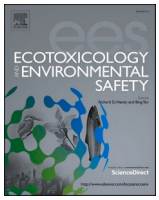
Ecotoxicology and Environmental Safety 281 (2024) 116634

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: www.elsevier.com/locate/ecoenv



Health effect of multiple air pollutant mixture on sarcopenia among middle-aged and older adults in China

Yinqiao Dong [a,b,1], Wangnan Cao [c,1], Jing Wei [d], Yingjie Chen [a,b], Yinghuan Zhang [a,b], Shengzhi Sun [e], Fan Hu [a,*], Yong Cai [a,*]

[a] Public Health Department, Hongqiao International Institute of Medicine, Tongren Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, PR China
[b] School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai, PR China
[c] Department of Social Medicine and Health Education, School of Public Health, Peking University, Beijing, PR China
[d] Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, MD, United States
[e] School of Public Health, Capital Medical University, Beijing 100069, China

ARTICLE INFO

Edited by Bing Yan

Keywords:
Air pollution
Sarcopenia
Creatinine
Cystatin C
Mixture effect

ABSTRACT

Background: As the global aging process accelerates, the health challenges posed by sarcopenia among middle-aged and older adults are becoming increasingly prominent. However, the available evidence on the adverse effects of air pollution on sarcopenia is limited, particularly in the Western Pacific region. This study aimed to explore relationships of multiple air pollutants with sarcopenia and related biomarkers using the nationally representative database.

Methods: Totally, 6585 participants aged over 45 years were enrolled from the China Health and Retirement Longitudinal Study (CHARLS) in 2011 and 3443 of them were followed up until 2015. Air pollutants were estimated from high-resolution satellite-based spatial-temporal models. In the cross-sectional analysis, we used generalized linear regression, unconditional logistic regression analytical and restricted cubic spline (RCS) methods to assess the single-exposure and non-linear effects of multiple air pollutants on sarcopenia and related surrogate biomarkers (serum creatinine and cystatin C). Several popular mixture analysis techniques such as Bayesian kernel machine regression (BKMR), weighted quantile sum (WQS) regression, and quantile-based g-computation (Qgcomp) were further used to examinate the combined effects of multiple air pollutants. Logistic regression was used to further analyze the longitudinal association between air pollution and sarcopenia.

Results: Each interquartile range increase in $PM_{2.5}$, PM_{10} and NO_2 was significantly associated with an increased risk of sarcopenia, with adjusted odds ratios (aORs) of 1.09 [95 % confidence interval (CI): 1.01, 1.20], 1.24 (95 % CI: 1.14, 1.35) and 1.18 (95 % CI: 1.08, 1.28), respectively. Our findings also showed that five air pollutants were significantly associated with the sarcopenia index. In addition, employing a mixture analysis approach, we confirmed significant combined effects of air pollution mixtures on sarcopenia risk and associated biomarkers, with PM_{10} and $PM_{2.5}$ identified as major contributors to the combined effect. The results of the exposure-response (E-R) relationships, subgroup analysis, longitudinal analysis and sensitivity analysis all showed the unfavorable impact of air pollution on sarcopenia risk and related vulnerable populations.

Conclusions: Single-exposure and co-exposure to multiple air pollutants were positively associated with sarcopenia among middle-aged and older adults in China. Our study provided new evidence that air pollution mixture was significantly associated with sarcopenia related biomarkers.

Abbreviations: ASM, appendicular skeletal muscle mass; AWGS, Asian Work Group for Sarcopenia; BKMR, Bayesian kernel machine regression; BMI, body mass index; CHARLS, China Health and Retirement Longitudinal Study; CI, confidence interval; DAG, Directed Acyclic Graph; IQR, inter-quartile range; NO_2, nitrogen oxides; OR, odds ratios; O_3, ozone; PM, particulate matter; Qgcomp, quantile-based g computation model; RCS, restricted cubic spline; SI, sarcopenia index; WQS, weighted quantile sum regression.

* Corresponding authors.
E-mail addresses: joyking2003@163.com (F. Hu), caiyong202028@hotmail.com (Y. Cai).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.ecoenv.2024.116634
Received 16 March 2024; Received in revised form 12 June 2024; Accepted 21 June 2024

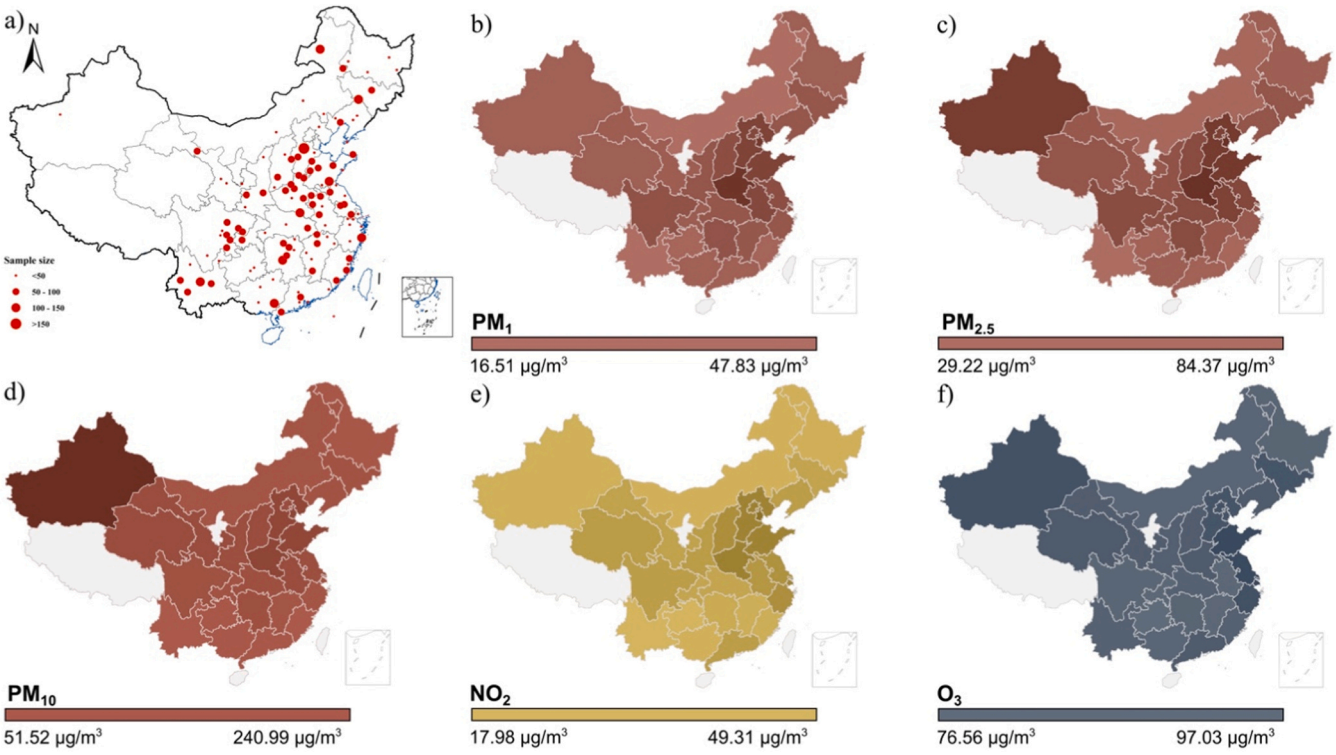


Fig. 1. Geographical distribution of study population and five air pollutants. The panel (a) presented sample distribution in 125 survey cities from 28 provinces of China. The panel (b)-(f) presented the average annual concentration of PM_1, $PM_{2.5}$, PM_{10}, NO_2 and O_3 during 2011–2015, respectively.

1. Introduction

Sarcopenia is a progressive condition associated with aging process manifested by a gradual decline in muscle mass, strength, or physical function(Cruz-Jentoft and Sayer, 2019). As the global demographic transforms into an aging society, sarcopenia emerges as a significant health concern deserving attention. Globally, meta-analysis studies report an approximate prevalence of 10 % or higher in people aged 60 years and over (Petermann-Rocha et al., 2022). In Asia, recent epidemiologic studies estimated the prevalence of sarcopenia ranging from 5.5 % to 25.7 % (Chen et al., 2020), with an estimated 18.6 % prevalence among the elderly population in China (Wu et al., 2021). Such a high prevalence further leads to various health-related outcomes, including fall-related injuries, increased hospitalizations, frailty-related illnesses, cardiovascular diseases, metabolic disorders, cognitive impairment, and mortality (Gao et al., 2022; Xia et al., 2020; Yuan and Larsson, 2023).

Identifying potential modifiable factors such as air pollution may have important public health implications for preventing or delaying age-related diseases (Collaborators, 2020). Initially, previous studies simply observed the adverse effects of air pollution on the single component of sarcopenia, including lower handgrip strength, reduced performance-based body functions, or decreased skeletal muscle mass (de Zwart et al., 2018; Tung et al., 2021; Zare Sakhvidi et al., 2022). Currently, there is growing evidence of the relationship between outdoor air pollution and sarcopenia(Cai et al., 2024; Chen et al., 2023; Lai et al., 2022; Shi et al., 2024; Shi et al., 2023; Zhang et al., 2023b). For example, Lai et al. and Cai et al., utilizing data from the UK biobank, both found positive associations between exposure to multiple air pollutants and the prevalence of probable sarcopenia in the European population (Cai et al., 2024; Lai et al., 2022). In the Chinese population, multiple individual air pollutants were also proved to have different levels of adverse health-related effects on sarcopenia (Chen et al., 2023; Shi et al., 2024, 2023). In reality, individuals are commonly co-exposed to multiple air pollutants rather than a single air pollutant in isolation. Nevertheless, the epidemiological evidence on the combined effects of exposure to air pollutant mixtures on sarcopenia based on the national population remains limited. Moreover, some potential biological indicators (i.e., Serum creatinine-to-cystatin C ratio) could be used for sarcopenia screening to complement the complex consensus process defined by international sarcopenia diagnosis standards (Lin et al., 2024). To our knowledge, there is no evidence on whether air pollution was associated with sarcopenia-related indicators.

