

SUPPLEMENTARY MATERIALS

Supplementary Text 1. Selection criteria for items used to construct the frailty index

The 29 health deficits were selected based on established principles for frailty index (FI) construction^[1] and covered multiple domains, including activities of daily living (ADLs), chronic diseases, sleep quality, self-rated health, mental health, physical activity, and anthropometric measurements.

Specifically, items were required to: 1) reflect a health deficit; 2) generally show an increasing prevalence with age within our population; 3) not exhibit premature saturation (i.e., not have a prevalence near 100% in the youngest age groups); 4) collectively cover a broad range of physiological systems; and 5) have a low missing rate (< 5% in our dataset). Regarding reliability and validity, although the internal consistency of the frailty index (FI) (e.g., Cronbach's alpha) was not formally assessed, its construct validity was evaluated. The frailty indices constructed in the study exhibited several well-recognized characteristics of a robust FI, including a positive association with age, a right-skewed distribution, higher mean FI scores in women than in men, and at least 99% of values below 0.7. These features indicate good construct validity. Furthermore, the FI has demonstrated high validity in a large population of middle-aged and older adults in China^[2].

Supplementary Text 2. Exposure assessment methods

The TAP database integrates satellite-derived aerosol optical depth estimation data, ground monitoring data, and emission inventory data, and uses the Weather Research and Forecasting model (WRF v3.9.1) coupled with the Community Multiscale Air Quality model (CMAQ v5.2) to evaluate daily concentrations in China since 2000^[1,3]. For the TAP dataset concerning PM_{2.5} mass concentration, the average out-of-bag cross-validation correlation coefficient (R) is 0.83. The estimates from TAP have been validated using in-situ observations; the Pearson correlation coefficients (R²) between observed and estimated values for total PM_{2.5}, black carbon (BC), nitrate (NO₃⁻), sulfate (SO₄²⁻), ammonium (NH₄⁺), and organic matter (OM) were 0.72, 0.66, 0.65, 0.75, 0.74, and 0.71, respectively^[4]. This indicates a high consistency between TAP's estimations of PM components and ground measurements. The platform has been widely used^[5].

Supplementary Table S1. List of 29 variables included in the frailty index

No.	Variables	Description	Value
1	N1	Need help to eat.	1.00 = Yes; 0.00 = No.
2	N2	Need help to bath.	1.00 = Yes; 0.00 = No.
3	N3	Need help to move from chair to bed.	1.00 = Yes; 0.00 = No.
4	N4	Need help to dress,	1.00 = Yes; 0.00 = No.
5	N7	Need help to use toilet.	1.00 = Yes; 0.00 = No.
6	N8	Need help to groom.	1.00 = Yes; 0.00 = No.
7	N9	Need help to walk.	1.00 = Yes; 0.00 = No.
8	N10	Need help to up/down stairs.	1.00 = Yes; 0.00 = No.
9	D1	Self-reported diagnosis of hypertension by a doctor, self-reported use of antihypertension drugs, systolic blood pressure measured to be ≥ 140 mmHg, or diastolic blood pressure measured to be ≥ 90 mmHg	1.00 = Yes; 0.00 = No.
10	D2	Self-reported diagnosis of dyslipidemia by a doctor, self-reported use of lipid-lowering drugs, serum total cholesterol ≥ 6.22 mmol/L, triglyceride ≥ 2.26 mmol/L, high density lipoprotein cholesterol < 1.04 mmol/L, or low density lipoprotein cholesterol ≥ 4.14 mmol/L	1.00 = Yes; 0.00 = No.
11	D3	Self-reported diagnosis of diabetes by a doctor, self-reported use of antidiabetic drugs, fasting blood glucose measured to be ≥ 7.0 mmol/L, or random blood glucose measured to be ≥ 11.1 mmol/L	1.00 = Yes; 0.00 = No.
12	D4	Self-reported diagnosis of heart disease by a doctor	1.00 = Yes; 0.00 = No.
13	D5	Self-reported diagnosis of stroke by a doctor	1.00 = Yes; 0.00 = No.
14	D6	Self-reported diagnosis of emphysema or chronic bronchitis by a doctor	1.00 = Yes; 0.00 = No.
15	D7	Self-reported diagnosis of tuberculosis by a doctor	1.00 = Yes; 0.00 = No.
16	D8	Self-reported diagnosis of asthma by a doctor	1.00 = Yes; 0.00 = No.
17	D9	Self-reported diagnosis of peptic ulcer by a doctor	1.00 = Yes; 0.00 = No.
18	D10	Self-reported diagnosis of gallstone disease by a doctor	1.00 = Yes; 0.00 = No.
19	D11	Self-reported diagnosis of malignant tumor by a doctor	1.00 = Yes; 0.00 = No.
20	Sleep	During the past month, did you have any of the following for ≥ 3 days per week: 1) taking > 30 min to fall asleep after going to bed or waking up in the middle of the night; 2) waking up early and not being able to go back to sleep; or 3) having difficulty staying alert while at work, eating, or meeting people during the daytime?	1.00 = Yes; 0.00 = No.

