.34 (95% CI 1.28-1.41), and 1.55 (95% CI 1.44-1.66) for those with high metabolic risk, compared with low metabolic risk. Similar results were observed for stroke and MI (Table 2 and Figure S2 in Supplement file).

There was a significant association with CVD risk as the number of unhealthy lifestyle factors adopted increased (*P* for trend <0.001, Figure 2C). The same pattern of results was observed when lifestyle categories was used instead of the number of unhealthy lifestyle factors. CVD risk also increased monotonically across unhealthy lifestyle categories (Figure 2D). In the multivariable model, the HRs for CVD were 1.10 (95% CI 1.03-1.17) for participants with moderately healthy lifestyle, and 1.23 (95% CI 1.15-2.30) for those with least healthy lifestyle, compared with most healthy lifestyle (*P* for trend <0.001, Table 3). With regards to all-cause mortality, the adjusted HR for the participants with moderately healthy lifestyle was 1.07 (95% CI 1.02-1.13), and 1.08 (95% CI 1.02-1.14) for those with least healthy lifestyle, compared with most healthy lifestyle. Similar results were observed for stroke. However, there was no significant between lifestyle and MI (Table 3 and Figure S3 in Supplement file).

## Joint Effects of Lifestyle and Metabolic Health Status with Clinical Outcomes

The joint associations of lifestyle and metabolic health status with CVD, stroke, MI and all-cause mortality are shown in Table 4. Our analyses indicate that the participants within the less metabolic risk components and most healthy lifestyle had the lowest risk of CVD, whereas those within the more metabolic risk components and least healthy lifestyle group had the highest risk (2.06 [95% CI 1.77-2.39]) of CVD. The association persisted for stroke but not presence for MI and all-cause mortality. The risk of CVD was associated with metabolic health in each lifestyle status. No significant interaction between metabolic risk and lifestyle factors was observed (all *P*=0.15).

Associations of lifestyle health status with CVD, stroke, MI and all-cause mortality were stratified according to the metabolic health status (Figure 2). Overall, participants who had the most healthy

lifestyle were associated with a lower risk of CVD across all metabolic health groups. Compared with those with the most healthy lifestyle, the HRs of CVD for participants with least healthy lifestyle was 1.26 (95% CI 1.17–1.37) in the category with low metabolic risk and was 1.16 (95% CI 1.03–1.31) and 1.07 (95% CI 0.90–1.27) for those with medium and high metabolic risk, respectively. Moreover, even a moderately healthy lifestyle conferred an obvious risk of CVD in those with medium metabolic risk (1.24 [95% CI 1.11–1.39]). Similar results were observed for stroke. There was no significant association between healthy lifestyle and MI among participants with different metabolic health status. For all-cause mortality, only in the category with low metabolic risk, the healthy lifestyle was significant association with all-cause mortality (Table S3 in Supplement file).

## Discussion

In this perspective cohort study, we described the joint associations of the lifestyle and metabolic risk factors with the incident of CVD and all-cause mortality. Our results indicate that participants with high metabolic risk and unfavorable lifestyle had a significantly higher risk of incident CVD and all-cause mortality compared with participants with low metabolic risk and a most healthy lifestyle. We found that the association between healthy lifestyle and the risk of CVD remained stable in different metabolic risk. The association between metabolic risk and the risk of CVD was not modified by healthy lifestyle.

Previous studies have reported similar but not identical associations of lifestyle factors and cardiometabolic outcomes[8, 9, 13, 25]. A recent meta-analysis has shown that the combination of multiple healthy lifestyle factors was associated with a substantially lower risk of incident diabetes and risk of mortality and incident CVD[11]. A previous study included over 40,000 Chinese participants aged 30-79, demonstrated that adherence to a healthy lifestyle may substantially lower the burden to diabetes. This study also indicates the population attributable risk percentage of diabetes appeared to be higher among old and obese participants[26]. In our study, lifestyle was not significantly associated with risk of MI, inconsistent with results from the INTERHEART Study analysis[27]. Individually, these lifestyle factors were more strongly associated with risk of stroke than MI, although power was limited by the few MI cases. Future studies should focus on differences in risk factors between CVD subtypes.

Data from the China Cardiometabolic Disease and Cancer Cohort (4C) study have presented robust effects of lifestyle status on new-onset diabetes and major cardiovascular events regardless of metabolic status[7], which is inconsistent with our results. However, our study indicates that the associations between metabolic risk and the risk of CVD, stroke and all-cause mortality was not modified by healthy lifestyle.