Accordingly, we sought to estimate the individual and combined effects of exposure to multiple air pollutants on sarcopenia risk and sarcopenia-related index among middle-aged and older Chinese adults using nationally representative survey data with longitudinal design.

2. Methods

2.1. Study population

The study population was from the China Health and Retirement Longitudinal Survey (CHARLS), an ongoing nationally representative longitudinal study involving Chinese adults aged 45 years and older. Using a multi-stage stratified sampling approach, CHARLS recruited 17,708 individuals across 10,257 households, 450 village units, 150 counties or districts and 28 provinces in China in 2011–2012. Of these, we excluded: (1) 249 participants with age<45 years, (2) 4909 participants with missing sarcopenia data, (3) 5448 participants with missing sarcopenia index (Cystatin C and creatinine in blood) data, (4) 112 participants who suffered from major accidental injuries, (5) 405 participants with missing sociodemographic and health-related information. Finally, the cross-sectional analysis at baseline included 6585 participants. The participants were then followed up every two to three years, with information on sociodemographic, lifestyle and health-related factors through face-to-face interviews using structured questionnaires and physical examinations. For the longitudinal analysis, 646 participants with sarcopenia at baseline in 2011 were excluded, and a further 2496 participants with missing information on sarcopenia

Table 1
Baseline characteristics of study participants (n=6585).

Characteristics	Overall	Sarcopenia		*P*-value
		No (n=5939)	Yes (n=646)	
Age, Mean ± SD	60.16 ± 9.57	58.00 ± 8.64	64.11 ± 9.92	<0.001
BMI, Mean (IQR)	23.07 (20.76, 25.72)	23.51 (21.39, 26.08)	19.90 (17.96, 20.25)	<0.001
Sex, n (%)				0.002
Male	3132 (47.6 %)	2863 (48.2 %)	269 (41.6 %)	
Female	3453 (52.4 %)	3076 (51.8 %)	377 (58.4 %)	
Residence, n (%)				<0.001
Urban Community	2313 (35.1 %)	2152 (36.2 %)	161 (24.9 %)	
Rural Village	4272 (64.9 %)	3787 (63.8 %)	485 (75.1 %)	
Region, n (%)				<0.001
East	2141 (32.5 %)	1968 (33.1 %)	173 (26.8 %)	
Midland	2525 (38.4 %)	2278 (38.4 %)	247 (38.2 %)	
West	1919 (29.1 %)	1693 (28.5 %)	226 (35.0 %)	
Education level, n (%)				<0.001
Primary school or below	4681 (71.1 %)	4091 (68.9 %)	590 (91.3 %)	
Middle school	1255 (19.0 %)	1212 (20.4 %)	43 (6.7 %)	
High school or above	649 (9.9 %)	636 (10.7 %)	13 (2.0 %)	
Marital status, n (%)				<0.001
Married/cohabitating	5485 (83.3 %)	5036 (84.8 %)	449 (69.5 %)	
Divorced/separated/ widowed/never married	1100 (16.7 %)	903 (15.2 %)	197 (30.5 %)	
Self-reported socioeconomic status, n (%)				0.013
Poor	2941 (44.7 %)	2629 (44.3 %)	312 (48.3 %)	
Fair	3465 (52.6 %)	3156 (53.1 %)	309 (47.8 %)	
Good	179 (2.7 %)	154 (2.6 %)	25 (3.9 %)	
Smoking status, n (%)				0.40
Non-smoker	3968 (60.3 %)	3569 (60.1 %)	399 (61.8 %)	
Smoker	2617 (39.7 %)	2370 (39.9 %)	247 (38.2 %)	
Drinking status, n (%)				<0.001
Non-drinker	4438 (67.4 %)	3961 (66.7 %)	477 (73.8 %)	
Drinker	2147 (32.6 %)	1978 (33.3 %)	169 (26.2 %)	
Heating, n (%)				<0.001
Solid fuel	3802 (57.7 %)	3378 (56.9 %)	424 (65.6 %)	
Non-solid fuel	2783 (42.3 %)	2561 (43.1 %)	222 (34.4 %)	
Cooking, n (%)				<0.001
Solid fuel	3789 (57.5 %)	3327 (56.0 %)	462 (71.5 %)	
Non-solid fuel	2796 (42.5 %)	2612 (44.0 %)	184 (28.5 %)	
Physical activity, n (%)				0.039
None	3993 (60.6 %)	3580 (60.3 %)	413 (63.9 %)	
Low intensity	661 (10.1 %)	590 (9.9 %)	71 (11.0 %)	
Middle or high intensity	1931 (29.3 %)	1769 (29.8 %)	162 (25.1 %)	
Night Sleep, n (%)				<0.001
Sleep debt	1991 (30.2 %)	1725 (29.0 %)	266 (41.2 %)	
Adequate sleep	4594 (69.8 %)	4214 (71.0 %)	380 (58.8 %)	
Health Status, n (%)				<0.001
Good/Very good	3051 (46.3 %)	2826 (47.6 %)	225 (34.8 %)	
Fair	2478 (37.6 %)	2195 (37.0 %)	283 (43.8 %)	
Poor	1056 (16.1 %)	918 (15.4 %)	138 (21.4 %)	
Comorbidity, n (%)				0.818
None	1633 (24.8 %)	1479 (24.9 %)	154 (23.8 %)	
1	2036 (30.9 %)	1836 (30.9 %)	200 (31.0 %)	
2 or above	2916 (44.3 %)	2624 (44.2 %)	292 (45.2 %)	
SBP (mmHg), Mean ± SD	130.63 ± 21.85	130.37 ± 21.47	133.03 ± 25.04	0.044
DBP (mmHg), Mean ± SD	75.39 ± 12.27	75.77 ± 12.21	71.89 ± 12.27	<0.001
Total cholesterol (mg/dL), Mean ± SD	193.70 ± 38.85	194.26 ± 38.92	188.56 ± 37.82	<0.001
Triglyceride (mg/dL), Mean (IQR)	105.32 (74.34, 153.99)	107.08 (76.11, 158.41)	88.06 (67.26, 123.01)	<0.001
HDL-C (mg/dL), Mean ± SD	51.27 ± 15.12	50.64 ± 14.95	57.03 ± 15.53	<0.001
LDL-C (mg/dL), Mean ± SD	116.98 ± 35.32	117.53 ± 35.44	111.98 ± 33.88	<0.001
HbA1c, Mean ± SD	5.26 ± 0.80	5.27 ± 0.81	5.15 ± 0.67	<0.001
FBG (mg/dL), Mean ± SD	109.94 ± 36.22	110.25 ± 36.35	107.10 ± 34.89	0.003
BUN (mg/dL), Mean ± SD	15.84 ± 4.62	15.75 ± 4.43	16.70 ± 6.00	<0.001
Uric acid (mg/dL), Mean ± SD	4.47 ±1.26	4.49 ± 1.25	4.28 ± 1.32	<0.001
Serum creatinine (mg/dL), Mean ± SD	0.79 ± 0.22	0.79 ± 0.20	0.79 ± 0.36	0.011
Cystatin C (mg/dL), Mean ± SD	1.02 ± 0.27	1.00 ± 0.25	1.16 ± 0.36	<0.001
Sarcopenia index, Mean ± SD	79.42 ± 19.83	80.55 ± 19.80	69.08 ± 16.67	<0.001
eGFR (mL/min/ 1.73 m^2), Mean ± SD	96.05 ± 15.84	96.83 ± 15.55	88.87 ± 15.81	<0.001
CRP (mg/L), Mean (IQR)	1.04 (0.55, 2.15)	1.05 (0.56, 2.12)	0.96 (0.54, 2.45)	<0.001

Notes: BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FBG, Fasting blood glucose; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; BUN, Blood urea nitrogen; CRP, C-Reactive Protein; SD, standard deviation; IQR, interquartile range.

measurements or lost to follow-up in 2013 and 2015 were excluded, resulting in 3443 participants being included (Figure S1). Detailed information on CHARLS could be found in previously studies (Zhao et al., 2014). The study protocol was approved by the Biomedical Ethics Review Board of Peking University (approval number: IRB00001052–11015), and all participants were informed of the contents of the disclosure statement and signed informed consent.

Table 2
Association between single air pollutant (per interquartile range (IQR) increase) and sarcopenia prevalence and levels of sarcopenia index.