21	Score	How is your current general health status?	Poor = 1.00; fair = 0.50; good = 0.25; excellent = 0.00.
22	Depression	PHQ-2 score ≥ 3 or self-reported use of antidepressant in last two weeks	1.00 = Yes; 0.00 = No.
23	Anxiety	GAD-2 score ≥ 3 or self-reported use of anti-anxiolytic in last two weeks	1.00 = Yes; 0.00 = No.
24	Suicide	The thought of "dying" or hurting yourself in some way in last two weeks	1.00 = Yes; 0.00 = No.
25	BMI	Body-mass index (kg/m^2)	< 18.5 or $\geq 28.0 = 1.00$; ≥ 24.0 and $< 28.0 = 0.50$; ≥ 18.5 and $< 24.0 = 0.00$. ≥ 0.95 for men or ≥ 0.90 for women = 1.00;
26	WHR	Waist circumference (cm) to hip circumference ratio	≥ 0.90 and < 0.95 for men or ≥ 0.85 and < 0.90 for women = 0.50; < 0.90 for men or < 0.85 for women = 0.00
27	GS	Handgrip strength	< 28.0 kg for men or < 18.0 kg for women = 1.00; ≥ 28.0 kg for men or ≥ 18.0 kg for women = 0.00.
28	HR	Measured heart rate, beats per min	< 60 or $> 100 = 1.00$; ≥ 60 and $\leq 100 = 0.00$
29	Exercise	Physical activity in the past 12 months, including the usual type and duration of activities in occupational, commuting, domestic, and leisure time-related domains	Lowest quintile stratified by sex = 1.00; other = 0.00

Supplementary Table S2. The distribution of the frailty index

Age group	Overall	Men	Women	P-value
45-	0.09 \pm 0.06	0.10 \pm 0.06	0.08 \pm 0.05	< 0.001
50-	0.10 \pm 0.06	0.10 \pm 0.06	0.10 \pm 0.06	0.020
55-	0.11 \pm 0.06	0.10 \pm 0.06	0.11 \pm 0.06	< 0.001
60-	0.12 \pm 0.07	0.11 \pm 0.07	0.13 \pm 0.07	< 0.001
65-	0.13 \pm 0.08	0.12 \pm 0.07	0.14 \pm 0.08	< 0.001
70-	0.14 \pm 0.08	0.13 \pm 0.08	0.16 \pm 0.08	< 0.001
75-	0.16 \pm 0.09	0.14 \pm 0.08	0.17 \pm 0.09	< 0.001
Total	0.12 \pm 0.07	0.11 \pm 0.07	0.13 \pm 0.08	< 0.001

Supplementary Table S3. Basic demographic characteristics of the study participants according to frailty status

Variables	Robust (n = 10,113)	Prefrailty (n = 12,483)	Frailty (n = 1,341)	P
Age (year, mean ± SD)	59.69 ± 8.92	63.34 ± 9.01	68.67 ± 7.67	< 0.001
Gender				< 0.001
Men	4,119 (40.73)	4,512 (36.15)	400 (29.83)	
Women	5,994 (59.27)	7,971 (63.85)	941 (70.17)	
Education level (n, %)				< 0.001
Illiterate	1,441 (14.25)	2,691 (21.56)	478 (35.64)	
Elementary school	2,791 (27.60)	3,908 (31.31)	486 (36.24)	
Junior high school	4,377 (43.28)	4,400 (35.25)	299 (22.30)	
Senior high school or above	1,504 (14.87)	1,484 (11.89)	78 (5.82)	
Marital status (n, %)				< 0.001
Married/cohabiting	9,148 (90.46)	10,695 (85.68)	1,067 (79.57)	
Widowed/divorced/separated/single	965 (9.54)	1,788 (14.32)	274 (20.43)	
Average monthly income (n, %)				< 0.001
< 500 RMB	2,857 (28.25)	4,388 (35.15)	650 (48.47)	
500- RMB	2,732 (27.02)	3,384 (27.11)	351 (26.18)	
≥ 1000 RMB	4,524 (44.73)	4,711 (37.74)	340 (25.35)	
Smoking status (n, %)				< 0.001
No current smoking	8,106 (80.15)	10,693 (85.66)	1,272 (94.85)	
Current smoking	2,007 (19.85)	1,790 (14.34)	69 (5.15)	
Drinking status (n, %)				< 0.001
No current drinking	8,437 (83.43)	10,792 (86.45)	1,275 (95.08)	
Current drinking	1,676 (16.57)	1,691 (13.55)	66 (4.92)	
High-fat diet (n, %)				< 0.001
No	7,945 (78.56)	10,321 (82.68)	1,196 (89.19)	
Yes	2,168 (21.44)	2,162 (17.32)	145 (10.81)	
More fruits & vegetables intake (n, %)				< 0.001
No	5,074 (50.17)	6,890 (55.2)	836 (62.34)	
Yes	5,039 (49.83)	5,593 (44.8)	505 (37.66)	
PM _{2.5} (µg/ m ³ , mean ± SD)	58.91 ± 8.95	59.88 ± 9.73	61.90 ± 10.38	< 0.001
PM _{2.5} components				
BC (µg/ m ³ , mean ± SD)	2.40 ± 0.31	2.43 ± 0.34	2.49 ± 0.36	< 0.001
NO ₃ ⁻ (µg/ m ³ , mean ± SD)	14.89 ± 1.95	15.12 ± 2.12	15.56 ± 2.26	< 0.001
SO ₄ ²⁻ (µg/ m ³ , mean ± SD)	10.84 ± 1.44	11.02 ± 1.56	11.35 ± 1.67	< 0.001
NH ₄ ⁺ (µg/ m ³ , mean ± SD)	9.47 ± 1.31	9.62 ± 1.42	9.92 ± 1.52	< 0.001
OM (µg/ m ³ , mean ± SD)	13.21 ± 1.54	13.39 ± 1.68	13.74 ± 1.79	< 0.001

