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RESEARCH PAPER

Individual and joint exposures to $PM_{2.5}$ constituents and mortality risk among the oldest-old in China

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Cohort evidence linking long-term survival of older adults with exposure to fine particulate matter ($PM_{2.5}$) constituents remains scarce in China. By constructing a dynamic cohort based on the Chinese Longitudinal Healthy Longevity Study, we aimed to assess the individual and joint associations of major $PM_{2.5}$ constituents with all-cause death in Chinese oldest-old (⩾80 years) adults. Time-dependent Cox proportional hazards models were adopted to estimate death risks of long-term exposure to $PM_{2.5}$ constituents. Among 14,884 participants, totaling 56,342 person-years of follow-up, 12,346 deaths were identified. The highest mortality risk associated with an interquartile range (IQR) increase in exposure was 1.081 (95% confidence interval [CI]: 1.055–1.108) for sulfate (IQR=4.1 μg m^{-3}), followed by 1.078 (95% CI: 1.056–1.101) for black carbon (IQR=1.6 μg m^{-3}), 1.056 (95% CI: 1.028–1.084) for ammonium (IQR=3.2 μg m^{-3}), 1.050 (95% CI: 1.021–1.080) for nitrate (IQR=5.8 μg m^{-3}), and 1.049 (95% CI: 1.024–1.074) for organic matter (IQR=10.3 μg m^{-3}). In joint exposure, each IQR-equivalent rise of all five $PM_{2.5}$ constituents was associated with an 8.2% (95% CI: 4.0%–12.6%) increase in mortality risk. The weight analysis indicated the predominant role of sulfate and black carbon in driving $PM_{2.5}$-related mortality. Octogenarians (aged 80–89 years) and rural dwellers were at significantly greater risk of mortality from individual and joint exposures to $PM_{2.5}$ constituents. This study suggests that later-life exposure to $PM_{2.5}$ constituents, particularly sulfate and black carbon, may curtail long-term survival of the oldest-old in China.

particulate air pollution | $PM_{2.5}$ constituents | mortality | oldest-old Chinese | cohort study | joint exposure

INTRODUCTION

Rapid population aging posed a great challenge for alleviating air pollution-related health burden across the globe, particularly in low- and middle-income countries (LMICs) (Southerland et al., 2022). The number of oldest-old adults (⩾80 years) has amounted to 35.8 million, accounting for nearly 2.5% of Chinese population in 2020 (Yang, 2022). It is projected that this demographic in China will surge to 125.4 million, making up one-tenth of the national population by 2050 (Vollset et al., 2020). Given the increasing growth of the oldest-old population in the coming decades, discerning modifiable risks that threaten their well-being is of great importance to achieve healthy longevity and reduce economic loss in a population-ageing era.

Accumulating evidence indicated that the older adults were disproportionally affected by exposure to ambient air pollutants because of the decline in physical function and immune defense systems (Di et al., 2017; Peled, 2011; Shi et al., 2022). In 2021, ambient fine particulate matter ($PM_{2.5}$) pollution contributed to 0.8 million premature deaths of the oldest-old in China, accounting for over one-third (36.7%) of total $PM_{2.5}$-related deaths across all ages (Brauer et al., 2024). Of note, population aging was identified as a dominant driver of growing $PM_{2.5}$-related deaths in China, which had nearly offset the health benefits from the Air Pollution Prevention and Control Action Plan over the past decade (Huang et al., 2018). Therefore, characterizing risk patterns in $PM_{2.5}$-mortality association among the oldest-old is crucial for achieving sustainable development and healthy aging, particularly in the context of a growing aging population.