This discrepancy may be caused by the differences in population characteristics and follow-up duration. We used a long-term follow-up cohort study to analysis a risk evaluation strategy based on the combination of lifestyle and metabolic health status to prevent CVD and all-cause mortality risk.

The current study has several strengths. The Kailuan study enrolled a large population-based cohort of Chinese adults. Standardized protocols were used for data collection, including lifestyle health factors,

metabolic health components and potential confounders such as income and education. Additionally, long-term follow-up was available during which CVD events were identified and adjudicated by trained staff. Despite these strengths, several limitations should be taken into consideration. First, lifestyle factors were self-reported, which might be susceptible to self-report bias in estimation the associations. Second, females were underrepresented in this cohort so that the generalizability of the results are limited. Third, lifestyle and metabolic health status is artificial, indicating that considerable caution should be taken in quantifying the precise effect of risk factors. Finally, the population of this study came from China, may cannot directly promote the results on other ethnicities. Further studies, including other geographic regions, ethnicities, and races, are needed to confirm the generalizability of the current results.

## Conclusions

We found that healthy lifestyle and metabolic health were associated with a lower risk of CVD, whereas unhealthy lifestyle and high metabolic risk were associated with a higher risk of CVD. The association between healthy lifestyle and the risk of CVD remained stable in different metabolic risk. Our findings highlight the importance of both lifestyle and metabolic health status in the prevention of CVD and suggest the healthy lifestyle should be promoted even for people with high metabolic risk.

## Declarations

### Ethics Approval and Consent to Participate

The study was performed according to the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of Kailuan General Hospital (approval number: 2006-05) and Beijing Tiantan Hospital (approval number: 2010-014-01). All participants were agreed to take part in the study and provided informed written consent.

### Consent for Publication

Not applicable

### Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

### Competing Interests

These authors declare that they have no conflicts of interests.

### Funding

## Authors' contributions

YZ and HL wrote the manuscript. YZ, AW, SC, XT and HL collected the data. SC, XT researched data and contributed to discussion. SW and DM reviewed and edited the manuscript. AX contributed to the discussion and reviewed/edited the manuscript. All authors read and approved the final manuscript.

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# Tables

Table 1. Baseline characteristics of the study population according to the baseline metabolic health status.

|  | Overall | Metabolic health status | | | P value |
| --- | --- | --- | --- | --- | --- |
|  |  | Low metabolic risk | Medium metabolic risk | High metabolic risk |  |
| Participants (n) | 94831 | 69612 (73.41) | 17810 (18.78) | 7409 (7.81) |  |
| Sociodemographic |  |  |  |  |  |
| Age, years | 51.60 (43.47-58.87) | 50.72 (42.40-57.80) | 53.83 (47.24-61.05) | 54.78 (48.84-61.41) | <0.001 |
| Male, sex | 75640 (79.76) | 55853 (80.23) | 14242 (79.97) | 5545 (74.84) | <0.001 |
| Education, high school or above | 18984 (20.03) | 14775 (21.24) | 2961 (16.65) | 1248 (16.86) | <0.001 |
| Income, yuan/month, ≥¥800 | 13622 (14.38) | 10015 (14.40) | 2446 (13.75) | 1161 (15.69) | <0.001 |
| Metabolic risk factors |  |  |  |  |  |
| BMI, kg/m$^2$ | 24.86 (22.64-27.24) | 24.09 (22.04-26.26) | 26.78 (24.79-28.80) | 27.70 (25.86-29.76) | <0.001 |
| Waist circumference, cm | 87.00 (80.00-93.00) | 84.00 (79.00-90.00) | 93.00 (88.00-98.00) | 95.00 (91.00-100.00) | <0.001 |
| Systolic blood pressure, mmHg | 130.00 (119.30-141.30) | 121.00 (111.30-140.00) | 140.00 (130.00-151.30) | 142.00 (130.70-160.00) | <0.001 |
| Diastolic blood pressure, mmHg | 80.00 (78.70-90.00) | 80.00 (73.30-89.30) | 90.00 (80.00-97.30) | 90.00 (81.30-100.00) | <0.001 |
| Fasting plasma glucose, mmol/L | 5.11 (4.67-5.71) | 5.00 (4.59-5.40) | 5.61 (4.92-6.34) | 6.27 (5.77-7.63) | <0.001 |
| Triglycerides, mmol/L | 1.27 (0.90-1.93) | 1.11 (0.81-1.50) | 1.94 (1.36-2.81) | 2.49 (1.95-3.63) | <0.001 |
| LDL cholesterol, mmol/L | 2.34 (1.84-2.83) | 2.32 (1.84-2.80) | 2.40 (1.86-2.90) | 2.40 (1.80-2.96) | <0.001 |
| HDL cholesterol, mmol/L | 1.51 (1.28-1.77) | 1.53 (1.31-1.78) | 1.46 (1.23-1.73) | 1.35 (1.10-1.64) | <0.001 |
| Total cholesterol, mmol/L | 4.93 (4.28-5.60) | 4.86 (4.24-5.49) | 5.11 (4.40-5.83) | 5.22 (4.49-5.98) | <0.001 |
| Lifestyle risk factors |  |  |  |  |  |
| Current smoking | 29428 (31.03) | 22007 (31.61) | 5305 (29.79) | 2116 (28.56) | <0.001 |