Note. SD, standard deviation; PM_{2.5}, particulate matter with an aerodynamic diameter ≤ 2.5µm; BC, Black carbon; NO₃⁻, nitrate; SO₄²⁻, Sulfate; NH₄⁺, ammonium; OM, organic matter.

Supplementary Table S4. Summary statistics of 3-year averaged concentrations of ambient PM_{2.5} and its components

Variables	Mean	SD	IQR	Min	P ₂₅	Median	P ₇₅	Max
PM _{2.5}	59.58	9.48	22.54	46.82	49.43	56.40	71.97	78.78
Components								
BC	2.42	0.33	0.78	1.87	2.06	2.34	2.84	3.25
NO ₃ ⁻	15.05	2.07	4.83	11.70	12.96	14.54	17.79	18.85
SO ₄ ²⁻	10.96	1.52	3.48	8.67	9.50	10.48	12.98	14.02
NH ₄ ⁺	9.58	1.39	3.22	7.53	8.19	9.21	11.41	12.13
OM	13.33	1.63	3.59	10.95	11.83	12.83	15.42	17.27

Note. SD, standard deviation; BC, Black carbon; NO₃⁻, nitrate; SO₄²⁻, Sulfate; NH₄⁺, ammonium; OM, organic matter.

Supplementary Table S5. Weights of PM_{2.5} components in the Weighted Quantile Sum results

Mix_name	Weight	
	Prefrailty	Frailty
OM	0.415433	0.160554
NO ₃ ⁻	0.281246	0.659815
SO ₄ ²⁻	0.197047	0.000001
BC	0.100517	0.166632
NH ₄ ⁺	0.005757	0.012998

Note. BC, Black carbon; NO₃⁻, nitrate; SO₄²⁻, Sulfate; NH₄⁺, ammonium; OM, organic matter.

Supplementary Table S6. Sensitivity analyses associations of 3-year averaged PM_{2.5} and its components (each SD increment) with prefrailty and frailty when using cut-off value 1 of FI to define frailty status.

	Single-pollutant model ^a OR (95% CI)	Component- PM _{2.5} model ^b OR (95% CI)	Component-residual model ^c OR (95% CI)
Prefrailty			
PM _{2.5}	1.118 (1.087, 1.151)	-	-
BC	1.105 (1.074, 1.137)	0.256 (0.187, 0.350)	0.014 (0.006, 0.038)
NO ₃ ⁻	1.124 (1.093, 1.157)	1.515 (1.215, 1.890)	1.251 (1.123, 1.394)
SO ₄ ²⁻	1.130 (1.099, 1.163)	1.526 (1.301, 1.790)	1.354 (1.218, 1.505)
NH ₄ ⁺	1.127 (1.096, 1.159)	1.424 (1.206, 1.681)	1.326 (1.175, 1.497)
OM	1.126 (1.094, 1.158)	1.263 (1.100, 1.450)	1.174 (1.078, 1.279)
Frailty			
PM _{2.5}	1.325 (1.263, 1.390)	-	-
BC	1.301 (1.240, 1.366)	0.086 (0.050, 0.149)	0.001 (0.000, 0.003)
NO ₃ ⁻	1.331 (1.269, 1.396)	1.650 (1.113, 2.448)	1.329 (1.100, 1.605)
SO ₄ ²⁻	1.337 (1.275, 1.401)	1.775 (1.326, 2.375)	1.568 (1.296, 1.898)
NH ₄ ⁺	1.332 (1.270, 1.397)	1.544 (1.142, 2.087)	1.475 (1.188, 1.832)
OM	1.330 (1.268, 1.394)	1.357 (1.058, 1.741)	1.271 (1.092, 1.478)

Note. OR, odds ratio; 95% CI, 95% confidence interval; PM_{2.5}, particulate matter with an

aerodynamic diameter $\leq 2.5 \mu\text{m}$; BC, Black carbon; NO_3^- , nitrate; SO_4^{2-} , Sulfate; NH_4^+ , ammonium; OM, organic matter. Model was adjusted for age, gender, marital status, educational level, per capital monthly income, smoking status, drinking status, high-fat diet and adequate vegetables and fruits intake. a: $\text{PM}_{2.5}$ and its components were included by origin value to assess associations with outcomes. b: additionally adjust for $\text{PM}_{2.5}$ mass based on single-pollutant model. c: the original value was replaced with the residual of each component to $\text{PM}_{2.5}$ mass based on single-pollutant model.