Population-based cohort studies have consistently presented compelling evidence linking elevated mortality risk with long-term exposure to ambient $PM_{2.5}$ on a global scale (Beelen et al., 2014; Chen and Hoek, 2020), but the effects from individual $PM_{2.5}$ constituents remained largely unstudied due to data sparsity, particularly in the oldest-old from LMICs. Recently, several pilot investigations in China reported the nexus between long-term exposure to $PM_{2.5}$ major constituents (i.e., black carbon [BC], organic matter [OM], sulfate [SO_4^{2-}], nitrate [NO_3^-], ammonium [NH_4^+]) and increased all-cause (Liu et al., 2022), non-accidental (Chen et al., 2021), and cardiovascular (Liang et al., 2020) mortality in general adults. Though satellite-derived estimates from chemical transport models were utilized for exposure assessment in these studies, it could be unable to well capture the spatiotemporal variations of $PM_{2.5}$ constituents in China due to the lack of model validation from native ground-based monitoring measurements (Hammer et al., 2020; van Donkelaar et al., 2019). Hence, the observed cohort findings may still have been prone to criticism for its potential bias and uncertainty from exposure misclassification in association analysis.

To address this knowledge gap, we conducted a dynamic cohort study by integrating well-validated high-resolution (approximately 1 km×1 km) satellite-based estimates with a nationwide cohort of oldest-old adults from the Chinese Longitudinal Healthy Longevity Survey (CLHLS). We primarily aimed to investigate individual and joint associations of all-cause mortality with long-term exposure to $PM_{2.5}$ constituents, through time-dependent Cox analysis incorporated with quantile-based g-computation approach. Our secondary purpose was to check potential effect modification by demographic and geographical factors.

RESULTS

Summary statistics of study population

Table 1 describes the baseline characteristics of 14,884 CLHLS eligible respondents in this study. During the survey spanning over a decade, the high incidence of mortality events (82.9%) gave rise to a short median follow-up duration of 3.0 years during totaling 56,342 person-years of observation. The mean age of participants at baseline was 92.9 (standard deviation [SD]: 7.3) years, and more than a quarter (28.3%) were centenarians (aged 100+ years). Women comprised 61.8% of the cohort, which was slightly higher than the reported estimate in the Seventh National Population Census in China (57.4%, 2020). The exposure levels of five selected chemical constituents varied greatly during study period, with average concentrations ranging from 23.9 (SD: 7.4) $\mu g\ m^{-3}$ for OM to 4.1 (SD: 1.3) $\mu g\ m^{-3}$ for BC (Table 2). We observed moderate to high correlations among $PM_{2.5}$ constituents, with Spearman's correlation coefficients ranging from 0.47 to 0.89 (Figure S1 in Supporting Information).

$PM_{2.5}$ constituents-mortality associations

Figure 1 estimates the individual and joint effects of long-term exposure to five $PM_{2.5}$ constituents on all-cause mortality, as determined by multiple models. Despite some heterogeneities in the magnitude of effect estimates, analyses from different models indicated robustly positive relationships of individual and joint exposures to $PM_{2.5}$ components with mortality risk. In multivariable-adjusted models, the greatest hazard ratio (HR) associated with an interquartile range (IQR) increase in exposure was 1.081 (95% confidence interval [CI]: 1.055–1.108) for SO_4^{2-} (IQR=4.1 $\mu g\ m^{-3}$), followed by 1.078 (95% CI: 1.056–1.101) for BC (IQR=1.6 $\mu g\ m^{-3}$), 1.056 (95% CI: 1.028–1.084) for NH_4^+ (IQR=3.2 $\mu g\ m^{-3}$), 1.050 (95% CI: 1.021–1.080) for NO_3^- (IQR =5.8 $\mu g\ m^{-3}$), and 1.049 (95% CI: 1.024–1.074) for OM (IQR =10.3 $\mu g\ m^{-3}$). In joint exposure, an IQR-equivalent increase of all five $PM_{2.5}$ constituents was associated with an 8.2% (95% CI: 4.0%–12.6%) rise in mortality risk. In the multivariable-adjusted model, the weight analysis of joint exposure identified the greatest positive weight in SO_4^{2-} (+45.1%), followed by BC (+43.3%) and NO_3^- (+11.6%), highlighting the predominance of SO_4^{2-} and BC in triggering $PM_{2.5}$-related mortality (Figure 2).