Air pollutants (IQR)	DAG-based model	Model 1	Model 2	Model 3
Sarcopenia prevalence (OR and 95 % CIs)				
PM1 (13.84 μg /m3)	1.07 (0.99, 1.16)	1.07 (0.99, 1.16)	1.08 (1.00, 1.17)	1.08 (1.00, 1.17)
PM2.5 (28.39 μg /m3)	**1.10 (1.01, 1.21)**	**1.10 (1.01, 1.20)**	**1.11 (1.01, 1.21)**	**1.09 (1.01, 1.20)**
PM10 (47.51 μg /m3)	**1.25 (1.15, 1.36)**	**1.25 (1.15, 1.36)**	**1.26 (1.16, 1.37)**	**1.24 (1.14, 1.35)**
NO2 (15.15 μg /m3)	**1.15 (1.05, 1.25)**	**1.15 (1.06, 1.25)**	**1.17 (1.08, 1.28)**	**1.18 (1.08, 1.28)**
O3 (8.19 μg /m3)	1.03 (0.94, 1.13)	1.03 (0.95, 1.11)	1.06 (0.99, 1.15)	1.08 (1.00, 1.17)
Sarcopenia index (CCR) (Estimated changes and 95 % CIs)				
PM1 (13.84 μg /m3)	**−2.20 (−2.84, −1.55)**	**−2.23 (−2.87, −1.60)**	**−2.25 (−2.90, −1.61)**	**−2.18 (−2.82, −1.54)**
PM2.5 (28.39 μg /m3)	**−2.79 (−3.50, −2.09)**	**−2.78 (−3.48, −2.08)**	**−2.88 (−3.59, −2.17)**	**−2.76 (−3.47, −2.05)**
PM10 (47.51 μg /m3)	**−3.44 (−4.11, −2.77)**	**−3.41 (−4.07, −2.75)**	**−3.56 (−4.23, −2.88)**	**−3.38 (−4.05, −2.70)**
NO2 (15.15 μg /m3)	**−2.30 (−2.99, −1.61)**	**−2.31 (−2.99, −1.63)**	**−2.29 (−2.99, −1.60)**	**−2.33 (−3.02, −1.64)**
O3 (8.19 μg /m3)	**−1.55 (−2.18, −0.92)**	**−1.40 (−2.02, −0.78)**	**−1.39 (−2.03, −0.76)**	**−1.64 (−2.28, −1.01)**

Notes: Bold represents *P*-value < 0.05
DAG-based model: adjusted confounders selected from directed acyclic graph.
Model 1: adjusted for the sociodemographic status (age, gender, residence, educational level, marital status and self-reported socioeconomic status).
Model 2: further adjusted for health behaviors (smoking, drinking, sleep duration and physical activity) and physical condition (BMI, comorbidity and health status) based on model 1.
Model 3: further adjusted for geographical region and solid fuel use based on model 2.

2.2. Air pollution exposure assessment

The average annual concentration data for air pollutants (PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3) from 2009 to 2015 in this study were obtained from the ChinaHighAirPollution (CHAP) dataset. Employing big data and artificial intelligence, this dataset generates high-resolution air pollution data with a spatial resolution of 1 km × 1 km, except for NO_2, which has a resolution of 10 km × 10 km. Detailed information on the CHAP dataset have been previously documented (Wei et al., 2019, 2022a, 2021a, 2021b, 2022b). Briefly, the dataset estimates air pollutant concentrations by integrating extensive big data from surface observations, satellite remote sensing products, emission inventories, and atmospheric reanalysis combined with model simulations using the space-time extremely randomized trees. The model parameters of the 10-fold cross-validation showed high accuracy and predictive power, which indicated that the estimated air pollutants in this study align well with ground-based measurements (Table S1). We derived participants' long-term air pollution exposure by calculating the one-year average air pollution concentrations before the baseline survey and matching them to the county-level geocode corresponding to each participant's residential address. The spatial distribution of the included participants (n=6585) and averaged air pollutants during 2011–2015 were shown in Fig. 1.

2.3. Ascertainment of sarcopenia

According to the consensus updated by the Asian Work Group for Sarcopenia (AWGS) in 2019, sarcopenia is defined as containing the following three components: muscle strength, appendicular skeletal muscle mass (ASM), and physical performance (Chen et al., 2020). The diagnosis of sarcopenia requires the presence of low muscle mass in combination with low muscle strength or low physical performance (Chen et al., 2020).

1) Low muscle strength is defined as handgrip strength <28 kg for males and <18 kg for females (Chen et al., 2020);
2) ASM was measured with validated anthropometric equations applicable to Chinese population:
$$\text{ASM} = 0.193 * \text{Weight (kg)} + 0.107 * \text{Height (cm)} - 4.157 * \text{Gender (Males} = 1 \text{ and Females} = 2) - 0.037 * \text{Age (years)} - 2.631$$
Referring to previous studies, the threshold for categorizing low muscle mass was based on the lowest 20 % of the gender-specific height-adjusted muscle mass (ASM/Ht^2) within the study population. In this study, the ASM/Ht^2 values of <6.97 kg/m^2 for men and <5.23 kg/m^2 for women were regarded as low muscle mass.
3) Low physical performance was ascertained when participants took 12 seconds or more for 5-time chair stand test based on AWGS 2019 consensus recommendations (Chen et al., 2020). More details about the criteria for measuring and definition of sarcopenia components are available elsewhere or on the CHARLS website https://charls.charlsdata.com (Gao et al., 2022; Zhang et al., 2023a).

In addition, considering the time and cost involved in performing primary prevention and in clinical practice, some economical and available serum indicators have been used as potential biomarkers to assess sarcopenia. Numerous studies have consistently identified the sarcopenia index (SI) as a reliable surrogate marker for the evaluation of sarcopenia (Ballew et al., 2023; Kitago et al., 2023; Wu et al., 2023; Zhu et al., 2022a). The SI is calculated using the equation: $SI = \frac{\text{serum creatinine (mg/dL)}}{\text{cystatin C (mg/dL)}} * 100$. A lower SI could signify reduced skeletal muscle mass and increased vulnerability to sarcopenia. Detailed procedures for venous blood collection, storage, and bioassay analysis were described in previous articles (Zhao et al., 2014; Zhu et al., 2022b).

2.4. Covariates

Covariates were chosen based on potential confounders associated with both air pollution and sarcopenia, including sociodemographic, lifestyle and health-related variables. Trained interviewers collected sociodemographic information, including gender (male versus female), age, education, marital status, birth place (rural versus urban), region (eastern, midland, and western), self-reported socioeconomic status (poor, fair, and good). Lifestyle information included smoking and drinking status (yes versus no), physical activity (none, low intensity, and high intensity) and sleep duration (<6 h versus ≥ 6 h). We used the variable of the use of biofuel for heating and cooking (solid/clean) to represent indoor air pollution. We used both blood tests and questionnaires to ascertain health-related diseases. Hypertension, diabetes mellitus, and dyslipidemia were determined based on comprehensive diagnostic criteria, which took considering physical examination, blood parameters, self-reported disease history and/or history of relevant medications (Zhang et al., 2023a). The other 10 chronic diseases were based on self-reported physician-diagnosed disease histories collected from questionnaires. Number of chronic diseases was considered as a covariate (none/1 chronic disease/2 and more chronic diseases). In addition, self-reported health status (excellent or good/fair/poor) was selected to assess the personal health. In addition to the blood indicators used above, other blood indicators, such as blood urea nitrogen, serum urine acid and C-reactive protein (CRP) were also analyzed by bioassay.

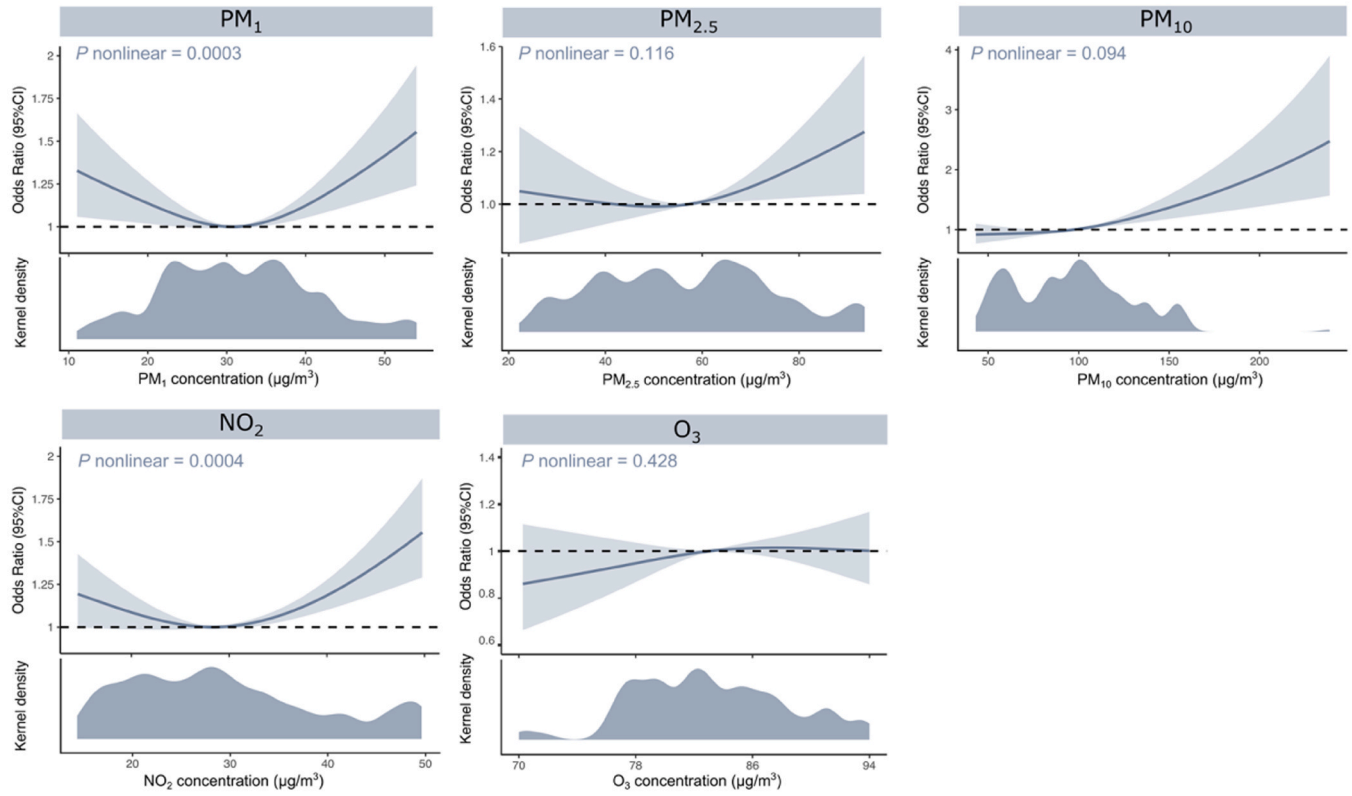


Fig. 2. Concentration-response associations of five air pollutants with sarcopenia. Dashed area represents the 95 % confidence interval (CI).

