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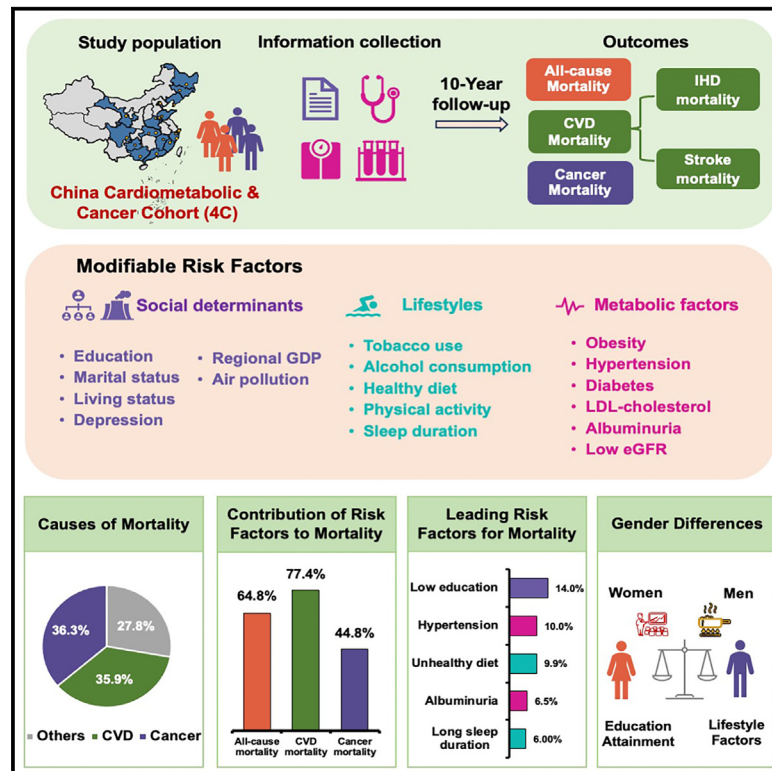# Association of social determinants, lifestyle, and metabolic factors with mortality in Chinese adults: A nationwide 10-year prospective cohort study

Graphical abstract

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In brief

Lu et al. reveal the impact of social determinants, lifestyle, and metabolic factors on mortality in China. Targeted strategies are crucial in improving metabolic health to reduce cardiovascular mortality, promoting healthy lifestyles to lower cancer mortality, and addressing lifestyles among men, as well as enhancing educational opportunities for women.

Highlights

- Cardiovascular disease and cancer account for over 72% of all-cause mortality in China

- Modifiable risk factors explain 64.8% of all-cause mortality

- Low education emerges as the leading factor for both all-cause and cancer mortality

- Hypertension is the predominant factor for cardiovascular mortality

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Association of social determinants, lifestyle, and metabolic factors with mortality in Chinese adults: A nationwide 10-year prospective cohort study

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SUMMARY

Nationwide estimates of the impact of common modifiable risk factors on mortality remain crucial. We aim to assess the influence of social determinants, lifestyle, and metabolic factors on mortality in 174,004 adults aged $\geq$ 40 years from the China Cardiometabolic Disease and Cancer Cohort (4C) Study. We reveal that 17 modifiable factors are independently associated with mortality, accounting for 64.8% of all-cause mortality, 77.4% of cardiovascular mortality, and 44.8% of cancer mortality. Low education emerges as the leading factor for both all-cause and cancer mortality, while hypertension is predominant for cardiovascular mortality. Moreover, low gross domestic product per capita and high ambient particulate matter with a diameter of <2.5 μm (PM$_{2.5}$) air pollution account for 7.8% and 4.3% for all-cause mortality, respectively, using a different method. Gender-specific analyses reveal distinct patterns, with women's mortality primarily associated with social determinants and men exhibiting stronger associations with lifestyle factors. Targeted health interventions are essential to mitigate mortality risks effectively in China.

INTRODUCTION

Cardiovascular disease and cancer are rising rapidly and have recently become recognized as the predominant burden of mor-

tality in China.[1] The estimated number of deaths in China was 10.7 million in 2019. Of these, 4.6 million deaths were from cardiovascular disease and 2.7 million from cancer.[2] Identification of preventable risk factors of cardiovascular and cancer

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mortality can aid in formulating prevention and intervention strategies during transition of disease epidemiology in countries experiencing rapid economic growth, such as China. Furthermore, targeted public health policies accounting for the disparities in risk factor distributions and contributions to health outcomes in men and women are urgently needed.

Existing studies assessing the associations between modifiable risk factors and all-cause mortality were predominantly carried out in the European ancestry.[3–7] It is well known that there are non-negligible differences in lifestyle, metabolic features, and social determinants of health across Chinese and Europeans and between men and women.[8,9] The spectrum of causes of death and the burden of mortality vary across different countries and ethnicities, with China exhibiting a higher stroke incidence rate and stroke-related deaths compared to other regions.[10–12] However, large-scale population-based cohorts are scarce in the Chinese population, which limited the capacity of identifying important associations between modifiable risk factors and mortality in the general population and in subpopulations (e.g., in men and women). Previously, the Global Burden of Disease Study[1,13,14] has comprehensively estimated the associations of a large number of risk factors with mortality in China. However, the findings from the Global Burden of Disease Study were based on data pooling from diverse sources using different modeling strategies. The subgroup analysis of Prospective Urban Rural Epidemiology study among 46,727 middle-aged Chinese adults[15] identified hypertension, low education, and poor diet as three leading risk factors for all-cause mortality, and hypertension, low education, and high non-high-density lipoprotein cholesterol for cardiovascular disease, which is similar to the findings from the overall cohort and other regions.[16] Other prospective cohort studies, including the China Kadoorie Biobank etc., have also explored the risk factors for mortality in the Chinese population.[17,18] These studies underlie the substantial influence of metabolic factors and socioeconomic status on health outcomes. However, cardiovascular and cancer mortality were not investigated in the Prospective Urban Rural Epidemiology study, and the distinct risk factor profiles and associations with all-cause and cause-specific mortalities in subpopulations were less investigated.

To explore whether and how modifiable risk factors influenced all-cause mortality and mortalities attributed to cardiovascular disease and cancer in China, the prospective China Cardiometabolic Disease and Cancer Cohort (4C) Study was established among Chinese adults aged ≥40 years from 20 study sites across mainland China and followed up between 2011 and 2021, using standardized methods to measure risk factors and outcomes.[19–24] In this analysis, we aimed to quantify the individual and overall contributions of 17 modifiable social determinants, lifestyle, and metabolic risk factors to all-cause and cause-specific mortalities in the overall population and in men and women separately in China.

RESULTS

A total of 193,846 participants aged 40 years or older were enrolled in the 4C study between January 2011 and December 2012. After excluding 15,697 participants with cardiovascular disease or cancer at baseline, 178,149 participants were followed until November 30, 2021. During a median of 10.1 years of follow-up, 4,145 participants were lost to follow-up. The remaining 174,004 participants were included in the final analysis (Figure S1).

Baseline characteristics of social determinants, lifestyle, and metabolic risk factors of the study participants are presented in Table 1. The average age of the participants was 56.5 (standard deviation [SD] 9.1) years old, and 34.8% were men. A total of 9,274 deaths were documented, including 3,330 cardiovascular deaths (1,247 ischemic heart disease deaths, 1,355 stroke deaths, and 728 other cardiovascular deaths) and 3,365 cancer deaths.

For social determinants of health, 50,699 (29.1%) participants had primary school education level or less, 13,706 (7.9%) participants were single, divorced, separated, or widowed, and 7,737 (4.4%) lived alone. 1,546 (0.9%) participants reported symptoms of moderate or severe depression. For lifestyle risk factors, 34,803 (20.0%) participants were current or former smokers, and 7,264 (4.2%) participants had current high alcohol consumption (11.2% in men and 0.4% in women). Mean diet score was 1.7 (SD 0.7; a lower score indicates worse diet), and

Table 1. Baseline characteristics of the study population

	Total (*n* = 174,004)	Women (*n* = 113,437)	Men (*n* = 60,567)
Age, years	56.5 ± 9.1	56.0 ± 8.9	57.3 ± 9.5
Social determinants			
Educational attainment			
High school or above	63,519 (36.5)	38,384 (33.8)	25,135 (41.5)
Middle school	59,786 (34.4)	37,742 (33.3)	22,044 (36.4)
Primary education or less	50,699 (29.1)	37,311 (32.9)	13,388 (22.1)
Marital status			
Married	160,298 (92.1)	102,038 (90.0)	58,260 (96.2)
Single, divorced, separated, or widowed	13,706 (7.9)	11,399 (10.0)	2,307 (3.8)
Living alone	7,737 (4.4)	5,809 (5.1)	1,928 (3.2)
Moderate or severe depression	1,546 (0.9)	1,171 (1.0)	375 (0.6)
Gross domestic product per capita <36,262 (yuan)	56,817 (32.7)	36,642 (32.3)	20,175 (33.3)
$PM_{2.5}$ (µg/m^3)	47.5 ± 13.0	47.5 ± 12.8	47.6 ± 13.2
Ambient $PM_{2.5}$ air pollution >59.11 (µg/m^3)	49,133 (28.2)	31,778 (28.0)	17,355 (28.7)
Lifestyle factors			
Tobacco use			
Never	139,201 (80.0)	111,225 (98.1)	27,976 (46.2)
Former	8,192 (4.7)	495 (0.4)	7,697 (12.7)
Current	26,611 (15.3)	1,717 (1.5)	24,894 (41.1)
Alcohol consumption			
Never	150,967 (86.8)	110,977 (97.8)	39,990 (66.0)
Former	3,832 (2.2)	484 (0.4)	3,348 (5.5)
Current			
Low	4,223 (2.4)	1,026 (0.9)	3,197 (5.3)
Moderate	7,718 (4.4)	455 (0.4)	7,263 (12.0)
High	7,264 (4.2)	495 (0.4)	6,769 (11.2)
Diet score	1.7 ± 0.7	1.7 ± 0.7	1.7 ± 0.7
Diet score category			
3–4	26,744 (15.4)	17,060 (15.0)	9,684 (16.0)
2	68,396 (39.3)	44,931 (39.6)	23,465 (38.7)
0–1	78,864 (45.3)	51,446 (45.4)	27,418 (45.3)
Physical activity			
High	47,177 (27.1)	30,718 (27.1)	16,459 (27.2)
Moderate	67,064 (38.6)	44,346 (39.1)	22,718 (37.5)
Low	59,763 (34.3)	38,373 (33.8)	21,390 (35.3)
Sleep duration (hours per night)	7.9 ± 1.4	7.9 ± 1.4	7.9 ± 1.4
Sleep duration category (hours per night)			
<6	8,945 (5.1)	5,785 (5.1)	3,160 (5.2)
6–8	105,943 (60.9)	69,424 (61.2)	36,519 (60.3)
>8	59,116 (34.0)	38,228 (33.7)	20,888 (34.5)
Metabolic factors			
Waist-to-hip ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1
Abdominal obesity	47,028 (27.0)	34,626 (30.5)	12,402 (20.5)
Blood pressure			
Systolic blood pressure (mmHg)	133.2 ± 20.8	131.9 ± 21.0	135.7 ± 20.2
Diastolic blood pressure (mmHg)	78.5 ± 11.3	77.3 ± 11.0	80.8 ± 11.5
Hypertension	76,024 (43.7)	46,469 (41.0)	29,555 (48.8)
Glucose			

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Table 1. *Continued*

	Total (*n* = 174,004)	Women (*n* = 113,437)	Men (*n* = 60,567)
Fasting blood glucose (mmol/L)	6.0 ± 1.7	5.9 ± 1.6	6.1 ± 1.8
2-h postload glucose (mmol/L)	8.2 ± 3.9	8.2 ± 3.7	8.4 ± 4.2
Hemoglobin A1c (%)	6.0 ± 1.0	6.0 ± 1.0	6.0 ± 1.1
Diabetes	40,133 (23.1)	24,530 (21.6)	15,603 (25.8)
Low-density lipoprotein cholesterol (mmol/L)	2.9 ± 0.9	3.0 ± 0.9	2.8 ± 0.8
<3.4	127,247 (73.1)	80,717 (71.2)	46,530 (76.8)
3.4 to <4.9	43,490 (25.0)	30,230 (26.6)	13,260 (21.9)
≥4.9	3,267 (1.9)	2,490 (2.2)	777 (1.3)
Urine albumin-creatinine ratio (mg/g)	6.5 (3.9–12.8)	7.0 (4.2–13.8)	5.5 (3.5–10.7)
<30	155,501 (89.4)	100,742 (88.8)	54,759 (90.4)
30 to <300	16,320 (9.4)	11,288 (10.0)	5,032 (8.3)
≥300	2,183 (1.3)	1,407 (1.2)	776 (1.3)
Estimated glomerular filtration rate (mL/min per 1.73 m^2)	95.6 ± 13.2	95.6 ± 12.7	95.7 ± 14.0
<60	3,107 (1.8)	1,837 (1.6)	1,270 (2.1)

Values are means ± standard deviation, or number of participants (%), or the median (interquartile range). PM$_{2.5}$ denotes particulate matter with a diameter of <2.5 μm. The sum of the percentages of all subgroups may not add up as 100% because of rounding.
Data are presented for the 174,004 participants after imputation. In the unimputed data, there were 5,259 (3.02%) missing values for educational attainment, 4,066 (2.34%) for marital status, 4,695 (2.70%) for living arrangements, 20,771 (11.94%) for depression status, 7,752 (4.45%) for tobacco use, 10,268 (5.90%) for alcohol consumption, 25,222 (14.50%) for diet score, 9,188 (5.28%) for physical activity, 23,934 (13.75%) for sleep duration, 5,289 (3.04%) for waist-to-hip ratio, 1,554 (0.89%) for systolic blood pressure, 1,565 (0.90%) for diastolic blood pressure, 2,008 (1.15%) for fasting blood glucose, 6,023 (3.46%) for 2-h post-load glucose, 1,391 (0.80%) for hemoglobin A1c, 529 (0.30%) for low-density lipoprotein cholesterol, 16,896 (9.71%) for urinary albumin-creatinine ratio, and 555 (0.32%) for estimated glomerular filtration rate.

147,260 (84.6%) participants had unhealthy diet (score 0–2). 59,763 (34.3%) participants reported low physical activity. The mean sleep duration was 7.9 (SD 1.4) hours; therefore, 8 h was used as the cutoff for sleep duration to estimate the population-attributable fractions (PAFs) in this study, which resulted in 59,116 (34.0%) participants with sleep duration >8 h. For metabolic risk factors, mean waist-to-hip ratio was 0.9 (SD 0.1), and 47,028 (27.0%) participants had abdominal obesity. Mean systolic blood pressure was 133.2 (SD 20.8) mmHg, mean hemoglobin A1c was 6.0% (SD 1.0%), mean low-density lipoprotein cholesterol (LDL-C) was 2.9 (SD 0.9) mmol/L, and median urine albumin-creatinine ratio was 6.5 (interquartile range 3.9–12.8) mg/g. A total of 76,024 (43.7%) participants had hypertension, 40,133 (23.1%) had diabetes, 46,757 (26.9%) had LDL-C ≥ 3.4 mmol/L, 18,503 (10.7%) had albuminuria, and 3,107 (1.8%) had a low estimated glomerular filtration rate (<60 mL/min per 1.73 m^2).

When considering gender, baseline social determinants and lifestyle risk factors were substantially different between men and women. More women had low educational attainment than men (32.9% in women vs. 22.1% in men). For lifestyle risk factors, a larger proportion of men had current tobacco use (41.1% in men vs. 1.5% in women) or current alcohol consumption (28.5% in men vs. 1.7% in women) than women. A similar proportion of women and men had unhealthy diet habit (85.0% in women vs. 84.0% in men), low physical activity (33.8% in women vs. 35.3% in men), and long sleep duration (33.7% in women vs. 34.5% in men). For metabolic risk factors, women were more likely to have abdominal obesity (30.5% in women

vs. 20.5% in men) and higher LDL-C (28.8% in women vs. 23.2% in men). By contrast, the proportions of hypertension (41.0% in women vs. 48.8% in men), diabetes (21.6% in women vs. 25.8% in men), and a low estimated glomerular filtration rate (1.6% in women vs. 2.1% in men) were higher in men than in women.

Cumulative incidence of all-cause, cardiovascular, and cancer mortalities with each risk factor using Kaplan-Meier analysis is presented in Figures S2–S4. Multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of each of the modifiable risk factors in associations with all-cause, cardiovascular, and cancer mortalities are presented in Tables 2, 3, and 4, and the results for subtypes of cardiovascular mortality (ischemic heart disease and stroke mortality) are presented in Tables S1 and S2. Among social determinants, low educational attainment; marital status of being single, divorced, separated, or widowed; and living alone were significantly and independently associated with all-cause and cardiovascular mortality, with depression additionally associated with all-cause and cancer mortality (Tables 2, 3, and 4). Low educational attainment was additionally associated with ischemic heart disease and stroke mortality (Tables S1 and S2). Among these factors, moderate or severe depression showed the largest HRs for all-cause (HR = 1.52, 95% CI = 1.24–1.85) and cancer mortality (HR = 1.67, 95% CI = 1.21–2.30; Tables 2 and 4). Gender-specific analysis showed that low education was associated with cardiovascular and ischemic heart disease mortality more strongly in women than in men ($p_{interaction}$ < 0.01; Tables 3 and S1).

Table 2. Multivariable-adjusted hazard ratios and 95% confidence intervals for all-cause mortality in overall population and by gender using the Cox regression model

	Overall		Women		Men		$p_{interaction}$
	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	of women and men
Social determinants							
Educational attainment							
High school or above	2,195/63,519 (3.5)	1.00 (reference)	762/38,384 (2.0)	1.00 (reference)	1,433/25,135 (5.7)	1.00 (reference)	0.466
Middle school	2,609/59,786 (4.4)	1.13 (1.07–1.20)	1,002/37,742 (2.7)	1.09 (0.99–1.20)	1,608/22,044 (7.3)	1.16 (1.07–1.25)	
Primary school or less	4,470/50,699 (8.8)	1.35 (1.27–1.44)	2,577/37,311 (6.9)	1.32 (1.20–1.44)	1,893/13,388 (14.1)	1.37 (1.26–1.48)	
Marital status							
Married	7,984/160,298 (5.0)	1.00 (reference)	3,424/102,038 (3.4)	1.00 (reference)	4,560/58,260 (7.8)	1.00 (reference)	0.922
Single, divorced, separated, or widowed	1,290/13,706 (9.4)	1.14 (1.06–1.22)	917/11,399 (8.1)	1.11 (1.02–1.21)	373/2,307 (16.2)	1.18 (1.03–1.34)	
Living alone							
No	8,524/166,267 (5.1)	1.00 (reference)	3,857/107,628 (3.6)	1.00 (reference)	4,666/58,639 (8.0)	1.00 (reference)	0.975
Yes	750/7,737 (9.7)	1.21 (1.11–1.32)	484/5,809 (8.3)	1.20 (1.08–1.34)	267/1,928 (13.8)	1.20 (1.03–1.40)	
Moderate or severe depression							
No	9,168/172,458 (5.3)	1.00 (reference)	4,280/112,266 (3.8)	1.00 (reference)	4,888/60,192 (8.1)	1.00 (reference)	0.807
Yes	106/1,546 (6.8)	1.52 (1.24–1.85)	61/1,171 (5.2)	1.50 (1.16–1.95)	45/375 (11.9)	1.55 (1.14–2.11)	
Gross domestic product per capita (yuan)*							
≥36,262	5,556/117,187 (4.7)	1.00 (reference)	2,628/76,795 (3.4)	1.00 (reference)	2,928/40,392 (7.3)	1.00 (reference)	0.800
<36,262	3,718/56,817 (6.5)	1.26 (1.20–1.33)	1,713/36,642 (4.7)	1.28 (1.19–1.38)	2,005/20,175 (9.9)	1.25 (1.16–1.34)	
Ambient $PM_{2.5}$ air pollution ($\mu g/m^3$)*							
<59.11	5,912/124,871 (4.7)	1.00 (reference)	2,793/81,659 (3.4)	1.00 (reference)	3,119/43,212 (7.2)	1.00 (reference)	0.422
≥59.11	3,362/49,133 (6.8)	1.16 (1.11–1.22)	1,548/31,778 (4.9)	1.13 (1.05–1.21)	1,814/17,355 (10.5)	1.19 (1.11–1.27)	
Lifestyle risk factors							
Tobacco use							
Never	6,440/139,201 (4.6)	1.00 (reference)	4,196/111,225 (3.8)	1.00 (reference)	2,244/27,976 (8.0)	1.00 (reference)	0.870
Former	768/8,192 (9.4)	1.20 (1.10–1.30)	42/495 (8.5)	1.30 (0.95–1.78)	726/7,697 (9.4)	1.18 (1.08–1.29)	
Current	2,066/26,611 (7.8)	1.35 (1.27–1.44)	103/1,717 (6.0)	1.35 (1.10–1.65)	1,963/24,894 (7.9)	1.34 (1.25–1.43)	
Alcohol consumption							
Never	7,525/150,967 (5.0)	1.00 (reference)	4,235/110,977 (3.8)	1.00 (reference)	3,290/39,990 (8.2)	1.00 (reference)	0.688
Former	393/3,832 (10.3)	1.16 (1.04–1.30)	27/484 (5.5)	1.18 (0.79–1.76)	366/3,348 (10.9)	1.16 (1.03–1.30)	
Current: low	259/4,223 (6.1)	0.85 (0.74–0.96)	41/1,026 (4.0)	0.96 (0.70–1.31)	218/3,197 (6.8)	0.83 (0.72–0.96)	
Current: moderate	522/7,718 (6.8)	0.87 (0.79–0.96)	19/455 (4.2)	0.93 (0.57–1.49)	503/7,263 (6.9)	0.87 (0.79–0.96)	
Current: high	575/7,264 (7.9)	1.06 (0.96–1.17)	19/495 (3.8)	0.83 (0.52–1.33)	556/6,769 (8.2)	1.07 (0.97–1.18)	
Diet score							
3–4	1,046/26,744 (3.9)	1.00 (reference)	485/17,060 (2.8)	1.00 (reference)	562/9,684 (5.8)	1.00 (reference)	0.185
2	3,341/68,396 (4.9)	1.09 (1.01–1.18)	1,540/44,931 (3.4)	1.00 (0.90–1.11)	1,801/23,465 (7.7)	1.17 (1.06–1.29)	
0–1	4,886/78,864 (6.2)	1.17 (1.08–1.26)	2,316/51,446 (4.5)	1.06 (0.95–1.18)	2,570/27,418 (9.4)	1.26 (1.14–1.39)	