Supplementary Table S7. Sensitivity analyses associations of 3-year averaged $\text{PM}_{2.5}$ and its components (each SD increment) with prefrailty and frailty when using cut-off value 2 of FI to define frailty status

	Single-pollutant model ^a OR (95% CI)	Component- $\text{PM}_{2.5}$ model ^b OR (95% CI)	Component-residual model ^c OR (95% CI)
Prefrailty			
$\text{PM}_{2.5}$	1.126 (1.093, 1.160)	-	-
BC	1.111 (1.079, 1.145)	0.223 (0.161, 0.308)	0.009 (0.003, 0.025)
NO_3^-	1.133 (1.100, 1.167)	1.621 (1.291, 2.034)	1.296 (1.160, 1.449)
SO_4^{2-}	1.141 (1.108, 1.175)	1.655 (1.405, 1.949)	1.429 (1.282, 1.592)
NH_4^+	1.137 (1.104, 1.171)	1.529 (1.289, 1.815)	1.398 (1.234, 1.584)
OM	1.136 (1.103, 1.170)	1.327 (1.151, 1.530)	1.210 (1.108, 1.321)
Frailty			
$\text{PM}_{2.5}$	1.396 (1.309, 1.489)	-	-
BC	1.371 (1.284, 1.463)	0.070 (0.033, 0.147)	0.000 (0.000, 0.002)
NO_3^-	1.402 (1.315, 1.496)	1.727 (1.005, 2.968)	1.362 (1.049, 1.768)
SO_4^{2-}	1.408 (1.321, 1.501)	1.848 (1.243, 2.748)	1.636 (1.260, 2.125)
NH_4^+	1.404 (1.317, 1.496)	1.599 (1.062, 2.409)	1.534 (1.141, 2.064)
OM	1.401 (1.315, 1.494)	1.415 (1.008, 1.987)	1.317 (1.071, 1.620)

Note. OR, odds ratio; 95% CI, 95% confidence interval; $\text{PM}_{2.5}$, particulate matter with an aerodynamic diameter $\leq 2.5\mu\text{m}$; BC, Black carbon; NO_3^- , nitrate; SO_4^{2-} , Sulfate; NH_4^+ , ammonium; OM, organic matter. Model was adjusted for age, gender, marital status, educational level, per capital monthly income, smoking status, drinking status, high-fat diet and adequate vegetables and fruits intake. ^a: $\text{PM}_{2.5}$ and its components were included by origin value to assess associations with outcomes. ^b: additionally adjust for $\text{PM}_{2.5}$ mass based on single-pollutant model. ^c: the original value was replaced with the residual of each component to $\text{PM}_{2.5}$ mass based on single-pollutant model.

Supplementary Table S8. Associations of 3-year averaged PM_{2.5} and its components (each SD increment) with prefrailty and frailty after adjust O₃ and NO₂

