Supplemental Material

Data S1.

Supplemental Methods

Data collection and quality control

As described in the manuscript, the cohort was conducted in Sichuan province using a multistage stratified cluster sampling method to obtain community-based populations. In the first stage, geography, development state, and settlements were fully considered to achieve representation. In the second stage, with the cooperation of the local Centers for Disease Control and Prevention, communities with various migration, local health, and economic status were selected.

The baseline survey was comprised of three processes, including an electronic questionnaire with a face-to-face interview (sociodemographic, health behaviors, prior physician diagnosis of diseases, etc.), medical examinations (anthropometric measurements including weight, height, waist circumference, etc.), and clinical laboratory tests (fasting blood glucose, lipid levels, etc.). All the investigators and clinicians were systematically well-trained before the baseline survey. Moreover, the whole face-to-face interview was audio recorded to assess and correct the potential investigation bias during the survey.

Covariates

According to the minimally sufficient adjustment set from the DAG, the covariates in the manuscript are selected as follows:

Age (refers to age at baseline), sex (male and female), education (no formal school, primary school, middle school, high school, college and above), marital status (married or cohabitating, separated or divorced, widow, and unmarried), annual household income (<12000 yuan, 12000-19999 yuan, 20000-59999 yuan, 60000-99999 yuan, and ≥100000 yuan), urbanicity (rural and urban), family history of hypertension (yes and no), BMI, smoke (never, smoking and quitted), second-hand smoke (yes and no), alcohol (yes and no), indoor air pollution (yes and no), physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension (yes and no), and diabetes (yes and no).

Among the above covariates, some variables were not obtained directly from the questionnaire but were redefined by referring to the related former studies to integrate several questions. BMI was calculated as the weight (kg) divided by the square of the height (m). Alcohol was assessed based on the frequency of drinking and was subsequently classified as a binary variable. Indoor air pollution is evaluated after integrating cooking behavior (frequency of home cooking), fuel type (gas, coal, electricity, etc.), and ventilation equipment (fans, chimneys, etc.) and is redefined as binary. Based on a series of questions including type, mode, and duration of work, housework, leisure, and travel, physical activity was calculated using various weights and qualified by metabolic equivalent tasks per day (MET-h/day)[19]. The DASH-style

diet is used to lower the risk of cardiometabolic diseases. In this study, we calculated a modified score to represent the DASH-style diet based on the quantitative food frequency questionnaire (FFQ). Detailed information on FFQ and scoring criteria were described elsewhere[20]. The three-year average temperature was obtained from the European Centre for Medium-Range Weather Forecasts reanalysis v5 (ERA5) and was assigned to each participant based on the geocoded address. Hypertension and diabetes status were determined based on participants' self-reports of clinical diagnoses.

Statistical methods

Quantile g-computation (QGC)

QGC is a statistical method newly developed in environmental studies to encounter high-dimensional datasets, especially joint-exposure scenarios[21]. Combining the weighted quantile sum (WQS) regression and g-computation, QGC estimates with a soft constraint on the direction of weights. In other words, the weights for QGC can be positive and negative simultaneously. In contrast, WQS only allowed the same direction of weights, so the application of WQS may be limited in real-world scenarios. Under the unconfounding scenario, the QGC method first assumes that the directional homogeneity holds and fits the model such as $g(\mu) = \beta_0 + \sum_{i=1}^{n} \beta_i a_i$. Here, g is the link function in the generalized linear model, μ represents the mean value of the outcome, β_0 is the intercept, n is the number of exposures, β_1 is the effect for the

i^{th} exposure (or component), a_i is the quantile of the ith exposure. Then, the total

effect φ for mixed exposure can be given as $\sum_{i=1}^{n} \beta_i$, the weight w_i for each

exposure is given as $w_i = \beta_i / \varphi$. On the other hands, if the weights are not in same

direction, the g-computation would redefine the weights. The new weights would be

interpreted as the proportion of the negative or positive partial effect due to the exposure.

Further, the variance can be estimated with a nonparametric bootstrap. We used the R

package *qgcomp* to conduct the QGC analyses, detailed codes were represented

elsewhere.

False-discovery rate (FDR) correction

We used FDR correction for multiple comparisons in Cox proportional hazard models

and logistic models. The P values of PM$_{2.5}$ and its chemical constituents were co-

adjusted except for mixed pollutants in each outcome. Further, P values in subgroup

analyses were co-adjusted in each modifier and outcome.

R code for analyses

QGC

```
# example: CVD as outcome of interest
# Packages
library(tidyverse)
library(qgcomp)
# Loading data
```

```
data <- load('data.rdata')
# Assigning exposure, outcome, and covariate, all variables were prepared in advance
exposure <- c('NO3', 'NH4', 'OM', 'BC', 'Cl', 'SO4')
outcome <- c('CVD')
covariate <- c('age', 'sex', 'income', 'education', 'marital', 'urbanicity',
               'hypertension family history', 'smoking', 'passive smoking', 'alcohol',
               'physical activity', 'dash score', 'indoor air pollution', 'temperature',
               'hypertension', 'diabetes')
# Quantile g-computation method
formula_QGC <-   sprintf('Surv(%s, %s) ~ %s + %s',
                         time,
                         outcome,
                         paste(exposure, collapse = '+'),
                         paste(c(covariate), collapse = '+')) %>% as.formula()
model <- qgcomp.boot.cox( formula_QGC,
                          expnms = exposure, family = 'binomial',
                          data, q = 4, B = 200)
summary(qc)
```

Mediation analysis

```
# example: CVD as outcome of interest; OM as exposure
# Packages
library(tidyverse)
library(CMAverse)
# Loading data
data <- load('data.rdata')
# Assigning exposure, mediator, outcome, and covariate, all variables were prepared in
advance
exposure <- c('OM')
mediator <- c('MetS')
outcome <- c('CVD')
covariate <- c('age', 'sex', 'income', 'education', 'marital', 'urbanicity',
               'hypertension family history', 'smoking', 'passive smoking', 'alcohol',
               'physical activity', 'dash score', 'indoor air pollution', 'temperature')
model <- cmest(   data = data,
                  model = 'rb',
                  estimation = 'paramfunc',
                  inference = ' bootstrap ',
                  outcome = time,
                  event = outcome,
                  exposure = exposure,
                  mediator = mediator,
                  EMint = FALSE,
                  basec = covariate,
                  postc = NULL,
                  yreg = 'coxph',
                  mreg = rep(list('logistic'), num_med),
                  mval = rep(list(0), num_med),
                  yval = NULL,
                  nboot = 2000,
                  basecval = NULL)
summary(model)
```

Figure S1. Participant inclusion process for the study.

CMEC, China Multi-Ethnic Cohort.

Figure S2. Directed acyclic graph for the study.

PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; CVD, cardiovascular disease; SES, social economic status; BMI; body mass index; DASH, dietary approaches to stop hypertension.

Figure S3. Spearman correlation matrix among three-year average concentrations of PM$_{2.5}$ chemical constituents.

PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; OM, organic matter; Cl$^-$, chloride; SO$_4^{2-}$, sulfate.

Figure S4. The study area (Sichuan province) and spatial distribution of PM$_{2.5}$ chemical constituents in this study.

PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; BC, black carbon; OM, organic matter.

Figure S5. Hazard ratios (95% CIs) of CVD risks associated with per IQR increase in the PM$_{2.5}$ chemical constituents.

CVD, total cardiovascular disease; IHD, ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; NO$_3^-$, nitrate; NH$_4^+$, ammonium; OM, organic matter; BC, black carbon; Cl$^-$, chloride; SO$_4^{2-}$, sulfate. Model 1: adjusted for age, sex; Model 2: additionally adjusted for education, marital status, annual household income, urbanicity, family history of hypertension and BMI; Model 3: additionally adjusted for smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature; Model 4: additionally adjusted for hypertension and diabetes.

Figure S6. Weight estimations of PM$_{2.5}$ chemical constituents associated with CVD risks by QGC method.

CVD, total cardiovascular disease; IHD, ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; QGC, quantile g-computation; NO$_3^-$, nitrate; SO$_4^{2-}$, sulfate; Cl$^-$, chloride; OM, organic matter; BC, black carbon; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 µm; NH$_4^+$, ammonium.

Figure S7. Estimated OR and corresponding 95% CI of associations between PM$_{2.5}$ constituents and MetS and its components.

Units are per IQR in pollutants. All model was adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, BMI, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, DASH score, three-year average temperature, hypertension, and diabetes. PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose; BMI, body mass index; DASH, dietary approaches to stop hypertension.

Table S1. Cardiovascular diseases corresponding ICD-10 codes in the study.