The Directed Acyclic Graph (DAG) method is used to reduce model estimation bias by selecting the minimal covariate set that contains sufficient information from numerous confounding variables (Figure S2).

2.5. Statistical analysis

Descriptive statistics were conducted to analyze the baseline characteristics of the sarcopenia and control groups. Parametric or nonparametric tests and chi-square tests were used to compare the differences in continuous and categorical variables between the two groups, respectively. Spearman rank correlation method was conducted to analyze the pairwise correlations among five air pollutants.

In the cross-sectional stage, binary logistic regression and generalized linear models were employed to examinate the relationship of air pollution with sarcopenia prevalence and sarcopenia index, respectively. In the multivariate regression models, various potential confounders were adjusted based on DAG and the currently available evidence (Hu et al., 2023; Wang et al., 2023). including DAG-based model (gender, age, residence, region, education, socioeconomic status drinking, smoking and physical activity); Model 1 (adjusted for socio-demographic information), Model 2 (further adjusted for health behavioral and physical condition information based on Model 1), and Model 3 (further adjusted for region and solid fuels based on Model 2). The optimal restricted cubic spline (RCS) with three nodes (10th, 50th, and 90th percentiles) was used to further explore the concentration-response associations between air pollution and sarcopenia prevalence. In addition, subgroup analysis further stratified study populations by gender, age, education, residence and smoking to examine possible modifying effects among various vulnerable populations.

Considering the reality of air pollution mixture exposure, the effects of single-exposure and co-exposure to multiple air pollutants on the sarcopenia index and prevalence were further analyzed by weighted quantile sum (WQS) regression model and Bayesian kernel machine regression (BKMR) model. In the WQS model, WQS indexes (ranging from 0 to 1) were calculated based on quartiles of air pollutants to identify the relative importance of each air pollutant to the joint effect (Carrico et al., 2015). During the model fit process, the complete samples were performed 5000 iterations of bootstrap procedure in a training set (40 %) and a validation set (60 %). The binary outcome (sarcopenia or non-sarcopenia) used a logit link function, and the continuous variable (sarcopenia index) used a linear link function. In the BKMR model, the overall effect of multiple air pollutants on study outcomes was assessed by fixing the pollutants at different quantiles of exposure compared to the median (Bobb et al., 2015). When evaluating the individual effects of multiple pollutants, the model used the changes in a single pollutant at different quartiles while holding the other pollutants fixed at the specific quartile concentration levels. PM_1, $PM_{2.5}$, and PM_{10} exposures were grouped together for analysis in the BKMR model due to significant correlations among them. The modeling analysis was based on the Markov Chain Monte Carlo algorithm with 10,000 iterations. In the longitudinal stage, we applied multinomial logistic regression to estimate the longitudinal relationship between baseline air pollution and follow-up sarcopenia during the four-year follow-up period (Hu et al., 2022; Zhang et al., 2023c).

Finally, we conducted several sensitivity analyses to test the robustness of the results: (1) analyzed the combined effect of mixed air pollution exposure using quantile-based g computation (qgcomp) model based on “qgcomp” R software package. (Keil et al., 2020). This approach was adopted to overcome the shortcoming of directional homogeneity assumption in the WQS regression model. (2) adjusted the exposure window to two years before the baseline survey (Jiang et al., 2023; Shi et al., 2024; Zhang et al., 2023b). (3) excluded participants with eGFR <60 mL/min/1.73 m^2 and with arthritis or rheumatic disease. (4) further examined the relationship between each environmental pollutant and sarcopenia components. All statistical analyses were performed in R Studio software and $P<0.05$ (two-sided) was defined

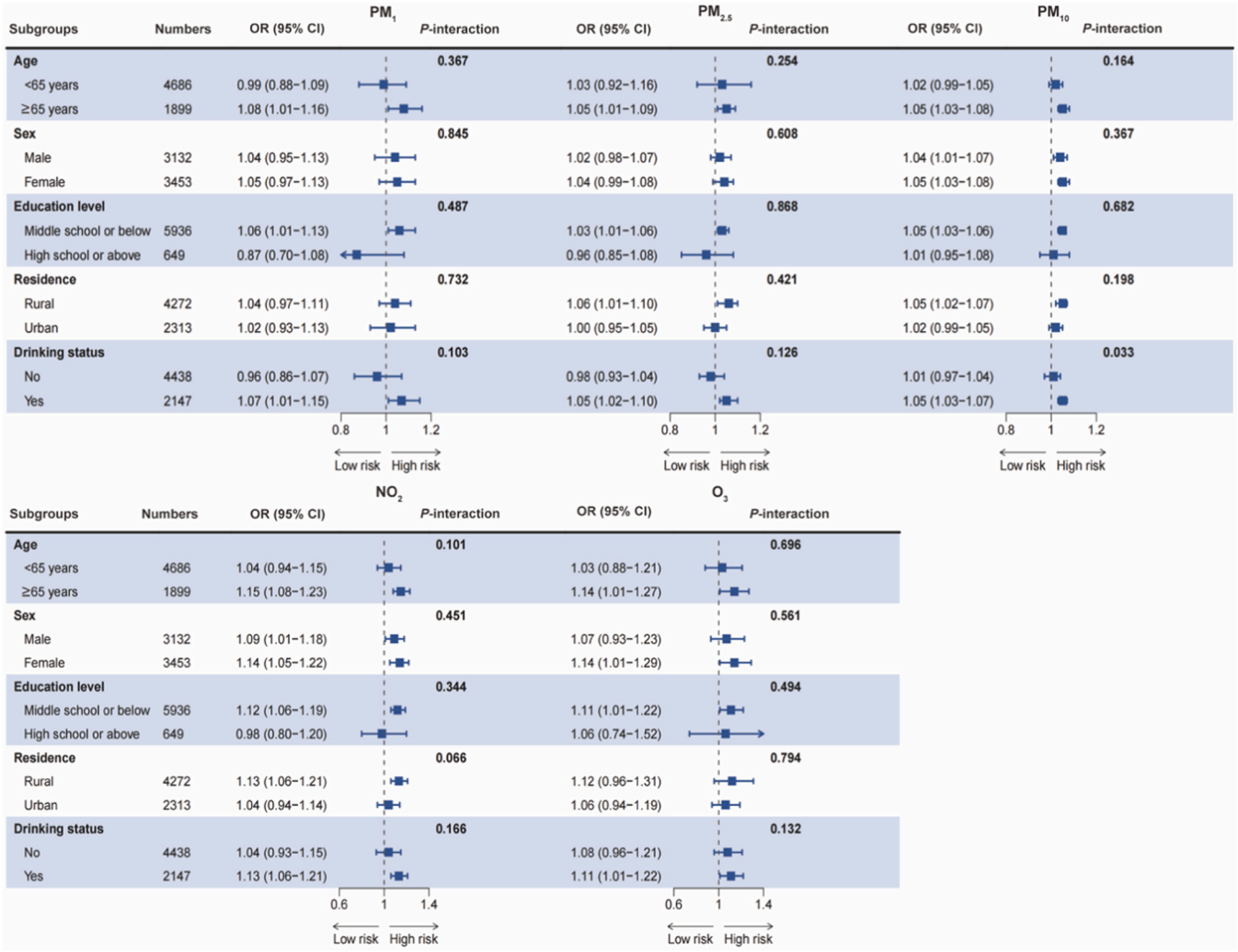


Fig. 3. Forest plot for subgroup analyses of air pollutants with sarcopenia prevalence. The model adjusted for all covariates.

statistically significant.

3. Results

3.1. Characteristics of study population

The present study enrolled 6585 participants (3132 males and 3453 females) from 28 provinces of China at baseline, in which 646 were diagnosed with sarcopenia. In summary, participants who suffered from sarcopenia were prone to be older, resident in rural areas, have less education, be unmarried, have poorer socioeconomic status, have unhealthy lifestyle and use indoor solid fuels compared with non-sarcopenia participants (Table 1). The detailed baseline characteristics of the participants included in the longitudinal analyses was presented in Table S2. The distribution of characteristics of the follow-up participants was observed to be largely consistent with those of participants in the cross-sectional studies (Table S2). Annual average concentration distributions and correlation matrix of air pollutants were summarized in Table S3 and Table S4.