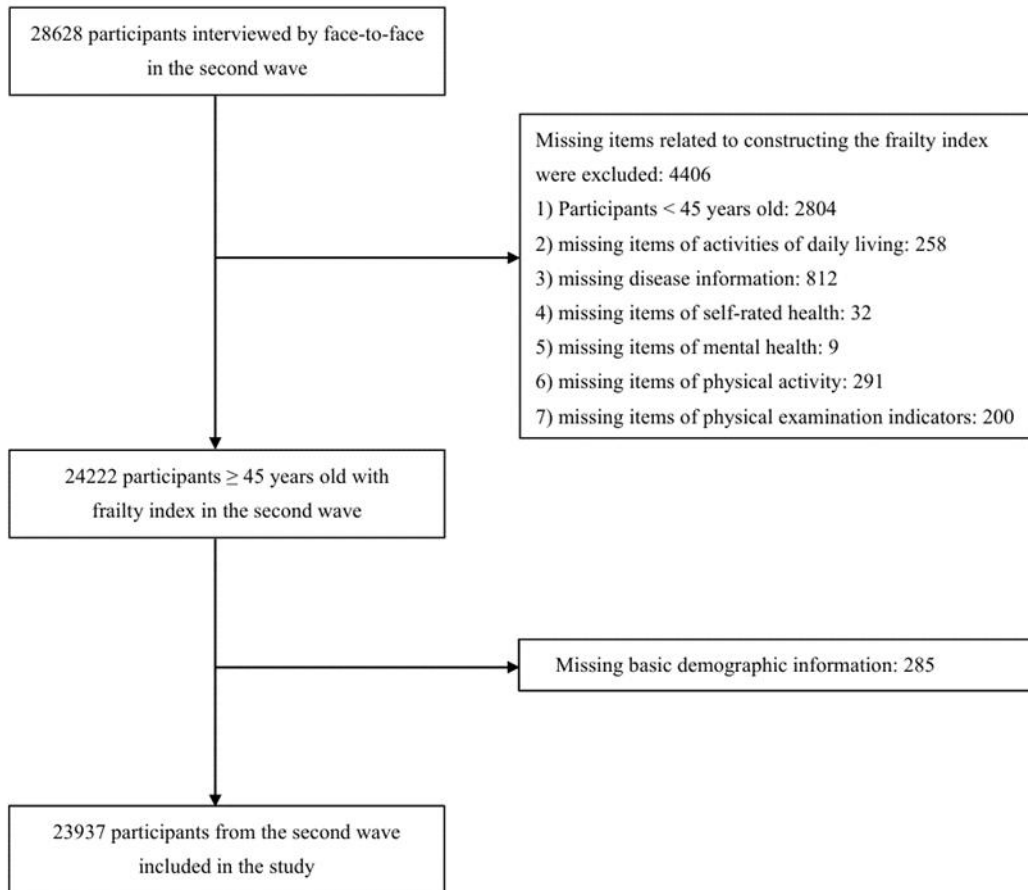
Pollution	Single-pollutant model ^a OR (95% CI)	Component-PM _{2.5} model ^b OR (95% CI)	Component-residual model ^c OR (95% CI)
Prefrailty			
PM _{2.5}	1.315 (1.158, 1.493)		
BC	1.125 (1.000, 1.266)	0.319 (0.223, 0.458)	0.035 (0.011, 0.105)
NO ₃ ⁻	1.206 (1.079, 1.348)	0.751 (0.550, 1.027)	0.929 (0.799, 1.080)
SO ₄ ²⁻	1.217 (1.079, 1.373)	0.376 (0.227, 0.624)	0.589 (0.423, 0.822)
NH ₄ ⁺	1.199 (1.058, 1.360)	0.600 (0.427, 0.844)	0.651 (0.508, 0.833)
OM	1.119 (0.978, 1.279)	0.407 (0.294, 0.565)	0.532 (0.438, 0.646)
Frailty			
PM _{2.5}	2.323 (1.694, 3.185)		
BC	1.599 (1.192, 2.145)	0.088 (0.037, 0.205)	0.001 (0.000, 0.016)
NO ₃ ⁻	1.807 (1.374, 2.377)	0.490 (0.231, 1.040)	0.830 (0.578, 1.191)
SO ₄ ²⁻	1.902 (1.409, 2.568)	0.098 (0.029, 0.330)	0.310 (0.143, 0.672)
NH ₄ ⁺	1.858 (1.360, 2.537)	0.311 (0.134, 0.723)	0.345 (0.189, 0.631)
OM	1.778 (1.280, 2.470)	0.267 (0.122, 0.586)	0.328 (0.206, 0.522)

Note. OR, odds ratio; 95% CI, 95% confidence interval; PM_{2.5}, particulate matter with an aerodynamic diameter ≤ 2.5 μm; BC, Black carbon; NO₃⁻, nitrate; SO₄²⁻, Sulfate; NH₄⁺, ammonium; OM, organic matter. Model was adjusted for age, gender, marital status, educational level, per capital monthly income, smoking status, drinking status, high-fat diet, adequate vegetables and fruits intake, O₃ and NO₂. ^a: PM_{2.5} and its components were included by origin value to assess associations with outcomes. ^b: additionally adjust for PM_{2.5} mass based on single-pollutant model. ^c: the original value was replaced with the residual of each component to PM_{2.5} mass based on single-pollutant model.

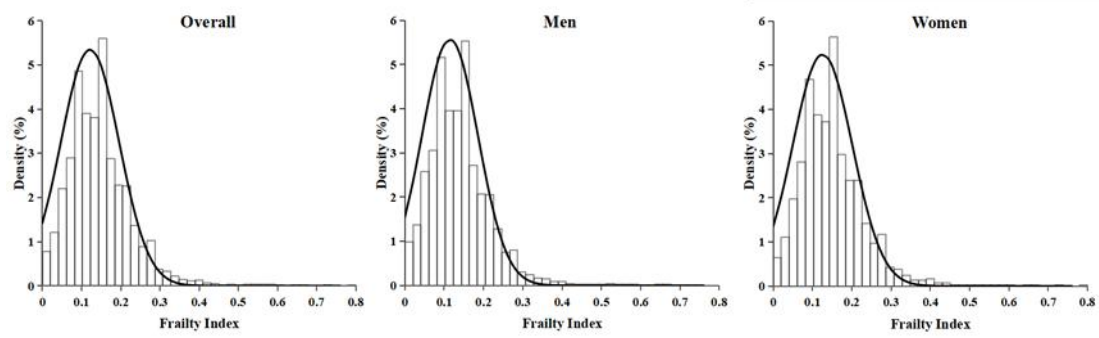
Supplementary Table S9. Collinearity diagnostics for the association between PM_{2.5}, its components, and frailty.