ICD-10 code	Cardiovascular Diseases
I00 - I99	Total CVD
I20 - I25	Ischemic heart disease
I30 - I51	Cardiac arrest
G45, I60 - I69	Cerebrovascular disease

Table S2. Sensitivity analyses for associations of PM$_{2.5}$ with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
Total CVD	Manuscript	1.67(1.52,1.84)	<0.001	2.73
	2-year average	1.54(1.42,1.67)	<0.001	2.45
	4-year average	1.69(1.53,1.87)	<0.001	2.77
IHD	Manuscript	1.26(1.03,1.54)	0.038	1.82
	2-year average	1.18(1.00,1.40)	0.071	1.65
	4-year average	1.25(1.01,1.54)	0.060	1.80
CAR	Manuscript	1.49(1.21,1.83)	<0.001	2.33
	2-year average	1.39(1.17,1.66)	<0.001	2.13
	4-year average	1.54(1.24,1.92)	<0.001	2.46
CBVD	Manuscript	2.11(1.82,2.43)	<0.001	3.63
	2-year average	1.90(1.68,2.15)	<0.001	3.21
	4-year average	2.09(1.80,2.43)	<0.001	3.60

Note: Units are per IQR increase in PM$_{2.5}$. PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

† All P values were adjusted by the adjustment strategy in the manuscript.

Table S3. Sensitivity analyses for associations of NO_3^- with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
	Manuscript	1.30(1.21,1.40)	<0.001	1.93
Total CVD	2-year average	1.39(1.30,1.49)	<0.001	2.13
	4-year average	1.16(1.08,1.25)	<0.001	1.59
	Manuscript	1.52(1.32,1.74)	<0.001	2.40
IHD	2-year average	1.43(1.25,1.63)	<0.001	2.22
	4-year average	1.47(1.29,1.68)	<0.001	2.31
	Manuscript	1.26(1.07,1.48)	0.008	1.83
CAR	2-year average	1.34(1.15,1.55)	<0.001	2.01
	4-year average	1.19(1.02,1.39)	0.033	1.67
	Manuscript	1.41(1.28,1.56)	<0.001	2.17
CBVD	2-year average	1.54(1.40,1.69)	<0.001	2.45
	4-year average	1.19(1.07,1.31)	<0.001	1.66

Note: Units are per IQR increase in NO_3^-. NO_3^-, nitrate; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.
† All P values were adjusted by the adjustment strategy in the manuscript.

Table S4. Sensitivity analyses for associations of NH_4^+ with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
	Manuscript	1.56(1.46,1.67)	<0.001	2.50
Total CVD	2-year average	1.61(1.50,1.73)	<0.001	2.60
	4-year average	1.78(1.63,1.95)	<0.001	2.96
	Manuscript	1.29(1.12,1.48)	0.001	1.90
IHD	2-year average	1.31(1.13,1.52)	0.001	1.95
	4-year average	1.38(1.15,1.67)	0.002	2.11
	Manuscript	1.44(1.24,1.66)	<0.001	2.23
CAR	2-year average	1.49(1.28,1.74)	<0.001	2.34
	4-year average	1.63(1.35,1.99)	<0.001	2.65
	Manuscript	1.83(1.65,2.02)	<0.001	3.06
CBVD	2-year average	1.90(1.71,2.12)	<0.001	3.21
	4-year average	2.16(1.89,2.46)	<0.001	3.74

Note: Units are per IQR increase in NH_4^+. NH_4^+, ammonium; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

† All P values were adjusted by the adjustment strategy in the manuscript.

Table S5. Sensitivity analyses for associations of OM with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
	Manuscript	1.63(1.46,1.83)	<0.001	2.65
Total CVD	2-year average	1.60(1.44,1.78)	<0.001	2.59
	4-year average	1.62(1.45,1.82)	<0.001	2.63
	Manuscript	1.05(0.82,1.34)	0.678	1.29
IHD	2-year average	1.05(0.84,1.32)	0.659	1.29
	4-year average	1.04(0.81,1.33)	0.881	1.23
	Manuscript	1.44(1.13,1.84)	0.005	2.25
CAR	2-year average	1.43(1.14,1.79)	0.003	2.21
	4-year average	1.46(1.14,1.88)	0.005	2.29
	Manuscript	2.00(1.69,2.36)	<0.001	3.41
CBVD	2-year average	1.97(1.68,2.29)	<0.001	3.34
	4-year average	1.93(1.63,2.28)	<0.001	3.27

Note: Units are per IQR increase in OM. OM, organic matter; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

† All P values were adjusted by the adjustment strategy in the manuscript.

Table S6. Sensitivity analyses for associations of BC with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
	Manuscript	1.42(1.30,1.56)	<0.001	2.20
Total CVD	2-year average	1.36(1.26,1.48)	<0.001	2.07
	4-year average	1.46(1.32,1.60)	<0.001	2.27
	Manuscript	1.30(1.07,1.59)	0.016	1.94
IHD	2-year average	1.24(1.03,1.48)	0.035	1.77
	4-year average	1.33(1.08,1.63)	0.013	1.99
	Manuscript	1.24(1.01,1.51)	0.042	1.78
CAR	2-year average	1.19(1.00,1.42)	0.050	1.67
	4-year average	1.29(1.05,1.59)	0.022	1.91
	Manuscript	1.79(1.57,2.05)	<0.001	2.99
CBVD	2-year average	1.68(1.49,1.89)	<0.001	2.75
	4-year average	1.80(1.57,2.06)	<0.001	3.00

Note: Units are per IQR increase in BC. BC, black carbon; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

† All P values were adjusted by the adjustment strategy in the manuscript.

Table S7. Sensitivity analyses for associations of Cl⁻ with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
	Manuscript	1.40(1.25,1.57)	<0.001	2.15
Total CVD	2-year average	1.41(1.27,1.57)	<0.001	2.17
	4-year average	1.36(1.21,1.52)	<0.001	2.05
	Manuscript	1.39(1.10,1.74)	0.013	2.12
IHD	2-year average	1.35(1.08,1.68)	0.017	2.04
	4-year average	1.42(1.13,1.79)	0.007	2.19
	Manuscript	1.24(0.97,1.58)	0.082	1.78
CAR	2-year average	1.31(1.05,1.65)	0.022	1.96
	4-year average	1.25(0.98,1.60)	0.069	1.82
	Manuscript	1.52(1.30,1.78)	<0.001	2.41
CBVD	2-year average	1.63(1.41,1.89)	<0.001	2.64
	4-year average	1.47(1.26,1.71)	<0.001	2.30

Note: Units are per IQR increase in Cl⁻. Cl⁻, chloride; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

† All *P* values were adjusted by the adjustment strategy in the manuscript.

Table S8. Sensitivity analyses for associations of SO$_4^{2-}$ with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	P†	E value
Total CVD	Manuscript	1.54(1.41,1.67)	<0.001	2.45
	2-year average	1.60(1.45,1.76)	<0.001	2.57
	4-year average	1.57(1.40,1.76)	<0.001	2.51
IHD	Manuscript	1.13(0.95,1.35)	0.208	1.51
	2-year average	1.20(0.98,1.47)	0.093	1.69
	4-year average	0.98(0.76,1.26)	0.881	1.16
CAR	Manuscript	1.56(1.29,1.87)	<0.001	2.49
	2-year average	1.65(1.34,2.03)	<0.001	2.69
	4-year average	1.83(1.43,2.35)	<0.001	3.06
CBVD	Manuscript	1.83(1.62,2.07)	<0.001	3.07
	2-year average	1.92(1.68,2.20)	<0.001	3.26
	4-year average	1.93(1.65,2.27)	<0.001	3.28

Note: Units are per IQR increase in SO$_4^{2-}$. SO$_4^{2-}$, sulfate; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

† All P values were adjusted by the adjustment strategy in the manuscript.

Table S9. Sensitivity analyses for associations of mixture pollutant with CVD risks. *

Outcome	Sensitivity strategy	HR (95%CI)	*P*	E value
	Manuscript	1.79(1.63,1.97)	<0.001	2.98
Total CVD	2-year average	1.66(1.52,1.80)	<0.001	2.70
	4-year average	1.79(1.61,1.99)	<0.001	2.98
	Manuscript	1.48(1.21,1.81)	<0.001	2.32
IHD	2-year average	1.47(1.22,1.78)	<0.001	2.30
	4-year average	1.49(1.19,1.86)	<0.001	2.34
	Manuscript	1.70(1.35,2.14)	<0.001	2.80
CAR	2-year average	1.60(1.31,1.95)	<0.001	2.57
	4-year average	1.83(1.45,2.32)	<0.001	3.07
	Manuscript	2.25(1.94,2.62)	<0.001	3.93
CBVD	2-year average	2.08(1.83,2.38)	<0.001	3.59
	4-year average	2.20(1.90,2.55)	<0.001	3.83

Note: CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 µm.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, three-year average temperature, hypertension, and diabetes.

Table S10. Sensitivity analyses for associations between PM$_{2.5}$ and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	P†	E value
MetS	Manuscript	1.37(1.23,1.53)	<0.001	1.61
	2-year average	1.31(1.20,1.44)	<0.001	1.55
	4-year average	1.35(1.20,1.52)	<0.001	1.60
Obesity	Manuscript	1.48(1.33,1.65)	<0.001	1.73
	2-year average	1.42(1.29,1.55)	<0.001	1.67
	4-year average	1.42(1.27,1.59)	<0.001	1.67
Raised TG	Manuscript	1.14(1.06,1.23)	0.001	1.33
	2-year average	1.11(1.05,1.19)	0.001	1.30
	4-year average	1.13(1.05,1.23)	0.006	1.33
Raised HDL	Manuscript	1.08(1.00,1.17)	0.092	1.24
	2-year average	1.08(1.02,1.15)	0.034	1.24
	4-year average	1.10(1.01,1.19)	0.059	1.27
Raised BP	Manuscript	1.42(1.31,1.55)	<0.001	1.67
	2-year average	1.36(1.27,1.46)	<0.001	1.61
	4-year average	1.42(1.30,1.55)	<0.001	1.67
Raised FBG	Manuscript	0.95(0.88,1.02)	0.200	1.20
	2-year average	0.95(0.89,1.01)	0.127	1.20
	4-year average	0.95(0.88,1.03)	0.357	1.18

Note: Units are per IQR increase in PM$_{2.5}$. PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.