Table 1. Baseline characteristics of study participants[a)]

Variables	Statistics
Population	
No. of subject, *n*	14,884
No. of death, *n*	12,346
Total person-years of follow-up	56,342
Median years of follow-up per person	3.0
Demographic characteristics, *n* (%)	
Age, mean±SD	92.9±7.3
Octogenarians (aged 80–89 years)	5,287 (35.5)
Nonagenarians (aged 90–99 years)	5,388 (36.2)
Centenarians (aged 100+ years)	4,209 (28.3)
Women	9,201 (61.8)
Han ethnicity	13,842 (93.0)
Married	2733 (18.4)
Illiterate	11,104 (74.6)
Per capita GDP (CNY), mean±SD	17,420±26,053
Beds/1000 population, mean±SD	2.0±1.3
Behavioral factors, *n* (%)	
Regular physical activity	3,431 (23.1)
Smokers	
Current	2,184 (14.7)
Former	2,132 (14.3)
Never	10,568 (71.0)
Alcohol drinkers	
Current	2,606 (17.5)
Former	1,796 (12.1)
Never	10,482 (70.4)
Night sleep duration, hours	
<6	3,777 (25.4)
6–8	4,950 (33.3)
>8	6,157 (41.4)
Chronic disease, *n* (%)	
Diabetes	1,390 (9.3)
Hypertension	3,709 (24.9)
Stroke	1,554 (10.4)
Heart disease	2,134 (14.3)
Respiratory disease	2,148 (14.4)
Geography, *n* (%)	
Region	
North	1,880 (12.6)
Midwest	4,506 (30.3)
Southeast	8,498 (57.1)
Residence	
City	2,779 (18.7)
Town	2,865 (19.2)
Village	9,240 (62.1)

a) The sum of percentages from multiple subgroups may not equal 100% exactly due to the use of rounding-off method. SD, standard deviation; GDP, gross domestic product; CNY, Chinese Yuan.

Figure 3 displays concentration-response (C-R) relationships of long-term exposure to $PM_{2.5}$ constituents with all-cause mortality risk, as fitted from the multivariable-adjusted model. We did not identify clear violations of linearity in the C-R associations (nonlinear P>0.05) of death risk with individual exposure to

Table 2. Summary statistics of $PM_{2.5}$ constituents during study period[a)]

Pollutants (μg m^{-3})	Mean	SD	Min	Percentile			Max	IQR
				P_{25}	P_{50}	P_{75}		
BC	4.0	1.3	1.3	3.2	3.7	4.7	10.1	1.6
OM	23.9	7.4	5.6	18.3	23.2	28.6	67.3	10.3
NO_3^-	10.9	3.5	2.6	7.8	11.4	13.7	30.4	5.8
NH_4^+	7.6	2.1	2.0	5.9	7.7	9.1	22.9	3.2
SO_4^{2-}	12.1	2.8	2.7	10.1	11.7	14.2	32.0	4.1

a) The IQR value may not equal to difference between P_{75} and P_{25} exactly due to rounding-off. SD, standard deviation; IQR, interquartile range; BC, black carbon; OM, organic matter; NO_3^-, nitrate; NH_4^+, ammonium; SO_4^{2-}, sulfate.