3.2. Individual associations of multiple air pollutants with sarcopenia risk

Table 2 presented the change in sarcopenia prevalence (odds ratios (OR) and 95 % CIs) and sarcopenia index (beta coefficients and 95 % CIs) for each interquartile range (IQR) increase in air pollutant exposure. $PM_{2.5}$, PM_{10}, and NO_2 increased the risk of sarcopenia by 10 % (DAG-based adjusted OR: 1.10, 95 %CI: 1.01–1.21), 25 % (DAG-based adjusted OR: 1.25, 95 %CI: 1.15–1.36), and 15 % (DAG-based adjusted OR: 1.15, 95%CI: 1.05–1.25), respectively. Similarly, our findings revealed that three air pollutants had higher sarcopenia prevalence in the full-adjusted model (model 3) and the aOR (95% CIs) were 1.09 (1.01–1.20), 1.24 (1.14–1.35) and 1.18 (1.08–1.28), respectively. In the DAG-based covariate-adjusted model, all air pollutants were associated with a reduced sarcopenia index, which also potentially revealed increased sarcopenia risk. PM_1 ($\beta = -2.18$, 95% CI : -2.82, -1.54), $PM_{2.5}$ ($\beta = -2.76$, 95%CI : -3.47, -2.05), PM_{10} ($\beta = -3.38$, 95% CI : -4.05, -2.70), NO_2 ($\beta = -2.33$, 95%CI : -3.02, -1.64),O_3 ($\beta = -1.64$, 95%CI : -2.28, -1.01) were also associated with decreased sarcopenia index after adjusting for all potential variables. In addition, the concentration-response (C-R) relationships of air pollutant exposure with the prevalence of sarcopenia were displayed in Fig. 2. The C-R curves show insignificant violation of the linear relationship in $PM_{2.5}$, PM_{10} and O_3. Notably, we found significant nonlinear relationships between PM_1 and NO_2 and the prevalence of sarcopenia according to the shape of C-R curves ($P_{nonlinear}$ <0.001 in both pollutants).

3.3. Subgroup analysis

The relationships of air pollution with the sarcopenia risk were mostly consistent with the main results among different subgroups

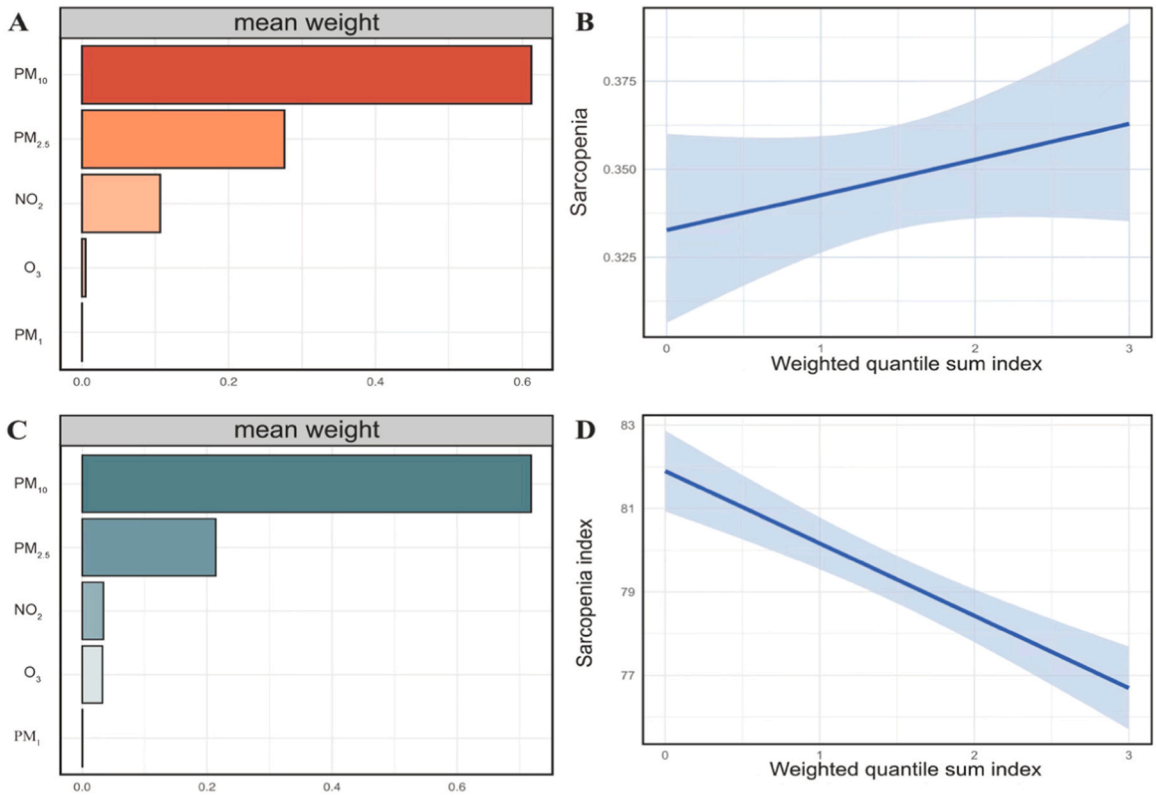


Fig. 4. Associations of air pollutants with sarcopenia risk and sarcopenia index based on WQS model. (A) Weights of five air pollutants; (B) Association between air pollutant mixtures and sarcopenia. (C) Weights of five air pollutants; (D) Association between air pollutant mixtures and sarcopenia index.

(Fig. 3). No significant interactions were found across age, gender, education, residence, and drinking status subgroups ($P_{\text{interaction}}>0.05$). Exposure to air pollution appeared to have more prominent risk of developing sarcopenia in susceptible populations aged >65 years, females, those with lower educational levels, those living in rural areas and drinking alcohol.

3.4. Overall associations of co-exposure to air pollution on the risk of sarcopenia

Based on WQS regression models, PM_{10} and $PM_{2.5}$ contributed great weight to the mixed effect of co-exposure to air pollution on sarcopenia risk, and the highest exposure weight was PM_{10} (Fig. 4A). WQS index-sarcopenia curves demonstrated the positive linear relationship between air pollution mixtures and sarcopenia (Fig. 4B). The risk of sarcopenia significantly increased with each quartile of the air pollutant mixture (OR = 1.10; 95 % CI: 1.03, 1.17). PM_{10} also dominated the mixed effect of the five air pollutants on the sarcopenia index, followed by $PM_{2.5}$ (Fig. 4C). Fig. 4D shows that there were significant adverse overall effects of air pollution mixtures with sarcopenia index.

Subsequently, the joint effect of five air pollutants fitted by the BKMR model on sarcopenia prevalence and sarcopenia index were mainly consistent with the WQS analysis (Fig. 5). When air pollution mixture concentrations were at or greater than the 55th percentile, the overall effect between mixture concentration and risk of developing sarcopenia was significantly positive compared to the 50th percentile (Fig. 5A). When other air pollutants were held at the 25th, 50th, and 75th percentiles, only PM_{10} had a significantly positive association with an increased risk of sarcopenia (Fig. 5B). In addition, individuals co-exposed to air pollution mixtures above the 55th percentile had the decreased trends and lower sarcopenia index compared to the median, which further demonstrated increased sarcopenia risk (Fig. 5C). Fig. 5D further reveals negative effects of PM_{10}, $PM_{2.5}$ and O_3 on the sarcopenia index when controlling for other pollutants at different percentiles.

3.5. Longitudinal associations between air pollution and incident sarcopenia

After 4 years of follow-up, we found that 342 (9.9 %) participants developed sarcopenia. There were significant positive effects of baseline $PM_{2.5}$, PM_{10} and NO_2 with incident sarcopenia (Table 3). Compared to the lowest reference group, $PM_{2.5}$, PM_{10} and NO_2 in the highest tertiles were associated with increased risk of developing sarcopenia.

3.6. Sensitivity analyses

In the sensitivity analyses, the qgcomp model, which estimates exposure weights in both the positive and negative directions, found similar relationships of air pollution mixtures with sarcopenia risk and the sarcopenia index. The positive and negative weights in each air pollutant associated with sarcopenia risk and the sarcopenia index were displayed in detail in Figure S3. The positive overall effect (OR = 1.08; 95 % CI: 1.02, 1.14) and main drivers of air pollution mixtures were similar to those found in the WQS and BKMR models. After changing the exposure window from 1-year to 2-year average concentrations of air pollutants, the associations of air pollutants with risk of sarcopenia and sarcopenia index remained evident (Table S5 and Table S6). After excluding participants with kidney disease and arthritis or rheumatism associated with health outcomes of this study, the sensitivity analysis results were in agreement with the main findings, which increased the robustness of the findings (Table S5 and Table S6). Sensitivity analyses further revealed that all air pollutants had varying degrees of adverse effects on physical performance, and that PM_{10} also significantly impaired muscle strength (Table S7).