† All P values were adjusted by the adjustment strategy in the manuscript.

Table S11. Sensitivity analyses for associations between NO$_3^-$ and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	P†	E value
MetS	Manuscript	1.38(1.26,1.52)	<0.001	1.63
	2-year average	1.42(1.31,1.54)	<0.001	1.67
	4-year average	1.30(1.19,1.42)	<0.001	1.54
Obesity	Manuscript	1.54(1.40,1.68)	<0.001	1.78
	2-year average	1.57(1.44,1.70)	<0.001	1.81
	4-year average	1.39(1.27,1.51)	<0.001	1.63
Raised TG	Manuscript	1.09(1.02,1.15)	0.012	1.25
	2-year average	1.10(1.04,1.16)	0.001	1.27
	4-year average	1.07(1.01,1.14)	0.026	1.23
Raised HDL	Manuscript	1.05(0.99,1.12)	0.180	1.18
	2-year average	1.06(1.00,1.12)	0.073	1.20
	4-year average	1.04(0.98,1.11)	0.237	1.17
Raised BP	Manuscript	1.22(1.14,1.31)	<0.001	1.45
	2-year average	1.28(1.20,1.36)	<0.001	1.52
	4-year average	1.12(1.05,1.19)	<0.001	1.31
Raised FBG	Manuscript	0.96(0.90,1.02)	0.258	1.16
	2-year average	0.96(0.90,1.01)	0.134	1.18
	4-year average	0.97(0.91,1.03)	0.401	1.14

Note: Units are per IQR increase in NO$_3^-$. NO$_3^-$, nitrate. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.
† All P values were adjusted by the adjustment strategy in the manuscript.

Table S12. Sensitivity analyses for associations between NH$_4^+$ and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	P†	E value
MetS	Manuscript	1.22(1.13,1.32)	<0.001	1.45
	2-year average	1.24(1.14,1.35)	<0.001	1.47
	4-year average	1.27(1.15,1.41)	<0.001	1.50
Obesity	Manuscript	1.31(1.22,1.42)	<0.001	1.56
	2-year average	1.36(1.25,1.47)	<0.001	1.61
	4-year average	1.38(1.25,1.53)	<0.001	1.63
Raised TG	Manuscript	1.11(1.05,1.17)	<0.001	1.29
	2-year average	1.12(1.06,1.18)	<0.001	1.31
	4-year average	1.14(1.06,1.22)	0.002	1.33
Raised HDL	Manuscript	1.06(1.01,1.11)	0.092	1.20
	2-year average	1.09(1.03,1.15)	0.015	1.26
	4-year average	1.10(1.02,1.18)	0.042	1.27
Raised BP	Manuscript	1.20(1.13,1.27)	<0.001	1.41
	2-year average	1.18(1.11,1.26)	<0.001	1.40
	4-year average	1.20(1.11,1.30)	<0.001	1.42
Raised FBG	Manuscript	0.94(0.90,0.99)	0.106	1.21
	2-year average	0.93(0.88,0.98)	0.038	1.23
	4-year average	0.93(0.87,1.00)	0.205	1.22

Note: Units are per IQR increase in NH$_4^+$. NH$_4^+$, ammonium. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.
† All P values were adjusted by the adjustment strategy in the manuscript.

Table S13. Sensitivity analyses for associations between OM and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	*P*†	E value
MetS	Manuscript	1.37(1.20,1.56)	<0.001	1.62
	2-year average	1.35(1.19,1.52)	<0.001	1.59
	4-year average	1.33(1.16,1.52)	<0.001	1.57
Obesity	Manuscript	1.44(1.26,1.64)	<0.001	1.69
	2-year average	1.43(1.26,1.61)	<0.001	1.68
	4-year average	1.35(1.18,1.54)	<0.001	1.59
Raised TG	Manuscript	1.12(1.03,1.23)	0.012	1.31
	2-year average	1.12(1.03,1.21)	0.010	1.30
	4-year average	1.11(1.02,1.22)	0.026	1.30
Raised HDL	Manuscript	1.12(1.02,1.22)	0.092	1.30
	2-year average	1.11(1.02,1.21)	0.034	1.30
	4-year average	1.13(1.03,1.24)	0.042	1.32
Raised BP	Manuscript	1.48(1.34,1.64)	<0.001	1.73
	2-year average	1.47(1.34,1.62)	<0.001	1.72
	4-year average	1.44(1.30,1.60)	<0.001	1.69
Raised FBG	Manuscript	0.97(0.88,1.06)	0.487	1.14
	2-year average	0.96(0.88,1.04)	0.326	1.17
	4-year average	0.98(0.89,1.08)	0.692	1.11

Note: Units are per IQR increase in OM. OM, organic matter. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.
† All *P* values were adjusted by the adjustment strategy in the manuscript.

Table S14. Sensitivity analyses for associations between BC and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	*P*†	E value
MetS	Manuscript	1.22(1.10,1.36)	<0.001	1.45
	2-year average	1.20(1.10,1.32)	<0.001	1.43
	4-year average	1.20(1.08,1.34)	0.001	1.42
Obesity	Manuscript	1.35(1.22,1.50)	<0.001	1.59
	2-year average	1.31(1.20,1.44)	<0.001	1.55
	4-year average	1.30(1.17,1.45)	<0.001	1.54
Raised TG	Manuscript	1.12(1.04,1.20)	0.005	1.30
	2-year average	1.11(1.04,1.18)	0.001	1.29
	4-year average	1.12(1.04,1.20)	0.007	1.30
Raised HDL	Manuscript	1.01(0.94,1.09)	0.754	1.08
	2-year average	1.02(0.96,1.09)	0.574	1.12
	4-year average	1.01(0.93,1.09)	0.827	1.07
Raised BP	Manuscript	1.41(1.31,1.53)	<0.001	1.66
	2-year average	1.38(1.28,1.48)	<0.001	1.63
	4-year average	1.42(1.30,1.54)	<0.001	1.67
Raised FBG	Manuscript	0.94(0.87,1.01)	0.161	1.22
	2-year average	0.94(0.88,1.00)	0.089	1.22
	4-year average	0.94(0.87,1.02)	0.283	1.20

Note: Units are per IQR increase in BC. BC, black carbon. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.
† All *P* values were adjusted by the adjustment strategy in the manuscript.

Table S15. Sensitivity analyses for associations between Cl⁻ and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	P†	E value
MetS	Manuscript	1.17(1.02,1.33)	0.023	1.37
	2-year average	1.12(0.99,1.27)	0.070	1.31
	4-year average	1.12(0.98,1.28)	0.089	1.31
Obesity	Manuscript	1.32(1.16,1.50)	<0.001	1.56
	2-year average	1.29(1.14,1.46)	<0.001	1.53
	4-year average	1.29(1.13,1.48)	<0.001	1.53
Raised TG	Manuscript	1.17(1.07,1.28)	0.001	1.38
	2-year average	1.15(1.06,1.25)	0.001	1.35
	4-year average	1.14(1.04,1.25)	0.007	1.34
Raised HDL	Manuscript	0.97(0.89,1.06)	0.538	1.15
	2-year average	0.98(0.90,1.07)	0.696	1.10
	4-year average	0.97(0.88,1.06)	0.551	1.15
Raised BP	Manuscript	0.90(0.82,0.99)	0.038	1.29
	2-year average	0.90(0.82,0.99)	0.024	1.29
	4-year average	0.87(0.79,0.96)	0.006	1.35
Raised FBG	Manuscript	0.91(0.83,0.99)	0.106	1.28
	2-year average	0.89(0.82,0.97)	0.038	1.30
	4-year average	0.91(0.83,0.99)	0.205	1.28

Note: Units are per IQR increase in Cl⁻. Cl⁻, chloride. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.
† All P values were adjusted by the adjustment strategy in the manuscript.

Table S16. Sensitivity analyses for associations between SO_4^{2-} and MetS and its components. *

Mediator	Sensitivity strategy	OR (95%CI)	P†	E value
MetS	Manuscript	1.32(1.19,1.45)	<0.001	1.56
	2-year average	1.29(1.15,1.44)	<0.001	1.53
	4-year average	1.32(1.15,1.52)	<0.001	1.57
Obesity	Manuscript	1.40(1.27,1.55)	<0.001	1.65
	2-year average	1.42(1.27,1.59)	<0.001	1.67
	4-year average	1.37(1.19,1.58)	<0.001	1.62
Raised TG	Manuscript	1.08(1.01,1.16)	0.020	1.25
	2-year average	1.08(1.00,1.17)	0.037	1.25
	4-year average	1.03(0.94,1.13)	0.559	1.13
Raised HDL	Manuscript	1.06(0.99,1.13)	0.180	1.20
	2-year average	1.09(1.01,1.18)	0.051	1.26
	4-year average	1.07(0.98,1.18)	0.237	1.23
Raised BP	Manuscript	1.23(1.14,1.33)	<0.001	1.46
	2-year average	1.14(1.05,1.24)	0.002	1.34
	4-year average	1.21(1.09,1.35)	<0.001	1.44
Raised FBG	Manuscript	0.94(0.88,1.01)	0.161	1.21
	2-year average	0.92(0.85,0.99)	0.071	1.26
	4-year average	0.93(0.85,1.03)	0.283	1.23

Note: Units are per IQR increase in SO_4^{2-}. SO_4^{2-}, sulfate. MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose.
* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes.
† All P values were adjusted by the adjustment strategy in the manuscript.