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Table 2. *Continued*

	Overall		Women		Men		$p_{interaction}$
	Case/*n* (%)	HR (95% CI)	Case/*n* (%)	HR (95% CI)	Case/*n* (%)	HR (95% CI)	of women and men
Physical activity							
High	2,619/47,177 (5.6)	1.00 (reference)	1,182/30,718 (3.9)	1.00 (reference)	1,437/16,459 (8.7)	1.00 (reference)	0.291
Moderate	3,456/67,064 (5.2)	1.00 (0.95–1.05)	1,670/44,346 (3.8)	0.99 (0.92–1.07)	1,786/22,718 (7.9)	1.00 (0.93–1.07)	
Low	3,199/59,763 (5.4)	1.08 (1.02–1.14)	1,489/38,373 (3.9)	1.04 (0.96–1.13)	1,710/21,390 (8.0)	1.10 (1.02–1.19)	
Sleep duration (hours per night)							
6–8	4,753/105,943 (4.5)	1.00 (reference)	2,226/69,424 (3.2)	1.00 (reference)	2,526/36,519 (6.9)	1.00 (reference)	0.691
<6	451/8,945 (5.0)	0.94 (0.85–1.05)	217/5,785 (3.8)	0.92 (0.79–1.08)	234/3,160 (7.4)	0.97 (0.82–1.13)	
>8	4,070/59,116 (6.9)	1.18 (1.12–1.24)	1,897/38,228 (5.0)	1.18 (1.10–1.27)	2,173/20,888 (10.4)	1.18 (1.11–1.26)	
Metabolic risk factors							
Abdominal obesity							
No	6,334/126,976 (5.0)	1.00 (reference)	2,543/78,811 (3.2)	1.00 (reference)	3,792/48,165 (7.9)	1.00 (reference)	0.532
Yes	2,940/47,028 (6.3)	1.06 (1.01–1.11)	17,998/34,626 (5.2)	1.04 (0.97–1.10)	1,141/12,402 (9.2)	1.08 (1.01–1.15)	
Hypertension							
No	3,398/97,980 (3.5)	1.00 (Reference)	1,591/66,968 (2.4)	1.00 (reference)	1,807/31,012 (5.8)	1.00 (reference)	0.064
Yes	5,876/76,024 (7.7)	1.19 (1.14–1.25)	2,750/46,469 (5.9)	1.22 (1.14–1.30)	3,126/29,555 (10.6)	1.17 (1.10–1.24)	
Diabetes							
No	5,935/133,871 (4.4)	1.00 (reference)	2,774/88,907 (3.1)	1.00 (reference)	3,161/44,964 (7.0)	1.00 (reference)	0.430
Yes	3,339/40,133 (8.3)	1.31 (1.25–1.37)	1,567/24,530 (6.4)	1.26 (1.18–1.35)	1,772/15,603 (11.4)	1.35 (1.27–1.43)	
Low-density lipoprotein cholesterol (mmol/L)							
<3.4	6,843/127,247 (5.4)	1.00 (reference)	2,977/80,717 (3.7)	1.00 (reference)	3,867/46,530 (8.3)	1.00 (reference)	0.245
3.4 - <4.9	2,233/43,490 (5.1)	0.90 (0.86–0.95)	1,234/30,230 (4.1)	0.92 (0.86–0.99)	999/13,260 (7.5)	0.88 (0.82–0.94)	
≥4.9	198/3,267 (6.1)	1.04 (0.90–1.20)	130/2,490 (5.2)	1.03 (0.87–1.23)	67/777 (8.7)	1.04 (0.82–1.33)	
Urine albumin-creatinine ratio (mg/g)							
<30	7,064/155,501 (4.5)	1.00 (reference)	3,127/100,742 (3.1)	1.00 (reference)	3,937/54,759 (7.2)	1.00 (reference)	0.008
30 - <300	1,707/16,320 (10.5)	1.50 (1.42–1.59)	946/11,288 (8.4)	1.59 (1.47–1.72)	761/5,032 (15.1)	1.41 (1.29–1.53)	
≥300	503/2,183 (23.0)	2.85 (2.57–3.15)	268/1,407 (19.0)	3.07 (2.67–3.53)	235/776 (30.3)	2.63 (2.28–3.04)	
Estimated glomerular filtration rate <60 (mL/min per 1.73 m^2)							
No	8,588/170,897 (5.0)	1.00 (reference)	4,021/111,600 (3.6)	1.00 (reference)	4,567/59,297 (7.7)	1.00 (reference)	0.335
Yes	686/3,107 (22.1)	1.46 (1.35–1.59)	320/1,837 (17.4)	1.47 (1.30–1.66)	366/1,270 (28.8)	1.46 (1.30–1.64)	

For the 15 individual-level risk factors (excluding gross domestic product per capita and ambient PM$_{2.5}$ air pollution), each model was adjusted for age, gender, region (urban or rural), and all other individual-level risk factors. *For the two community-level risk factors of gross domestic product per capita and ambient PM$_{2.5}$ air pollution, a separate model was employed with adjustment for age, gender, region (urban or rural), and the remaining 15 individual-level risk factors.

See also Table S4, Figures S2, and S5.

Table 3. Multivariable-adjusted hazard ratios and 95% confidence intervals for cardiovascular mortality in overall population and by gender using the competing risk regression model

	Overall		Women		Men		$p_{interaction}$ of women and men
	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	
Social determinants							
Educational attainment							0.002
High school or above	655/63,519 (1.0)	1.00 (reference)	202/38,384 (0.5)	1.00 (reference)	453/25,135 (1.8)	1.00 (reference)	
Middle school	802/59,786 (1.3)	1.11 (0.99–1.24)	310/37,742 (0.8)	1.18 (0.98–1.43)	492/22,044 (2.2)	1.09 (0.95–1.25)	
Primary school or less	1,873/50,699 (3.7)	1.46 (1.31–1.63)	1141/37,311 (3.1)	1.57 (1.32–1.86)	732/13,388 (5.5)	1.40 (1.22–1.62)	
Marital status							0.300
Married	2,785/160,298 (1.7)	1.00 (reference)	1,272/102,038 (1.3)	1.00 (reference)	1,513/58,260 (2.6)	1.00 (reference)	
Single, divorced, separated, or widowed	545/13,706 (4.0)	1.17 (1.04–1.31)	381/11,399 (3.3)	1.07 (0.93–1.23)	164/2,307 (7.1)	1.34 (1.08–1.66)	
Living alone							0.517
No	3,024/166,267 (1.8)	1.00 (reference)	1,457/107,628 (1.4)	1.00 (reference)	1,568/58,639 (2.7)	1.00 (reference)	
Yes	306/7,737 (4.0)	1.18 (1.02–1.36)	196/5,809 (3.4)	1.14 (0.96–1.35)	109/1,928 (5.7)	1.20 (0.93–1.55)	
Moderate or severe depression							0.873
No	3,301/172,458 (1.9)	1.00 (reference)	1,635/112,266 (1.5)	1.00 (reference)	1,666/60,192 (2.8)	1.00 (reference)	
Yes	29/1,546 (1.9)	1.22 (0.81–1.83)	18/1,171 (1.6)	1.32 (0.80–2.16)	11/375 (3.0)	1.10 (0.56–2.15)	
Gross domestic product per capita (yuan)*							0.003
≥36,262	1,693/117,187 (1.4)	1.00 (reference)	813/76,795 (1.1)	1.00 (reference)	880/40,392 (2.2)	1.00 (reference)	
<36,262	1,637/56,817 (2.9)	1.46 (1.34–1.59)	840/36,642 (2.3)	1.60 (1.43–1.80)	797/20,175 (4.0)	1.34 (1.19–1.51)	
Ambient $PM_{2.5}$ air pollution ($\mu g/m^3$)*							0.469
<59.11	1,743/124,871 (1.4)	1.00 (reference)	860/81,659 (1.1)	1.00 (Reference)	883/43,212 (2.0)	1.00 (Reference)	
≥59.11	1,587/49,133 (3.2)	1.55 (1.43–1.67)	793/31,778 (2.5)	1.45 (1.30–1.62)	794/17,355 (4.6)	1.62 (1.45–1.81)	
Lifestyle risk factors							
Tobacco use							0.061
Never	2,447/139,201 (1.8)	1.00 (reference)	1,591/111,225 (1.4)	1.00 (reference)	856/27,976 (3.1)	1.00 (reference)	
Former	247/8,192 (3.0)	1.05 (0.91–1.22)	17/495 (3.5)	1.26 (0.76–2.11)	230/7,697 (3.0)	1.00 (0.86–1.16)	
Current	636/26,611 (2.4)	1.21 (1.08–1.35)	45/1,717 (2.6)	1.54 (1.13–2.08)	591/24,894 (2.4)	1.13 (1.01–1.28)	
Alcohol consumption							0.517
Never	2,771/150,967 (1.8)	1.00 (reference)	1,614/110,977 (1.5)	1.00 (reference)	1,156/39,990 (2.9)	1.00 (reference)	
Former	146/3,832 (3.8)	1.26 (1.05–1.52)	8/484 (1.7)	0.90 (0.42–1.91)	138/3,348 (4.1)	1.30 (1.08–1.57)	
Current: low	81/4,223 (1.9)	0.77 (0.61–0.98)	14/1,026 (1.4)	0.86 (0.50–1.48)	67/3,197 (2.1)	0.76 (0.59–0.99)	
Current: moderate	148/7,718 (1.9)	0.72 (0.60–0.87)	5/455 (1.1)	0.61 (0.23–1.59)	143/7,263 (2.0)	0.73 (0.61–0.88)	
Current: high	184/7,264 (2.5)	0.98 (0.82–1.16)	11/495 (2.3)	1.21 (0.68–2.18)	173/6,769 (2.6)	0.99 (0.83–1.18)	
Diet score							0.315
3–4	321/26,744 (1.2)	1.00 (reference)	154/17,060 (0.9)	1.00 (reference)	167/9,684 (1.7)	1.00 (reference)	
2	1,132/68,396 (1.7)	1.16 (1.02–1.32)	566/44,931 (1.3)	1.10 (0.92–1.33)	566/23,465 (2.4)	1.20 (1.00–1.45)	

Table 3.   Continued

	Overall		Women		Men		$p_{\text{interaction}}$ of women and men
	Case/*n* (%)	HR (95% CI)	Case/*n* (%)	HR (95% CI)	Case/*n* (%)	HR (95% CI)	
0–1	1,877/78,864 (2.4)	1.30 (1.14–1.48)	933/51,446 (1.8)	1.18 (0.98–1.41)	944/27,418 (3.4)	1.43 (1.19–1.71)	
Physical activity							0.922
High	959/47,177 (2.0)	1.00 (reference)	444/30,718 (1.5)	1.00 (reference)	515/16,459 (3.1)	1.00 (reference)	
Moderate	1,193/67,064 (1.8)	0.94 (0.86–1.03)	623/44,346 (1.4)	0.99 (0.87–1.13)	569/22,718 (2.5)	0.89 (0.79–1.02)	
Low	1,178/59,763 (2.0)	1.02 (0.93–1.12)	586/38,373 (1.5)	1.00 (0.87–1.15)	593/21,390 (2.8)	1.04 (0.91–1.18)	
Sleep duration (hours per night)							0.089
6–8	1,567/105,943 (1.5)	1.00 (reference)	759/69,424 (1.1)	1.00 (reference)	808/36,519 (2.2)	1.00 (reference)	
<6	136/8,945 (1.5)	0.85 (0.65–1.11)	66/5,785 (1.1)	0.81 (0.58–1.13)	70/3,160 (2.2)	0.90 (0.64–1.26)	
>8	1,627/59,116 (2.8)	1.22 (1.12–1.34)	828/38,228 (2.2)	1.25 (1.10–1.40)	799/20,888 (3.8)	1.20 (1.07–1.35)	
Metabolic risk factors							
Abdominal obesity							0.041
No	2,243/126,976 (1.8)	1.00 (reference)	970/78,811 (1.2)	1.00 (reference)	1,273/48,165 (2.6)	1.00 (reference)	
Yes	1,087/47,028 (2.3)	1.03 (0.96–1.12)	683/34,626 (2.0)	0.95 (0.86–1.06)	404/12,402 (3.3)	1.12 (1.00–1.26)	
Hypertension							0.002
No	886/97,980 (0.9)	1.00 (reference)	408/66,968 (0.6)	1.00 (reference)	478/31,012 (1.5)	1.00 (reference)	
Yes	2,444/76,024 (3.2)	1.67 (1.54–1.82)	1,245/46,469 (2.7)	1.82 (1.60–2.05)	1,199/29,555 (4.1)	1.53 (1.36–1.72)	
Diabetes							0.450
No	2,051/133,871 (1.5)	1.00 (reference)	1,014/88,907 (1.1)	1.00 (reference)	1,037/44,964 (2.3)	1.00 (reference)	
Yes	1,279/40,133 (3.2)	1.34 (1.24–1.45)	639/24,530 (2.6)	1.30 (1.17–1.45)	640/15,603 (4.1)	1.38 (1.24–1.53)	
Low-density lipoprotein cholesterol (mmol/L)							0.816
<3.4	2,340/127,247 (1.8)	1.00 (reference)	1,076/80,717 (1.3)	1.00 (reference)	1,264/46,530 (2.7)	1.00 (reference)	
3.4 - <4.9	890/43,490 (2.1)	1.04 (0.96–1.12)	516/30,230 (1.7)	1.06 (0.96–1.18)	374/13,260 (2.8)	1.00 (0.89–1.13)	
≥4.9	100/3,267 (3.1)	1.52 (1.24–1.87)	61/2,490 (2.5)	1.33 (1.03–1.72)	39/777 (5.1)	1.96 (1.40–2.76)	
Urine albumin-creatinine ratio (mg/g)							0.066
<30	2,322/155,501 (1.5)	1.00 (reference)	1,073/100,742 (1.1)	1.00 (reference)	1,249/54,759 (2.3)	1.00 (reference)	
30 - <300	767/16,320 (4.7)	1.68 (1.54–1.84)	447/11,288 (4.0)	1.74 (1.53–1.98)	320/5,032 (6.4)	1.58 (1.38–1.82)	
≥300	241/2,183 (11.0)	3.15 (2.70–3.68)	133/1,407 (9.5)	3.25 (2.66–3.98)	108/776 (13.9)	2.98 (2.35–3.78)	
Estimated glomerular filtration rate <60 (ml/min per 1.73 m^2)							0.808
No	3,037/170,897 (1.8)	1.00 (reference)	1,515/111,600 (1.4)	1.00 (reference)	1,522/59,297 (2.6)	1.00 (reference)	
Yes	293/3,107 (9.4)	1.34 (1.17–1.54)	138/1,837 (7.5)	1.30 (1.07–1.57)	155/1,270 (12.2)	1.41 (1.16–1.71)	

For the 15 individual-level risk factors (excluding gross domestic product per capita and ambient PM$_{2.5}$ air pollution), each model was adjusted for age, gender, region (urban or rural), and all other individual-level risk factors. *For the two community-level risk factors of gross domestic product per capita and ambient PM$_{2.5}$ air pollution, a separate model was employed with adjustment for age, gender, region (urban or rural), and the remaining 15 individual-level risk factors.

See also Tables S1, S2, and S4 and Figures S3 and S5.

Table 4. Multivariable-adjusted hazard ratios and 95% confidence intervals for cancer mortality in overall population and by gender using the competing risk regression model

	Overall		Women		Men		$p_{interaction}$ of women and men
	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	
Social determinants							
Educational attainment							0.064
High school or above	934/63,519 (1.5)	1.00 (reference)	346/38,384 (0.9)	1.00 (reference)	588/25,135 (2.3)	1.00 (reference)	
Middle school	1,057/59,786 (1.8)	1.10 (1.00–1.20)	413/37,742 (1.1)	1.06 (0.92–1.23)	644/22,044 (2.9)	1.11 (0.99–1.25)	
Primary school or less	1,374/50,699 (2.7)	1.19 (1.08–1.31)	711/37,311 (1.9)	1.14 (0.98–1.32)	662/13,388 (5.0)	1.25 (1.10–1.42)	
Marital status							0.882
Married	3,039/160,298 (1.9)	1.00 (reference)	1,244/102,038 (1.2)	1.00 (reference)	1,795/58,260 (3.1)	1.00 (reference)	
Single, divorced, separated, or widowed	326/13,706 (2.4)	0.92 (0.80–1.05)	226/11,399 (2.0)	0.93 (0.79–1.10)	100/2,307 (4.3)	0.91 (0.72–1.16)	
Living alone							0.691
No	3,159/166,267 (1.9)	1.00 (reference)	1,343/107,628 (1.3)	1.00 (reference)	1,816/58,639 (3.1)	1.00 (reference)	
Yes	206/7,737 (2.7)	1.16 (0.98–1.36)	127/5,809 (2.2)	1.20 (0.97–1.48)	79/1,928 (4.1)	1.11 (0.85–1.43)	
Moderate or severe depression							0.723
No	3,323/172,458 (1.9)	1.00 (reference)	1,445/112,266 (1.3)	1.00 (reference)	1,878/60,192 (3.1)	1.00 (reference)	
Yes	42/1,546 (2.7)	1.67 (1.21–2.30)	25/1,171 (2.1)	1.72 (1.14–2.58)	17/375 (4.5)	1.60 (0.96–2.65)	
Gross domestic product per capita (yuan)*							0.005
≥36,262	2,032/117,187 (1.7)	1.00 (reference)	937/76,795 (1.2)	1.00 (reference)	1,095/40,392 (2.7)	1.00 (reference)	
<36,262	1,333/56,817 (2.4)	1.28 (1.18–1.39)	533/36,642 (1.5)	1.19 (1.05–1.35)	800/20,175 (4.0)	1.35 (1.21–1.50)	
Ambient PM$_{2.5}$ air pollution (μg/m^3)*							0.001
<59.11	2,243/124,871 (1.8)	1.00 (reference)	1,032/81,659 (1.3)	1.00 (reference)	1,211/43,212 (2.8)	1.00 (reference)	
≥59.11	1,122/49,133 (2.3)	1.06 (0.98–1.15)	438/31,778 (1.4)	0.96 (0.85–1.10)	684/17,355 (3.9)	1.14 (1.03–1.27)	
Lifestyle risk factors							
Tobacco use							0.169
Never	2,167/139,201 (1.6)	1.00 (reference)	1427/111,225 (1.3)	1.00 (reference)	740/27,976 (2.7)	1.00 (reference)	
Former	314/8,192 (3.8)	1.43 (1.25–1.64)	14/495 (2.8)	1.46 (0.85–2.50)	300/7,697 (3.9)	1.47 (1.28–1.69)	
Current	884/26,611 (3.3)	1.55 (1.41–1.72)	29/1,717 (1.7)	1.18 (0.81–1.73)	855/24,894 (3.4)	1.61 (1.45–1.79)	
Alcohol consumption							0.473
Never	2,618/150,967 (1.7)	1.00 (reference)	1,429/110,977 (1.3)	1.00 (reference)	1,188/39,990 (3.0)	1.00 (reference)	
Former	137/3,832 (3.6)	1.11 (0.92–1.34)	14/484 (2.8)	1.93 (1.13–3.33)	124/3,348 (3.7)	1.04 (0.86–1.27)	
Current: low	108/4,223 (2.6)	0.96 (0.79–1.17)	15/1,026 (1.4)	1.05 (0.62–1.79)	93/3,197 (2.9)	0.94 (0.76–1.17)	
Current: moderate	250/7,718 (3.2)	1.08 (0.94–1.24)	8/455 (1.7)	1.21 (0.58–2.54)	242/7,263 (3.3)	1.07 (0.93–1.23)	
Current: high	252/7,264 (3.5)	1.20 (1.04–1.39)	4/495 (0.9)	0.63 (0.24–1.69)	248/6,769 (3.7)	1.20 (1.04–1.39)	
Diet score							0.258
3–4	449/26,744 (1.7)	1.00 (reference)	204/17,060 (1.2)	1.00 (reference)	245/9,684 (2.5)	1.00 (reference)	
2	1,255/68,396 (1.8)	1.01 (0.90–1.13)	536/44,931 (1.2)	0.89 (0.75–1.05)	719/23,465 (3.1)	1.11 (0.96–1.29)	

(Continued on next page)

Table 4. *Continued*

	Overall		Women		Men		$p_{interaction}$ of women and men
	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	Case/n (%)	HR (95% CI)	
0–1	1,661/78,864 (2.1)	1.03 (0.92–1.15)	729/51,446 (1.4)	0.93 (0.79–1.10)	931/27,418 (3.4)	1.12 (0.97–1.30)	
Physical activity							0.276
High	927/47,177 (2.0)	1.00 (reference)	409/30,718 (1.3)	1.00 (reference)	518/16,459 (3.2)	1.00 (reference)	
Moderate	1,306/67,064 (2.0)	1.06 (0.97–1.15)	573/44,346 (1.3)	0.99 (0.86–1.12)	733/22,718 (3.2)	1.12 (1.00–1.26)	
Low	1,132/59,763 (1.9)	1.07 (0.98–1.17)	488/38,373 (1.3)	1.02 (0.89–1.17)	644/21,390 (3.0)	1.11 (0.99–1.26)	
Sleep duration, hours per night							0.381
6–8	1,839/105,943 (1.7)	1.00 (reference)	823/69,424 (1.2)	1.00 (reference)	1016/36,519 (2.8)	1.00 (reference)	
<6	173/8,945 (1.9)	0.96 (0.75–1.23)	82/5,785 (1.4)	0.98 (0.70–1.38)	91/3,160 (2.9)	0.95 (0.72–1.26)	
>8	1,353/59,116 (2.3)	1.10 (1.02–1.19)	565/38,228 (1.5)	1.09 (0.96–1.23)	788/20,888 (3.8)	1.12 (1.01–1.24)	
Metabolic risk factors							
Abdominal obesity							0.744
No	2,361/126,976 (1.9)	1.00 (reference)	890/78,811 (1.1)	1.00 (reference)	1,471/48,165 (3.1)	1.00 (reference)	
Yes	1,004/47,028 (2.1)	1.09 (1.01–1.18)	580/34,626 (1.7)	1.12 (1.01–1.25)	424/12,402 (3.4)	1.08 (0.97–1.21)	
Hypertension							0.761
No	1,438/97,980 (1.5)	1.00 (reference)	664/66,968 (1.0)	1.00 (reference)	774/31,012 (2.5)	1.00 (reference)	
Yes	1,927/76,024 (2.5)	1.12 (1.04–1.21)	806/46,469 (1.7)	1.13 (1.01–1.26)	1,121/29,555 (3.8)	1.13 (1.03–1.25)	
Diabetes							0.357
No	2,336/133,871 (1.7)	1.00 (reference)	1,037/88,907 (1.2)	1.00 (reference)	1,299/44,964 (2.9)	1.00 (reference)	
Yes	1,029/40,133 (2.6)	1.14 (1.05–1.23)	433/24,530 (1.8)	1.08 (0.96–1.22)	596/15,603 (3.8)	1.19 (1.07–1.31)	
Low-density lipoprotein cholesterol (mmol/L)							0.551
<3.4	2,529/127,247 (2.0)	1.00 (reference)	1,031/80,717 (1.3)	1.00 (reference)	1,498/46,530 (3.2)	1.00 (reference)	
3.4 - <4.9	780/43,490 (1.8)	0.89 (0.82–0.96)	402/30,230 (1.3)	0.90 (0.80–1.01)	378/13,260 (2.9)	0.88 (0.79–0.99)	
≥4.9	56/3,267 (1.7)	0.86 (0.66–1.13)	37/2,490 (1.5)	0.91 (0.66–1.27)	19/777 (2.5)	0.78 (0.50–1.23)	
Urine albumin-creatinine ratio (mg/g)							0.125
<30	2,878/155,501 (1.9)	1.00 (reference)	1,218/100,742 (1.2)	1.00 (reference)	1,660/54,759 (3.0)	1.00 (reference)	
30 - <300	424/16,320 (2.6)	1.03 (0.92–1.15)	218/11,288 (1.9)	1.12 (0.95–1.31)	207/5,032 (4.1)	0.96 (0.82–1.12)	
≥300	63/2,183 (2.9)	0.98 (0.75–1.30)	34/1,407 (2.4)	1.21 (0.84–1.75)	28/776 (3.6)	0.81 (0.54–1.21)	
Estimated glomerular filtration rate <60 (ml/min per 1.73 m^2)							0.186
No	3,245/170,897 (1.9)	1.00 (reference)	1,415/111,600 (1.3)	1.00 (reference)	1,831/59,297 (3.1)	1.00 (reference)	
Yes	120/3,107 (3.9)	0.93 (0.77–1.13)	55/1,837 (3.0)	1.08 (0.81–1.44)	64/1,270 (5.1)	0.84 (0.65–1.09)	

For the 15 individual-level risk factors (excluding gross domestic product per capita and ambient PM$_{2.5}$ air pollution), each model was adjusted for age, gender, region (urban or rural), and all other individual-level risk factors. *For the two community-level risk factors of gross domestic product per capita and ambient PM$_{2.5}$ air pollution, a separate model was employed with adjustment for age, gender, region (urban or rural), and the remaining 15 individual-level risk factors.