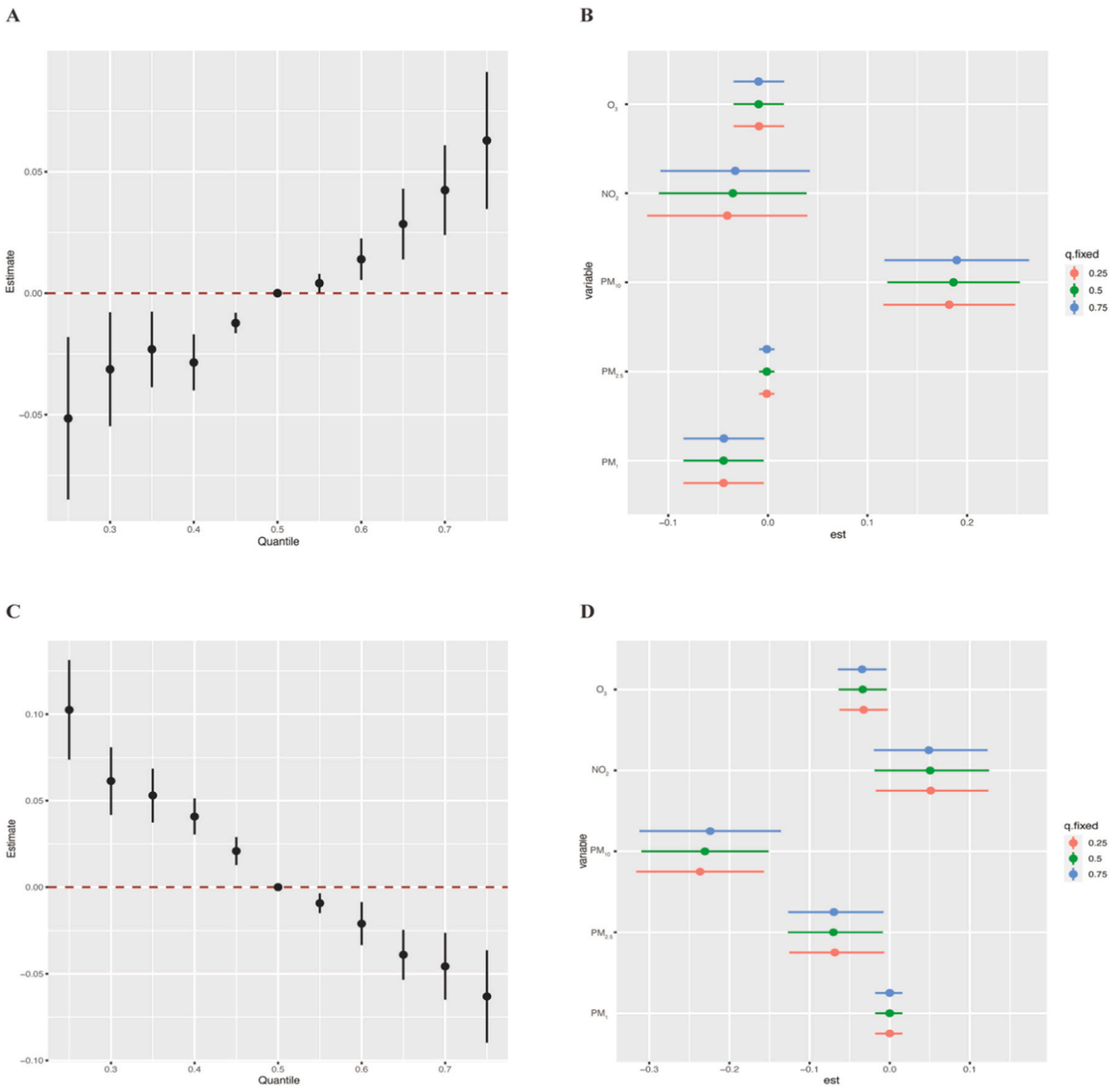


Fig. 5. Association of air pollutants with sarcopenia prevalence and sarcopenia index estimated by BKMR model. The joint effect of the air pollution mixture on sarcopenia prevalence (A) and sarcopenia index (C) when comparing all the air pollutants at particular percentiles were compared to all the air pollutants at their median. Single air pollutant-exposure effect (95 % CI) to sarcopenia (B) and sarcopenia index (D) when other air pollutants were fixed at a specific exposure percentile (25th, 50th, or 75th, respectively). BKMR model adjusted for covariates in full adjusted regression model.

4. Discussion

This study provided additional evidence to explore the cross-sectional and longitudinal relationships between multiple ambient air pollutants and risk of sarcopenia. In the cross-sectional analysis, single-exposure to multiple air pollutants were associated with risk of sarcopenia and sarcopenia index. Co-exposure to air pollutants mixture also increased sarcopenia risk, and the mixing effect was mainly driven by PM_{10} and $PM_{2.5}$. Notably, the mixed exposure analysis further showed significantly negative associations between all environmental pollutants and the sarcopenia index, which in turn revealed increased sarcopenia risk owing to air pollution. In the longitudinal analysis, the results further confirmed the findings from the cross-sectional study based on this nationally representative survey of middle-aged and older adults in Chinese communities.

Currently, epidemiologic evidence on the relationship of outdoor air pollution with risk of sarcopenia remains limited, especially in the Western Pacific region. Lai et al. observed that $PM_{2.5}$, PM_{10} and NO_2 per IQR increase were connected with increased probable sarcopenia risk among UK adults, which is consistent with our findings (Lai et al., 2022). Another cross-sectional study in central China also showed that each 1 μg/m^3 increase in $PM_{2.5}$ and PM_{10} correspondingly increased the risk of sarcopenia by 11.1 % and 4.3 % (Zhang et al., 2023b). A recent epidemiological study also found significantly positive relationships of ambient $PM_{2.5}$ exposure (each 10 μg/m^3 increase) with probable sarcopenia and sarcopenia, while the associations were only assessed in a single pollutant (Shi et al., 2023). Moreover, our sensitivity analysis regarding the adverse impact of multiple air pollutants on sarcopenia components was similar with previous findings (de Zwart et al., 2018; Lin et al., 2020). For instance, a prospective cohort study reported that most air pollutants, including $PM_{2.5}$, NO_2 and PM_{10}, were linked to decreased physical function among older Dutch adults (de Zwart et al., 2018). Our study found additional evidence of significant associations between PM_1 and O_3 and reduced physical performance, although the positive association with risk of sarcopenia was not significant.

It is well known that people are commonly subjected to multiple air pollutants together in daily life. However, the current evidence on the associations between co-exposure to air pollution and the risk of

Table 3
Longitudinal associations between multiple air pollutants and sarcopenia.

Air pollutants	DAG-based model	Full-adjusted Model
	OR (95 % CI)	OR (95 % CI)
PM_1		
Lowest tertiles	1 (Ref)	1 (Ref)
Middle tertiles	1.05 (0.88, 1.26)	1.08 (0.90, 1.30)
Highest tertiles	1.14 (0.95, 1.36)	1.17 (0.97, 1.40)
P for trend	0.149	0.083
PM2.5		
Lowest tertiles	1 (Ref)	1 (Ref)
Middle tertiles	1.01 (0.84, 1.20)	1.04 (0.86, 1.24)
Highest tertiles	1.27 (1.06, 1.52)	1.26 (1.06, 1.51)
P for trend	0.013	0.010
PM10		
Lowest tertiles	1 (Ref)	1 (Ref)
Middle tertiles	1.11 (0.93, 1.33)	1.17 (0.98, 1.40)
Highest tertiles	1.34 (1.12, 1.60)	1.22 (1.22, 1.75)
P for trend	0.001	<0.001
NO_2		
Lowest tertiles	1 (Ref)	1 (Ref)
Middle tertiles	1.02 (0.85, 1.22)	1.01 (0.86, 1.20)
Highest tertiles	1.25 (1.05, 1.49)	1.23 (1.03, 1.48)
P for trend	0.015	0.026
O_3		
Lowest tertiles	1 (Ref)	1 (Ref)
Middle tertiles	0.91 (0.76, 1.08)	0.87 (0.73, 1.04)
Highest tertiles	1.10 (0.92, 1.31)	1.12 (0.93, 1.34)
P for trend	0.329	0.275

Note: DAG-based model: adjusting confounders selected from directed acyclic graph; Full-adjusted model: adjusted for the sociodemographic status (age, gender, residence, educational level, marital status and self-reported socioeconomic status), health behaviors (smoking and drinking habits, sleep time and physical activity) and physical condition (BMI, comorbidity and self-reported health status), geographical region and solid fuel use.

sarcopenia were unclear and relatively sparse. The present study found significant overall effects of air pollution mixtures with sarcopenia prevalence, which echoed the previous cross-sectional study conducted in a single region (Zhang et al., 2023b). We also found significant PM_{10}-driven joint effects between air pollutants and sarcopenia risk based on multiple mixture analysis methods. Despite the lack of available epidemiologic evidence from other countries on the combined effect between air pollution mixtures and sarcopenia, stronger effects of PM_{10} on sarcopenia risk has been confirmed in the European population (de Zwart et al., 2018; Lai et al., 2022). Importantly, our study is the first study to examine individual and combined impacts between air pollution and surrogate biomarkers (SI) for sarcopenia. The available evidence suggested that the sarcopenia index could accurately assess muscle mass and muscle function and show potential for the screening of sarcopenia among healthy older individuals (He et al., 2018; Sim et al., 2022; Tabara et al., 2020). Thus, the sarcopenia index will expect to facilitate large-scale community-based early sarcopenia screening and clinical practice, which will further promote community health by identifying vulnerable populations and provide targeted primary health care.

The biological mechanisms underlying the effects remain poorly elucidated. Several potential explanations and clues have been revealed by some population-based and experimental studies. First, the induction of sarcopenia by air pollution is partly explained by insulin resistance and the mediating role of the gut microbiota (Rajagopalan et al., 2020; Zhao et al., 2022), leading to deficits in skeletal muscle mass and function (Wang et al., 2022; Wiedmer et al., 2021). Second, emerging evidence demonstrated that air pollution would trigger oxidative stress and inflammatory responses in the pathogenesis of sarcopenia (Bano et al., 2017; Hahad et al., 2020; Piao et al., 2018), which might result in decreased sarcopenia components by causing oxidative damage to biomolecules (Sayer et al., 2013). Additionally, mitochondrial damage may be another potential source of sarcopenia. It is reported that air pollution induces mitochondrial damage and aging (Fetterman et al., 2017; Hou et al., 2013), which leads to the loss of muscle fiber cross-sectional area related to sarcopenia (Parise and De Lisio, 2010).