Table S17. The associations between PM$_{2.5}$ chemical constituents and CVD risks with different age groups. *

Outcome	Exposure	Age group <65 ($n = 12,269$)	Age group ≥65 ($n = 2,158$)	P for heterogeneity
Total CVD	PM$_{2.5}$	1.67(1.48,1.88)*	1.67(1.42,1.98)*	0.977
	NO$_3^-$	1.31(1.20,1.43)*	1.26(1.10,1.44)*	0.591
	NH$_4^+$	1.56(1.43,1.69)*	1.56(1.39,1.75)*	0.987
	OM	1.60(1.39,1.83)*	1.71(1.41,2.09)*	0.565
	BC	1.45(1.29,1.62)*	1.36(1.15,1.60)*	0.513
	Cl$^-$	1.54(1.35,1.76)*	1.11(0.90,1.36)	0.009
	SO$_4^{2-}$	1.53(1.38,1.70)*	1.52(1.31,1.76)*	0.949
	Mixture pollutants	1.81(1.60,2.04)*	1.55(1.31,1.83)*	0.153
IHD	PM$_{2.5}$	1.36(1.03,1.79)	1.11(0.81,1.50)	0.323
	NO$_3^-$	1.70(1.42,2.03)*	1.25(0.99,1.58)	0.041
	NH$_4^+$	1.33(1.10,1.61)*	1.21(0.98,1.49)	0.508
	OM	1.07(0.77,1.48)	1.01(0.70,1.47)	0.837
	BC	1.50(1.15,1.96)*	1.04(0.76,1.42)	0.076
	Cl$^-$	1.65(1.22,2.22)*	1.04(0.72,1.50)	0.055
	SO$_4^{2-}$	1.18(0.93,1.50)	1.04(0.79,1.37)	0.481
	Mixture pollutants	1.66(1.27,2.16)*	1.22(0.87,1.73)	0.171
CAR	PM$_{2.5}$	1.64(1.24,2.17)*	1.35(0.98,1.85)	0.354
	NO$_3^-$	1.30(1.06,1.60)*	1.22(0.93,1.61)	0.715
	NH$_4^+$	1.49(1.23,1.81)*	1.39(1.12,1.73)*	0.642
	OM	1.58(1.14,2.18)*	1.34(0.92,1.94)	0.509
	BC	1.40(1.08,1.82)*	1.05(0.77,1.44)	0.163
	Cl$^-$	1.31(0.96,1.79)	1.09(0.74,1.61)	0.464
	SO$_4^{2-}$	1.66(1.30,2.12)*	1.44(1.08,1.92)*	0.458
	Mixture pollutants	1.81(1.36,2.42)*	1.39(0.96,2.01)	0.260
CBVD	PM$_{2.5}$	2.16(1.81,2.59)*	1.98(1.55,2.54)*	0.581
	NO$_3^-$	1.43(1.27,1.62)*	1.31(1.08,1.59)*	0.449
	NH$_4^+$	1.82(1.61,2.07)*	1.83(1.54,2.17)*	0.988
	OM	2.01(1.64,2.46)*	1.96(1.47,2.60)*	0.887
	BC	1.88(1.60,2.21)*	1.62(1.28,2.05)*	0.307
	Cl$^-$	1.67(1.38,2.01)*	1.21(0.91,1.62)	0.069
	SO$_4^{2-}$	1.77(1.52,2.05)*	1.94(1.57,2.40)*	0.476
	Mixture pollutants	2.20(1.86,2.61)*	2.03(1.58,2.61)*	0.600

Note: Units are per IQR increase in pollutants. Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes. PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; BC, black carbon; OM, organic matter; Cl$^-$, chloride; NO$_3^-$, nitrate; NH$_4^+$, ammonium; SO$_4^{2-}$, sulfate; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, ischemic heart disease; CBVD, cerebrovascular disease.
* indicates adjusted P value < 0.05.

Table S18. The associations between PM$_{2.5}$ chemical constituents and CVD risks with different sex groups. *

Outcome	Exposure	Sex Male ($n = 6,321$)	Female ($n = 8,106$)	P for heterogeneity
Total CVD	PM$_{2.5}$	1.51(1.31,1.74)*	1.83(1.60,2.09)*	0.053
	NO$_3^-$	1.07(0.95,1.21)	1.48(1.35,1.62)*	< 0.001
	NH$_4^+$	1.49(1.35,1.65)*	1.63(1.48,1.78)*	0.216
	OM	1.55(1.31,1.83)*	1.72(1.47,2.00)*	0.371
	BC	**1.26(1.10,1.45)***	**1.58(1.39,1.79)***	**0.019**
	Cl$^-$	1.27(1.08,1.51)*	1.51(1.30,1.75)*	0.147
	SO$_4^{2-}$	1.51(1.33,1.71)*	1.57(1.40,1.76)*	0.635
	Mixture pollutants	1.60(1.39,1.84)*	1.89(1.68,2.12)*	0.073
IHD	PM$_{2.5}$	1.08(0.79,1.48)	1.36(1.04,1.78)	0.282
	NO$_3^-$	1.21(0.95,1.56)	1.70(1.43,2.01)*	0.028
	NH$_4^+$	1.17(0.94,1.45)	1.37(1.14,1.65)*	0.269
	OM	0.99(0.68,1.45)	1.06(0.76,1.46)	0.802
	BC	1.09(0.80,1.49)	1.43(1.10,1.86)*	0.196
	Cl$^-$	1.04(0.71,1.51)	1.70(1.26,2.29)*	0.042
	SO$_4^{2-}$	1.01(0.76,1.33)	1.22(0.97,1.55)	0.301
	Mixture pollutants	1.28(0.90,1.82)	1.61(1.18,2.19)*	0.344
CAR	PM$_{2.5}$	1.89(1.38,2.57)*	1.20(0.91,1.60)	0.036
	NO$_3^-$	1.28(1.00,1.63)	1.25(1.00,1.55)	0.880
	NH$_4^+$	1.64(1.32,2.03)*	1.28(1.05,1.56)*	0.095
	OM	1.92(1.34,2.74)*	1.11(0.79,1.55)	0.028
	BC	1.51(1.13,2.03)*	1.03(0.79,1.36)	0.064
	Cl$^-$	1.18(0.83,1.69)	1.29(0.92,1.80)	0.734
	SO$_4^{2-}$	1.71(1.31,2.23)*	1.42(1.10,1.84)*	0.325
	Mixture pollutants	1.92(1.33,2.76)*	1.45(1.07,1.97)*	0.246
CBVD	PM$_{2.5}$	1.82(1.46,2.27)*	2.36(1.95,2.85)*	0.083
	NO$_3^-$	**1.21(1.01,1.44)***	**1.53(1.35,1.73)***	**0.033**
	NH$_4^+$	1.75(1.49,2.04)*	1.91(1.67,2.17)*	0.404
	OM	1.73(1.34,2.23)*	2.22(1.79,2.76)*	0.144
	BC	1.60(1.30,1.97)*	1.94(1.63,2.31)*	0.161
	Cl$^-$	1.53(1.19,1.96)*	1.54(1.26,1.88)*	0.980
	SO$_4^{2-}$	1.85(1.53,2.24)*	1.84(1.57,2.15)*	0.964
	Mixture pollutants	2.09(1.66,2.62)*	2.45(2.07,2.89)*	0.264

Note: Units are per IQR increase in pollutants. Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, body mass index, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, dietary approaches to stop hypertension score, three-year average temperature, hypertension, and diabetes. PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; BC, black carbon; OM, organic matter; Cl$^-$, chloride; NO$_3^-$, nitrate; NH$_4^+$, ammonium; SO$_4^{2-}$, sulfate; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, ischemic heart disease; CBVD, cerebrovascular disease.
* indicates adjusted P value < 0.05.
The bold means P value < 0.05 for both the subgroup and the heterogeneity test.