| | | | | |
|---|---|---|---|---|---|
| Current alcohol | 17034 (17.96) | 12320 (17.70) | 3402 (19.10) | 1312 (17.71) | <0.001 |
| Physical inactivity | 79947 (84.30) | 59303 (85.19) | 14796 (83.08) | 5848 (78.93) | <0.001 |
| Sedentary time, h/week, ≥30 | 10290 (10.85) | 7242 (10.40) | 2110 (11.85) | 938 (12.66) | <0.001 |
| Salt intake, g/day, ≥6 | 24037 (25.35) | 17597 (25.28) | 4434 (24.90) | 2006 (27.08) | 0.001 |

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; N, number.

Values are the number (proportion), mean (SD), or median (interquartile range).

*P values were for the ANOVA or analyses across the three categories of metabolic health status.

Table 2. Risk of incident cardiovascular disease, stroke, myocardial infarction and all-cause mortality according to metabolic health categories.

| | Metabolic health status | | |
|---|---|---|---|
| | Low metabolic risk | Medium metabolic risk | High metabolic risk |
| **Cardiovascular disease** | | | |
| Case, n (%) | 3925 (5.64) | 1749 (9.82) | 916 (12.36) |
| Incidence rate, per 1000-person, y (95% CI) | 5.42 (5.25-5.59) | 9.75 (9.30-10.21) | 12.48 (11.70-13.32) |
| HR (95% CI) | Reference | 1.47 (1.39-1.56) | 1.85 (1.72-2.00) |
| *P* value for trend | <0.001 | | |
| **Stroke** | | | |
| Case, n (%) | 3141 (4.51) | 1386 (7.78) | 706 (9.53) |
| Incidence rate, per 1000-person, y (95% CI) | 4.31 (4.17-4.47) | 7.65 (7.26-8.07) | 9.51 (8.83-10.23) |
| HR (95% CI) | Reference | 1.45 (1.36-1.55) | 1.77 (1.62-1.93) |
| *P* value for trend | <0.001 | | |
| **Myocardial infarction** | | | |
| Case, n (%) | 868 (1.25) | 413 (2.32) | 238 (3.21) |
| Incidence rate, per 1000-person, y (95% CI) | 1.18 (1.10-1.26) | 2.23 (2.03-2.46) | 3.12 (2.75-3.54) |
| HR (95% CI) | Reference | 1.56 (1.38-1.76) | 2.13 (1.82-2.48) |
| *P* value for trend | <0.001 | | |
| **All-cause mortality** | | | |
| Case, n (%) | 5938 (8.53) | 2249 (12.63) | 1031 (13.92) |
| Incidence rate, per 1000-person, y (95% CI) | 8.02 (7.81-8.22) | 12.03 (11.54-12.54) | 13.34 (12.55-14.18) |
| HR (95% CI) | Reference | 1.34 (1.28-1.41) | 1.55 (1.44-1.66) |
| *P* value for trend | <0.001 | | |

Abbreviation: HR, hazard ratio.

*Adjusted for age, sex, body mass index, education and family income at baseline.