Stratified analysis found that women seem to be more susceptible to the positive effects of PM10, NO2, and O_3 on sarcopenia compared to men, which has been confirmed in previous studies (Zhang et al., 2023b). Furthermore, we have found evidence to protect the vulnerable elderly population, which contributes to preventing the development of sarcopenia due to air pollution. This finding could be explained by the fact that sarcopenia is widespread among the elderly and that air pollution also poses greater health risks to the elderly population (Coll et al., 2021). Our study also identified positive associations of air pollution with sarcopenia among the less educated populations, which might be attributable to socioeconomic status differences regarding the health consequences from air pollution (Christensen et al., 2022). In addition, population-based and experimental studies have found that drinkers are more vulnerable to the adverse health impact of air pollutants on the risk of sarcopenia due to reduced lean body mass and protein synthesis in the gastrocnemius muscle caused by chronic alcohol consumption (Korzick et al., 2013; Zhang et al., 2023b), which is in line with our subgroup analysis. Future studies are needed to further clarify vulnerable individuals for implementation of sarcopenia-related preventive measures and behavioral interventions.

The advantages of this study are summarized as follows: first, this study is the initial study to explore individual and combined effects of exposure to multiple air pollutants on sarcopenia risk and surrogate biomarkers based on a national population-based database. Second, this study is one of the limited studies exploring the relationship between air pollution and sarcopenia in Asia. Our study will provide additional research evidence to further understand associations between air pollution and sarcopenia risk among middle-aged and elderly adults, and to develop early prevention and protection measures for relevant agencies and policymakers. However, there are several limitations in our study. First, we could only estimate air pollution exposure at the city level of participants due to sensitive information protection, such as detailed residential addresses in the CHARLS database, which may lead to misclassification bias. Nevertheless, this study used high-resolution and high-quality meteorological data and considered indoor air pollution as a covariate to minimize this shortcoming. Second, causality is difficult to determine due to the observational study design for the assessment of sarcopenia in the CHARLS database. Third, despite the high resolution of air pollution data, individual exposure to pollutants may be biased due to uneven distribution of emission sources, dilution, and physicochemical transformations of the atmosphere. Finally, because of the limitations in the CHARLS database regarding self-reported information and the lack of other information related to sarcopenia, it might cause unavoidable potential confounding and bias.

5. Conclusions

Our findings supported the opinion that air pollution, particularly $PM_{2.5}$, PM_{10} and NO_2, potentially increased the risk of sarcopenia among middle-aged and older adults in China. Meanwhile, mixed exposure analysis provided additional evidence that exposure to air pollution mixtures was significantly associated with sarcopenia prevalence, and was primarily driven by PM_{10} and $PM_{2.5}$. Notably, we found significant individual and combined effects between air pollution and sarcopenia biomarkers, which provides novel insights into the early screening and early prevention of sarcopenia. Future well- designed prospective and biological research is necessary to further address the above potential relationships.

Ethical approval

The study protocol was approved by the Biomedical Ethics Review Board of Peking University (approval number: IRB00001052–11015),

and all participants were informed of the contents of the disclosure statement and signed informed consent.

Funding

This work was supported by grants from Shanghai Municipal Health Commission (Grant Number: Shanghai three-year Action Plan for Public Health GWVI-11.1–29); Shanghai Municipal Education Commission (Grant number: 2024-Sports, Health, Arts and Science Department 01–43) and Shanghai Municipal Commission of Science and Technology (Grant number: 20JC1410204).

CRediT authorship contribution statement

Wangnan Cao: Writing – review & editing, Supervision, Resources, Investigation. **Yinqiao Dong:** Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation. **Yingjie Chen:** Investigation, Data curation. **Jing Wei:** Validation, Resources, Data curation. **Shengzhi Sun:** Writing – review & editing, Validation, Supervision, Project administration. **Yinghuan Zhang:** Investigation, Data curation. **Yong Cai:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Fan Hu:** Visualization, Validation, Software.

Declaration of Competing Interest

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

Data Availability

Data will be made available on request.

Acknowledgments

Thanks to the China Center for Economic Research, National Development Research Institute, Peking University, for providing CHARLS data. We also thank the National Earth System Science Data Sharing Platform for providing air pollution data. We are grateful to all the participants and researchers in this project.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2024.116634.

References

Ballew, S.H., Zhou, L., Surapaneni, A., et al., 2023. A Novel creatinine muscle index based on creatinine filtration: associations with frailty and mortality. J. Am. Soc. Nephrol. 34, 495–504. https://doi.org/10.1681/ASN.0000000000000037.

Bano, G., Trevisan, C., Carraro, S., et al., 2017. Inflammation and sarcopenia: a systematic review and meta-analysis. Maturitas 96, 10–15. https://doi.org/10.1016/j.maturitas.2016.11.006.

Bobb, J.F., Valeri, L., Claus Henn, B., et al., 2015. Bayesian kernel machine regression for estimating the health effects of multi-pollutant mixtures. Biostatistics 16, 493–508. https://doi.org/10.1093/biostatistics/kxu058.

Cai, L., Tan, J., Chen, X., et al., 2024. Ambient air pollution exposure and the risk of probable sarcopenia: a prospective cohort study. Ecotoxicol. Environ. Saf. 275, 116273 https://doi.org/10.1016/j.ecoenv.2024.116273.

Carrico, C., Gennings, C., Wheeler, D.C., Factor-Litvak, P., 2015. Characterization of weighted quantile sum regression for highly correlated data in a risk analysis setting. J. Agric. Biol. Environ. Stat. 20, 100–120. https://doi.org/10.1007/s13253-014-0180-3.

Chen, L.K., Woo, J., Assantachai, P., et al., 2020. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. e2 J. Am. Med. Dir. Assoc. 21, 300–307. https://doi.org/10.1016/j.jamda.2019.12.012.

Chen, S.W., Lin, C.Y., Chen, C.Y., et al., 2023. Long-term exposure to air pollution and risk of Sarcopenia in adult residents of Taiwan: a nationwide retrospective cohort study. BMC Public Health 23, 2172. https://doi.org/10.1186/s12889-023-17091-8.

Christensen, G.M., Li, Z., Pearce, J., et al., 2022. The complex relationship of air pollution and neighborhood socioeconomic status and their association with cognitive decline. Environ. Int. 167, 107416 https://doi.org/10.1016/j.envint.2022.107416.

Coll, P.P., Phu, S., Hajjar, S.H., et al., 2021. The prevention of osteoporosis and sarcopenia in older adults. J. Am. Geriatr. Soc. 69, 1388–1398. https://doi.org/10.1111/jgs.17043.

Collaborators, G.B.D.R.F., 2020. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 396, 1223–1249. https://doi.org/10.1016/S0140-6736(20)30752-2.

Cruz-Jentoft, A.J., Sayer, A.A., 2019. Sarcopenia. Lancet 393, 2636–2646. https://doi.org/10.1016/S0140-6736(19)31138-9.

Fetterman, J.L., Sammy, M.J., Ballinger, S.W., 2017. Mitochondrial toxicity of tobacco smoke and air pollution. Toxicology 391, 18–33. https://doi.org/10.1016/j.tox.2017.08.002.

Gao, K., Cao, L.F., Ma, W.Z., et al., 2022. Association between sarcopenia and cardiovascular disease among middle-aged and older adults: findings from the China health and retirement longitudinal study. EClinicalMedicine 44, 101264. https://doi.org/10.1016/j.eclinm.2021.101264.

Hahad, O., Lelieveld, J., Birklein, F., et al., 2020. Ambient air pollution increases the risk of cerebrovascular and neuropsychiatric disorders through induction of inflammation and oxidative stress. Int. J. Mol. Sci. 21 https://doi.org/10.3390/ijms21124306.

He, Q., Jiang, J., Xie, L., Zhang, L., Yang, M., 2018. A sarcopenia index based on serum creatinine and cystatin C cannot accurately detect either low muscle mass or sarcopenia in urban community-dwelling older people. Sci. Rep. 8, 11534 https://doi.org/10.1038/s41598-018-29808-6.

Hou, L., Zhang, X., Dioni, L., et al., 2013. Inhalable particulate matter and mitochondrial DNA copy number in highly exposed individuals in Beijing, China: a repeated-measure study. Part Fibre Toxicol. 10, 17. https://doi.org/10.1186/1743-8977-10-17.

Hu, Y., Peng, W., Ren, R., Wang, Y., Wang, G., 2022. Sarcopenia and mild cognitive impairment among elderly adults: the first longitudinal evidence from CHARLS. J. Cachex. Sarcopenia Muscle 13, 2944–2952. https://doi.org/10.1002/jcsm.13081.

Hu, Z., Tian, Y., Song, X., Zeng, F., Yang, A., 2023. Associations between indoor air pollution for cooking and heating with muscle and sarcopenia in Chinese older population. J. Cachex. Sarcopenia Muscle 14, 2029–2043. https://doi.org/10.1002/jcsm.13281.

Jiang, H., Zhang, S., Yao, X., et al., 2023. Does physical activity attenuate the association between ambient PM(2.5) and physical function? Sci. Total Environ. 874, 162501 https://doi.org/10.1016/j.scitotenv.2023.162501.

Keil, A.P., Buckley, J.P., O'Brien, K.M., et al., 2020. A Quantile-based g-computation approach to addressing the effects of exposure mixtures. Environ. Health Perspect. 128, 47004. https://doi.org/10.1289/EHP5838.

Kitago, M., Seino, S., Shinkai, S., et al., 2023. Cross-sectional and longitudinal associations of creatinine-to-cystatin c ratio with sarcopenia parameters in older adults. J. Nutr. Health Aging 27, 946–952. https://doi.org/10.1007/s12603-023-2029-3.