See also Table S4 and Figures S4 and S5.

For lifestyle risk factors, tobacco use, former alcohol consumption, unhealthy diet, low physical activity, and long sleep duration were significantly and independently associated with an increased risk of all-cause mortality (Table 2). For cardiovascular outcomes, tobacco use, former alcohol consumption, unhealthy diet, and long sleep duration were associated with cardiovascular and ischemic heart disease mortality, whereas unhealthy diet and long sleep duration were associated with stroke mortality. Tobacco use, current high alcohol consumption, and long sleep duration were associated with cancer mortality. Gender-specific analysis showed that current tobacco use had a stronger association with stroke mortality in women than in men ($p_{interaction}$ = 0.037; Table S2).

For metabolic risk factors, abdominal obesity, hypertension, diabetes, microalbuminuria or macroalbuminuria, and a low estimated glomerular filtration rate were significantly and independently associated with an increased risk of all-cause mortality (Table 2). Hypertension, diabetes, microalbuminuria or macroalbuminuria, and a low estimated glomerular filtration rate were associated with an increased risk of cardiovascular, ischemic heart disease, and stroke mortality. Abdominal obesity, hypertension, and diabetes were associated with an increased risk of cancer mortality (Table 4).

It is important to highlight that our study revealed distinct impacts of LDL-C levels on cardiovascular and cancer mortality. We did not observe a significant association between LDL-C and all-cause mortality (Table 2). However, high LDL-C levels were strongly associated with cardiovascular mortality, especially with ischemic heart disease mortality (Tables 3 and S1). Furthermore, the cubic spline analysis demonstrated a consistent link between LDL-C levels above 3.4 mmol/L and an increased risk of cardiovascular mortality. Conversely, LDL-C levels below 3.4 mmol/L were associated with an elevated risk of cancer mortality (Figure S5), indicating a potential trade-off between cardiovascular health benefits and an increased risk of cancer mortality for low LDL-C levels.

Gender-specific analysis showed that albuminuria had a stronger association with all-cause mortality in women than in men ($p_{interaction}$ = 0.008; Table 2), and hypertension had a stronger association with cardiovascular and ischemic heart disease mortality in women than in men ($p_{interaction}$<0.01; Tables 3 and S1).

PAFs of all-cause, cardiovascular, ischemic heart disease, stroke, and cancer mortality associated with individual risk factors or combinations of risk factors are shown in Figures 1, 2, and 3. In the overall population, 64.8% of all-cause mortality was attributable to the 15 individual-level risk factors. Social determinants, lifestyle, and metabolic factors accounted for 17.9%, 20.8%, and 26.1% for all-cause mortality, respectively, with low educational attainment (14.0%) being the top leading contributor, followed by hypertension (10.0%), unhealthy diet (9.9%), albuminuria (6.5%), and long sleep duration (6.0%) (Figure 1). The 15 individual-level risk factors explained more PAFs for cardiovascular mortality than cancer mortality. Approximately 77.4% of cardiovascular mortality could be explained by the 15 risk factors (79.2% and 83.4% for ischemic heart disease and stroke mortality, respectively), whereas 44.8% of cancer mortality could be explained. Metabolic risk factors (37.3%)

were the most predominant contributors to cardiovascular mortality compared to social determinants (18.5%) and lifestyle factors (21.6%). Hypertension (20.2%), low educational attainment (14.4%), unhealthy diet (12.7%), albuminuria (8.2%), and long sleep duration (7.4%) were the top five leading factors for cardiovascular mortality (Figure 2). For ischemic heart disease mortality, unhealthy diet, hypertension, low educational attainment, albuminuria, and long sleep duration were the top five leading factors (Figure 2), whereas hypertension, low educational attainment, unhealthy diet, long sleep duration, and diabetes were the top five factors for stroke mortality (Figure 2). For cancer mortality, lifestyle factors had the highest contribution (18.2%), followed by metabolic factors (14.1%) and social determinants (12.5%). Low educational attainment (10.7%), tobacco use (9.1%), hypertension (7.7%), long sleep duration (4.4%), and unhealthy diet (3.6%) were the top five leading risk factors for cancer mortality (Figure 3).

Analysis in men and women separately demonstrated that social determinants (e.g., low education) contributed larger PAFs to all-cause mortality in women (21.4%) than in men (14.9%) and lifestyle risk factors (e.g., unhealthy diet and tobacco use) contributed larger PAFs to all-cause mortality in men (27.6%) than in women (12.6%), whereas metabolic factors were leading contributors in both men (22.8%) and women (29.9%). For individual risk factors, low education attainment was one of the leading contributors to all-cause mortality in both women and men (15.6% in women vs. 12.6% in men) (Figure 1). For cardiovascular mortality, hypertension was the largest contributing risk factor in both women and men (22.7% in women vs. 17.1% in men), followed by low educational attainment (19.4%) in women and unhealthy diet (16.5%) in men (Figure 2). For cancer mortality in men, tobacco use was the largest contributing risk factor (15.8%), followed by low educational attainment (10.2%) and unhealthy diet (8.6%). In women, low education was the largest contributing risk factor to cancer mortality (10.9%), followed by hypertension (8.7%) and abdominal obesity (4.7%) (Figure 3).

The associations of gross domestic product per capita and ambient particulate matter with a diameter of <2.5 μm ($PM_{2.5}$) air pollution with all-cause, cardiovascular, ischemic heart disease, stroke, and cancer mortality were estimated (Tables 2, 3, 4, S1, and S2). Low gross domestic product per capita was associated with increased risks of all-cause mortality (HR = 1.26, 95% CI = 1.20–1.33), cardiovascular mortality (1.46, 1.34–1.59), ischemic heart disease mortality (1.27, 1.10–1.46), stroke mortality (1.29, 1.14–1.46), and cancer mortality (1.28, 1.18–1.39). We estimated that low gross domestic product per capita accounted for 7.8% of the PAF for all-cause mortality, 13.3% for cardiovascular mortality, 8.9% for ischemic heart disease mortality, 9.2% for stroke mortality, and 8.7% for cancer mortality. The PAF of low gross domestic product per capita for cardiovascular mortality was higher in women (16.2%) than in men (10.2%), whereas the PAF for cancer mortality was higher in men (10.7%) than women (6.4%) (Table S3). Ambient $PM_{2.5}$ air pollution was associated with increased risk of all-cause mortality (HR = 1.16, 95% CI = 1.11–1.22), cardiovascular mortality (1.55, 1.43–1.67), ischemic heart disease mortality (2.37, 2.09–2.70), and stroke mortality (1.34, 1.19–1.52). Approximately 4.3% of the PAF for all-cause mortality, 13.4% for cardiovascular
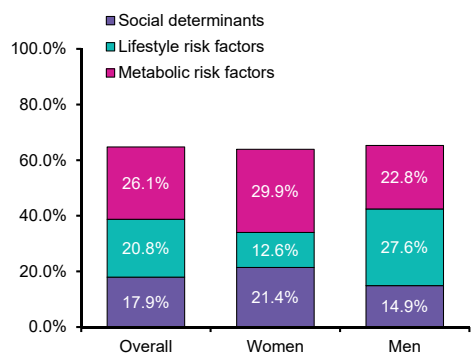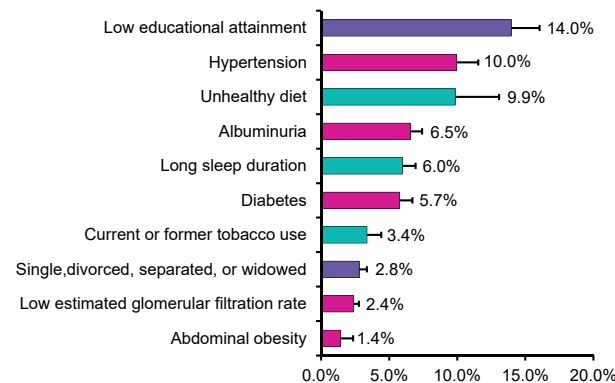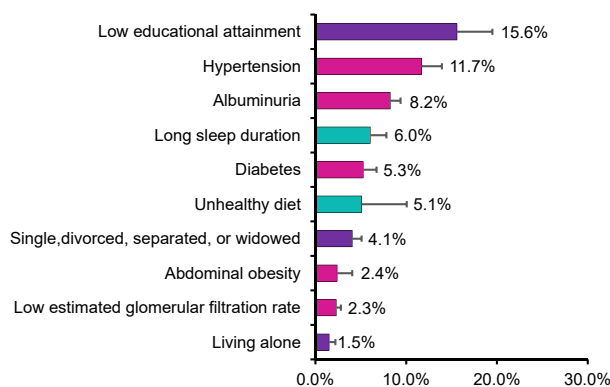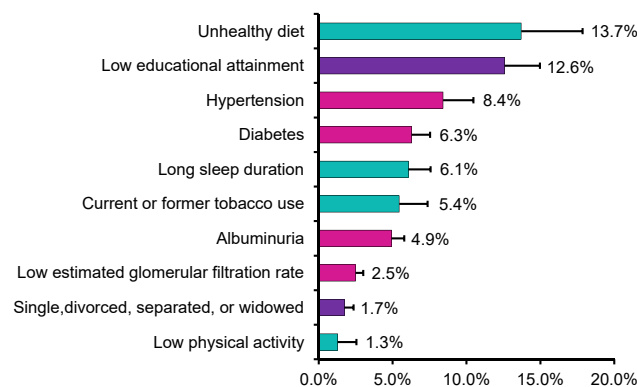
Figure 1. Population-attributable fractions (PAFs) for all-cause mortality
(A) PAFs associated with clusters of risk factors in the overall population, women, and men.
(B–D) PAFs associated with individual risk factors in the overall population, women, and men.
Models were adjusted for age, gender, and region, and individual risk factors were mutually adjusted. We showed the top ten most contributed risk factors based on population-attributable fractions of each mortality outcome. Gross domestic product per capita and ambient PM$_{2.5}$ air pollution were not included in this figure since they were community-level risk factors and analyzed using separate model. The negative population-attributable fractions were truncated at a lower limit of 0 when calculating the cluster estimates. See also Table S3.

mortality, 28.3% for ischemic heart disease mortality, 9.7% for stroke mortality, and 2.2% for cancer mortality were attributable to ambient PM$_{2.5}$ air pollution (Table S3). It is worth mentioning that the statistical approach used to calculate the PAF for ambient air pollution and low gross domestic product per capita (as a community-level risk factor) was different from the approach used to calculate the effect of all other risk factors (which were based on individual-level data). Therefore, these two types of PAFs are not strictly comparable.

DISCUSSION

In this study, we described the establishment of the 4C study, which is a large-scale population-based prospective cohort study with comprehensive measurements of social determinants, lifestyle, and metabolic factors during 10.1 years of follow-up. Recently, the concept of pan-risk factors for cardiovascular health and mortality has been raised by us but not been fully examined.[25] Utilizing the enriched data in the 4C study, we estimated the asso-

ciations between a comprehensive list of risk factors and mortality, which brings several novel insights for disease- and gender-specific risk factors for mortality. First, we showed that 72.2% of deaths in China were due to cardiovascular disease or cancer, and the identified risk factors explained 64.8% of the PAFs for all-cause mortality, 77.4% for cardiovascular mortality, and 44.8% for cancer mortality. Regarding disease-specific mortality, metabolic factors such as hypertension and albuminuria were leading contributors to all-cause and cardiovascular mortality, whereas lifestyle factors such as unhealthy diet and tobacco use were leading contributors to cancer mortality. Considering gender differences, while hypertension contributed a substantial proportion to mortality in both men and women, social determinants (e.g., low education) were leading risk factors for mortality in women, and lifestyle factors (e.g., unhealthy diet) were leading risk factors for mortality in men. Collectively, our study provides timely evidence to support the development of targeted health policies to control metabolic risk factors for the total population, control lifestyle risk factors for men, and increase social status
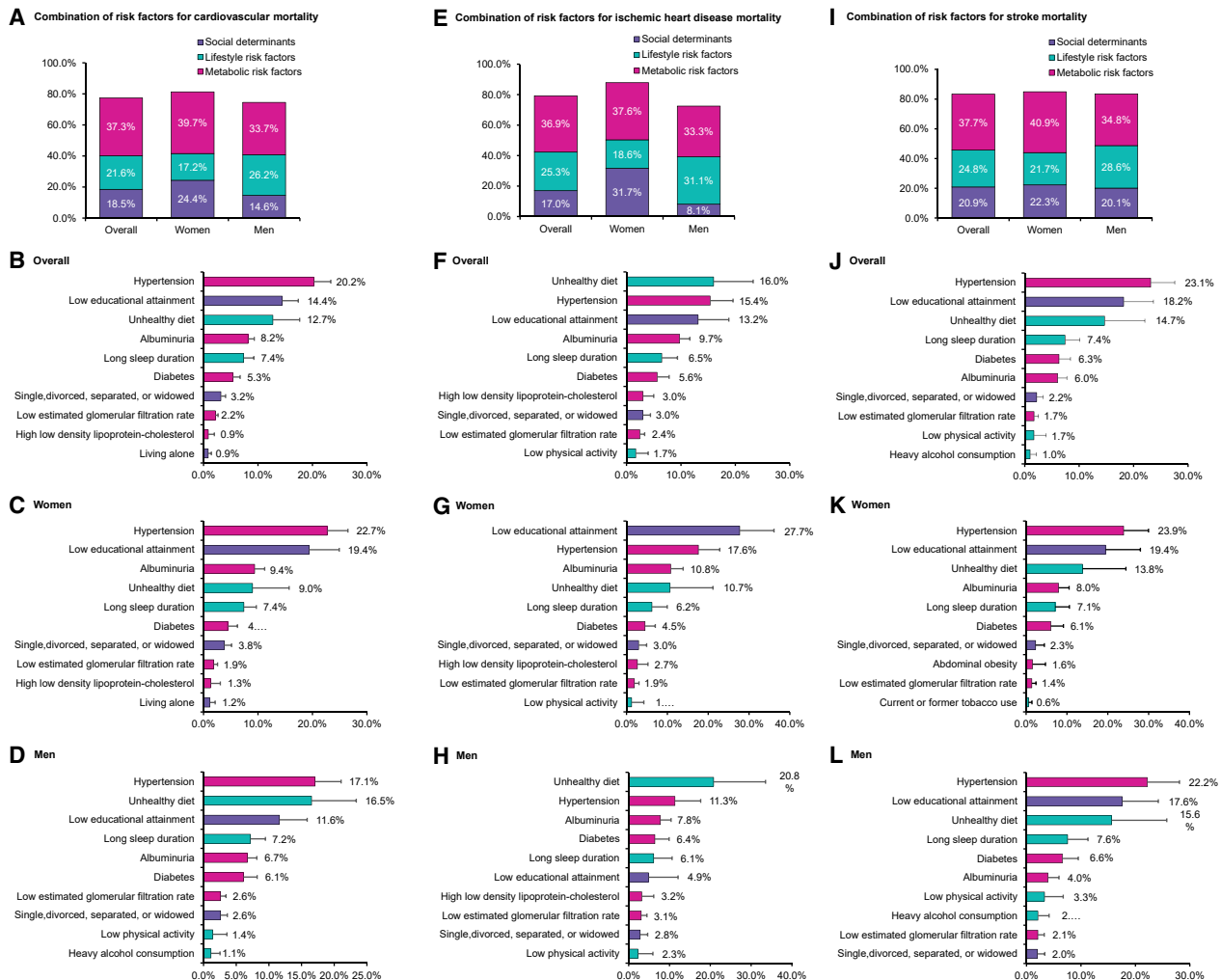
Figure 2. Population-attributable fractions (PAFs) for cardiovascular mortality

(A–D) PAFs for cardiovascular mortality associated with clusters or individual risk factors in the overall population, women, and men.

(E–H) PAFs for ischemic heart disease mortality associated with clusters or individual risk factors in the overall population, women, and men.

(I–L) PAFs for stroke mortality associated with clusters or individual risk factors in the overall population, women, and men.
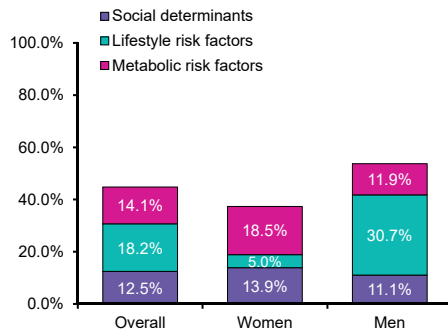
Models were adjusted for age, gender, and region, and individual risk factors were mutually adjusted. We showed the top ten most contributed risk factors based on population-attributable fractions of each mortality outcome. Gross domestic product per capita and ambient PM$_{2.5}$ air pollution were not included in this figure since they were community-level risk factors and analyzed using separate models. The negative population-attributable fractions were truncated at a lower limit of 0 when calculating the cluster estimates. See also Table S3.

for women. These policies may reduce the mortality rate in countries facing fast economic growth such as China.