Variable	Tolerance	VIF
Gender	0.556	1.799
Age	0.722	1.386
Culture	0.759	1.318
Marry	0.912	1.097
Income	0.898	1.113
Smoking	0.656	1.523
Drinking	0.742	1.347
High fat	0.935	1.069
Vegetables	0.906	1.104
NO ₂	0.086	11.586
O ₃	0.178	5.633

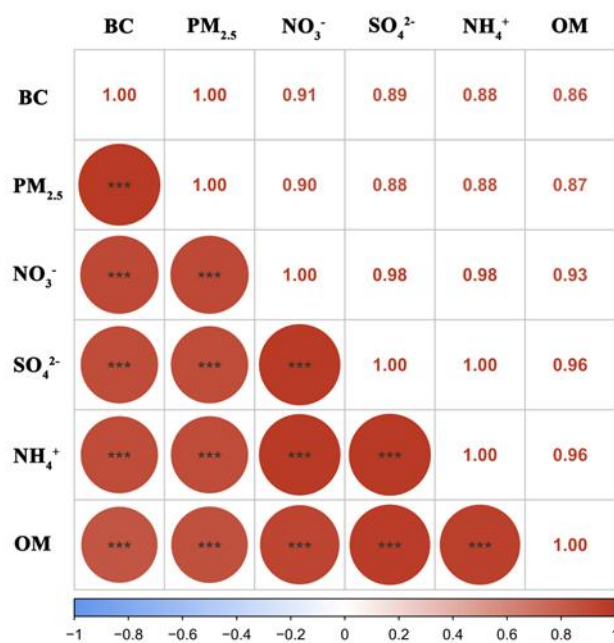
Note. NO₂, Nitrogen Dioxide; O₃, Ozone; VIF, Variance inflation factor.



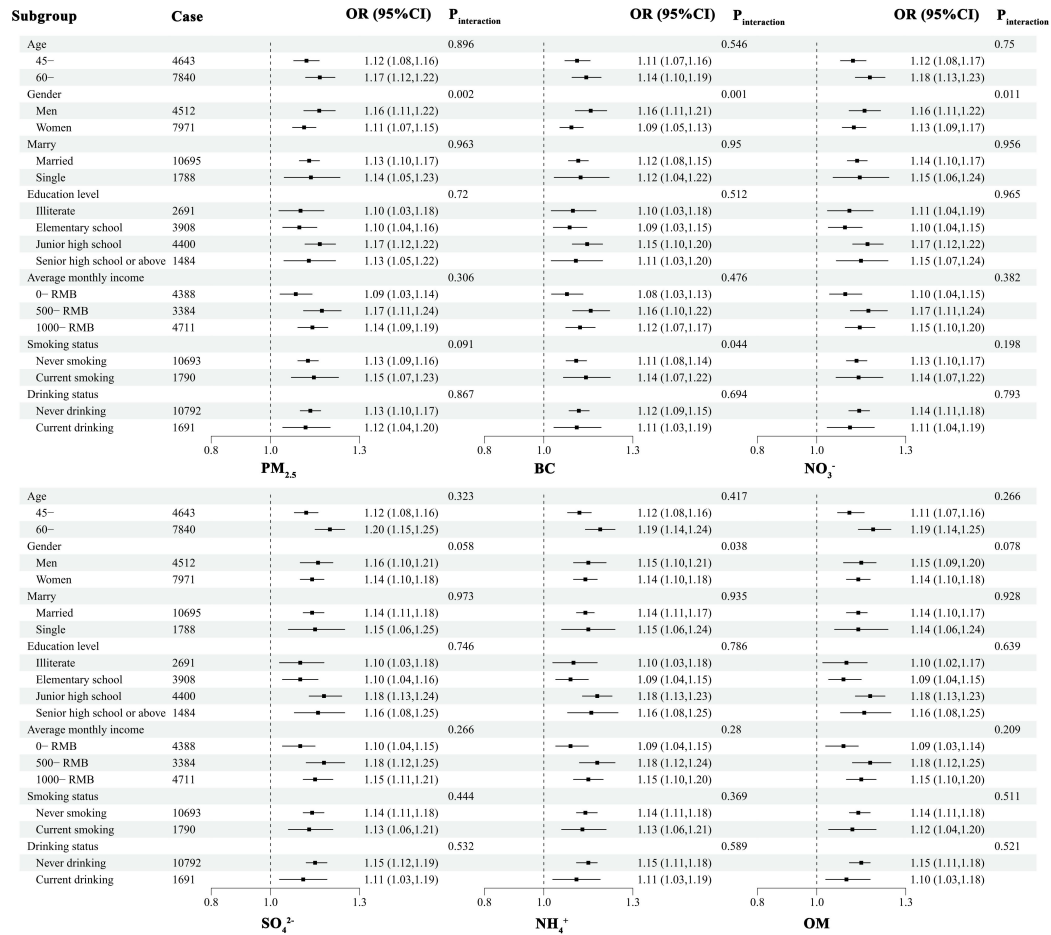
Supplementary Figure S1. Inclusion and exclusion criteria for study subjects.