Table 3. Risk of incident cardiovascular disease, stroke, myocardial infarction and all-cause mortality according to lifestyle health categories.

|  | Lifestyle health status | | |
|---|---|---|---|
|  | Most healthy lifestyle | Moderately healthy lifestyle | Least healthy lifestyle |
| Cardiovascular disease | | | |
|   Case, n (%) | 3492 (6.76) | 1536 (6.76) | 1562 (7.65) |
|   Incidence rate, per 1000-person, y (95% CI) | 6.57 (6.36-6.79) | 6.55 (6.23-6.88) | 7.40 (7.04-7.78) |
|   HR (95% CI) | Reference | 1.10 (1.03-1.17) | 1.23 (1.15-1.30) |
|   *P* value for trend | <0.001 | | |
| Stroke | | | |
|   Case, n (%) | 2758 (5.34) | 1207 (5.31) | 1268 (6.21) |
|   Incidence rate, per 1000-person, y (95% CI) | 5.16 (4.97-5.35) | 5.11 (4.83-5.41) | 5.97 (5.65-6.31) |
|   HR (95% CI) | Reference | 1.10 (1.03-1.18) | 1.27 (1.18-1.36) |
|   *P* value for trend | <0.001 | | |
| Myocardial infarction | | | |
|   Case, n (%) | 826 (1.60) | 358 (1.58) | 335 (1.64) |
|   Incidence rate, per 1000-person, y (95% CI) | 1.52 (1.42-1.63) | 1.49 (1.35-1.66) | 1.55 (1.39-1.72) |
|   HR (95% CI) | Reference | 1.04 (0.92-1.18) | 1.08 (0.95-1.23) |
|   *P* value for trend | 0.226 | | |
| All-cause mortality | | | |
|   Case, n (%) | 5235 (10.13) | 2161 (9.51) | 1822 (8.92) |
|   Incidence rate, per 1000-person, y (95% CI) | 9.59 (9.33-9.85) | 8.96 (8.59-9.35) | 8.37 (7.99-8.76) |
|   HR (95% CI) | Reference | 1.07 (1.02-1.13) | 1.08 (1.02-1.14) |
|   *P* value for trend | 0.003 | | |

Abbreviation: HR, hazard ratio.

*Adjusted for age, sex, body mass index, education and family income at baseline.

Table 4. Risk of cardiovascular disease, stroke, myocardial infarction and all-cause mortality in participants according to the combinations of baseline lifestyle and metabolic health status.

|  | Lifestyle health status | | |
| --- | --- | --- | --- |
|  | Most healthy lifestyle | Moderately healthy lifestyle | Least healthy lifestyle |
| Cardiovascular disease | | | |
| Metabolic health status | | | |
| Low metabolic risk | Reference | 1.05 (0.97-1.14) | 1.25 (1.16-1.35) |
| Medium metabolic risk | 1.42 (1.31-1.54) | 1.78 (1.60-1.98) | 1.72 (1.53-1.92) |
| High metabolic risk | 1.93 (1.75-2.14) | 1.92 (1.66-2.22) | 2.06 (1.77-2.39) |
| Stroke | | | |
| Metabolic health status | | | |
| Low metabolic risk | Reference | 1.06 (0.96-1.15) | 1.28 (1.17-1.39) |
| Medium metabolic risk | 1.39 (1.27-1.52) | 1.74 (1.54-1.96) | 1.77 (1.56-2.00) |
| High metabolic risk | 1.83 (1.63-2.05) | 1.85 (1.57-2.18) | 2.07 (1.75-2.44) |
| Myocardial infarction | | | |
| Metabolic health status | | | |
| Low metabolic risk | Reference | 1.03 (0.87-1.22) | 1.18 (1.00-1.40) |
| Medium metabolic risk | 1.58 (1.34-1.86) | 1.83 (1.47-2.27) | 1.53 (1.20-1.95) |
| High metabolic risk | 2.37 (1.95-2.89) | 2.05 (1.53-2.74) | 2.01 (1.46-2.75) |
| All-cause mortality | | | |
| Metabolic health status | | | |
| Low metabolic risk | Reference | 1.07 (1.01-1.14) | 1.13 (1.06-1.21) |
| Medium metabolic risk | 1.39 (1.30-1.48) | 1.47 (1.34-1.61) | 1.33 (1.20-1.48) |
| High metabolic risk | 1.61 (1.47-1.76) | 1.68 (1.48-1.91) | 1.53 (1.31-1.78) |

The Cox proportional hazards model was used to detect adjusted HRs (95% CIs).