Social determinants were known to affect a wide range of health outcomes.[26,27] Several previous studies have examined the effect of a limited number of social determinants on mortality.[5,28] In a meta-analysis of 48 prospective cohort studies with >1.75 million participants, low socioeconomic status (indexed by occupational position) was associated with a higher risk of all-cause mortality compared to high socioeconomic status (HR = 1.42, 95% CI = 1.38–1.45 for men; 1.34, 1.28–1.39 for women). In another study, adults with low socioeconomic status had higher risks of all-cause mortality compared with those with high socioeconomic status, in both National Health and Nutrition Examination Survey (HR = 2.13, 95% CI = 1.90–2.38) and the UK

Biobank (1.96, 1.87–2.06) after adjusting for lifestyle risk factors.[5] In our study, a set of social determinants also showed strong associations with all-cause and disease-specific mortalities. For factors with individual-level data, education, living arrangement, and depression were significantly associated with mortality, with education being the most important factor. For factors with community-level data, gross domestic product per capita and PM$_{2.5}$ air pollution were significantly associated with mortality. As indicated by our data, increasing the entire population's education level to middle school or above would reduce all-cause mortality by 14.0%, cardiovascular mortality by 14.4%, and cancer mortality by 10.7%, which highlighted the importance of improving the educational level in China. Although the educational attainment of the Chinese population is continuously improving during
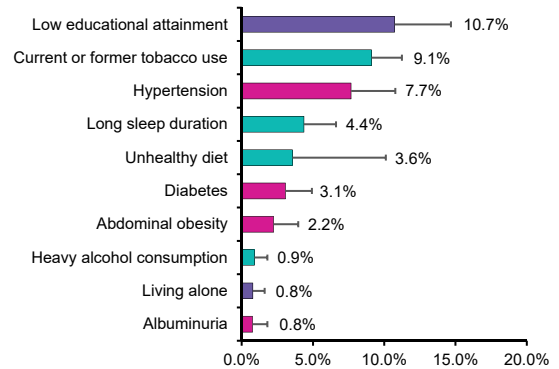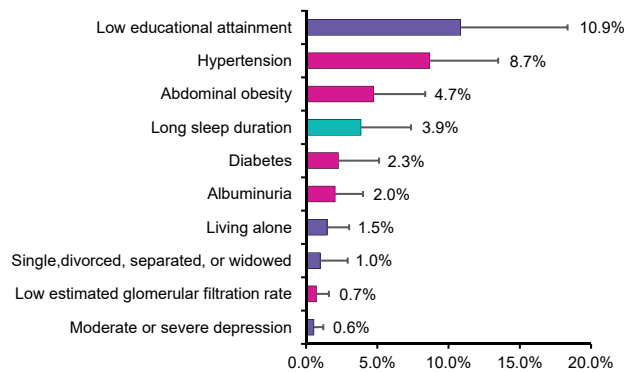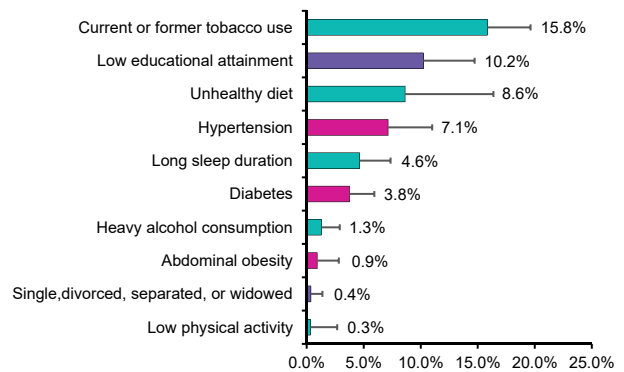
Figure 3. Population-attributable fractions (PAFs) for cancer mortality
(A) PAFs associated with clusters of risk factors in the overall population, women, and men.
(B–D) PAFs associated with individual risk factors in the overall population, women, and men.
Models were adjusted for age, gender, and region, and individual risk factors were mutually adjusted. We showed the top ten most contributed risk factors based on population-attributable fractions of each mortality outcome. Gross domestic product per capita and ambient $PM_{2.5}$ air pollution were not included in this figure since they were community-level risk factors and analyzed using separate model. The negative population-attributable fractions were truncated at a lower limit of 0 when calculating the cluster estimates. See also Table S3.

the past decades, low educational attainment remains a currently important issue in Chinese society. Apart from education, depression and living alone also exhibited associations with all-cause mortality, albeit with weaker contributions compared to education. Notably, the HR estimates for depression were stronger than those for education in relation to all-cause and cancer mortality. These findings imply that these social factors also pose significant threats to life and should receive increased attentions in future policy-making endeavors.

The associations of lifestyle and metabolic risk factors with mortality have been discussed before. Previous studies suggested that lifestyle factors interacted with social status, which increased mortality rate.[5] Other studies suggested that unhealthy diet habits such as increased red meat and processed meat consumption were associated with increasing mortality rates,[29] but not for dairy intake.[30] The Prospective Urban Rural Epidemiology study suggested that metabolic factors were the predominant risk factors for all-cause and cardiovascular mortality, with hypertension and lipid markers as key factors.[16,31] But most of these studies were conducted in participants with

European ancestry. Our study moves one key step forward by identifying lifestyle and metabolic risk factors for all-cause, cardiovascular, and cancer mortality in men and women in China.

Among lifestyle risk factors, tobacco use was one of the leading contributors to cancer mortality, while unhealthy diet was the third leading factor for all-cause and cardiovascular mortality. Our study further showed that high alcohol consumption (compared with never drinkers) was not significantly associated with risks of all-cause and cardiovascular mortality but was significantly associated with a higher risk of cancer mortality. These results are consistent with the findings reported in many other studies, which showed that the results could be biased by sick quitter/healthy survivor bias.[32,33] Furthermore, we found a significant association of binge drinking with a higher risk of all-cause mortality (HR = 1.21, 95% CI = 1.06–1.39) and cancer mortality (HR = 1.40, 95% CI = 1.15–1.71; Table S4).

Our findings corroborate the notion that air pollution is an increasingly important public health issue in China.[34–36] It was estimated that 1.24 million (95% CI: 1.08–1.40 million) deaths in China were attributable to air pollution in 2017, including

0.85 million (0.71–0.99 million) from ambient $PM_{2.5}$ pollution.[34] To promote national-wide air pollution control, the National Air Pollution Prevention and Control Action Plan has set up a wide range of control and prevention strategies and measures since 2013.[37] In our study, the annual average $PM_{2.5}$ exposure (47.5 $\mu g/m^3$) was much higher than the annual average $PM_{2.5}$ concentration threshold (5 $\mu g/m^3$) recommended by the World Health Organization Air Quality Guidelines 2021.[38] Of note, due to the absence of a real control group, this study is likely to underestimate the effect of ambient $PM_{2.5}$ pollution on mortality.

Among metabolic risk factors, hypertension was the leading factor for cardiovascular mortality and the second leading factor for all-cause mortality. Albuminuria was associated with a 1.5- to 3-fold higher risk of all-cause and cardiovascular mortality, which needs more attention when designing future health policies. For LDL-C, our study revealed that elevated levels of LDL-C were linked to an increased risk of cardiovascular mortality, whereas lower levels of LDL-C were associated with an elevated risk of cancer mortality. This noteworthy trade-off between cardiovascular health and increased cancer risk provides valuable insights into the potential implications for clinical management and risk assessment in the context of cardiovascular disease and cancer.

Thus far, the most comprehensive estimates of the associations between risk factors and health outcomes among Chinese adults are from the Global Burden of Disease Study by pooling data from diverse sources using modeling strategies.[1,13,14] While the subgroup analysis of Prospective Urban Rural Epidemiology study in Chinese adults focused on all-cause and cardiovascular mortality,[15] our study represents a significant advancement beyond existing studies. Specifically, we conducted a rigorous comparative analysis of the contributions of modifiable factors to cardiovascular and cancer mortality using centralized data and standardized statistical models. Furthermore, we delved deeper into risk factors associated with different subtypes of cardiovascular disease. Our finding revealed distinct leading risk factors for cardiovascular and cancer mortality (hypertension vs. low education, respectively), as well as different leading risk factors for specific cardiovascular disease subtypes (unhealthy diet for ischemic heart disease and hypertension for stroke mortality). These findings together with insights gained from LDL-C analysis highlighted the importance of setting up targeted prevention strategies and optimal thresholds for controlling modifiable risk factors based on individuals' disease status.

For gender difference, the sub-study of Prospective Urban Rural Epidemiology in 47,262 Chinese previously suggested that mortality rate was higher in men compared with women, but leading risk factors (e.g., lifestyle, hypertension and education) for men and women were similar.[15,30,31] Our results confirmed the findings that metabolic factors (e.g., hypertension) were leading factors for all-cause and cardiovascular mortality in both men and women. Our study also provided robust evidence to support that social determinants and lifestyle factors contributed differently to mortality in men and in women. Social determinants contributed 6.5% and 9.8% higher PAFs to all-cause and cardiovascular mortality in women than in men, respectively, whereas lifestyle factors contributed 15.0%, 9.0%, and 25.7% higher PAFs to all-cause, cardiovascular, and cancer mortality

in men than in women, respectively. For instance, low education was the top leading risk factor for ischemic heart disease mortality in women (27.7%) but only the sixth-ranked factor in men (4.9%). This aligns with previous studies that showed that mortality was mainly associated with women's social status.[39,40] Our finding provides evidence to support the prioritization of policies aimed at elevating the social status of women in China, which is expected to yield significant social and health benefits in the near future. Another well-known example was the influence of tobacco use on cancer mortality in men rather than in women,[41,42] which partly explained why lifestyle factors, such as smoking, were leading causes of mortality only in men.[43,44] We also demonstrated that unhealthy diet was the top-ranking risk factor for all-cause, ischemic heart disease, and cancer mortality in men, but showed much lower contributions in women. This finding aligns with evidence from existing literatures.[45]

The strengths and uniqueness of our study stem from several key aspects. First, we completed follow-up for a large sample of 174,004 Chinese adults aged $\geq$40 years from 20 study sites across mainland China. Second, we conducted a 10.1-year follow-up, allowing us to assess the long-term impact of risk factors on mortality outcomes. Third, we employed standardized methods to measure risk factors and outcomes, ensuring data consistency. Last, our study simultaneously analyzed all-cause mortality, cardiovascular mortality, and cancer mortality, providing comprehensive insights into different causes of death. It also unveiled novel observations regarding the relationships between established risk factors and mortality, specifically emphasizing the heterogeneous effects of LDL-C on both cancer mortality and cardiovascular mortality. These findings offer valuable contributions to the existing knowledge in this field.

Conclusions

In conclusion, our study indicates that cardiovascular disease and cancer accounted for over 70% of all causes of death in China. The majority of all-cause and cause-specific mortalities can be attributed to the 17 modifiable risk factors examined in the current study. The leading modifiable risk factors were largely different between mortalities caused by cardiovascular disease or cancer, between different cardiovascular disease subtypes, and between women and men. This study provides timely evidence to reduce the burden of metabolic disease to control cardiovascular disease mortality, set up different control targets for LDL-C to prevent cardiovascular and cancer death, and address unhealthy diet for ischemic heart disease and hypertension for stroke. It is crucial to promote healthy lifestyle for cancer mortality, address tobacco use and unhealthy diet among men, and enhance educational opportunities for women.

Limitations of the study

There are some limitations in this study. First, data on several important social determinants, including neighborhood and physical environment, safe housing, food security, social support, stress, community engagement, healthcare coverage, and access and quality of care were not collected. In addition, data on indoor air pollution and individual economic status were not collected. Second, the 4C study was not designed to reflect a nationally representative sample by stratified multistage

sampling strategy. Consequently, the presence of selection bias cannot be ruled out, and therefore the results might not be applicable to the whole Chinese population. Nevertheless, this nationwide prospective cohort study covered various geographic regions with substantial heterogeneity in social and economic circumstances, which enabled the capacity of evaluating the contributions of modifiable risk factors to mortality in the general adult population of China. Third, the interplay between age and various risk factors is substantial; thus, age-specific analyses are warranted in future studies to offer additional insights for targeted health interventions. Fourth, although the PAF calculation method in the present study offers advantages over traditional formulaic calculations by mitigating redundant contributions from multiple factors, it does not account for time variables. Fifth, premature cardiovascular and cancer deaths impose significant burdens on the majority of middle-income countries. However, our cohort primarily comprised middle to elderly participants, thereby restricting our capacity to examine premature deaths. Future studies should be conducted to explore this aspect further. Finally, since this study is observational in nature, it inherently limits the ability to infer causation from the association observed.

STAR★METHODS

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SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.xcrm.2024.101656.

AUTHOR CONTRIBUTIONS

G.N., Y.B., and W.W. conceived and designed the study. J.L., M.L., R.Z., C.H., and Q.C. did the statistical analysis. All authors contributed to acquisition,

analysis, or interpretation of data. J.L., J.H., Y.B., Y.X., J. Zheng, and M.L. contributed to drafting the manuscript and the revisions. G.N., Y.B., and W.W. supervised the study.

REFERENCES

1. Zhou, M., Wang, H., Zeng, X., Yin, P., Zhu, J., Chen, W., Li, X., Wang, L., Wang, L., Liu, Y., et al. (2019). Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet *394*, 1145–1158. https://doi.org/10.1016/S0140-6736(19)30427-1.

2. (2020). Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Results, 1736–1788. https://vizhub.healthdata.org/gbd-results/;.

3. GBD 2017 Causes of Death Collaborators (2018). Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet *392*, 1736–1788. https://doi.org/10.1016/S0140-6736(18)32203-7.

4. GBD 2015 Mortality and Causes of Death Collaborators (2016). Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet *388*, 1459–1544. https://doi.org/10.1016/S0140-6736(16)31012-1.

5. Zhang, Y.B., Chen, C., Pan, X.F., Guo, J., Li, Y., Franco, O.H., Liu, G., and Pan, A. (2021). Associations of healthy lifestyle and socioeconomic status with mortality and incident cardiovascular disease: two prospective cohort studies. BMJ *373*, n604. https://doi.org/10.1136/bmj.n604.

6. Celis-Morales, C.A., Lyall, D.M., Anderson, J., Iliodromiti, S., Fan, Y., Ntuk, U.E., Mackay, D.F., Pell, J.P., Sattar, N., and Gill, J.M. (2017). The association between physical activity and risk of mortality is modulated by grip strength and cardiorespiratory fitness: evidence from 498 135 UK-Biobank participants. Eur. Heart J. *38*, 116–122. https://doi.org/10.1093/eurheartj/ehw249.

7. GBD 2019 Diseases and Injuries Collaborators (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet *396*, 1204–1222. https://doi.org/10.1016/S0140-6736(20)30925-9.

8. Anand, S.S., Yusuf, S., Vuksan, V., Devanesen, S., Teo, K.K., Montague, P.A., Kelemen, L., Yi, C., Lonn, E., Gerstein, H., et al. (2000). Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: the Study of Health Assessment and Risk in Ethnic groups (SHARE). Lancet *356*, 279–284. https://doi.org/10.1016/s0140-6736(00)02502-2.

9. Kataoka, M., Venn, B.J., Williams, S.M., Te Morenga, L.A., Heemels, I.M., and Mann, J.I. (2013). Glycaemic responses to glucose and rice in people of Chinese and European ethnicity. Diabet. Med. *30*, e101–e107. https://doi.org/10.1111/dme.12080.

10. Ma, Q., Li, R., Wang, L., Yin, P., Wang, Y., Yan, C., Ren, Y., Qian, Z., Vaughn, M.G., McMillin, S.E., et al. (2021). Temporal trend and attributable risk factors of stroke burden in China, 1990-2019: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health *6*, e897–e906. https://doi.org/10.1016/S2468-2667(21)00228-0.

11. GBD 2019 Stroke Collaborators (2021). Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis

for the Global Burden of Disease Study 2019. Lancet Neurol 20, 795–820. https://doi.org/10.1016/S1474-4422(21)00252-0.

12. Roth, G.A., Mensah, G.A., Johnson, C.O., Addolorato, G., Ammirati, E., Baddour, L.M., Barengo, N.C., Beaton, A.Z., Benjamin, E.J., Benziger, C.P., et al. (2020). Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J. Am. Coll. Cardiol. 76, 2982–3021. https://doi.org/10.1016/j.jacc.2020.11.010.

13. Zhou, M., Wang, H., Zhu, J., Chen, W., Wang, L., Liu, S., Li, Y., Wang, L., Liu, Y., Yin, P., et al. (2016). Cause-specific mortality for 240 causes in China during 1990-2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. Lancet 387, 251–272. https://doi.org/10.1016/S0140-6736(15)00551-6.

14. Cai, Z., Chen, M., Ye, P., and Yip, P.S.F. (2022). Socio-economic determinants of suicide rates in transforming China: A spatial-temporal analysis from 1990 to 2015. Lancet Reg. Health. West. Pac. 19, 100341. https://doi.org/10.1016/j.lanwpc.2021.100341.

15. Li, S., Liu, Z., Joseph, P., Hu, B., Yin, L., Tse, L.A., Rangarajan, S., Wang, C., Wang, Y., Islam, S., et al. (2022). Modifiable risk factors associated with cardiovascular disease and mortality in China: a PURE substudy. Eur. Heart J. 43, 2852–2863. https://doi.org/10.1093/eurheartj/ehac268.

16. Yusuf, S., Joseph, P., Rangarajan, S., Islam, S., Mente, A., Hystad, P., Brauer, M., Kutty, V.R., Gupta, R., Wielgosz, A., et al. (2020). Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 395, 795–808. https://doi.org/10.1016/S0140-6736(19)32008-2.

17. Xing, A., Tian, X., Wang, Y., Chen, S., Xu, Q., Xia, X., Zhang, Y., Zhang, X., Wang, A., and Wu, S. (2023). Life's Essential 8' cardiovascular health with premature cardiovascular disease and all-cause mortality in young adults: the Kailuan prospective cohort study. Eur. J. Prev. Cardiol. 30, 593–600. https://doi.org/10.1093/eurjpc/zwad033.

18. Sun, Q., Yu, D., Fan, J., Yu, C., Guo, Y., Pei, P., Yang, L., Chen, Y., Du, H., Yang, X., et al. (2022). Healthy lifestyle and life expectancy at age 30 years in the Chinese population: an observational study. Lancet Public Health 7, e994–e1004. https://doi.org/10.1016/S2468-2667(22)00110-4.

19. Lu, J., He, J., Li, M., Tang, X., Hu, R., Shi, L., Su, Q., Peng, K., Xu, M., Xu, Y., et al. (2019). Predictive Value of Fasting Glucose, Postload Glucose, and Hemoglobin A(1c) on Risk of Diabetes and Complications in Chinese Adults. Diabetes Care 42, 1539–1548. https://doi.org/10.2337/dc18-1390.

20. Lu, J., Wang, W., Li, M., Bi, Y., Xu, Y., Chen, L., Zhao, J., Mu, Y., DeFronzo, R.A., and Ning, G. (2018). Associations of Hemoglobin A(1c) With Cardiovascular Disease and Mortality in Chinese Adults With Diabetes. J. Am. Coll. Cardiol. 72, 3224–3225. https://doi.org/10.1016/j.jacc.2018.09.062.

21. Wang, T., Lu, J., Su, Q., Chen, Y., Bi, Y., Mu, Y., Chen, L., Hu, R., Tang, X., Yu, X., et al. (2019). Ideal Cardiovascular Health Metrics and Major Cardiovascular Events in Patients With Prediabetes and Diabetes. JAMA Cardiol. 4, 874–883. https://doi.org/10.1001/jamacardio.2019.2499.

22. Wang, T., Lu, J., Shi, L., Chen, G., Xu, M., Xu, Y., Su, Q., Mu, Y., Chen, L., Hu, R., et al. (2020). Association of insulin resistance and β-cell dysfunction with incident diabetes among adults in China: a nationwide, population-based, prospective cohort study. Lancet Diabetes Endocrinol. 8, 115–124. https://doi.org/10.1016/s2213-8587(19)30425-5.

23. Zheng, R., Xu, Y., Li, M., Gao, Z., Wang, G., Hou, X., Chen, L., Huo, Y., Qin, G., Yan, L., et al. (2023). Data-driven subgroups of prediabetes and the associations with outcomes in Chinese adults. Cell Rep. Med. 4, 100958. https://doi.org/10.1016/j.xcrm.2023.100958.

24. Wang, S., Li, M., Lin, H., Wang, G., Xu, Y., Zhao, X., Hu, C., Zhang, Y., Zheng, R., Hu, R., et al. (2022). Amino acids, microbiota-related metabolites, and the risk of incident diabetes among normoglycemic Chinese adults: Findings from the 4C study. Cell Rep. Med. 3, 100727. https://doi.org/10.1016/j.xcrm.2022.100727.

25. Zheng, R., Xu, Y., Li, M., Lu, J., Xu, M., Wang, T., Zhao, Z., Wang, S., Lin, H., Zhang, X., et al. (2022). Pan-risk factor for a comprehensive cardiovascular health management. J. Diabetes 14, 179–191. https://doi.org/10.1111/1753-0407.13258.

26. Marmot, M., Friel, S., Bell, R., Houweling, T.A., and Taylor, S.; Commission on Social Determinants of Health (2008). Closing the gap in a generation: health equity through action on the social determinants of health. Lancet 372, 1661–1669. https://doi.org/10.1016/s0140-6736(08)61690-6.

27. Hales, C.N., and Barker, D.J. (1992). Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. Diabetologia 35, 595–601. https://doi.org/10.1007/bf00400248.

28. Stringhini, S., Carmeli, C., Jokela, M., Avendaño, M., Muennig, P., Guida, F., Ricceri, F., d'Errico, A., Barros, H., Bochud, M., et al. (2017). Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. Lancet 389, 1229–1237. https://doi.org/10.1016/s0140-6736(16)32380-7.

29. Zheng, Y., Li, Y., Satija, A., Pan, A., Sotos-Prieto, M., Rimm, E., Willett, W.C., and Hu, F.B. (2019). Association of changes in red meat consumption with total and cause specific mortality among US women and men: two prospective cohort studies. BMJ 365, l2110. https://doi.org/10.1136/bmj.l2110.

30. Ding, M., Li, J., Qi, L., Ellervik, C., Zhang, X., Manson, J.E., Stampfer, M., Chavarro, J.E., Rexrode, K.M., Kraft, P., et al. (2019). Associations of dairy intake with risk of mortality in women and men: three prospective cohort studies. BMJ 367, l6204. https://doi.org/10.1136/bmj.l6204.

31. Walli-Attaei, M., Rosengren, A., Rangarajan, S., Breet, Y., Abdul-Razak, S., Sharief, W.A., Alhabib, K.F., Avezum, A., Chifamba, J., Diaz, R., et al. (2022). Metabolic, behavioural, and psychosocial risk factors and cardiovascular disease in women compared with men in 21 high-income, middle-income, and low-income countries: an analysis of the PURE study. Lancet 400, 811–821. https://doi.org/10.1016/S0140-6736(22)01441-6.

32. Xi, B., Veeranki, S.P., Zhao, M., Ma, C., Yan, Y., and Mi, J. (2017). Relationship of Alcohol Consumption to All-Cause, Cardiovascular, and Cancer-Related Mortality in U.S. Adults. J. Am. Coll. Cardiol. 70, 913–922. https://doi.org/10.1016/j.jacc.2017.06.054.

33. Ding, C., O'Neill, D., Bell, S., Stamatakis, E., and Britton, A. (2021). Association of alcohol consumption with morbidity and mortality in patients with cardiovascular disease: original data and meta-analysis of 48,423 men and women. BMC Med. 19, 167. https://doi.org/10.1186/s12916-021-02040-2.

34. Yin, P., Brauer, M., Cohen, A.J., Wang, H., Li, J., Burnett, R.T., Stanaway, J.D., Causey, K., Larson, S., Godwin, W., et al. (2020). The effect of air pollution on deaths, disease burden, and life expectancy across China and its provinces, 1990-2017: an analysis for the Global Burden of Disease Study 2017. Lancet Planet. Health 4, e386–e398. https://doi.org/10.1016/s2542-5196(20)30161-3.

35. Huang, C., Moran, A.E., Coxson, P.G., Yang, X., Liu, F., Cao, J., Chen, K., Wang, M., He, J., Goldman, L., et al. (2017). Potential Cardiovascular and Total Mortality Benefits of Air Pollution Control in Urban China. Circulation 136, 1575–1584. https://doi.org/10.1161/circulationaha.116.026487.