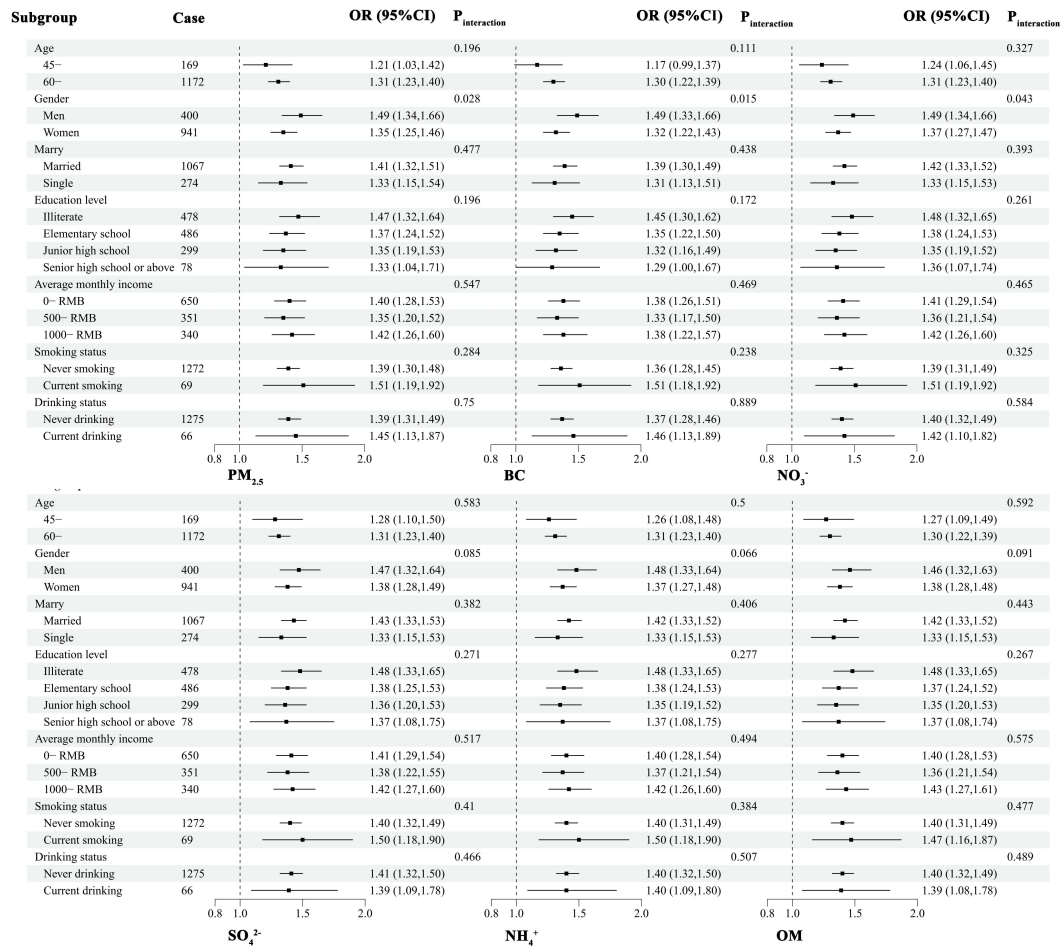


Supplementary Figure S2. Distribution of FI at baseline. The solid line represents the fitted density plot of the FI.

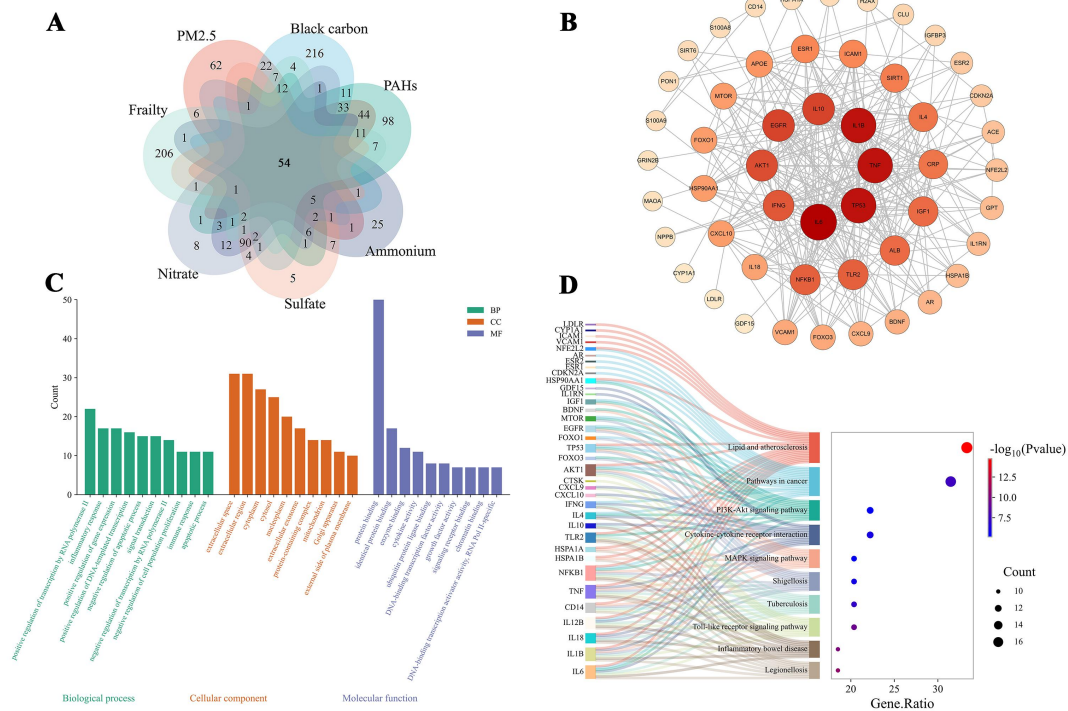


Supplementary Figure S3. Correlation between 3-year averaged concentrations of ambient PM_{2.5} and its components. PM_{2.5}, particulate matter with an aerodynamic diameter ≤ 2.5 μm; BC, Black carbon; NO₃⁻, nitrate; SO₄²⁻, Sulfate; NH₄⁺, ammonium; OM, organic matter.