Korzick, D.H., Sharda, D.R., Pruznak, A.M., Lang, C.H., 2013. Aging accentuates alcohol-induced decrease in protein synthesis in gastrocnemius. Am. J. Physiol. Regul. Integr. Comp. Physiol. 304, R887–R898. https://doi.org/10.1152/ajpregu.00083.2013.

Lai, Z., Yang, Y., Qian, Z.M., et al., 2022. Is ambient air pollution associated with sarcopenia? Results from a nation-wide cross-sectional study. Age Ageing 51. https://doi.org/10.1093/ageing/afac249.

Lin, H., Guo, Y., Ruan, Z., et al., 2020. Association of indoor and outdoor air pollution with hand-grip strength among adults in six low- and middle-income countries. J. Gerontol. A Biol. Sci. Med. Sci. 75, 340–347. https://doi.org/10.1093/gerona/glz038.

Lin, T., Jiang, T., Huang, X., et al., 2024. Diagnostic test accuracy of serum creatinine and cystatin C-based index for sarcopenia: a systematic review and meta-analysis. Age Ageing 53. https://doi.org/10.1093/ageing/afad252.

Parise, G., De Lisio, M., 2010. Mitochondrial theory of aging in human age-related sarcopenia. Inter. Top. Gerontol. 37, 142–156. https://doi.org/10.1159/000319999.

Petermann-Rocha, F., Balntzi, V., Gray, S.R., et al., 2022. Global prevalence of sarcopenia and severe sarcopenia: a systematic review and meta-analysis. J. Cachex. Sarcopenia Muscle 13, 86–99. https://doi.org/10.1002/jcsm.12783.

Piao, M.J., Ahn, M.J., Kang, K.A., et al., 2018. Particulate matter 2.5 damages skin cells by inducing oxidative stress, subcellular organelle dysfunction, and apoptosis. Arch. Toxicol. 92, 2077–2091. https://doi.org/10.1007/s00204-018-2197-9.

Rajagopalan, S., Park, B., Palanivel, R., et al., 2020. Metabolic effects of air pollution exposure and reversibility. J. Clin. Invest. 130, 6034–6040. https://doi.org/10.1172/JCI137315.

Sayer, A.A., Robinson, S.M., Patel, H.P., et al., 2013. New horizons in the pathogenesis, diagnosis and management of sarcopenia. Age Ageing 42, 145–150. https://doi.org/10.1093/ageing/afs191.

Shi, W., Zhang, T., Yu, Y., Luo, L., 2023. Association of indoor solid fuel use and long-term exposure to ambient PM(2.5) with sarcopenia in China: a nationwide cohort study. Chemosphere 344, 140356. https://doi.org/10.1016/j.chemosphere.2023.140356.

Shi, W., Li, Y., Zhao, J.V., 2024. Long-term exposure to ambient air pollution with sarcopenia among middle-aged and older adults in China. J. Nutr. Health Aging 28, 100029. https://doi.org/10.1016/j.jnha.2023.100029.

Sim, M., Dalla Via, J., Scott, D., et al., 2022. Creatinine to cystatin C ratio, a biomarker of sarcopenia measures and falls risk in community-dwelling older women. J. Gerontol. A Biol. Sci. Med. Sci. 77, 1389–1397. https://doi.org/10.1093/gerona/glab369.

Tabara, Y., Kohara, K., Okada, Y., Ohyagi, Y., Igase, M., 2020. Creatinine-to-cystatin C ratio as a marker of skeletal muscle mass in older adults: J-SHIPP study. Clin. Nutr. 39, 1857–1862. https://doi.org/10.1016/j.clnu.2019.07.027.

Tung, N.T., Lee, Y.L., Lin, S.Y., et al., 2021. Associations of ambient air pollution with overnight changes in body composition and sleep-related parameters. Sci. Total Environ. 791, 148265 https://doi.org/10.1016/j.scitotenv.2021.148265.

Wang, M., Hu, L., Peng, H., et al., 2023. The longitudinal association between indoor air pollution and sarcopenia in China: the mediating role of depression. Environ. Sci. Pollut. Res. Int. 30, 115506–115516. https://doi.org/10.1007/s11356-023-30379-x.

Wang, Y., Zhang, Y., Lane, N.E., et al., 2022. Population-based metagenomics analysis reveals altered gut microbiome in sarcopenia: data from the Xiangya Sarcopenia Study. J. Cachex-.-. Sarcopenia Muscle 13, 2340–2351. https://doi.org/10.1002/jcsm.13037.

Wei, J., Li, Z., Guo, J., et al., 2019. Satellite-derived 1-km-resolution PM(1) concentrations from 2014 to 2018 across China. Environ. Sci. Technol. 53, 13265–13274. https://doi.org/10.1021/acs.est.9b03258.

Wei, J., Li, Z., Xue, W., et al., 2021b. The ChinaHighPM(10) dataset: generation, validation, and spatiotemporal variations from 2015 to 2019 across China. Environ. Int 146, 106290. https://doi.org/10.1016/j.envint.2020.106290.

Wei, J., Li, Z., Lyapustin, A., et al., 2021a. Reconstructing 1-km-resolution high-quality PM2.5 data records from 2000 to 2018 in China: spatiotemporal variations and policy implications. Remote Sens. Environ. 252, 112136 https://doi.org/10.1016/j.rse.2020.112136.

Wei, J., Liu, S., Li, Z., et al., 2022b. Ground-Level NO(2) surveillance from space across China for high resolution using interpretable spatiotemporally weighted artificial intelligence. Environ. Sci. Technol. 56, 9988–9998. https://doi.org/10.1021/acs.est.2c03834.

Wei, J., Li, Z., Li, K., et al., 2022a. Full-coverage mapping and spatiotemporal variations of ground-level ozone (O3) pollution from 2013 to 2020 across China. Remote Sens. Environ. 270, 112775 https://doi.org/10.1016/j.rse.2021.112775.

Wiedmer, P., Jung, T., Castro, J.P., et al., 2021. Sarcopenia - molecular mechanisms and open questions. Ageing Res. Rev. 65, 101200 https://doi.org/10.1016/j.arr.2020.101200.

Wu, X., Li, X., Xu, M., et al., 2021. Sarcopenia prevalence and associated factors among older Chinese population: findings from the China Health and Retirement Longitudinal Study. PLoS One 16, e0247617. https://doi.org/10.1371/journal.pone.0247617.

Wu, Y., Wang, H., Tong, Y., et al., 2023. Sarcopenia index based on serum creatinine and cystatin C is associated with mortality in middle-aged and older adults in Chinese: a retrospective cohort study from the China Health and Retirement Longitudinal Study. Front. Public Health 11, 1122922. https://doi.org/10.3389/fpubh.2023.1122922.

Xia, L., Zhao, R., Wan, Q., et al., 2020. Sarcopenia and adverse health-related outcomes: an umbrella review of meta-analyses of observational studies. Cancer Med. 9, 7964–7978. https://doi.org/10.1002/cam4.3428.

Yuan, S., Larsson, S.C., 2023. Epidemiology of sarcopenia: Prevalence, risk factors, and consequences. Metabolism 144, 155533. https://doi.org/10.1016/j.metabol.2023.155533.

Zare Sakhvidi, M.J., Lafontaine, A., Yang, J., et al., 2022. Association between outdoor air pollution exposure and handgrip strength: findings from the French CONSTANCES study. Environ. Health Perspect. 130, 57701. https://doi.org/10.1289/EHP10464.

Zhang, B., Huang, L., Zhu, X., et al., 2023a. Impact of household solid fuel use on sarcopenia in China: a nationwide analysis. Sci. Total Environ. 877, 162814 https://doi.org/10.1016/j.scitotenv.2023.162814.

Zhang, F., Li, T., Chen, B., et al., 2023b. Air pollution weaken your muscle? Evidence from a cross-sectional study on sarcopenia in central China. Ecotoxicol. Environ. Saf. 258, 114962 https://doi.org/10.1016/j.ecoenv.2023.114962.

Zhang, J., Jia, X., Li, Y., Li, H., Yang, Q., 2023c. The longitudinal bidirectional association between sarcopenia and cognitive function in community-dwelling older adults: findings from the China Health and Retirement Longitudinal Study. J. Glob. Health 13, 04182. https://doi.org/10.7189/jogh.13.04182.

Zhao, L., Fang, J., Tang, S., et al., 2022. PM2.5 and serum metabolome and insulin resistance, potential mediation by the gut microbiome: a population-based panel study of older adults in China. Environ. Health Perspect. 130, 27007. https://doi.org/10.1289/EHP9688.

Zhao, Y., Hu, Y., Smith, J.P., Strauss, J., Yang, G., 2014. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). Int. J. Epidemiol. 43, 61–68. https://doi.org/10.1093/ije/dys203.

Zhu, Y., Guo, X., Zhang, X., et al., 2022a. Sex differences in the relationship of serum creatinine to cystatin C ratio and depressive symptoms among middle-aged and older adults in China. J. Affect Disord. 319, 57–61. https://doi.org/10.1016/j.jad.2022.09.030.

Zhu, Y., Tan, Z., Li, S., et al., 2022b. Serum creatinine to cystatin C ratio and cognitive function among middle-aged and older adults in China. Front Aging Neurosci. 14, 919430 https://doi.org/10.3389/fnagi.2022.919430.

de Zwart, F., Brunekreef, B., Timmermans, E., Deeg, D., Gehring, U., 2018. Air pollution and performance-based physical functioning in Dutch older adults. Environ. Health Perspect. 126, 017009 https://doi.org/10.1289/EHP2239.