36. Liu, C., Chen, R., Sera, F., Vicedo-Cabrera, A.M., Guo, Y., Tong, S., Coelho, M., Saldiva, P.H.N., Lavigne, E., Matus, P., et al. (2019). Ambient Particulate Air Pollution and Daily Mortality in 652 Cities. N. Engl. J. Med. 381, 705–715. https://doi.org/10.1056/NEJMoa1817364.

37. The General Office of the State Council of China (2013). On the publication of the Action Plan against Atmospheric Pollution. http://www.gov.cn/zwgk/2013-09/12/content_2486773.htm.

38. Hoffmann, B., Boogaard, H., de Nazelle, A., Andersen, Z.J., Abramson, M., Brauer, M., Brunekreef, B., Forastiere, F., Huang, W., Kan, H., et al. (2021). WHO Air Quality Guidelines 2021–Aiming for Healthier Air for all: A Joint Statement by Medical, Public Health, Scientific Societies and Patient Representative Organisations. Int. J. Publ. Health 66, 1604465. https://doi.org/10.3389/ijph.2021.1604465.

39. Wu, H., Bragg, F., Yang, L., Du, H., Guo, Y., Jackson, C.A., Zhu, S., Yu, C., Luk, A.O.Y., Chan, J.C.N., et al. (2019). Sex differences in the association

between socioeconomic status and diabetes prevalence and incidence in China: cross-sectional and prospective studies of 0.5 million adults. Diabetologia *62*, 1420–1429. https://doi.org/10.1007/s00125-019-4896-z.

40. Ross, S., Armas Rojas, N., Sawatzky, J., Varona-Perez, P., Burrett, J.A., Calderon Martinez, M., Lorenzo-Vazquez, E., Bess Constanten, S., Sherliker, P., Morales Rigau, J.M., et al. (2022). Educational inequalities and premature mortality: the Cuba Prospective Study. Lancet Public Health *7*, e923–e931. https://doi.org/10.1016/S2468-2667(22)00237-7.

41. Millwood, I.Y., Walters, R.G., Mei, X.W., Guo, Y., Yang, L., Bian, Z., Bennett, D.A., Chen, Y., Dong, C., Hu, R., et al. (2019). Conventional and genetic evidence on alcohol and vascular disease aetiology: a prospective study of 500 000 men and women in China. Lancet *393*, 1831–1842. https://doi.org/10.1016/S0140-6736(18)31772-0.

42. Chan, K.H., Wright, N., Xiao, D., Guo, Y., Chen, Y., Du, H., Yang, L., Millwood, I.Y., Pei, P., Wang, J., et al. (2022). Tobacco smoking and risks of more than 470 diseases in China: a prospective cohort study. Lancet Public Health *7*, e1014–e1026. https://doi.org/10.1016/S2468-2667(22)00227-4.

43. Chen, W., Xia, C., Zheng, R., Zhou, M., Lin, C., Zeng, H., Zhang, S., Wang, L., Yang, Z., Sun, K., et al. (2019). Disparities by province, age, and sex in site-specific cancer burden attributable to 23 potentially modifiable risk factors in China: a comparative risk assessment. Lancet Global Health *7*, e257–e269. https://doi.org/10.1016/S2214-109X(18)30488-1.

44. Islami, F., Goding Sauer, A., Miller, K.D., Siegel, R.L., Fedewa, S.A., Jacobs, E.J., McCullough, M.L., Patel, A.V., Ma, J., Soerjomataram, I., et al. (2018). Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA A Cancer J. Clin. *68*, 31–54. https://doi.org/10.3322/caac.21440.

45. Shan, Z., Guo, Y., Hu, F.B., Liu, L., and Qi, Q. (2020). Association of Low-Carbohydrate and Low-Fat Diets With Mortality Among US Adults. JAMA Intern. Med. *180*, 513–523. https://doi.org/10.1001/jamainternmed.2019.6980.

46. Kroenke, K., Spitzer, R.L., and Williams, J.B. (2001). The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. *16*, 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x.

47. Craig, C.L., Marshall, A.L., Sjostrom, M., Bauman, A.E., Booth, M.L., Ainsworth, B.E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J.F., and Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. Med. Sci. Sports Exerc. *35*, 1381–1395. https://doi.org/10.1249/01.MSS.0000078924.61453.FB.

48. Zhao, W.-H., Huang, Z.-P., Zhang, X., He, L., Willett, W., Wang, J.-L., Hasegawa, K., and Chen, J.-S. (2010). Reproducibility and Validity of a Chinese Food Frequency Questionnaire. Biomed. Environ. Sci. *23*, 1–38. https://doi.org/10.1016/s0895-3988(11)60014-7.

49. Bi, Y., Jiang, Y., He, J., Xu, Y., Wang, L., Xu, M., Zhang, M., Li, Y., Wang, T., Dai, M., et al. (2015). Status of cardiovascular health in Chinese adults. J. Am. Coll. Cardiol. *65*, 1013–1025. https://doi.org/10.1016/j.jacc.2014.12.044.

50. World Health Organization (2011). Waist Circumference and Waist-hip Ratio. Report of a WHO Expert Consultation (World Health Organization).

51. American Diabetes Association (2019). 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care *42*, S13–S28. https://doi.org/10.2337/dc19-S002.

52. Mach, F., Baigent, C., Catapano, A.L., Koskinas, K.C., Casula, M., Badimon, L., Chapman, M.J., De Backer, G.G., Delgado, V., Ference, B.A., et al. (2020). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur. Heart J. *41*, 111–188. https://doi.org/10.1093/eurheartj/ehz455.

53. Arnett, D.K., Blumenthal, R.S., Albert, M.A., Buroker, A.B., Goldberger, Z.D., Hahn, E.J., Himmelfarb, C.D., Khera, A., Lloyd-Jones, D., McEvoy, J.W., et al. (2019). 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J. Am. Coll. Cardiol. *74*, 1376–1414. https://doi.org/10.1016/j.jacc.2019.03.009.

54. Xu, Y., Li, M., Qin, G., Lu, J., Yan, L., Xu, M., Wang, T., Zhao, Z., Dai, M., Zhang, D., et al. (2021). Cardiovascular Risk Based on ASCVD and KDIGO Categories in Chinese Adults: A Nationwide, Population-Based, Prospective Cohort Study. J. Am. Soc. Nephrol. *32*, 927–937. https://doi.org/10.1681/asn.2020060856.

55. Levey, A.S., Stevens, L.A., Schmid, C.H., Zhang, Y.L., Castro, A.F., CKD-EPI Chronic Kidney Disease Epidemiology Collaboration; Feldman, H.I., 3rd, Kusek, J.W., Eggers, P., Van Lente, F., et al. (2009). A new equation to estimate glomerular filtration rate. Ann. Intern. Med. *150*, 604–612. https://doi.org/10.7326/0003-4819-150-9-200905050-00006.

56. Hammer, M.S., van Donkelaar, A., Li, C., Lyapustin, A., Sayer, A.M., Hsu, N.C., Levy, R.C., Garay, M.J., Kalashnikova, O.V., Kahn, R.A., et al. (2022). Global Annual PM2.5 Grids from MODIS, MISR and SeaWiFS Aerosol Optical Depth (AOD), 1998-2019, V4.GL.03 (NASA Socioeconomic Data and Applications Center (SEDAC)).

57. Resche-Rigon, M., and White, I.R. (2018). Multiple imputation by chained equations for systematically and sporadically missing multilevel data. Stat. Methods Med. Res. *27*, 1634–1649. https://doi.org/10.1177/0962280216666564.

58. Raghunathan, T.E. (2004). What do we do with missing data? Some options for analysis of incomplete data. Annu. Rev. Publ. Health *25*, 99–117. https://doi.org/10.1146/annurev.publhealth.25.102802.124410.

59. Eide, G.E., and Gefeller, O. (1995). Sequential and average attributable fractions as aids in the selection of preventive strategies. J. Clin. Epidemiol. *48*, 645–655. https://doi.org/10.1016/0895-4356(94)00161-i.

60. Ferguson, J., Alvarez-Iglesias, A., Newell, J., Hinde, J., and O'Donnell, M. (2018). Estimating average attributable fractions with confidence intervals for cohort and case-control studies. Stat. Methods Med. Res. *27*, 1141–1152. https://doi.org/10.1177/0962280216655374.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
SAS version 9.4	SAS Institute	https://www.sas.com/
R version 4.2.3	R-Project	https://www.r-project.org/
STAR Methods. Average PAFs analysis: R package averisk version 1.0.3	R CRAN	https://mirrors.ustc.edu.cn/CRAN/web/packages/averisk/index.html
Biological samples		
Serum and urinary samples of the participants	4C BioBank	N/A

RESOURCE AVAILABILITY

Lead contact
Further information and request for resources and reagents should be directed to and will be fulfilled by the lead contact, Weiqing Wang (wqingw61@shsmu.edu.cn).

Materials availability
This study did not generate new unique reagents.

Data and code availability
- Data generated and/or analyzed in this study, excluding identifying personal information, are available from the lead contact, Weiqing Wang (wqingw61@shsmu.edu.cn) with reasonable request to protect research participant privacy.
- This paper does not report the original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

EXPERIMENTAL MODEL AND SUBJECT DETAILS

Study design and population
The 4C Study is a multicenter, population-based, prospective cohort study that was designed to investigate the risk factors of cardiovascular, cancer, and all-cause mortality in the Chinese population. In brief, a total of 20 communities from various geographic regions were selected to represent the general population in mainland China. The selection of communities considered the coverage of different geographic regions with various economic development status, as well as the feasibility of centralized sample collection and successfully achieving long-term follow-up. Based on the national criteria for coordinated regional development according to their socioeconomic development status at the time of recruitment, these 16 provinces were categorized into Eastern (Beijing, Zhejiang, Guangzhou, Fujian, Shanghai, Liaoning, Shandong), Central (Heilongjiang, Jilin, Henan, Hubei, Jiangxi), and Western regions (Guizhou, Sichuan, Gansu, Guangxi). Within each community, potential study participants were identified from the local residence registration records and must be 40 years or older. There was no restriction on gender or ethnicity. Each eligible subject was approached by trained local community workers using a door-to-door invitation method. Overall, 204,467 agreed to participate and signed informed consent, and were scheduled for a personal interview and a clinic visit within a week after the invitation. After excluding 10,621 (5.2%) individuals who did not meet age eligibility criteria or withdrew their consents, 193,846 (94.8%) participants underwent a detailed baseline examination and were enrolled in the 4C study between January 2011 and December 2012.

The study was approved by the Medical Ethics Committee of Ruijin Hospital, Shanghai Jiao-Tong University School of Medicine. All study participants provided written informed consent prior to study participation.

Baseline data collection
We used standardized methods to collect information on risk factors at baseline. The personal interview was conducted by trained study personnel using a structured questionnaire. All participants underwent an oral glucose tolerance test, and plasma glucose was obtained at zero and 2 h during the test. Blood specimens and first morning spot urine samples were collected and aliquoted into 0.5-mL Eppendorf tubes within 2 h of collection and shipped in dry ice to the central laboratory of the study located at Shanghai Institute of Endocrine and Metabolic Diseases, which is accredited by the College of American Pathologists. All biochemical tests were performed at the central clinical laboratory using validated and standardized protocols and procedures.

We collected and evaluated 15 baseline individual-level and two community-level modifiable risk factors in this study. The 17 risk factors were categorized into six social determinants (community level data of low gross domestic product per capita and high ambient $PM_{2.5}$ air pollution, and individual level data of low educational attainment, marital status of being single, divorced, separated, or widowed, living alone and moderate or severe depression), five lifestyle risk factors (current or former tobacco use, former, or high current alcohol consumption, unhealthy diet, low physical activity and long sleep duration), and six metabolic risk factors (abdominal obesity, hypertension, diabetes, high low-density lipoprotein cholesterol (LDL-C), albuminuria and low estimated glomerular filtration rate). Depression, recognized as a multifaceted construct that mirrors social factors, has been classified as a social determinant in many studies,[15,16] including the current study. A detailed summary of each risk factor, its measurement method, and its categorization used to calculate the PAF was available in Table S5. Spearman correlation coefficients and multicollinearity diagnosis indicated no high correlation or multicollinearity among these variables (Tables S6 and S7).

For social determinants, self-reported educational attainment was classified into three groups as primary education or less, middle school, and high school or above. Low educational attainment was defined as middle school or less education. Depression severity was assessed using the Patient Health Questionnaire-9, in which a score of ≥ 10 represents moderate or severe depression.[46] For lifestyle factors, physical activity was assessed using the International Physical Activity Questionnaire-Short Form.[47] A semi-quantitative Chinese Food Frequency Questionnaire recommended by the National Institute for Nutrition and Health of Chinese Center for Disease Control and Prevention was used to collect habitual dietary intake by asking about the consumption frequency and portion size of typical food items during the previous 12 months[48] A diet score was calculated according to the recommendation of the American Heart Association and was reported to associate with health outcomes in Chinese.[21,49] For metabolic factors, abdominal obesity was defined as waist-to-hip ratio ≥ 0.95 for men and waist-to-hip ratio ≥ 0.90 for women.[50] Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg using the mean value of three readings or treatment with antihypertensive medications. Diabetes was defined as fasting glucose ≥ 7.0 mmol/L (126 mg/dL) or 2-h postload glucose ≥ 11.1 mmol/L (200 mg/dL) or hemoglobin A1c ≥ 48 mmol/mol (6.5%) or self-reported history of diabetes.[51] LDL-C was divided into three subgroups: <3.4 mmol/L (<130 mg/dL), ≥ 3.4 and <4.9 mmol/L (130–190 mg/dL), and ≥ 4.9 mmol/L (≥ 190 mg/dL).[52,53] Non-high-density lipoprotein cholesterol was also used as an alternative risk factor to LDL-C. Albuminuria was defined as microalbuminuria (urine albumin-creatinine ratio: 30-299 mg/g) or macroalbuminuria (urine albumin-creatinine ratio ≥ 300 mg/g).[54] Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease-Epidemiology Collaboration equation, with low estimated glomerular filtration rate defined as <60 mL/min per $1.73m^2$.[55]

For community-level risk factors, gross domestic product per capita of the city was obtained from government administrative data, and low gross domestic product per capita was defined as gross domestic product per capita of the city lower than the average gross domestic product per capita across China in 2011. Data on the annual average residential $PM_{2.5}$ exposure in 2011 for each city were collected from the Global Annual $PM_{2.5}$ Grids,[56] and participants were categorized into two groups using the upper quartile of $PM_{2.5}$ levels (59.11 $\mu g/m^3$) in our study as a cut-off threshold.

METHOD DETAILS

Follow-up and outcome assessment
The follow-up was conducted till November 30, 2021 with a median follow-up duration of 10.1 years. Death was ascertained by death certificates from the local death registries of the National Disease Surveillance Point System, based on the International Classification of Diseases, 10th Revision (ICD-10) codes. ICD-10 Codes used in the 4C study for causes of death were provided in Table S8. Adjudications for cardiovascular deaths and cancer deaths were performed by the investigators from the adjudication committee of the 4C study, which was composed of cardiologists, neurologists, oncologists, and physicians of internal medicine. Each death was independently adjudicated by two members of the committee and discrepancies were discussed within the committee to make a final decision. During the adjudication, medical records including pathology reports were obtained and reviewed by the adjudicators. All members of the committee were unaware of the baseline risk factors of study participants.

QUANTIFICATION AND STATISTICAL ANALYSIS

Baseline characteristics of participants were summarized as mean ± SD, or number of participants and percentage, or median with interquartile range, depending on the normality distribution of continuous variables or numbers with proportions for categorical variables.

Missing data imputation
Multiple imputation by chained Equation 10 replications was conducted for all individual-level risk factors.[57] Details of the imputation process for risk factors, distributions of predictors before and after multiple imputations are provided in Table S9, Figures S6 and S7. All primary analyses were performed using multiple-imputed data and SAS software (version 9.4, SAS Institute). The estimates from each of the ten imputed datasets were combined into one overall estimate with the use of Rubin's rule.[58] Given the higher incidence rate of stroke in China compared to other countries,[10–12] we separated cardiovascular mortality into two subgroups, ischemic heart disease mortality and stroke mortality, and conducted statistical analyses separately.

Cox proportional hazards models

Cox proportional hazards models were used to calculate HRs and 95% CIs of individual risk factors associated with all-cause mortality, while competing risk regression models were employed for cause-specific mortality, including cardiovascular, ischemic heart disease, stroke and cancer mortality. The analyses were conducted by using SAS software (version 9.4, SAS Institute). The proportional hazards assumption was not violated according to the tests of the interaction terms of variables and follow-up duration. A single multivariable model was utilized to account for the mutually adjusted effects of the 15 individual-level risk factors, in addition to age, gender, and area of residence (urban or rural). Since the information on gross domestic product per capita and ambient air pollution was at community level, HRs were calculated in separate models after adjusting for age, gender, area of residence (urban or rural), and 15 individual-level risk factors. We also estimated the HR of each risk factor with mortality in men and women separately. Multiplicative interactions of gender with risk factors were examined by including the product term (e.g., gender × risk factor) in the models to assess whether the associations of risk factors with outcomes vary across different gender groups. Multiple testing was not performed as the risk factors were mutually adjusted in the regression model. In these time-to-event analyses, participants were censored at either the date of death or the date of last follow-up till November, 2021, whichever occurred first.

Average PAF calculation

Average PAFs of all-cause, cardiovascular, ischemic heart disease, stroke and cancer mortality related to individual and clusters of social determinants, lifestyle, and metabolic risk factors were calculated using the approach described by Eide and Gefeller.[59,60] PAFs quantify the proportional reduction in disease incidence that would be achieved if the risk factor is theoretically removed from the population. PAFs were calculated with adjustment for age, gender, area of residence (urban or rural), and 15 individual-level risk factors simultaneously, which enables to avoid the overlapping contributions of multiple factors to the same outcome. Since the information on gross domestic product per capita and ambient air pollution was at the community level, the PAFs for these two factors were calculated separately, using the fully adjusted HRs and the exposure distributions based on the aforementioned formula: PAF = p(HR-1)/(1 + p(HR-1)), where p is the population prevalence of the risk factor. Average PAF was calculated by using the R package 'averisk' (version 1.0.3) on R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

Supplemental information

Association of social determinants, lifestyle, and

metabolic factors with mortality in Chinese adults:

A nationwide 10-year prospective cohort study

Jieli Lu, Mian Li, Jiang He, Yu Xu, Ruizhi Zheng, Jie Zheng, Guijun Qin, Yingfen Qin, Yuhong Chen, Xulei Tang, Zhen Ye, Min Xu, Tiange Wang, Lixin Shi, Qing Su, Xuefeng Yu, Li Yan, Zhiyun Zhao, Qin Wan, Gang Chen, Zhengnan Gao, Guixia Wang, Feixia Shen, Xuejiang Gu, Zuojie Luo, Li Chen, Xinguo Hou, Yanan Huo, Qiang Li, Hong Qiao, Yinfei Zhang, Tianshu Zeng, Chunyan Hu, Qiuyu Cao, Xiaojing Jia, Chao Liu, Youmin Wang, Shengli Wu, Tao Yang, Huacong Deng, Hongyan Qi, Xueyan Wu, Di Zhang, Meng Dai, Donghui Li, Shenghan Lai, Lulu Chen, Jiajun Zhao, Yiming Mu, Weiguo Hu, Guang Ning, Ruying Hu, Yufang Bi, Weiqing Wang, and for the 4C Study Group
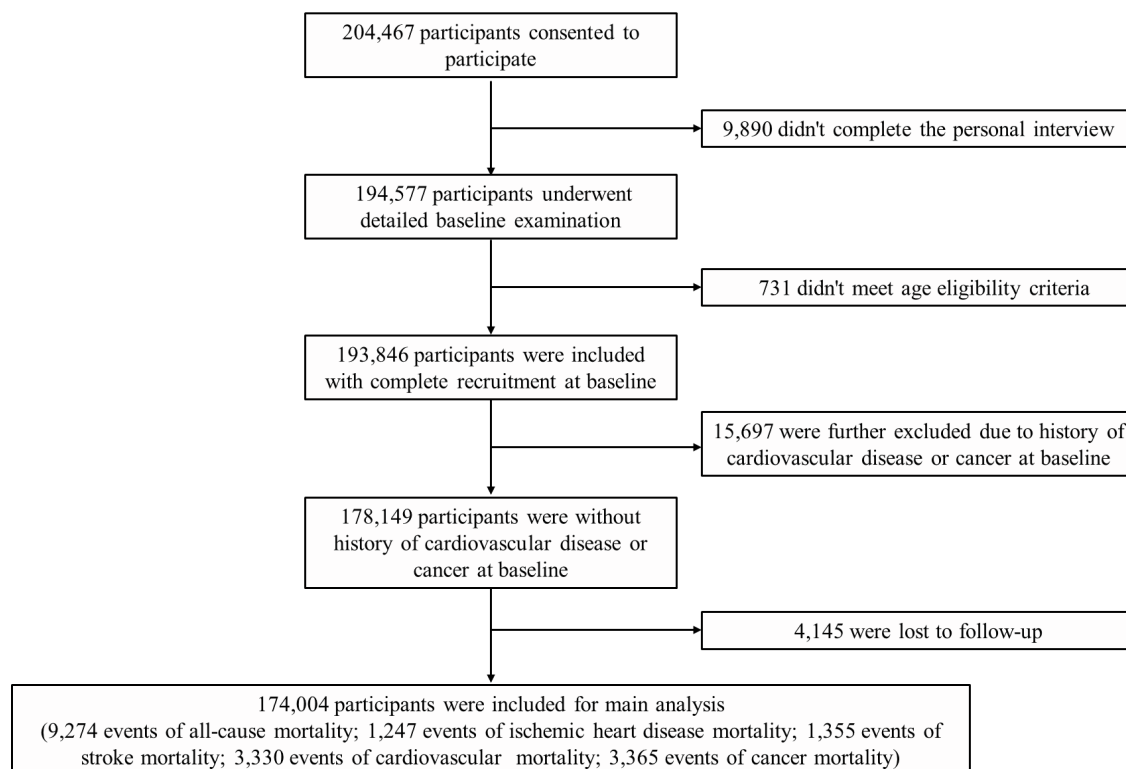
Supplementary Figures