Table S19. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by obesity. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	OM	1.58(1.43,1.77)	< 0.001	1.01(1.00,1.01)	0.035	1.4%
	PM$_{2.5}$	1.62(1.47,1.81)	< 0.001	1.01(1.00,1.01)	0.002	1.1%
IHD	Cl⁻	1.36(1.05,1.76)	0.021	1.00(1.00,1.01)	0.110	2.0%
	PM$_{2.5}$	1.23(1.00,1.55)	0.050	1.01(1.00,1.01)	0.003	2.4%
CAR	OM	1.42(1.12,1.82)	0.004	1.00(1.00,1.01)	0.042	1.3%
	PM$_{2.5}$	1.46(1.18,1.81)	< 0.001	1.00(1.00,1.01)	0.022	1.0%
CBVD	Cl⁻	1.49(1.26,1.78)	< 0.001	1.00(1.00,1.01)	0.094	1.3%
	PM$_{2.5}$	2.09(1.80,2.46)	< 0.001	1.00(1.00,1.01)	0.001	0.5%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S20. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by raised triglycerides. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	OM	1.59(1.43,1.78)	< 0.001	1.00(1.00,1.01)	0.056	1.0%
	PM$_{2.5}$	1.63(1.47,1.81)	< 0.001	1.00(1.00,1.01)	0.004	0.9%
IHD	Cl$^-$	1.37(1.07,1.79)	0.018	1.01(1.00,1.01)	0.012	3.2%
	PM$_{2.5}$	1.25(1.02,1.56)	0.035	1.01(1.00,1.01)	0.009	2.6%
CAR	OM	1.43(1.12,1.84)	0.006	1.00(1.00,1.01)	0.422	0.5%
	PM$_{2.5}$	1.48(1.18,1.85)	0.001	1.00(1.00,1.01)	0.399	0.4%
CBVD	Cl$^-$	1.50(1.28,1.78)	< 0.001	1.00(1.00,1.01)	0.031	1.2%
	PM$_{2.5}$	2.10(1.80,2.47)	< 0.001	1.00(1.00,1.01)	0.053	0.3%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; OM, organic matter; Cl$^-$, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S21. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by raised high-density lipoprotein. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	OM	1.60(1.43,1.79)	< 0.001	1.00(1.00,1.01)	0.080	0.5%
	PM$_{2.5}$	1.64(1.48,1.80)	< 0.001	1.00(1.00,1.00)	0.169	0.3%
IHD	Cl⁻	1.38(1.06,1.80)	0.019	1.00(0.99,1.00)	0.531	-
	PM$_{2.5}$	1.26(1.02,1.59)	0.032	1.00(1.00,1.00)	0.496	0.4%
CAR	OM	1.43(1.14,1.86)	0.002	1.00(1.00,1.01)	0.445	0.4%
	PM$_{2.5}$	1.48(1.20,1.84)	0.003	1.00(1.00,1.00)	0.518	0.2%
CBVD	Cl⁻	1.51(1.28,1.78)	< 0.001	1.00(0.99,1.00)	0.223	-
	PM$_{2.5}$	2.11(1.80,2.47)	< 0.001	1.00(1.00,1.00)	0.171	0.2%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S22. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by raised blood pressure. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	OM	1.56(1.40,1.76)	< 0.001	1.03(1.02,1.04)	< 0.001	5.8%
	PM$_{2.5}$	1.61(1.45,1.78)	< 0.001	1.01(1.01,1.02)	< 0.001	3.0%
IHD	Cl$^-$	1.38(1.07,1.80)	0.021	0.99(0.98,1.00)	0.023	-
	PM$_{2.5}$	1.24(1.00,1.55)	0.053	1.01(1.00,1.02)	0.001	4.2%
CAR	OM	1.42(1.12,1.82)	0.006	1.01(1.00,1.03)	0.045	3.2%
	PM$_{2.5}$	1.46(1.20,1.82)	< 0.001	1.01(1.00,1.01)	0.057	1.5%
CBVD	Cl$^-$	1.51(1.27,1.78)	< 0.001	1.00(0.99,1.00)	0.023	-
	PM$_{2.5}$	2.09(1.80,2.44)	< 0.001	1.00(1.00,1.01)	0.050	0.5%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; OM, organic matter; Cl$^-$, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S23. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by impaired fasting glucose. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	OM	1.60(1.43,1.79)	< 0.001	1.00(1.00,1.00)	0.760	-
	PM$_{2.5}$	1.65(1.50,1.82)	< 0.001	1.00(1.00,1.00)	0.267	-
IHD	Cl$^-$	1.38(1.06,1.77)	0.021	1.00(0.99,1.01)	0.885	-
	PM$_{2.5}$	1.26(1.03,1.59)	0.028	1.00(1.00,1.00)	0.875	-
CAR	OM	1.44(1.12,1.84)	0.003	1.00(1.00,1.00)	0.837	-
	PM$_{2.5}$	1.48(1.20,1.84)	< 0.001	1.00(1.00,1.00)	0.598	-
CBVD	Cl$^-$	1.51(1.27,1.79)	< 0.001	1.00(0.99,1.00)	0.236	-
	PM$_{2.5}$	2.11(1.82,2.49)	< 0.001	1.00(1.00,1.00)	0.449	-

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; OM, organic matter; Cl$^-$, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S24. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between other PM$_{2.5}$ chemical constituents and CVD mediated by MetS. *

Outcome	Exposure	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
Total CVD	NO$_3^-$	1.28(1.19,1.37)	< 0.001	1.00(1.00,1.00)	< 0.001	0.8%
	NH$_4^+$	1.53(1.43,1.64)	< 0.001	1.00(1.00,1.00)	0.060	0.7%
	BC	1.41(1.28,1.55)	< 0.001	1.01(1.00,1.01)	0.003	1.7%
	SO$_4^{2-}$	1.50(1.38,1.64)	< 0.001	1.00(1.00,1.00)	0.011	0.4%
IHD	NO$_3^-$	1.50(1.28,1.71)	< 0.001	1.00(1.00,1.00)	0.018	0.4%
	NH$_4^+$	1.28(1.11,1.49)	< 0.001	1.00(1.00,1.00)	0.070	0.8%
	BC	1.30(1.03,1.64)	0.022	1.00(1.00,1.01)	0.011	1.7%
	SO$_4^{2-}$	1.12(0.93,1.35)	0.252	1.00(1.00,1.00)	0.014	1.0%
CAR	NO$_3^-$	1.25(1.05,1.48)	0.020	1.00(1.00,1.00)	0.032	0.6%
	NH$_4^+$	1.42(1.22,1.66)	< 0.001	1.00(1.00,1.00)	0.093	0.5%
	BC	1.23(1.02,1.51)	0.038	1.00(1.00,1.01)	0.037	1.7%
	SO$_4^{2-}$	1.54(1.27,1.87)	< 0.001	1.00(1.00,1.00)	0.051	0.3%
CBVD	NO$_3^-$	1.40(1.25,1.56)	< 0.001	1.00(1.00,1.00)	0.018	0.3%
	NH$_4^+$	1.82(1.64,2.04)	< 0.001	1.00(1.00,1.00)	0.063	0.3%
	BC	1.80(1.57,2.07)	< 0.001	1.00(1.00,1.01)	0.019	0.5%
	SO$_4^{2-}$	1.82(1.62,2.06)	< 0.001	1.00(1.00,1.00)	0.021	0.2%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; SO$_4^{2-}$, sulfate.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S25. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between other PM$_{2.5}$ chemical constituents and CVD mediated by obesity. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	NO$_3^-$	1.27(1.18,1.37)	< 0.001	1.00(1.00,1.00)	< 0.001	1.2%
	NH$_4^+$	1.52(1.42,1.63)	< 0.001	1.00(1.00,1.00)	0.019	0.9%
	BC	1.40(1.28,1.54)	< 0.001	1.01(1.00,1.01)	< 0.001	2.3%
	SO$_4^{2-}$	1.50(1.37,1.64)	< 0.001	1.00(1.00,1.00)	0.014	0.7%
IHD	NO$_3^-$	1.49(1.28,1.74)	< 0.001	1.00(1.00,1.00)	0.006	0.6%
	NH$_4^+$	1.27(1.09,1.48)	0.003	1.00(1.00,1.00)	0.023	1.3%
	BC	1.29(1.04,1.62)	0.027	1.01(1.00,1.01)	0.002	2.7%
	SO$_4^{2-}$	1.11(0.91,1.36)	0.279	1.00(1.00,1.00)	0.011	1.9%
CAR	NO$_3^-$	1.24(1.05,1.47)	0.012	1.00(1.00,1.00)	0.023	0.9%
	NH$_4^+$	1.42(1.22,1.67)	< 0.001	1.00(1.00,1.00)	0.043	0.7%
	BC	1.23(1.01,1.52)	0.036	1.01(1.00,1.01)	0.021	2.6%
	SO$_4^{2-}$	1.53(1.25,1.88)	< 0.001	1.00(1.00,1.00)	0.034	0.5%
CBVD	NO$_3^-$	1.39(1.26,1.55)	< 0.001	1.00(1.00,1.00)	0.003	0.6%
	NH$_4^+$	1.81(1.64,2.02)	< 0.001	1.00(1.00,1.00)	0.023	0.5%
	BC	1.79(1.57,2.06)	< 0.001	1.00(1.00,1.01)	0.002	1.0%
	SO$_4^{2-}$	1.81(1.61,2.05)	< 0.001	1.00(1.00,1.00)	0.014	0.4%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; SO$_4^{2-}$, sulfate.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S26. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between other PM$_{2.5}$ chemical constituents and CVD mediated by raised triglycerides. *