*Adjusted for age, sex, body mass index, education and family income at baseline.
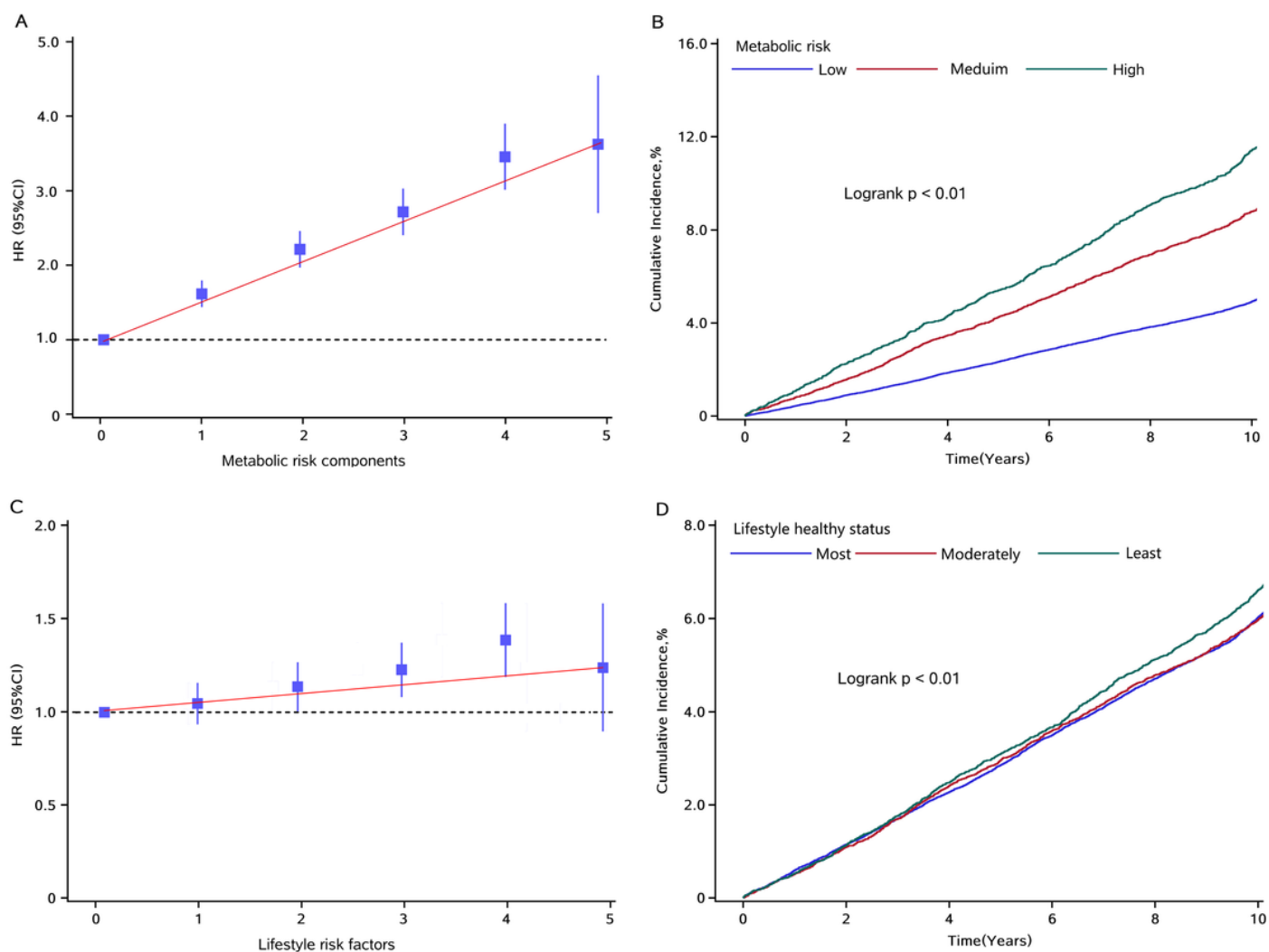
# Figures