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┌─────────────────────────────────┐
│ 204,467 participants consented to│
│           participate            │
└─────────────────────────────────┘
                │
                │────────────►┌──────────────────────────────────────────┐
                │             │ 9,890 didn't complete the personal interview│
                │             └──────────────────────────────────────────┘
                ▼
┌─────────────────────────────────┐
│ 194,577 participants underwent   │
│ detailed baseline examination    │
└─────────────────────────────────┘
                │
                │────────────►┌──────────────────────────────────────────┐
                │             │ 731 didn't meet age eligibility criteria  │
                │             └──────────────────────────────────────────┘
                ▼
┌─────────────────────────────────┐
│ 193,846 participants were included│
│ with complete recruitment at baseline│
└─────────────────────────────────┘
                │
                │────────────►┌──────────────────────────────────────────┐
                │             │ 15,697 were further excluded due to history of│
                │             │ cardiovascular disease or cancer at baseline│
                │             └──────────────────────────────────────────┘
                ▼
┌─────────────────────────────────┐
│ 178,149 participants were without│
│ history of cardiovascular disease or│
│       cancer at baseline         │
└─────────────────────────────────┘
                │
                │────────────►┌──────────────────────────────────────────┐
                │             │ 4,145 were lost to follow-up              │
                │             └──────────────────────────────────────────┘
                ▼
```

174,004 participants were included for main analysis
(9,274 events of all-cause mortality; 1,247 events of ischemic heart disease mortality; 1,355 events of stroke mortality; 3,330 events of cardiovascular mortality; 3,365 events of cancer mortality)

Figure S1. Participant flow diagram of the China Cardiometabolic Disease and Cancer Cohort (4C) Study, related to Table 1.
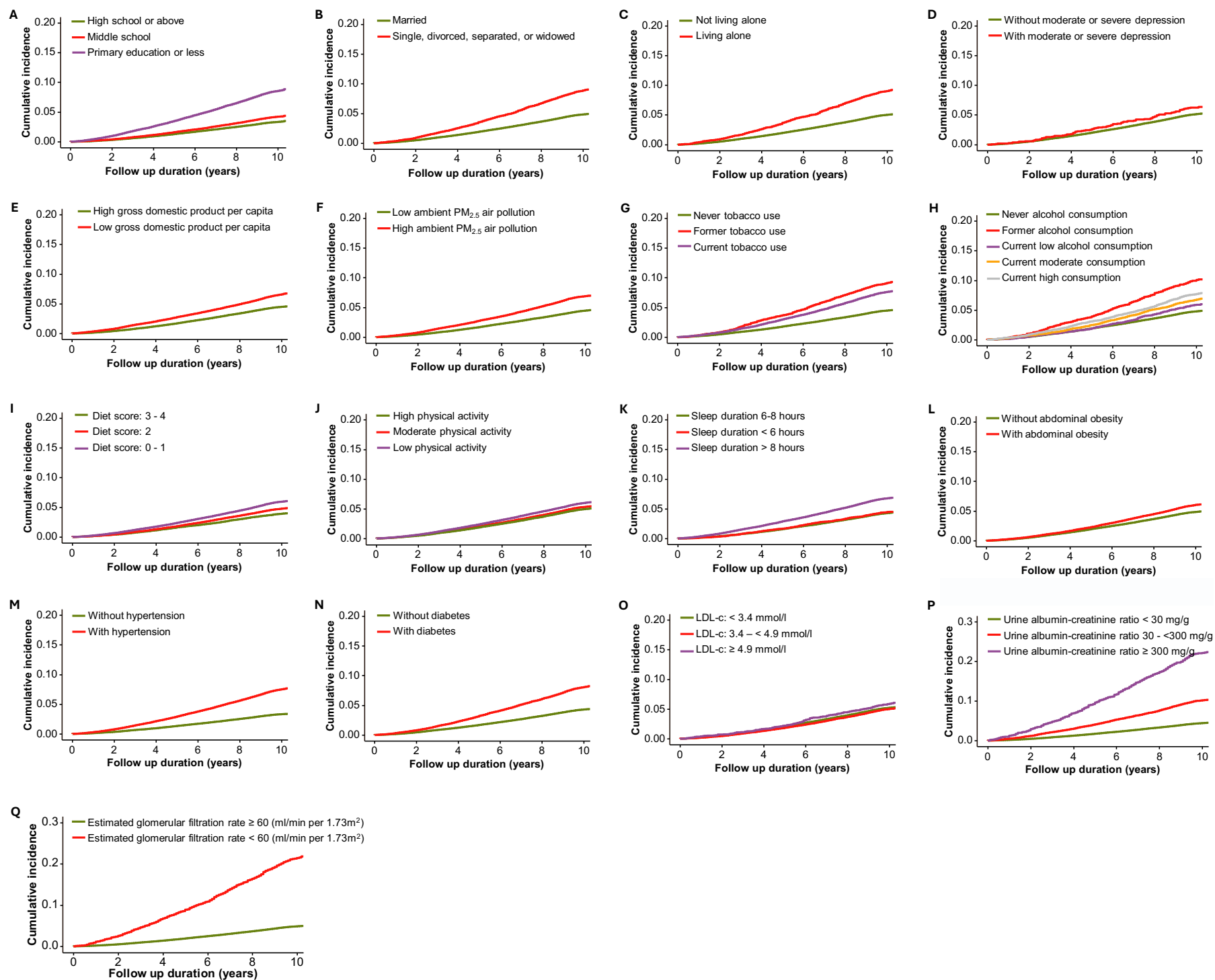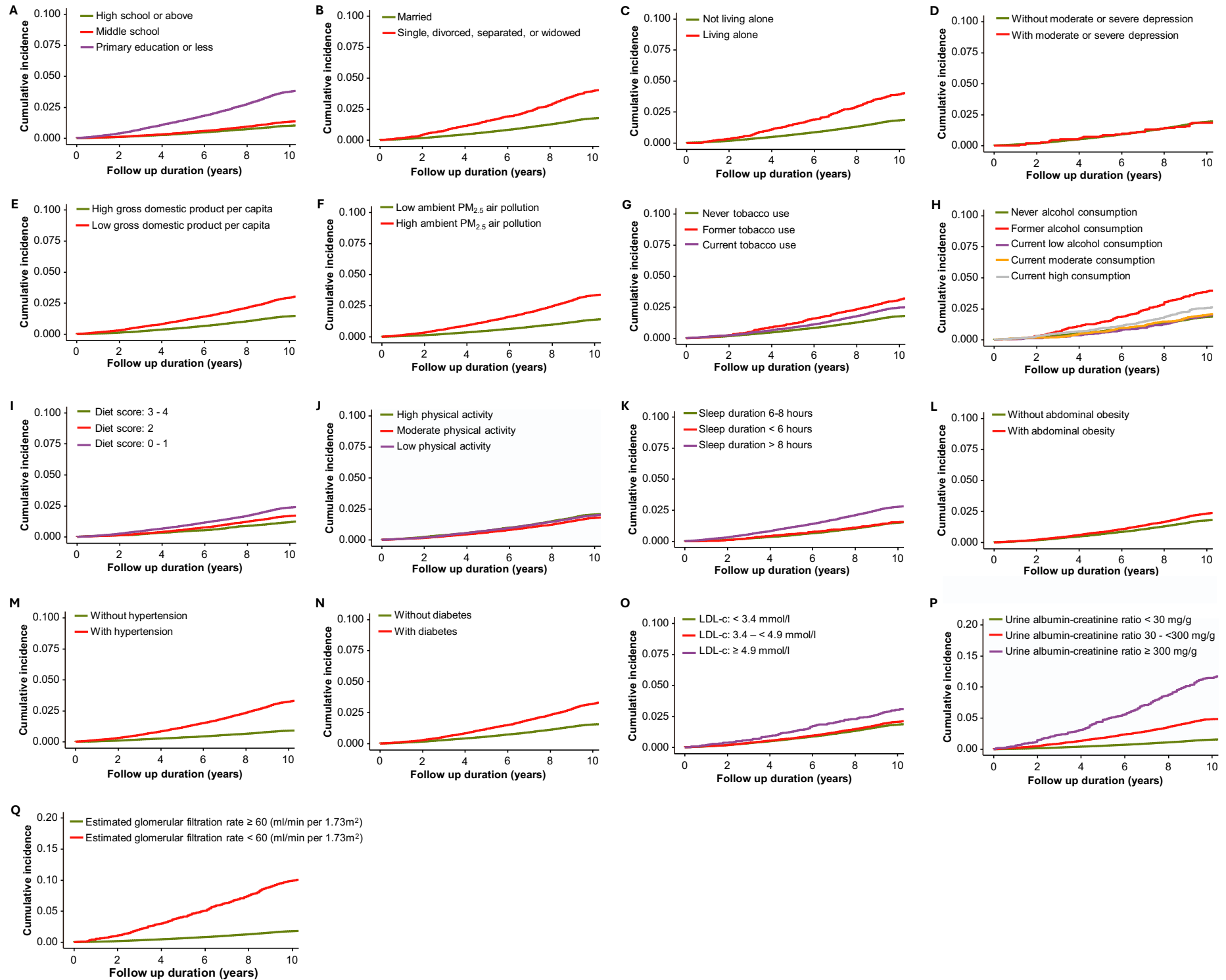
Figure S2. Cumulative incidence of all-cause mortality with each risk factor using Kaplan-Meier analysis, related to Table 2.

A, educational attainment; B, marital status; C, living status; D, depression status; E, gross domestic product per capita; F, ambient PM2.5 air pollution; G, tobacco use; H, alcohol consumption; I, diet score; J, physical activity; K, sleep duration; L, abdominal obesity; M, hypertension; N, diabetes; O, low-density lipoprotein cholesterol; P, urine albumin-creatinine ratio; Q, estimated glomerular filtration rate
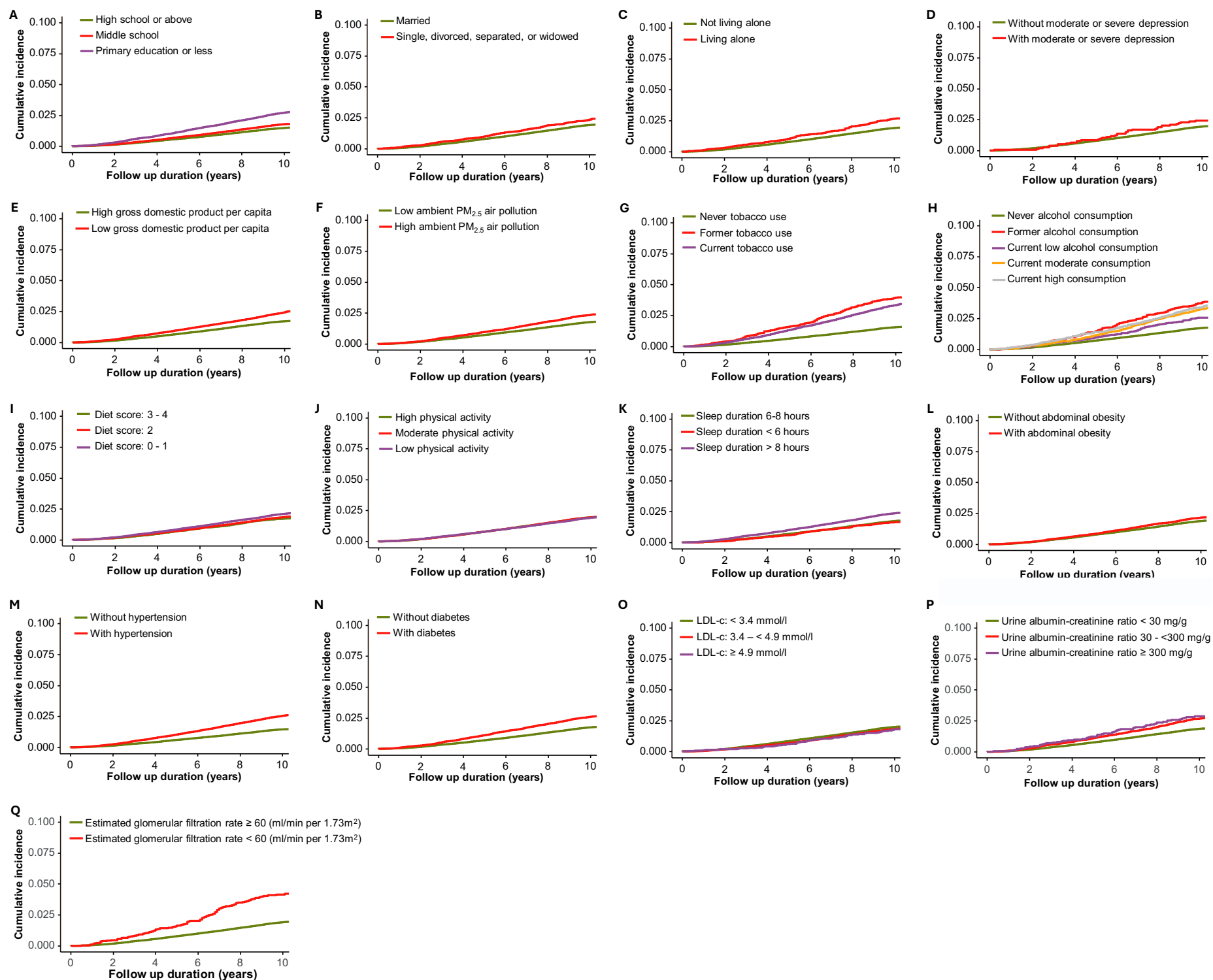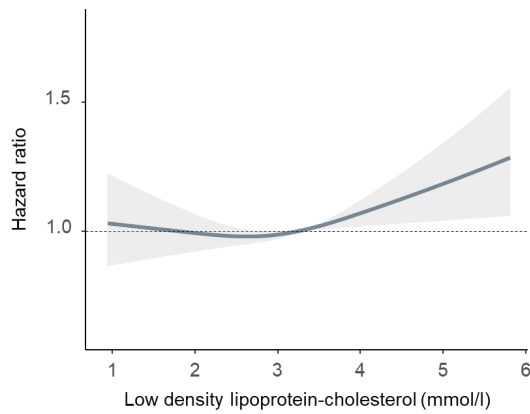
Figure S3. Cumulative incidence of cardiovascular mortality with each risk factor using Kaplan-Meier analysis, related to Table 3.
A, educational attainment; B, marital status; C, living status; D, depression status; E, gross domestic product per capita; F, ambient PM2.5 air pollution; G, tobacco use; H, alcohol consumption; I, diet score; J, physical activity; K, sleep duration; L, abdominal obesity; M, hypertension; N, diabetes; O, low-density lipoprotein cholesterol; P, urine albumin-creatinine ratio; Q, estimated glomerular filtration rate

Figure S4. Cumulative incidence of cancer mortality with each risk factor using Kaplan-Meier analysis, related to Table 4.
A, educational attainment; B, marital status; C, living status; D, depression status; E, gross domestic product per capita; F, ambient PM2.5 air pollution; G, tobacco use; H, alcohol consumption; I, diet score; J, physical activity; K, sleep duration; L, abdominal obesity; M, hypertension; N, diabetes; O, low-density lipoprotein cholesterol; P, urine albumin-creatinine ratio; Q, estimated glomerular filtration rate
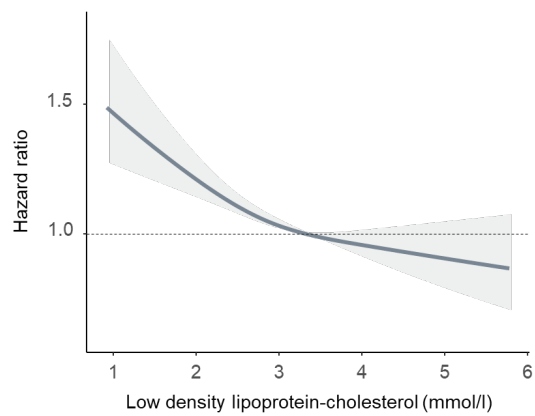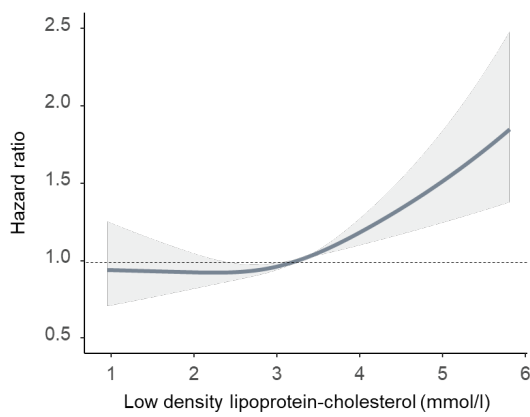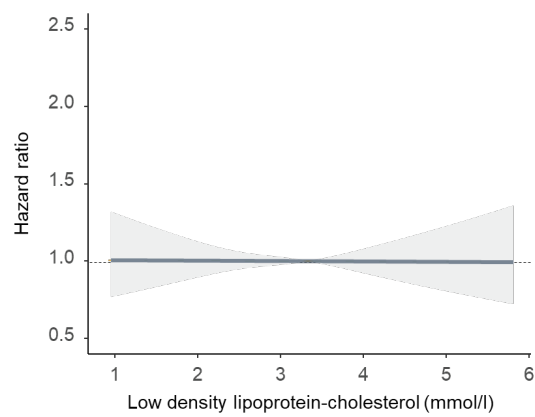
Figure S5. Multivariable-adjusted hazard ratios for cause-specific mortalities according to levels of low-density lipoprotein cholesterol on a continuous scale, related to Table 2-4.

Solid lines are multivariable adjusted hazard ratios, with shade showing 95% confidence intervals derived from restricted cubic spline regressions plotted with a reference value of 3.4 mmol/l for LDL-c using 3 knots at 5th, 50th, and 95th percentiles. Model was adjusted for age, sex, region and other individual risk factors. The highest and lowest 0.5% values of low-density lipoprotein cholesterol were trimmed.
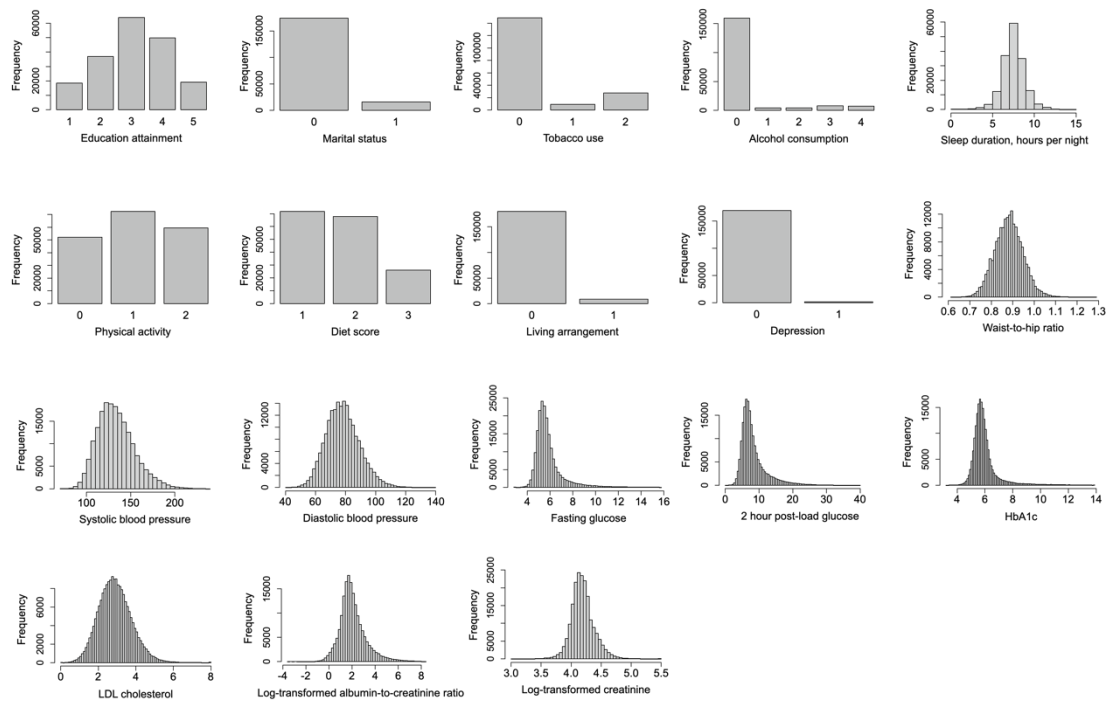
Figure S6. Distributions of variables used as predictors in multiple imputation, related to STAR Methods.
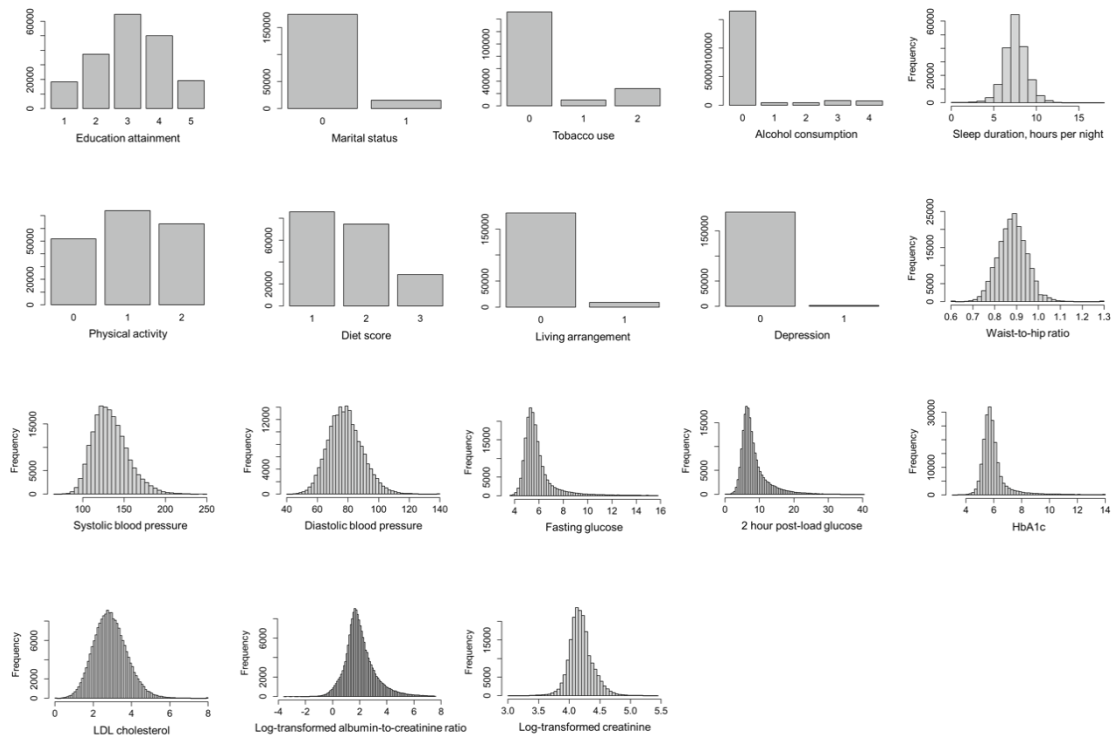
Figure S7. Distributions of predictors after multiple imputations, showing the first imputed data set, related to STAR Methods.

Table S1. Multivariable-adjusted hazard ratios and 95% CIs for ischemic heart disease mortality in overall population and by gender using competing risk regression model, related to Table 3

	Overall		Women		Men		P interaction of women and men
	Case/N (%)	HR (95%CI)	Case/N (%)	HR (95%CI)	Case/N (%)	HR (95%CI)	
Social determinants							
Educational attainment							<.0001
High school or above	230/63519 (0.4)	1.00 (Reference)	51/38384 (0.1)	1.00 (Reference)	179/25135 (0.7)	1.00 (Reference)	
Middle school	271/59786 (0.5)	1.02 (0.84-1.23)	106/37742 (0.3)	1.53 (1.07-2.20)	164/22044 (0.8)	0.88 (0.70-1.10)	
Primary school or less	746/50699 (1.5)	1.43 (1.20-1.70)	478/37311 (1.3)	2.19 (1.57-3.05)	268/13388 (2.0)	1.16 (0.93-1.45)	
Marital status							0.508
Married	1042/160298 (0.7)	1.00 (Reference)	494/102038 (0.5)	1.00 (Reference)	549/58260 (0.9)	1.00 (Reference)	
Single, divorced, separated, or widowed	205/13706 (1.5)	1.11 (0.92-1.33)	142/11399 (1.3)	0.99 (0.79-1.24)	62/2307 (2.7)	1.32 (0.94-1.85)	
Living alone							0.595
No	1133/166267 (0.7)	1.00 (Reference)	563/107628 (0.5)	1.00 (Reference)	570/58639 (1.0)	1.00 (Reference)	
Yes	114/7737 (1.5)	1.14 (0.91-1.43)	73/5809 (1.3)	1.07 (0.81-1.41)	41/1928 (2.1)	1.22 (0.82-1.79)	
Moderate or severe depression							0.305
No	1237/172458 (0.7)	1.00 (Reference)	629/112266 (0.6)	1.00 (Reference)	609/60192 (1.0)	1.00 (Reference)	
Yes	10/1546 (0.6)	1.10 (0.56-2.19)	7/1171 (0.6)	1.54 (0.71-3.35)	2/375 (0.6)	0.55 (0.13-2.30)	
Gross domestic product per capita (yuan)*							0.008
≥ 36,262	584/117187 (0.5)	1.00 (Reference)	279/76795 (0.4)	1.00 (Reference)	305/40392 (0.8)	1.00 (Reference)	
< 36,262	663/56817 (1.2)	1.27 (1.10-1.46)	357/36642 (1.0)	1.43 (1.18-1.73)	306/20175 (1.5)	1.14 (0.93-1.38)	
Ambient PM$_{2.5}$ air pollution (μg/m^3) *							0.742
< 59.11	519/124871 (0.4)	1.00 (Reference)	262/81659 (0.3)	1.00 (Reference)	257/43212 (0.6)	1.00 (Reference)	
≥ 59.11	728/49133 (1.5)	2.37 (2.09-2.70)	374/31778 (1.2)	2.13 (1.78-2.55)	354/17355 (2.0)	2.59 (2.16-3.11)	
Lifestyle Risk Factors							
Tobacco use							0.940
Never	915/139201 (0.7)	1.00 (Reference)	614/111225 (0.6)	1.00 (Reference)	301/27976 (1.1)	1.00 (Reference)	
Former	92/8192 (1.1)	1.15 (0.90-1.47)	8/495 (1.5)	1.42 (0.65-3.09)	84/7697 (1.1)	1.09 (0.84-1.41)	
Current	240/26611 (0.9)	1.31 (1.10-1.57)	14/1717 (0.8)	1.20 (0.70-2.06)	225/24894 (0.9)	1.29 (1.07-1.56)	
Alcohol consumption							0.344
Never	1051/150967 (0.7)	1.00 (Reference)	618/110977 (0.6)	1.00 (Reference)	433/39990 (1.1)	1.00 (Reference)	
Former	60/3832 (1.6)	1.36 (1.01-1.83)	6/484 (1.2)	1.57 (0.64-3.90)	54/3348 (1.6)	1.34 (0.99-1.82)	
Current: low	25/4223 (0.6)	0.63 (0.42-0.96)	7/1026 (0.6)	1.09 (0.48-2.47)	19/3197 (0.6)	0.54 (0.34-0.88)	
Current: moderate	51/7718 (0.7)	0.65 (0.48-0.89)	2/455 (0.6)	0.74 (0.19-2.91)	49/7263 (0.7)	0.64 (0.47-0.88)	
Current: high	60/7264 (0.8)	0.82 (0.61-1.09)	3/495 (0.7)	0.88 (0.29-2.66)	56/6769 (0.8)	0.83 (0.62-1.13)	
Diet score							0.781
3 - 4	110/26744 (0.4)	1.00 (Reference)	53/17060 (0.3)	1.00 (Reference)	57/9684 (0.6)	1.00 (Reference)	
2	392/68396 (0.6)	1.16 (0.93-1.46)	200/44931 (0.4)	1.10 (0.80-1.52)	192/23465 (0.8)	1.22 (0.87-1.70)	
0 - 1	745/78864 (1.0)	1.45 (1.17-1.81)	383/51446 (0.8)	1.29 (0.94-1.76)	362/27418 (1.3)	1.63 (1.21-2.19)	
Physical activity							0.498
High	370/47177 (0.8)	1.00 (Reference)	173/30718 (0.6)	1.00 (Reference)	197/16459 (1.2)	1.00 (Reference)	
Moderate	403/67064 (0.6)	0.84 (0.72-0.97)	216/44346 (0.5)	0.92 (0.74-1.13)	187/22718 (0.8)	0.76 (0.62-0.94)	
Low	474/59763 (0.8)	1.01 (0.87-1.17)	248/38373 (0.7)	1.03 (0.83-1.27)	227/21390 (1.1)	0.99 (0.81-1.22)	
Sleep duration (hours per night)							0.057
6 - 8	573/105943 (0.5)	1.00 (Reference)	277/69424 (0.4)	1.00 (Reference)	297/36519 (0.8)	1.00 (Reference)	
< 6	45/8945 (0.5)	0.79 (0.52-1.19)	23/5785 (0.4)	0.78 (0.45-1.35)	22/3160 (0.7)	0.80 (0.46-1.38)	
> 8	629/59116 (1.1)	1.14 (0.99-1.32)	336/38228 (0.9)	1.17 (0.97-1.40)	292/20888 (1.4)	1.12 (0.91-1.38)	
Metabolic Risk Factors							
Abdominal obesity							0.085
No	835/126976 (0.7)	1.00 (Reference)	376/78811 (0.5)	1.00 (Reference)	459/48165 (1.0)	1.00 (Reference)	
Yes	412/47028 (0.9)	1.05 (0.92-1.20)	260/34626 (0.8)	0.94 (0.79-1.11)	152/12402 (1.2)	1.18 (0.97-1.44)	
Hypertension							0.006
No	346/97980 (0.4)	1.00 (Reference)	156/66968 (0.2)	1.00 (Reference)	190/31012 (0.6)	1.00 (Reference)	
Yes	901/76024 (1.2)	1.46 (1.28-1.67)	480/46469 (1.0)	1.62 (1.32-1.97)	421/29555 (1.4)	1.30 (1.08-1.56)	
Diabetes							0.816
No	760/133871 (0.6)	1.00 (Reference)	385/88907 (0.4)	1.00 (Reference)	375/44964 (0.8)	1.00 (Reference)	
Yes	487/40133 (1.2)	1.40 (1.24-1.58)	251/24530 (1.0)	1.39 (1.17-1.64)	236/15603 (1.5)	1.39 (1.17-1.66)	
Low-density lipoprotein cholesterol (mmol/l)							0.353
< 3.4	842/127247 (0.7)	1.00 (Reference)	402/80717 (0.5)	1.00 (Reference)	440/46530 (0.9)	1.00 (Reference)	
3.4 - <4.9	362/43490 (0.8)	1.19 (1.05-1.35)	209/30230 (0.7)	1.19 (1.01-1.42)	153/13260 (1.2)	1.19 (0.98-1.44)	
≥4.9	43/3267 (1.3)	1.81 (1.32-2.48)	25/2490 (1.0)	1.50 (1.00-2.26)	18/777 (2.3)	2.52 (1.55-4.09)	
Urine albumin-creatinine ratio (mg/g)							0.045
< 30	826/155501 (0.5)	1.00 (Reference)	382/100742 (0.4)	1.00 (Reference)	444/54759 (0.8)	1.00 (Reference)	
30 - <300	322/16320 (2.0)	1.87 (1.62-2.15)	198/11288 (1.8)	2.00 (1.65-2.42)	124/5032 (2.5)	1.67 (1.34-2.08)	
≥ 300	99/2183 (4.5)	3.23 (2.55-4.08)	56/1407 (4.0)	3.32 (2.43-4.54)	43/776 (5.5)	3.05 (2.12-4.37)	
Estimated glomerular filtration rate < 60 (ml/min per 1.73m^2)							0.834
No	1125/170897 (0.7)	1.00 (Reference)	577/111600 (0.5)	1.00 (Reference)	549/59297 (0.9)	1.00 (Reference)	
Yes	122/3107 (3.9)	1.45 (1.17-1.79)	59/1837 (3.2)	1.38 (1.03-1.86)	62/1270 (4.9)	1.54 (1.14-2.08)	

For the 15 individual-level risk factors (excluding gross domestic product per capita and ambient PM$_{2.5}$ air pollution), each model was adjusted for age, sex, region (urban or rural), and all other individual-level risk factors. For the two community-level risk factors of gross domestic product per capita and ambient PM$_{2.5}$ air pollution, a separate model was employed with adjustment for age, sex, region (urban or rural) and the remaining 15 individual-level risk factors.

Table S2. Multivariable-adjusted hazard ratios and 95% CIs for stroke mortality in overall population and by gender using competing risk regression model, related to Table 3

	Overall		Women		Men		P interaction of women and men
	Case/N (%)	HR (95%CI)	Case/N (%)	HR (95%CI)	Case/N (%)	HR (95%CI)	
Social determinants							
Educational attainment							0.330
High school or above	239/63519 (0.4)	1.00 (Reference)	76/38384 (0.2)	1.00 (Reference)	163/25135 (0.7)	1.00 (Reference)	
Middle school	345/59786 (0.6)	1.28 (1.08-1.52)	127/37742 (0.3)	1.26 (0.94-1.68)	218/22044 (1.0)	1.31 (1.06-1.62)	
Primary school or less	771/50699 (1.5)	1.69 (1.43-2.00)	445/37311 (1.2)	1.67 (1.27-2.19)	326/13388 (2.4)	1.70 (1.36-2.11)	
Marital status							0.239
Married	1159/160298 (0.7)	1.00 (Reference)	518/102038 (0.5)	1.00 (Reference)	641/58260 (1.1)	1.00 (Reference)	
Single, divorced, separated, or widowed	196/13706 (1.4)	1.08 (0.90-1.30)	130/11399 (1.1)	0.99 (0.79-1.23)	66/2307 (2.9)	1.25 (0.89-1.76)	
Living alone							0.291
No	1246/166267 (0.8)	1.00 (Reference)	584/107628 (0.5)	1.00 (Reference)	662/58639 (1.1)	1.00 (Reference)	
Yes	109/7737 (1.4)	1.11 (0.88-1.39)	64/5809 (1.1)	1.01 (0.76-1.35)	45/1928 (2.4)	1.20 (0.80-1.79)	
Moderate or severe depression							0.308
No	1345/172458 (0.8)	1.00 (Reference)	644/112266 (0.6)	1.00 (Reference)	701/60192 (1.2)	1.00 (Reference)	
Yes	10/1546 (0.7)	1.12 (0.55-2.27)	4/1171 (0.4)	0.84 (0.31-2.26)	6/375 (1.5)	1.49 (0.58-3.83)	
Gross domestic product per capita (yuan)*							0.277