Outcome	Exposure	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
Total CVD	NO$_3^-$	1.29(1.19,1.39)	< 0.001	1.00(1.00,1.00)	0.025	1.3%
	NH$_4^+$	1.53(1.43,1.63)	< 0.001	1.00(1.00,1.00)	0.006	0.9%
	BC	1.41(1.29,1.55)	< 0.001	1.01(1.00,1.01)	0.003	1.7%
	SO$_4^{2-}$	1.51(1.40,1.65)	< 0.001	1.00(1.00,1.00)	0.185	0.6%
IHD	NO$_3^-$	1.51(1.28,1.76)	< 0.001	1.00(1.00,1.01)	0.021	1.2%
	NH$_4^+$	1.28(1.11,1.50)	< 0.001	1.00(1.00,1.01)	0.005	1.7%
	BC	1.30(1.06,1.63)	0.018	1.01(1.00,1.01)	0.005	2.8%
	SO$_4^{2-}$	1.13(0.94,1.37)	0.217	1.00(1.00,1.00)	0.190	2.2%
CAR	NO$_3^-$	1.26(1.05,1.49)	0.018	1.00(1.00,1.00)	0.370	0.5%
	NH$_4^+$	1.43(1.23,1.67)	< 0.001	1.00(1.00,1.00)	0.422	0.3%
	BC	1.24(1.02,1.53)	0.031	1.00(1.00,1.01)	0.364	0.9%
	SO$_4^{2-}$	1.55(1.28,1.89)	< 0.001	1.00(1.00,1.00)	0.456	0.2%
CBVD	NO$_3^-$	1.41(1.27,1.56)	< 0.001	1.00(1.00,1.00)	0.059	0.6%
	NH$_4^+$	1.82(1.64,2.03)	< 0.001	1.00(1.00,1.00)	0.063	0.4%
	BC	1.80(1.57,2.07)	< 0.001	1.01(1.00,1.01)	0.049	0.6%
	SO$_4^{2-}$	1.83(1.61,2.06)	< 0.001	1.00(1.00,1.00)	0.195	0.3%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; SO$_4^{2-}$, sulfate.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S27. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between other PM$_{2.5}$ chemical constituents and CVD mediated by raised high-density lipoprotein. *

Outcome	Exposure	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
Total CVD	NO$_3^-$	1.29(1.21,1.40)	< 0.001	1.00(1.00,1.00)	0.205	0.5%
	NH$_4^+$	1.54(1.44,1.65)	< 0.001	1.00(1.00,1.00)	0.255	0.3%
	BC	1.42(1.29,1.57)	< 0.001	1.00(1.00,1.00)	0.864	-
	SO$_4^{2-}$	1.52(1.40,1.66)	< 0.001	1.00(1.00,1.00)	0.452	0.3%
IHD	NO$_3^-$	1.52(1.31,1.76)	< 0.001	1.00(1.00,1.00)	0.550	0.2%
	NH$_4^+$	1.29(1.12,1.50)	0.001	1.00(1.00,1.00)	0.535	0.2%
	BC	1.32(1.05,1.66)	0.016	1.00(1.00,1.00)	0.943	-
	SO$_4^{2-}$	1.13(0.95,1.37)	0.189	1.00(1.00,1.00)	0.692	0.4%
CAR	NO$_3^-$	1.26(1.05,1.48)	0.016	1.00(1.00,1.00)	0.504	0.3%
	NH$_4^+$	1.43(1.24,1.69)	< 0.001	1.00(1.00,1.00)	0.536	0.2%
	BC	1.24(1.03,1.51)	0.031	1.00(1.00,1.00)	0.916	-
	SO$_4^{2-}$	1.55(1.29,1.89)	< 0.001	1.00(1.00,1.00)	0.646	0.2%
CBVD	NO$_3^-$	1.41(1.27,1.56)	< 0.001	1.00(1.00,1.00)	0.199	0.4%
	NH$_4^+$	1.82(1.64,2.03)	< 0.001	1.00(1.00,1.00)	0.278	0.2%
	BC	1.81(1.59,2.07)	< 0.001	1.00(1.00,1.00)	0.856	-
	SO$_4^{2-}$	1.83(1.63,2.06)	< 0.001	1.00(1.00,1.00)	0.467	0.2%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; SO$_4^{2-}$, sulfate.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S28. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between other PM$_{2.5}$ chemical constituents and CVD mediated by raised blood pressure. *

Outcome	Exposure	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
Total CVD	NO$_3^-$	1.27(1.18,1.37)	< 0.001	1.01(1.01,1.01)	< 0.001	3.9%
	NH$_4^+$	1.52(1.43,1.64)	< 0.001	1.01(1.00,1.01)	0.001	2.4%
	BC	1.38(1.26,1.52)	< 0.001	1.02(1.02,1.03)	< 0.001	7.4%
	SO$_4^{2-}$	1.50(1.37,1.63)	< 0.001	1.00(1.00,1.01)	0.001	1.2%
IHD	NO$_3^-$	1.50(1.28,1.75)	< 0.001	1.00(1.00,1.01)	0.009	1.5%
	NH$_4^+$	1.28(1.11,1.50)	< 0.001	1.00(1.00,1.01)	0.003	2.2%
	BC	1.29(1.02,1.63)	0.032	1.01(1.00,1.03)	0.008	5.9%
	SO$_4^{2-}$	1.12(0.93,1.35)	0.254	1.00(1.00,1.00)	0.003	2.2%
CAR	NO$_3^-$	1.25(1.05,1.47)	0.020	1.00(1.00,1.01)	0.045	1.7%
	NH$_4^+$	1.42(1.23,1.67)	< 0.001	1.00(1.00,1.01)	0.045	1.1%
	BC	1.23(1.00,1.51)	0.053	1.01(1.00,1.02)	0.045	4.9%
	SO$_4^{2-}$	1.54(1.27,1.86)	< 0.001	1.00(1.00,1.00)	0.050	0.5%
CBVD	NO$_3^-$	1.40(1.26,1.55)	< 0.001	1.00(1.00,1.00)	0.026	0.8%
	NH$_4^+$	1.82(1.63,2.04)	< 0.001	1.00(1.00,1.00)	0.028	0.6%
	BC	1.79(1.57,2.05)	< 0.001	1.01(1.00,1.01)	0.048	1.2%
	SO$_4^{2-}$	1.82(1.60,2.06)	< 0.001	1.00(1.00,1.00)	0.026	0.3%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; SO$_4^{2-}$, sulfate.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S29. Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between other PM$_{2.5}$ chemical constituents and CVD mediated by impaired fasting glucose. *

Outcome	Exposure	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
Total CVD	NO$_3^-$	1.30(1.20,1.39)	< 0.001	1.00(1.00,1.00)	0.270	-
	NH$_4^+$	1.54(1.44,1.65)	< 0.001	1.00(1.00,1.00)	0.041	-
	BC	1.42(1.30,1.56)	< 0.001	1.00(1.00,1.00)	0.321	-
	SO$_4^{2-}$	1.52(1.39,1.66)	< 0.001	1.00(1.00,1.00)	0.078	-
IHD	NO$_3^-$	1.53(1.31,1.77)	< 0.001	1.00(1.00,1.00)	0.860	-
	NH$_4^+$	1.29(1.11,1.50)	< 0.001	1.00(1.00,1.00)	0.799	-
	BC	1.32(1.07,1.66)	0.012	1.00(1.00,1.00)	0.906	-
	SO$_4^{2-}$	1.13(0.93,1.38)	0.185	1.00(1.00,1.00)	0.851	-
CAR	NO$_3^-$	1.26(1.04,1.48)	0.017	1.00(1.00,1.00)	0.595	-
	NH$_4^+$	1.43(1.23,1.67)	< 0.001	1.00(1.00,1.00)	0.421	-
	BC	1.24(1.02,1.54)	0.032	1.00(1.00,1.00)	0.640	-
	SO$_4^{2-}$	1.55(1.28,1.87)	< 0.001	1.00(1.00,1.00)	0.440	-
CBVD	NO$_3^-$	1.41(1.28,1.56)	< 0.001	1.00(1.00,1.00)	0.462	-
	NH$_4^+$	1.83(1.64,2.05)	< 0.001	1.00(1.00,1.00)	0.220	-
	BC	1.81(1.57,2.08)	< 0.001	1.00(1.00,1.00)	0.509	-
	SO$_4^{2-}$	1.83(1.62,2.08)	< 0.001	1.00(1.00,1.00)	0.243	-

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; IHD, chronic ischemic heart disease; CAR, cardiac arrests; CBVD, cerebrovascular disease; NO$_3^-$, nitrate; NH$_4^+$, ammonium; BC, black carbon; SO$_4^{2-}$, sulfate.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S30. Sensitivity analysis for Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by MetS. *