## Figure 1

Effect of metabolic and lifestyle factors on the risk of incident of CVD. Risk of incident of stroke (A), MI (C) and all-cause mortality (E) according metabolic risk components. The cumulative incidence of stroke (B), MI (D) and all-cause mortality (E) in low, medium and high metabolic risk groups. (A) Participants were divided into five groups according to their metabolic risk components, and the HRs for each group were compared with those in 0 of the metabolic risk components. (B) The cumulative incidence of CVD in low, medium and high metabolic risk groups. (C) Participants were divided into five groups according to the number of unhealthy lifestyle factors, and the HRs for each group were compared with those who adopted no unhealthy lifestyle factors. (D) The cumulative incidence of CVD in participants who had a most, moderately and least lifestyle healthy status. Abbreviation: CVD, cardiovascular disease; HRs, hazard ratios.
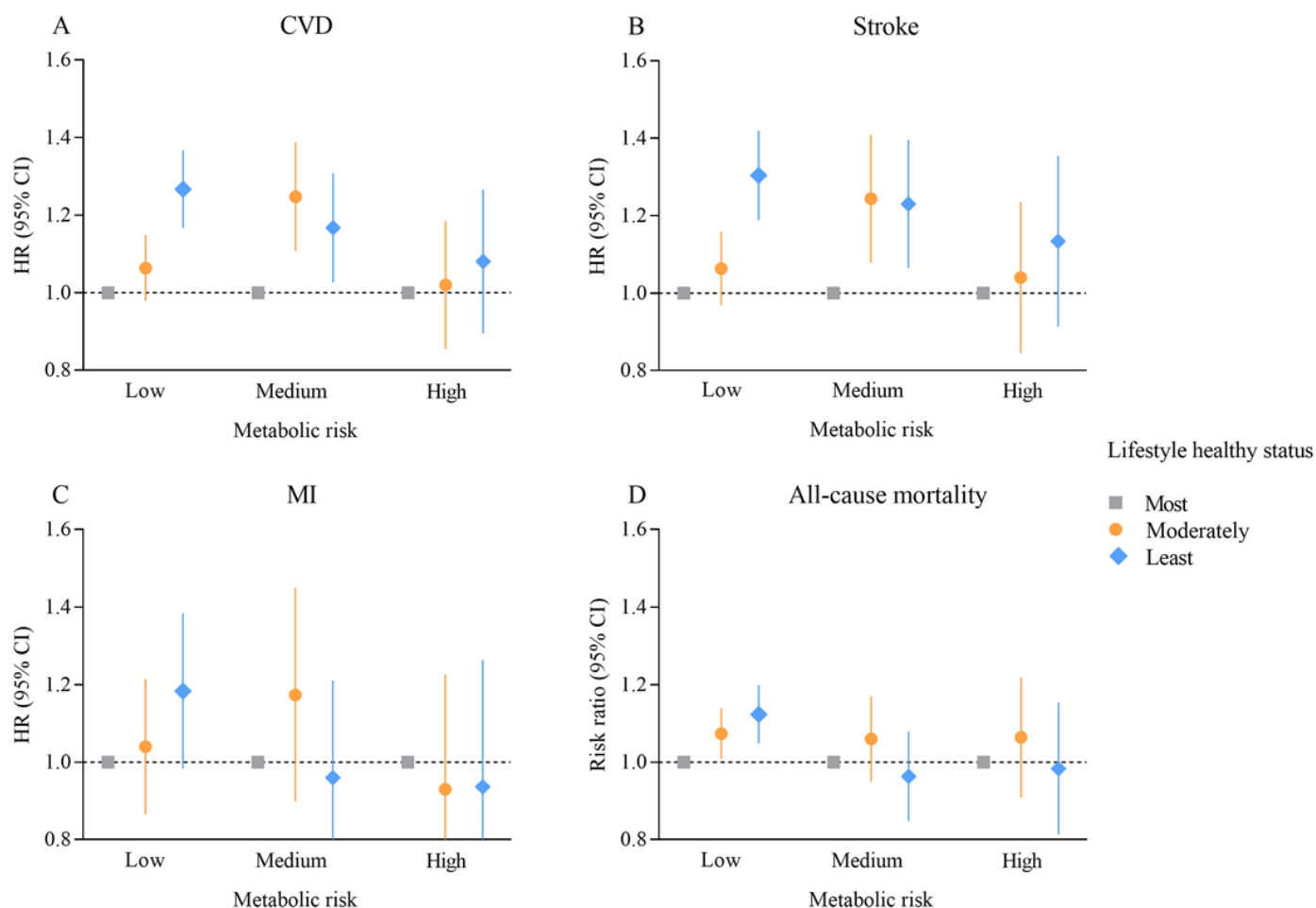
**Figure 2**

Combined associations of lifestyle and metabolic health status with CVD, stroke, MI and all-cause mortality. Association of lifestyle health status with CVD (A), stroke (B), MI (C) and all-cause mortality (D) across the metabolic health groups. Cox proportional hazards models were used to generate HRs and corresponding 95% CIs, adjusted for age, sex, body mass index, education and family income at baseline. Abbreviation: CVD, cardiovascular disease; MI, myocardial infarction; HRs, hazard ratios.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementalMaterial.docx