≥ 36,262	708/117187 (0.6)	1.00 (Reference)	336/76795 (0.4)	1.00 (Reference)	372/40392 (0.9)	1.00 (Reference)	
< 36,262	647/56817 (1.1)	1.29 (1.14-1.46)	312/36642 (0.9)	1.34 (1.13-1.59)	335/20175 (1.7)	1.25 (1.05-1.50)	
Ambient $PM_{2.5}$ air pollution ($\mu g/m^3$) *							0.455
< 59.11	746/124871 (0.6)	1.00 (Reference)	353/81659 (0.4)	1.00 (Reference)	393/43212 (0.9)	1.00 (Reference)	
≥ 59.11	609/49133 (1.2)	1.34 (1.19-1.52)	295/31778 (0.9)	1.32 (1.11-1.56)	314/17355 (1.8)	1.36 (1.14-1.62)	
Lifestyle Risk Factors							
Tobacco use							0.037
Never	1004/139201 (0.7)	1.00 (Reference)	624/111225 (0.6)	1.00 (Reference)	380/27976 (1.4)	1.00 (Reference)	
Former	90/8192 (1.1)	0.86 (0.68-1.09)	5/495 (1.1)	1.10 (0.46-2.62)	85/7697 (1.1)	0.81 (0.63-1.03)	
Current	261/26611 (1.0)	1.04 (0.88-1.24)	19/1717 (1.1)	1.67 (1.04-2.68)	242/24894 (1.0)	0.96 (0.80-1.15)	
Alcohol consumption							0.533
Never	1100/150967 (0.7)	1.00 (Reference)	633/110977 (0.6)	1.00 (Reference)	467/39990 (1.2)	1.00 (Reference)	
Former	57/3832 (1.5)	1.28 (0.96-1.70)	2/484 (0.3)	0.43 (0.06-2.88)	56/3348 (1.7)	1.37 (1.03-1.83)	
Current: low	32/4223 (0.8)	0.78 (0.54-1.14)	4/1026 (0.4)	0.71 (0.27-1.87)	27/3197 (0.9)	0.81 (0.54-1.21)	
Current: moderate	73/7718 (0.9)	0.90 (0.69-1.17)	2/455 (0.5)	0.71 (0.18-2.84)	70/7263 (1.0)	0.92 (0.70-1.21)	
Current: high	93/7264 (1.3)	1.20 (0.94-1.53)	7/495 (1.4)	1.86 (0.86-3.99)	86/6769 (1.3)	1.20 (0.93-1.55)	
Diet score							0.702
3 - 4	123/26744 (0.5)	1.00 (Reference)	54/17060 (0.3)	1.00 (Reference)	69/9684 (0.7)	1.00 (Reference)	
2	457/68396 (0.7)	1.23 (0.99-1.52)	224/44931 (0.5)	1.26 (0.91-1.73)	234/23465 (1.0)	1.20 (0.90-1.60)	
0 - 1	775/78864 (1.0)	1.40 (1.14-1.71)	370/51446 (0.7)	1.36 (1.00-1.84)	404/27418 (1.5)	1.44 (1.08-1.91)	
Physical activity							0.255
High	369/47177 (0.8)	1.00 (Reference)	172/30718 (0.6)	1.00 (Reference)	196/16459 (1.2)	1.00 (Reference)	
Moderate	478/67064 (0.7)	1.01 (0.88-1.16)	241/44346 (0.5)	1.01 (0.83-1.24)	236/22718 (1.0)	1.00 (0.82-1.22)	
Low	508/59763 (0.9)	1.12 (0.96-1.30)	234/38373 (0.6)	1.02 (0.82-1.26)	274/21390 (1.3)	1.21 (0.99-1.49)	
Sleep duration (hours per night)							0.563
6 - 8	623/105943 (0.6)	1.00 (Reference)	296/69424 (0.4)	1.00 (Reference)	327/36519 (0.9)	1.00 (Reference)	
< 6	50/8945 (0.6)	0.78 (0.55-1.11)	22/5785 (0.4)	0.69 (0.39-1.20)	28/3160 (0.9)	0.87 (0.56-1.35)	
> 8	682/59116 (1.2)	1.24 (1.09-1.40)	330/38228 (0.9)	1.23 (1.03-1.47)	352/20888 (1.7)	1.24 (1.05-1.46)	
Metabolic Risk Factors							
Abdominal obesity							0.706
No	919/126977 (0.7)	1.00 (Reference)	369/78811 (0.5)	1.00 (Reference)	550/48165 (1.1)	1.00 (Reference)	
Yes	436/47027 (0.9)	1.04 (0.92-1.17)	279/34626 (0.8)	1.05 (0.89-1.24)	157/12402 (1.3)	1.00 (0.83-1.20)	
Hypertension							0.152
No	333/97980 (0.3)	1.00 (Reference)	152/66968 (0.2)	1.00 (Reference)	180/31012 (0.6)	1.00 (Reference)	
Yes	1022/76024 (1.3)	1.93 (1.69-2.21)	496/46469 (1.1)	2.02 (1.65-2.46)	527/29555 (1.8)	1.84 (1.53-2.21)	
Diabetes							0.758
No	821/133871 (0.6)	1.00 (Reference)	384/88907 (0.4)	1.00 (Reference)	437/44964 (1.0)	1.00 (Reference)	
Yes	534/40133 (1.3)	1.47 (1.31-1.65)	264/24530 (1.1)	1.48 (1.25-1.75)	270/15603 (1.7)	1.46 (1.24-1.71)	
Low-density lipoprotein cholesterol (mmol/l)							0.644
< 3.4	984/127247 (0.8)	1.00 (Reference)	440/80717 (0.5)	1.00 (Reference)	545/46530 (1.2)	1.00 (Reference)	
3.4 - <4.9	335/43490 (0.8)	0.94 (0.82-1.06)	188/30230 (0.6)	0.95 (0.80-1.13)	146/13260 (1.1)	0.91 (0.76-1.10)	
≥ 4.9	36/3267 (1.1)	1.30 (0.93-1.82)	20/2490 (0.8)	1.04 (0.67-1.63)	16/777 (2.1)	1.87 (1.12-3.13)	
Urine albumin-creatinine ratio (mg/g)							0.056
< 30	972/155501 (0.6)	1.00 (Reference)	426/100742 (0.4)	1.00 (Reference)	546/54759 (1.0)	1.00 (Reference)	
30 - <300	301/16320 (1.8)	1.51 (1.31-1.73)	177/11288 (1.6)	1.69 (1.39-2.06)	124/5032 (2.5)	1.30 (1.05-1.60)	
≥ 300	82/2183 (3.8)	2.34 (1.82-3.01)	45/1407 (3.2)	2.50 (1.77-3.51)	37/776 (4.8)	2.16 (1.48-3.15)	
Estimated glomerular filtration rate < 60 (ml/min per $1.73m^2$)							0.973
No	1247/170897 (0.7)	1.00 (Reference)	599/111600 (0.5)	1.00 (Reference)	648/59297 (1.1)	1.00 (Reference)	
Yes	108/3107 (3.5)	1.33 (1.07-1.65)	49/1837 (2.7)	1.26 (0.92-1.72)	59/1270 (4.7)	1.41 (1.05-1.90)	

For the 15 individual-level risk factors (excluding gross domestic product per capita and ambient $PM_{2.5}$ air pollution), each model was adjusted for age, sex, region (urban or rural), and all other individual-level risk factors. For the two community-level risk factors of gross domestic product per capita and ambient $PM_{2.5}$ air pollution, a separate model was employed with adjustment for age, sex, region (urban or rural) and the remaining 15 individual-level risk factors.

Table S3. Population attributable fractions for all-cause and cause-specific mortalities associated with low gross domestic product per capita and high ambient PM$_{2.5}$ air pollution, related to Figure 1-3.

	All-cause mortality	Cardiovascular mortality	Ischemic heart disease mortality	Stroke mortality	Cancer mortality
Total population					
Low gross domestic product per capita	7.8% (6.1% - 9.7%)	13.3% (10.3% - 16.4%)	8.9% (3.8% - 14.1%)	9.2% (4.7% - 14.1%)	8.7% (5.8% - 11.6%)
High ambient PM$_{2.5}$ air pollution	4.3% (3.0% - 5.8%)	13.4% (10.8% - 16.1%)	28.3% (23.7% - 32.9%)	9.7% (5.6% - 13.6%)	2.2% (0.0% - 4.6%)
Women					
Low gross domestic product per capita	8.3% (5.8% - 10.9%)	16.2% (11.9% - 20.7%)	13.2% (6.1% - 20.5%)	10.4% (3.7% - 17.6%)	6.4% (2.2% - 10.7%)
High ambient PM$_{2.5}$ air pollution	3.5% (1.4% - 5.6%)	11.4% (7.7% - 15.2%)	24.5% (17.9% - 31.2%)	8.9% (3.3% - 14.8%)	-0.6% (-3.8% - 3.0%)
Men					
Low gross domestic product per capita	7.7% (5.1% - 10.2%)	10.2% (6.2% - 14.8%)	5.1% (-2.0% - 12.3%)	8.2% (1.6% - 15.0%)	10.7% (6.8% - 14.8%)
High ambient PM$_{2.5}$ air pollution	5.2% (3.1% - 7.2%)	15.3% (11.4% - 19.1%)	31.7% (25.1% - 38.3%)	10.3% (4.7% - 16.1%)	4.7% (1.4% - 7.9%)

Notes: The PAFs were calculated using the aforementioned formula: PAF = p(HR-1) / (1+ p(HR-1)), where p is the population prevalence of the risk factor.

Table S4. Multivariable-adjusted hazard ratios and 95% confidence intervals of alcohol consumption with all-cause and cause-specific mortalities, related to Table 2-4.

Alcohol consumption category	All-cause mortality	Cardiovascular mortality	Ischemic heart disease mortality	Stroke mortality	Cancer mortality
Never	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Former	1.16 (1.04 – 1.30)	1.25 (1.04 – 1.50)	1.34 (1.00 – 1.79)	1.27 (0.95 – 1.70)	1.11 (0.92 – 1.34)
Current: low	0.85 (0.74 – 0.96)	0.76 (0.61 – 0.96)	0.62 (0.41 – 0.93)	0.77 (0.53 – 1.11)	0.94 (0.77 – 1.15)
Current: moderate	0.87 (0.79 – 0.96)	0.72 (0.61 – 0.86)	0.65 (0.48 – 0.88)	0.89 (0.69 – 1.16)	1.07 (0.93 – 1.23)
Current: high but not binge drinking*	0.97 (0.86 – 1.10)	0.91 (0.73 – 1.13)	0.73 (0.50 – 1.06)	1.14 (0.85 – 1.54)	1.06 (0.88 – 1.28)
Current: high and binge drinking at least once a year*	1.21 (1.06 – 1.39)	1.09 (0.86 – 1.39)	0.96 (0.63 – 1.46)	1.32 (0.93 – 1.87)	1.40 (1.15 – 1.71)

Notes: *At the baseline of our cohort, we had asked the participants "How many times have you experienced binge drinking in the past year?" Based on their responses to this item, we further categorized the subjects with current high alcohol consumption into two groups: current: high and not experiencing binge drinking, and current: high and experiencing binge drinking at least once a year.

Table S5. Summary of Risk Factors: Definitions, Measurement Methods, and Categorizations for the Calculation of Population Attributable Fractions (PAFs), related to STAR Methods

Risk Factor	Measurement and definition	Risk category	Reference category
Social determinants			
Individual Level			
Educational attainment	Education was self-reported, and classified into three groups: primary school or less, middle school education, or high school or above).	Low educational attainment (primary school or less, middle school education)	High school or above
Marital status	Marital status was self-reported and categorized as married or having a partner; single, divorced, separated, or widowed.	Single, divorced, separated, or widowed	Married or having a partner
Living arrangements	Living arrangements were self-reported and categorized as living with children and/or a spouse; or living alone.	Living alone	Living with children and/or a spouse
Depression	Depression was assessed with the self-reported Patient Health Questionnaire 9 (PHQ-9). The PHQ-9 consists of nine items based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). Participants were asked how often they had been bothered by nine psychiatric symptoms over the past 2 weeks. Each of the nine items is scored as 0, 1, 2, or 3, which represents symptom severity of 'not at all', 'several days', 'more than half the days', or 'nearly every day', respectively. The nine items are summed to give the PHQ-9 total score. A score of ≥10 represents moderate or severe depression.[1]	Moderate or severe depression (PHQ-9 score ≥10)	PHQ-9 score< 10
Community level			
Gross domestic product per capita	Gross domestic product per capita was retrieved from the Statistical Report on the National Economy and Social Development for each city in 2011. Participants were categorized into two groups using a cut-off value equal to the average gross domestic product per capita in China in 2011 (5614.4 US$, 36,262 Chinese Yuan [CNY]) according to World Bank data.[2]	Low gross domestic product per capita (< 5614.4 US$)	≥ 5614.4 US$
Ambient fine particulate matter ($PM_{2.5}$) air pollution	Data on the annual average residential $PM_{2.5}$ exposure in 2011 for each city were collected from the Global Annual $PM_{2.5}$ Grids,[3] which combines AOD retrievals from multiple satellite algorithms including the NASA MODerate resolution Imaging Spectroradiometer Collection 6.1 (MODIS C6.1), Multi-angle Imaging SpectroRadiometer Version 23 (MISRv23), MODIS Multi-Angle Implementation of Atmospheric Correction Collection 6 (MAIAC C6), and the Sea-Viewing Wide Field-of-View Sensor (SeaWiFS) Deep Blue Version 4. Participants were categorized into two groups using a cut-off value equal to the upper quartile of $PM_{2.5}$ levels in our study (59.11 μg/m^3) according to World Health Organization [WHO] data).[4]	High $PM_{2.5}$ (> 59.11 μg/m^3)	≤ 59.11 μg/m^3
Lifestyle factors			
Tobacco use	Self-reported tobacco use using a standard tobacco use frequency questionnaire, categorized as never, former, or current. Never: never smoked or had not smoked cigarettes regularly (<100 cigarettes in a lifetime). Former: not currently smoking cigarettes but had smoked at least 7 cigarettes/week for at least 6 months in a lifetime. Current: smoke every day or almost every day, with at least 7 cigarettes/week for at least 6 months.	Current or former tobacco use	Never tobacco use
Alcohol consumption	Self-reported alcohol consumption using a standard alcohol consumption frequency questionnaire, categorized as never, former, or current. Never: never consumed alcohol. Former: not currently but had consumed alcohol once per week regularly for at least 6 months in a lifetime. Current: consumed alcohol once per week regularly during the past 6 months. Current drinkers' alcohol consumption was further classified as low (≤ 7 drinks/week), moderate (8-21 drinks/week for men and 8-14 drinks/week for women), or high (> 21 drinks/week for men and > 14 drinks/week for women).	Heavy alcohol consumption (Former, or high current consumption)	Never, or low or moderate current consumption
Diet score	Diet score was calculated according to recommendations from the American Heart Association, though whole grain consumption was replaced with bean consumption.[5,6] It was calculated as the sum of each of the following components: fruits and vegetables ≥ 4.5 cups/day (1 point); fish ≥ 198 g/week (1 point); sweets/sugar-sweetened beverages ≤ 450 kcal/week (1 point); and soy protein ≥ 25 g/day (1 point). Diet score was categorized into poor (0-1), intermediate (2), or healthy (3-4).	Unhealthy diet (Diet score: 0-2)	Diet score: 3-4
Physical activity	Physical activity was evaluated using the International Physical Activity Questionnaire,[7] and categorized as low (< 600 metabolic equivalents [MET] × minutes per week or < 150 minutes per week of moderate intensity physical activity), moderate (600-3,000 MET × minutes or 150-750 minutes per week) or high (> 3000 MET × minutes or > 750 minutes per week).[8,9]	Low physical activity	Moderate or high physical activity
Sleep duration	Sleep duration was self-reported with standardized questions and defined as the interval between evening bedtime and morning wake-up time. It was categorized into three groups (<6 hours/night, 6-8 hours/night, and > 8 hours/night).[10-12]	Long sleep duration (> 8 hours/night)	Sleep duration ≤ 8 hours/night