Exposure	Outcome	Sensitivity strategy	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
OM	Total CVD	manuscript	1.59(1.42,1.77)	< 0.001	1.01(1.00,1.01)	0.020	1.3%
		2-year average	1.56(1.40,1.73)	< 0.001	1.01(1.00,1.01)	0.021	1.2%
		4-year average	1.58(1.41,1.77)	< 0.001	1.01(1.00,1.01)	0.049	1.2%
	CAR	manuscript	1.42(1.11,1.81)	0.002	1.00(1.00,1.01)	0.052	1.1%
		2-year average	1.41(1.14,1.78)	0.004	1.00(1.00,1.01)	0.056	1.0%
		4-year average	1.44(1.14,1.87)	0.002	1.00(1.00,1.01)	0.085	0.9%
Cl⁻	IHD	manuscript	1.36(1.05,1.76)	0.024	1.00(1.00,1.01)	0.562	0.6%
		2-year average	1.33(1.04,1.70)	0.020	1.00(0.99,1.00)	0.819	0.3%
		4-year average	1.40(1.09,1.81)	0.012	1.00(0.99,1.01)	0.803	0.2%
	CBVD	manuscript	1.50(1.26,1.78)	< 0.001	1.00(1.00,1.00)	0.626	0.3%
		2-year average	1.61(1.38,1.89)	< 0.001	1.00(1.00,1.00)	0.807	0.1%
		4-year average	1.45(1.24,1.72)	< 0.001	1.00(1.00,1.00)	0.852	0.1%
PM$_{2.5}$	Total CVD	manuscript	1.63(1.48,1.80)	< 0.001	1.00(1.00,1.01)	0.002	0.9%
		2-year average	1.50(1.39,1.64)	< 0.001	1.00(1.00,1.00)	< 0.001	0.8%
		4-year average	1.65(1.49,1.84)	< 0.001	1.00(1.00,1.00)	0.006	0.8%
	CAR	manuscript	1.47(1.19,1.84)	< 0.001	1.00(1.00,1.01)	0.041	0.7%
		2-year average	1.38(1.16,1.67)	< 0.001	1.00(1.00,1.00)	0.051	0.7%
		4-year average	1.52(1.24,1.90)	< 0.001	1.00(1.00,1.00)	0.058	0.6%
	IHD	manuscript	1.24(1.01,1.56)	0.044	1.00(1.00,1.01)	0.005	1.6%
		2-year average	1.17(0.98,1.40)	0.089	1.00(1.00,1.01)	0.006	1.8%
		4-year average	1.23(0.99,1.56)	0.065	1.00(1.00,1.01)	0.007	1.6%
	CBVD	manuscript	2.10(1.81,2.46)	< 0.001	1.00(1.00,1.00)	0.017	0.3%
		2-year average	1.89(1.66,2.16)	< 0.001	1.00(1.00,1.00)	0.013	0.3%
		4-year average	2.08(1.79,2.44)	< 0.001	1.00(1.00,1.00)	0.025	0.3%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; MetS, metabolic syndrome; PM, proportion of mediation; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, chronic ischemic heart disease; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S31. Sensitivity analysis for Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by obesity. *

Exposure	Outcome	Sensitivity strategy	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
OM	Total CVD	manuscript	1.58(1.43,1.77)	< 0.001	1.01(1.00,1.01)	0.035	1.4%
		2-year average	1.56(1.41,1.73)	< 0.001	1.01(1.00,1.01)	0.025	1.3%
		4-year average	1.58(1.41,1.78)	< 0.001	1.00(1.00,1.01)	0.110	1.1%
	CAR	manuscript	1.42(1.12,1.82)	0.004	1.00(1.00,1.01)	0.042	1.3%
		2-year average	1.41(1.15,1.77)	0.002	1.00(1.00,1.01)	0.054	1.2%
		4-year average	1.44(1.13,1.85)	0.002	1.00(1.00,1.01)	0.104	1.0%
Cl⁻	IHD	manuscript	1.36(1.05,1.76)	0.021	1.00(1.00,1.01)	0.110	2.0%
		2-year average	1.32(1.02,1.71)	0.034	1.00(1.00,1.01)	0.098	1.9%
		4-year average	1.39(1.07,1.78)	0.018	1.00(1.00,1.01)	0.136	2.0%
	CBVD	manuscript	1.49(1.26,1.78)	< 0.001	1.00(1.00,1.01)	0.094	1.3%
		2-year average	1.60(1.38,1.89)	< 0.001	1.00(1.00,1.01)	0.086	1.0%
		4-year average	1.45(1.21,1.70)	< 0.001	1.00(1.00,1.01)	0.125	1.1%
PM$_{2.5}$	Total CVD	manuscript	1.62(1.47,1.81)	< 0.001	1.01(1.00,1.01)	0.002	1.1%
		2-year average	1.50(1.38,1.64)	< 0.001	1.00(1.00,1.01)	0.003	1.1%
		4-year average	1.64(1.48,1.83)	< 0.001	1.00(1.00,1.01)	0.007	1.0%
	CAR	manuscript	1.46(1.18,1.81)	< 0.001	1.00(1.00,1.01)	0.022	1.0%
		2-year average	1.38(1.14,1.67)	< 0.001	1.00(1.00,1.01)	0.038	1.0%
		4-year average	1.52(1.22,1.92)	< 0.001	1.00(1.00,1.01)	0.046	0.8%
	IHD	manuscript	1.23(1.00,1.55)	0.050	1.01(1.00,1.01)	0.003	2.4%
		2-year average	1.17(0.98,1.41)	0.101	1.00(1.00,1.01)	< 0.001	2.7%
		4-year average	1.22(0.99,1.53)	0.068	1.01(1.00,1.01)	0.010	2.6%
	CBVD	manuscript	2.09(1.80,2.46)	< 0.001	1.00(1.00,1.01)	0.001	0.5%
		2-year average	1.88(1.66,2.16)	< 0.001	1.00(1.00,1.01)	0.005	0.5%
		4-year average	2.07(1.79,2.45)	< 0.001	1.00(1.00,1.01)	0.008	0.4%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, chronic ischemic heart disease; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S32. Sensitivity analysis for Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by raised triglycerides. *

Exposure	Outcome	Sensitivity strategy	NDE†	P for NDE	NIE†	P for NIE	PM (%)‡
OM	Total CVD	manuscript	1.59(1.43,1.78)	< 0.001	1.00(1.00,1.01)	0.056	1.0%
		2-year average	1.56(1.41,1.74)	< 0.001	1.00(1.00,1.01)	0.050	1.0%
		4-year average	1.58(1.42,1.77)	< 0.001	1.00(1.00,1.01)	0.064	0.9%
	CAR	manuscript	1.43(1.12,1.84)	0.006	1.00(1.00,1.01)	0.422	0.5%
		2-year average	1.42(1.14,1.76)	0.005	1.00(1.00,1.01)	0.338	0.5%
		4-year average	1.45(1.13,1.86)	0.002	1.00(1.00,1.01)	0.502	0.4%
Cl$^-$	IHD	manuscript	1.37(1.07,1.79)	0.018	1.01(1.00,1.01)	0.012	3.2%
		2-year average	1.34(1.05,1.69)	0.015	1.01(1.00,1.01)	0.016	3.1%
		4-year average	1.41(1.08,1.82)	0.008	1.01(1.00,1.01)	0.052	2.3%
	CBVD	manuscript	1.50(1.28,1.78)	< 0.001	1.00(1.00,1.01)	0.031	1.2%
		2-year average	1.61(1.38,1.88)	< 0.001	1.00(1.00,1.01)	0.025	1.2%
		4-year average	1.45(1.23,1.72)	< 0.001	1.00(1.00,1.01)	0.062	1.1%
PM$_{2.5}$	Total CVD	manuscript	1.63(1.47,1.81)	< 0.001	1.00(1.00,1.01)	0.004	0.9%
		2-year average	1.51(1.39,1.65)	< 0.001	1.00(1.00,1.01)	0.002	0.9%
		4-year average	1.65(1.50,1.84)	< 0.001	1.00(1.00,1.01)	0.014	0.8%
	CAR	manuscript	1.48(1.18,1.85)	0.001	1.00(1.00,1.01)	0.399	0.4%
		2-year average	1.39(1.17,1.65)	< 0.001	1.00(1.00,1.00)	0.331	0.4%
		4-year average	1.53(1.23,1.92)	< 0.001	1.00(1.00,1.00)	0.500	0.3%
	IHD	manuscript	1.25(1.02,1.56)	0.035	1.01(1.00,1.01)	0.009	2.6%
		2-year average	1.18(0.97,1.43)	0.077	1.00(1.00,1.01)	0.005	2.9%
		4-year average	1.24(1.00,1.55)	0.048	1.01(1.00,1.01)	0.011	2.3%
	CBVD	manuscript	2.10(1.80,2.47)	< 0.001	1.00(1.00,1.01)	0.053	0.3%
		2-year average	1.89(1.66,2.17)	< 0.001	1.00(1.00,1.00)	0.028	0.4%
		4-year average	2.08(1.77,2.46)	< 0.001	1.00(1.00,1.00)	0.054	0.3%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, chronic ischemic heart disease; CBVD, cerebrovascular disease; OM, organic matter; Cl$^-$, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S33. Sensitivity analysis for Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by raised high-density lipoprotein. *