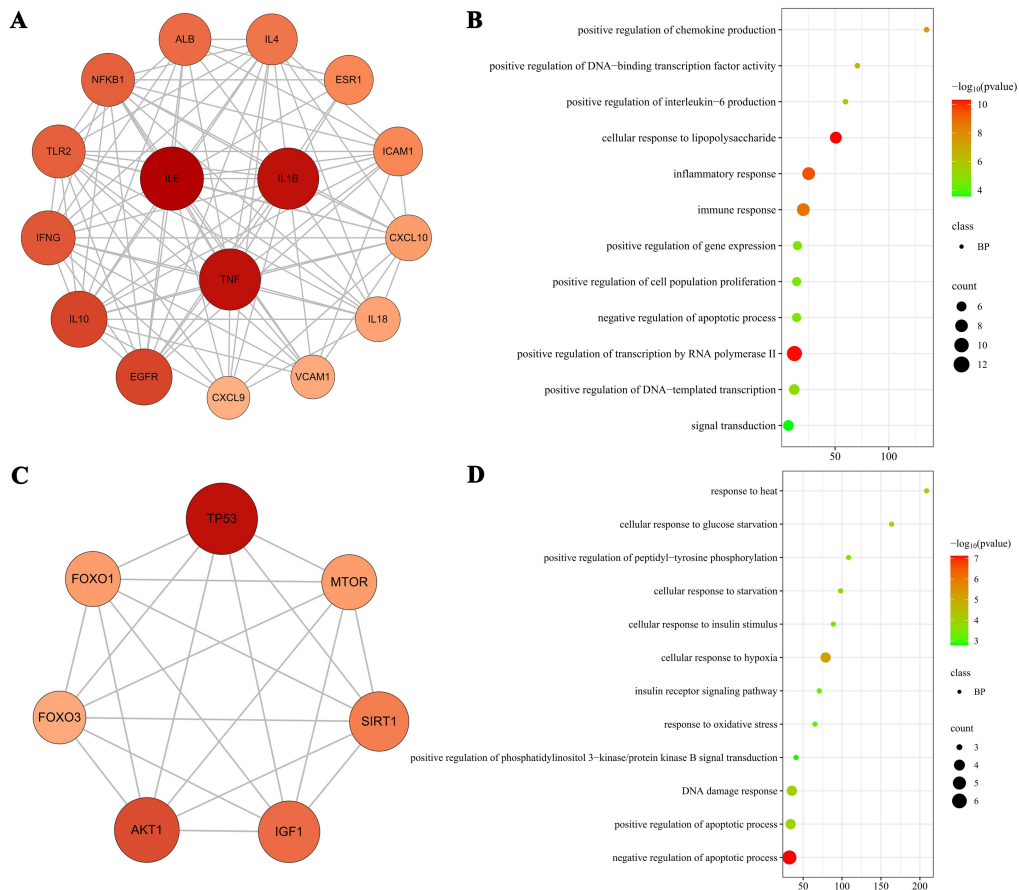




Supplementary Figure S5. Associations of 3-year averaged PM_{2.5} and its components (each SD increment) with frailty in stratified analyses. Model was adjusted for age, gender, marital status, educational level, per capital monthly income, smoking status, drinking status, high-fat diet and adequate vegetables and fruits intake. PM_{2.5}, particulate matter with an aerodynamic diameter ≤ 2.5 μm; BC, black carbon; NO₃⁻, nitrate; NH₄⁺, ammonium; SO₄²⁻, sulfate; OM, organic matter.



Supplementary Figure S6. Results of network toxicology. (A) Venn diagram showing frailty target genes associated with exposure to PM_{2.5} and its components. (B) The PPI network was constructed using the STRING database with a confidence score threshold of ≥ 0.7 , and it was further visualized and analyzed using Cytoscape 3.10.4. Nodes represent proteins, and edges indicate interactions between them. Nodes are colored and sized according to their degree values, with darker colors and larger circles indicating stronger interactions. (C) GO Enrichment Analysis of Air Pollutants-Frailty Targets. (D) KEGG Enrichment Analysis of Air Pollutants-Frailty Targets.



Supplementary Figure S7. Core gene clustering network diagram. The target network processing method uses the size of the point to represent the betweenness centrality. Node size represents betweenness centrality. Node color represents closeness centrality, with a redder color indicating a higher value. (A) The Cluster1 of PPI. (B) The GO-BP analysis of Cluster1. (C) The Cluster2 of PPI. (D) The GO-BP analysis of Cluster2.

Reference

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