Metabolic risk factors			
Abdominal obesity	Waist and hip circumference were measured and used to calculate the waist-to-hip ratio (WHR). Abdominal obesity was defined as WHR ≥ 0.95 for men and ≥ 0.90 for women.[13]	Abdominal obesity (WHR ≥ 0.95 in men and ≥ 0.90 in women)	WHR < 0.95 in men and < 0.90 in women
Hypertension	Three blood pressure measurements were obtained with participants in a seated position after five minutes of quiet rest using an automated electronic device (OMRON Model HEM-752 FUZZY, Dalian, China). Hypertension was defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg using the mean of three readings; or treatment with antihypertensive medications.	Definition of hypertension met	Definition of hypertension not met
Diabetes	Fasting and 2-hour postload glucose levels were measured using a glucose oxidase or hexokinase method. Hemoglobin A1c was measured using high-performance liquid chromatography (VARIANT II System, Bio-Rad Laboratories, CA, USA). Diabetes was defined as fasting glucose ≥7.0 mmol/L or 2-hour postload glucose ≥ 11.1mmol/L; hemoglobin A1c ≥ 48 mmol/mol (6.5%); self-reported history of diabetes.[14]	Definition of diabetes met	Definition of diabetes not met
Low-density lipoprotein cholesterol (LDL-C)	Serum fasting LDL-C was measured using an auto-analyzer (ARCHITECT ci16200 analyzer, Abbott Laboratories, Illinois, USA). LDL-C divided into three subgroups: <3.4 mmol/L (<130 mg/dL), ≥3.4 and <4.9 mmol/L (130-190 mg/dL), and ≥4.9 mmol/L (≥190 mg/dL). [15-16]	High LDL-C (LDL-C ≥ 3.4 mmol/L [130 mg/dL])	LDL-C < 3.4 mmol/L (130 mg/dL)
Albuminuria	Urinary albumin concentration was measured by immunonephelometry using Siemens BNII and BN ProSpec nephelometers (Siemens Healthcare Diagnostics, Marburg, Germany). Urinary creatinine was determined by an enzymatic method (ADVIA Chemistry XPT System; Siemens Healthcare, Erlangen, Germany). Urine albumin-creatinine ratio was calculated. Albuminuria was defined as microalbuminuria (urine albumin-creatinine ratio: 30-299 mg/g) or macroalbuminuria (urine albumin-creatinine ratio ≥ 300 mg/g).[17]	Albuminuria (Urine albumin-creatinine ratio ≥ 30 mg/g)	Urine albumin-creatinine ratio < 30 mg/g
Low estimated glomerular filtration rate	Serum fasting creatinine was measured using an auto-analyzer (ARCHITECT ci16200 analyzer, Abbott Laboratories, Illinois, USA). Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease-Epidemiology Collaboration equation.[18]	Low estimated glomerular filtration rate (estimated glomerular filtration rate < 60 ml/min per 1.73m^2)	Estimated glomerular filtration rate ≥ 60 ml/min per 1.73m^2

Table S6. Spearman correlation coefficients across risk factors, related to STAR Methods

	RF1	RF2	RF3	RF4	RF5	RF6	RF7	RF8	RF9	RF10	RF11	RF12	RF13	RF14	RF15	RF16	RF17
								Spearman correlation coefficients									
RF1	1.00	0.32	-0.01	0.03	0.01	-0.06	0.02	0.02	-0.04	-0.01	<0.01	-0.02	-0.01	-0.06	-0.02	<0.01	-0.02
RF2	0.32	1.00	-0.01	0.03	0.01	-0.02	0.06	0.02	-0.02	0.01	<0.01	0.04	0.01	-0.03	-0.01	<0.01	<0.01
RF3	-0.01	-0.01	1.00	0.05	0.07	0.01	0.03	0.01	-0.01	0.04	0.01	-0.05	0.07	0.02	0.01	<0.01	0.11
RF4	0.03	0.03	0.05	1.00	0.11	-0.01	-0.02	-0.05	-0.03	0.02	-0.01	0.08	0.11	-0.03	-0.03	<0.01	-0.01
RF5	0.01	0.01	0.07	0.11	1.00	-0.01	0.05	-0.01	<0.01	0.07	0.02	0.09	0.16	-0.02	-0.01	-0.02	0.06
RF6	-0.06	-0.02	0.01	-0.01	-0.01	1.00	0.11	0.14	0.06	0.07	0.04	-0.01	0.07	0.05	0.02	0.01	0.02
RF7	0.02	0.06	0.03	-0.02	0.05	0.11	1.00	0.16	0.07	0.18	0.07	0.10	0.10	0.02	0.01	-0.01	0.07
RF8	0.02	0.02	0.01	-0.05	-0.01	0.14	0.16	1.00	0.06	0.12	0.06	<0.01	0.02	0.02	0.02	0.01	0.03
RF9	-0.04	-0.02	-0.01	-0.03	<0.01	0.06	0.07	0.06	1.00	0.03	0.02	0.03	-0.01	0.02	0.01	<0.01	0.07
RF10	-0.01	0.01	0.04	0.02	0.07	0.07	0.18	0.12	0.03	1.00	0.12	0.04	0.08	0.03	0.02	<0.01	0.06
RF11	<0.01	<0.01	0.01	-0.01	0.02	0.04	0.07	0.06	0.02	0.12	1.00	-0.02	0.02	0.04	0.02	<0.01	-0.03
RF12	-0.02	0.04	-0.05	0.08	0.09	-0.01	0.10	<0.01	0.03	0.04	-0.02	1.00	0.07	-0.04	-0.01	<0.01	0.28
RF13	-0.01	0.01	0.07	0.11	0.16	0.07	0.10	0.02	-0.01	0.08	0.02	0.07	1.00	0.03	0.01	-0.02	0.03
RF14	-0.06	-0.03	0.02	-0.03	-0.02	0.05	0.02	0.02	0.02	0.03	0.04	-0.04	0.03	1.00	0.50	0.03	-0.02
RF15	-0.02	-0.01	0.01	-0.03	-0.01	0.02	0.01	0.02	0.01	0.02	0.02	-0.01	0.01	0.50	1.00	0.04	-0.03
RF16	<0.01	<0.01	<0.01	<0.01	-0.02	0.01	-0.01	0.01	<0.01	<0.01	<0.01	<0.01	-0.02	0.03	0.04	1.00	-0.02
RF17	-0.02	<0.01	0.11	-0.01	0.06	0.02	0.07	0.03	0.07	0.06	-0.03	0.28	0.03	-0.02	-0.03	-0.02	1.00

Spearman correlation analysis is conducted based on 174,004 participants after imputation.

RF1 = Tobacco use; RF2 = Alcohol excess; RF3 = Unhealthy diet; RF4 = Low physical activity; RF5 = Long sleep duration; RF6 = Abdominal obesity; RF7 = Hypertension; RF8 = Diabetes; RF9 = High low-density lipoprotein cholesterol; RF10 = Albuminuria; RF11 = Low estimated glomerular filtration rate; RF12 = Low gross domestic product per capita; RF13 = Low education; RF14 = Single, divorced, separated, or widowed; RF15 = Living alone; RF16 = Depression; RF17 = High ambient $PM_{2.5}$ air pollution

Table S7. Multicollinearity diagnostics of all the risk factors, related to STAR Methods

	Eigen Value	Condition Index	Tolerance	Variance Inflation
RF1	1.43	2.09	0.89	1.13
RF2	1.15	2.33	0.89	1.12
RF3	1.06	2.42	0.97	1.03
RF4	0.99	2.51	0.97	1.04
RF5	0.86	2.70	0.95	1.05
RF6	0.81	2.78	0.96	1.04
RF7	0.78	2.83	0.92	1.09
RF8	0.69	3.01	0.94	1.06
RF9	0.64	3.12	0.98	1.02
RF10	0.59	3.26	0.94	1.07
RF11	0.58	3.28	0.98	1.02
RF12	0.52	3.48	0.89	1.12
RF13	0.49	3.55	0.94	1.06
RF14	0.45	3.71	0.74	1.35
RF15	0.40	3.95	0.75	1.34
RF16	0.26	4.92	1.00	1.00
RF17	0.07	9.56	0.90	1.11

Regression analysis is conducted based on 174,004 participants after imputation with all-cause mortality as dependent variables and 17 individual risk factors as independent variables.

RF1 = Tobacco use; RF2 = Alcohol excess; RF3 = Unhealthy diet; RF4 = Low physical activity; RF5 = Long sleep duration; RF6 = Abdominal obesity; RF7 = Hypertension; RF8 = Diabetes; RF9 = High low-density lipoprotein cholesterol; RF10 = Albuminuria; RF11 = Low estimated glomerular filtration rate; RF12 = Low gross domestic product per capita; RF13 = Low education; RF14 = Single, divorced, separated, or widowed; RF15 = Living alone; RF16 = Depression; RF17 = High ambient $PM_{2.5}$ air pollution

Table S8. ICD-10 Codes used in the 4C study for causes of death, related to STAR Methods

Causes of death	ICD-10 codes
Cardiovascular disease	I00-I99
Fatal ischemic heart disease	I20-I25
Fatal stroke	I60-I64, I69
Fatal congestive heart failure	I50
Other cardiovascular deaths	I00-I99 (not including I20-I25, I50, I60-I64, I69)
Cancer	C00-C97, D00-D09
Renal disease	N17-N19
Diabetes mellitus	E10-E14
Respiratory disease (exclude pneumonia)	J20-J99
Pneumonia	J12-J18
Other infectious disease	A00-A99, B00-B09, B20-B99
Liver disease	B15-B19, K70-K77
Alzheimer's and related conditions	F00-F03, G30-G32
Injury and external causes	S00-W99, X00-X59, X85-X99, Y00-Y09, Y85-Y86
Intentional self-harm	X60-X84, Y87.0
All other causes combined	

Table S9. Variables used in the imputation algorithm, related to STAR Methods

Demographic factors	age, sex, study center
Lifestyle factors	tobacco use, alcohol consumption, sleep duration, physical activity, and diet score
Social determinants factors	educational attainment, marital status, living arrangements, urban/rural region, depression, and $PM_{2.5}$ air pollution
Family medical history	family history of cancer, family history of diabetes, family history of coronary heart disease, and family history of stroke
Health status	previous diagnosis of diabetes, current oral antidiabetic medication use, current insulin treatment, history of cardiovascular disease, current antihypertensive medication use, current lipid-lowering medication use, history of cancer, and previous diagnosis of hypertension
Physical examination	body mass index, waist-to-hip ratio, systolic blood pressure, and diastolic blood pressure
Biochemical measures	fasting glucose, 2-hour post-load glucose, hemoglobin A1c, fasting insulin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, total cholesterol, alanine transaminase, aspartate transaminase, glutamyl-transpeptidase, urinary albumin-creatinine ratio, and creatinine
Outcome at follow-up	all-cause mortality, ischemic heart disease mortality, stroke mortality, cancer mortality and the time to death or the last follow-up.

References

1.   Kroenke, K., Spitzer, R.L., and Williams, J.B. (2001). The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 16, 606-613. 10.1046/j.1525-1497.2001.016009606.x.

2.   World Bank. (2011). GDP per capita (current US$) – China. https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=CN

3.   Hammer, M.S., van Donkelaar, A., Li, C., Lyapustin, A., Sayer, A.M., Hsu, N.C., Levy, R.C., Garay, M.J., Kalashnikova, O.V., Kahn, R.A., et al. (2022). Global Annual PM2.5 Grids from MODIS, MISR and SeaWiFS Aerosol Optical Depth (AOD), 1998-2019, V4.GL.03. (NASA Socioeconomic Data and Applications Center (SEDAC)).

4.   World Health Organization. (2023). SDG Indicator 11.6.2 Concentrations of fine particulate matter (PM2.5). https://www.who.int/data/gho/data/indicators/indicator-details/GHO/concentrations-of-fine-particulate-matter-(pm2-5).

5.   Lloyd-Jones, D.M., Hong, Y., Labarthe, D., Mozaffarian, D., Appel, L.J., Van Horn, L., Greenlund, K., Daniels, S., Nichol, G., Tomaselli, G.F., et al. (2010). Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation 121, 586-613. 10.1161/circulationaha.109.192703.

6.   Bi, Y., Jiang, Y., He, J., Xu, Y., Wang, L., Xu, M., Zhang, M., Li, Y., Wang, T., Dai, M., et al. (2015). Status of cardiovascular health in Chinese adults. J Am Coll Cardiol 65, 1013-1025. 10.1016/j.jacc.2014.12.044.

7.   Craig, C.L., Marshall, A.L., Sjöström, M., Bauman, A.E., Booth, M.L., Ainsworth, B.E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J.F., and Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35, 1381-1395. 10.1249/01.Mss.0000078924.61453.Fb.

8.   Yusuf, S., Joseph, P., Rangarajan, S., Islam, S., Mente, A., Hystad, P., Brauer, M., Kutty, V.R., Gupta, R., Wielgosz, A., et al. (2020). Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 395, 795-808. 10.1016/s0140-6736(19)32008-2.

9.   Lear, S.A., Hu, W., Rangarajan, S., Gasevic, D., Leong, D., Iqbal, R., Casanova, A., Swaminathan, S., Anjana, R.M., Kumar, R., et al. (2017). The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. Lancet 390, 2643-2654. 10.1016/s0140-6736(17)31634-3.

10.   Leng, Y., Cappuccio, F.P., Wainwright, N.W., Surtees, P.G., Luben, R., Brayne, C., and Khaw, K.T. (2015). Sleep duration and risk of fatal and nonfatal stroke: a prospective study and meta-analysis. Neurology 84, 1072-1079. 10.1212/wnl.0000000000001371.

11.   Song, Q., Liu, X., Zhou, W., Wang, L., Zheng, X., Wang, X., and Wu, S. (2016). Long Sleep Duration and Risk of Ischemic Stroke and Hemorrhagic Stroke: the Kailuan Prospective Study. Sci Rep 6, 33664. 10.1038/srep33664.

12.   Qureshi, A.I., Giles, W.H., Croft, J.B., and Bliwise, D.L. (1997). Habitual sleep patterns and risk for stroke and coronary heart disease: a 10-year follow-up from NHANES I. Neurology 48, 904-911. 10.1212/wnl.48.4.904.

13.   World Health Organization. (2011). Waist Circumference and Waist-hip Ratio. Report of a WHO expert consultation.

14.   2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. (2019).

Diabetes Care 42, S13-s28. 10.2337/dc19-S002.

15. Grundy, S.M., Stone, N.J., Bailey, A.L., Beam, C., Birtcher, K.K., Blumenthal, R.S., Braun, L.T., de Ferranti, S., Faiella-Tommasino, J., Forman, D.E., et al. (2019). 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 139, e1082-e1143. 10.1161/cir.0000000000000625.

16. Mach, F., Baigent, C., Catapano, A.L., Koskinas, K.C., Casula, M., Badimon, L., Chapman, M.J., De Backer, G.G., Delgado, V., Ference, B.A., et al. (2020). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J 41, 111-188. 10.1093/eurheartj/ehz455.

17. Xu, Y., Li, M., Qin, G., Lu, J., Yan, L., Xu, M., Wang, T., Zhao, Z., Dai, M., Zhang, D., et al. (2021). Cardiovascular Risk Based on ASCVD and KDIGO Categories in Chinese Adults: A Nationwide, Population-Based, Prospective Cohort Study. J Am Soc Nephrol 32, 927-937. 10.1681/asn.2020060856.

18. Levey, A.S., Stevens, L.A., Schmid, C.H., Zhang, Y.L., Castro, A.F., 3rd, Feldman, H.I., Kusek, J.W., Eggers, P., Van Lente, F., Greene, T., and Coresh, J. (2009). A new equation to estimate glomerular filtration rate. Ann Intern Med 150, 604-612. 10.7326/0003-4819-150-9-200905050-00006.