Exposure	Outcome	Sensitivity strategy	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
OM	Total CVD	manuscript	1.60(1.43,1.79)	< 0.001	1.00(1.00,1.01)	0.080	0.5%
		2-year average	1.57(1.42,1.75)	< 0.001	1.00(1.00,1.01)	0.088	0.6%
		4-year average	1.59(1.42,1.77)	< 0.001	1.00(1.00,1.01)	0.037	0.6%
	CAR	manuscript	1.43(1.14,1.86)	0.002	1.00(1.00,1.01)	0.445	0.4%
		2-year average	1.42(1.15,1.80)	0.003	1.00(1.00,1.01)	0.433	0.5%
		4-year average	1.45(1.14,1.85)	< 0.001	1.00(1.00,1.01)	0.332	0.6%
Cl⁻	IHD	manuscript	1.38(1.06,1.80)	0.019	1.00(0.99,1.00)	0.531	-
		2-year average	1.35(1.04,1.71)	0.022	1.00(0.99,1.00)	0.537	-
		4-year average	1.42(1.11,1.84)	0.005	1.00(0.99,1.00)	0.783	-
	CBVD	manuscript	1.51(1.28,1.78)	< 0.001	1.00(0.99,1.00)	0.223	-
		2-year average	1.62(1.38,1.89)	< 0.001	1.00(0.99,1.00)	0.353	-
		4-year average	1.46(1.24,1.73)	< 0.001	1.00(0.99,1.00)	0.236	-
PM$_{2.5}$	Total CVD	manuscript	1.64(1.48,1.80)	< 0.001	1.00(1.00,1.00)	0.169	0.3%
		2-year average	1.52(1.40,1.66)	< 0.001	1.00(1.00,1.00)	0.095	0.4%
		4-year average	1.66(1.50,1.84)	< 0.001	1.00(1.00,1.00)	0.108	0.4%
	CAR	manuscript	1.48(1.20,1.84)	0.003	1.00(1.00,1.00)	0.518	0.2%
		2-year average	1.39(1.16,1.66)	< 0.001	1.00(1.00,1.00)	0.431	0.3%
		4-year average	1.53(1.23,1.90)	< 0.001	1.00(1.00,1.00)	0.365	0.3%
	IHD	manuscript	1.26(1.02,1.59)	0.032	1.00(1.00,1.00)	0.496	0.4%
		2-year average	1.19(1.00,1.43)	0.054	1.00(1.00,1.00)	0.378	0.6%
		4-year average	1.25(1.01,1.60)	0.045	1.00(1.00,1.00)	0.768	0.2%
	CBVD	manuscript	2.11(1.80,2.47)	< 0.001	1.00(1.00,1.00)	0.171	0.2%
		2-year average	1.90(1.68,2.16)	< 0.001	1.00(1.00,1.00)	0.108	0.3%
		4-year average	2.09(1.79,2.45)	< 0.001	1.00(1.00,1.00)	0.167	0.2%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, chronic ischemic heart disease; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S34. Sensitivity analysis for Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by raised blood pressure. *

Exposure	Outcome	Sensitivity strategy	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
OM	Total CVD	manuscript	1.56(1.40,1.76)	< 0.001	1.03(1.02,1.04)	< 0.001	5.8%
		2-year average	1.54(1.39,1.71)	< 0.001	1.03(1.02,1.04)	< 0.001	6.0%
		4-year average	1.57(1.40,1.74)	< 0.001	1.02(1.02,1.03)	< 0.001	5.3%
	CAR	manuscript	1.42(1.12,1.82)	0.006	1.01(1.00,1.03)	0.045	3.2%
		2-year average	1.41(1.13,1.78)	0.004	1.01(1.00,1.02)	0.058	3.2%
		4-year average	1.44(1.14,1.84)	< 0.001	1.01(1.00,1.02)	0.108	2.3%
Cl⁻	IHD	manuscript	1.38(1.07,1.80)	0.021	0.99(0.98,1.00)	0.023	-
		2-year average	1.35(1.07,1.73)	0.014	0.99(0.98,1.00)	0.020	-
		4-year average	1.42(1.09,1.84)	0.007	0.99(0.98,1.00)	0.008	-
	CBVD	manuscript	1.51(1.27,1.78)	< 0.001	1.00(0.99,1.00)	0.023	-
		2-year average	1.62(1.38,1.90)	< 0.001	1.00(0.99,1.00)	0.030	-
		4-year average	1.46(1.24,1.73)	< 0.001	0.99(0.99,1.00)	0.016	-
PM$_{2.5}$	Total CVD	manuscript	1.61(1.45,1.78)	< 0.001	1.01(1.01,1.02)	< 0.001	3.0%
		2-year average	1.49(1.37,1.62)	< 0.001	1.01(1.01,1.02)	< 0.001	3.0%
		4-year average	1.63(1.48,1.82)	< 0.001	1.01(1.01,1.02)	< 0.001	2.5%
	CAR	manuscript	1.46(1.20,1.82)	< 0.001	1.01(1.00,1.01)	0.057	1.5%
		2-year average	1.38(1.15,1.66)	< 0.001	1.00(1.00,1.01)	0.065	1.4%
		4-year average	1.52(1.24,1.92)	< 0.001	1.00(1.00,1.01)	0.142	0.9%
	IHD	manuscript	1.24(1.00,1.55)	0.053	1.01(1.00,1.02)	0.001	4.2%
		2-year average	1.17(0.98,1.41)	0.076	1.01(1.00,1.01)	0.002	4.7%
		4-year average	1.23(0.98,1.57)	0.070	1.01(1.00,1.01)	0.004	3.6%
	CBVD	manuscript	2.09(1.80,2.44)	< 0.001	1.00(1.00,1.01)	0.050	0.5%
		2-year average	1.89(1.67,2.16)	< 0.001	1.00(1.00,1.01)	0.065	0.5%
		4-year average	2.08(1.78,2.44)	< 0.001	1.00(1.00,1.01)	0.061	0.4%

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, chronic ischemic heart disease; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.

Table S35. Sensitivity analysis for Estimated natural direct effect, natural indirect effect, and corresponding 95% CI of the association between the most responsible PM$_{2.5}$ chemical constituents and CVD mediated by impaired fasting glucose. *

Exposure	Outcome	Sensitivity strategy	NDE†	*P* for NDE	NIE†	*P* for NIE	PM (%)‡
OM	Total CVD	manuscript	1.60(1.43,1.79)	< 0.001	1.00(1.00,1.00)	0.760	-
		2-year average	1.58(1.42,1.75)	< 0.001	1.00(1.00,1.00)	0.530	-
		4-year average	1.60(1.43,1.80)	< 0.001	1.00(1.00,1.00)	0.926	-
	CAR	manuscript	1.44(1.12,1.84)	0.003	1.00(1.00,1.00)	0.837	-
		2-year average	1.42(1.14,1.77)	< 0.001	1.00(1.00,1.00)	0.712	-
		4-year average	1.45(1.15,1.87)	0.004	1.00(1.00,1.00)	0.965	-
Cl⁻	IHD	manuscript	1.38(1.06,1.77)	0.021	1.00(0.99,1.01)	0.885	-
		2-year average	1.35(1.05,1.73)	0.020	1.00(0.99,1.00)	0.529	-
		4-year average	1.42(1.09,1.85)	0.014	1.00(0.99,1.01)	0.850	-
	CBVD	manuscript	1.51(1.27,1.79)	< 0.001	1.00(0.99,1.00)	0.236	-
		2-year average	1.62(1.37,1.89)	< 0.001	1.00(0.99,1.00)	0.191	-
		4-year average	1.46(1.22,1.73)	< 0.001	1.00(0.99,1.00)	0.392	-
PM$_{2.5}$	Total CVD	manuscript	1.65(1.50,1.82)	< 0.001	1.00(1.00,1.00)	0.267	-
		2-year average	1.52(1.40,1.66)	< 0.001	1.00(1.00,1.00)	0.191	-
		4-year average	1.67(1.52,1.84)	< 0.001	1.00(1.00,1.00)	0.419	-
	CAR	manuscript	1.48(1.20,1.84)	< 0.001	1.00(1.00,1.00)	0.598	-
		2-year average	1.39(1.17,1.68)	< 0.001	1.00(1.00,1.00)	0.493	-
		4-year average	1.54(1.25,1.96)	0.001	1.00(1.00,1.00)	0.783	-
	IHD	manuscript	1.26(1.03,1.59)	0.028	1.00(1.00,1.00)	0.875	-
		2-year average	1.19(0.99,1.43)	0.065	1.00(1.00,1.00)	0.637	-
		4-year average	1.25(1.00,1.60)	0.048	1.00(1.00,1.00)	0.904	-
	CBVD	manuscript	2.11(1.82,2.49)	< 0.001	1.00(1.00,1.00)	0.449	-
		2-year average	1.90(1.67,2.18)	< 0.001	1.00(1.00,1.00)	0.323	-
		4-year average	2.09(1.80,2.46)	< 0.001	1.00(1.00,1.00)	0.643	-

Note: Units are per IQR increase in pollutants. NDE, natural direct effect; NIE, natural indirect effect; PM$_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM, proportion of mediation; CVD, cardiovascular disease; CAR, cardiac arrests; IHD, chronic ischemic heart disease; CBVD, cerebrovascular disease; OM, organic matter; Cl⁻, chloride.

* Adjusted for age, sex, education, marital status, annual household income, urbanicity, family history of hypertension, smoke, second-hand smoke, alcohol, indoor air pollution, physical activity, the dietary approaches to stop hypertension (DASH) score, and three-year average temperature.

† Estimated effects of NDE and NIE were represented as HR (95% CI).

‡ Proportion < 0.1% was presented as '-'.