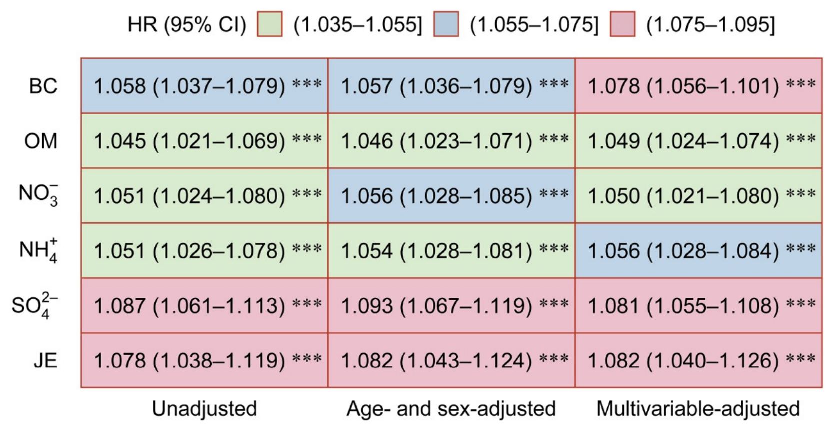

Figure 1. Risks of mortality associated with an IQR increase in exposure to individual $PM_{2.5}$ constituents or an IQR-equivalent increase in joint exposure. ***, P<0.001. HR, hazard ratio; CI, confidence interval; BC, black carbon; OM, organic matter; NO_3^-, nitrate; NH_4^+, ammonium; SO_4^{2-}, sulfate; JE, joint exposure.

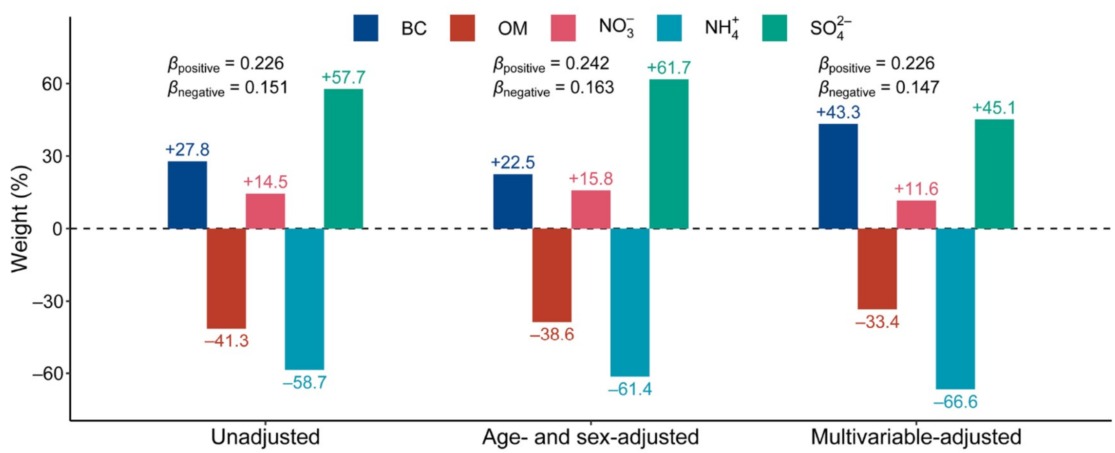

Figure 2. Estimated weights in joint-exposure analysis of $PM_{2.5}$ constituents-mortality associations. Positive and negative weights should not be compared with each other but rather only with others in the same direction. BC, Black carbon; OM, organic matter; NO_3^-, nitrate; NH_4^+, ammonium; SO_4^{2-}, sulfate.

$PM_{2.5}$ components. Despite insignificant effects being observed under low-percentile ranges (<50%), the C-R curve for joint exposure showed a super-linear growth of mortality risk in combined exposure to higher percentiles of $PM_{2.5}$ constituents.

Effect modification and sensitivity analyses

Figure 4 illustrates subgroup-specific associations of death risk with individual and joint exposures to $PM_{2.5}$ constituents, as estimated from the multivariable-adjusted model. We found greater risks of $PM_{2.5}$-associated mortality in octogenarians (aged 80–89 years) compared with centenarians, showing significant effect heterogeneity for individual exposure ($P\leqslant0.02$) to BC, OM, SO_4^{2-}, and NH_4^+ and joint exposure (P=0.04). Exposure-related risk effects were more pronounced in rural dwellers (HR: 1.072–1.131) compared with those residing in town (HR: 1.002–1.028) and city (HR: 1.000–1.055), suggesting rural-urban disparities in mortality associations with $PM_{2.5}$ constituents. Although we did not identify evident effect modifications by sex and education attainment (P>0.10), women and illiterate participants were seemingly at higher death risks when being exposed to $PM_{2.5}$ constituents.

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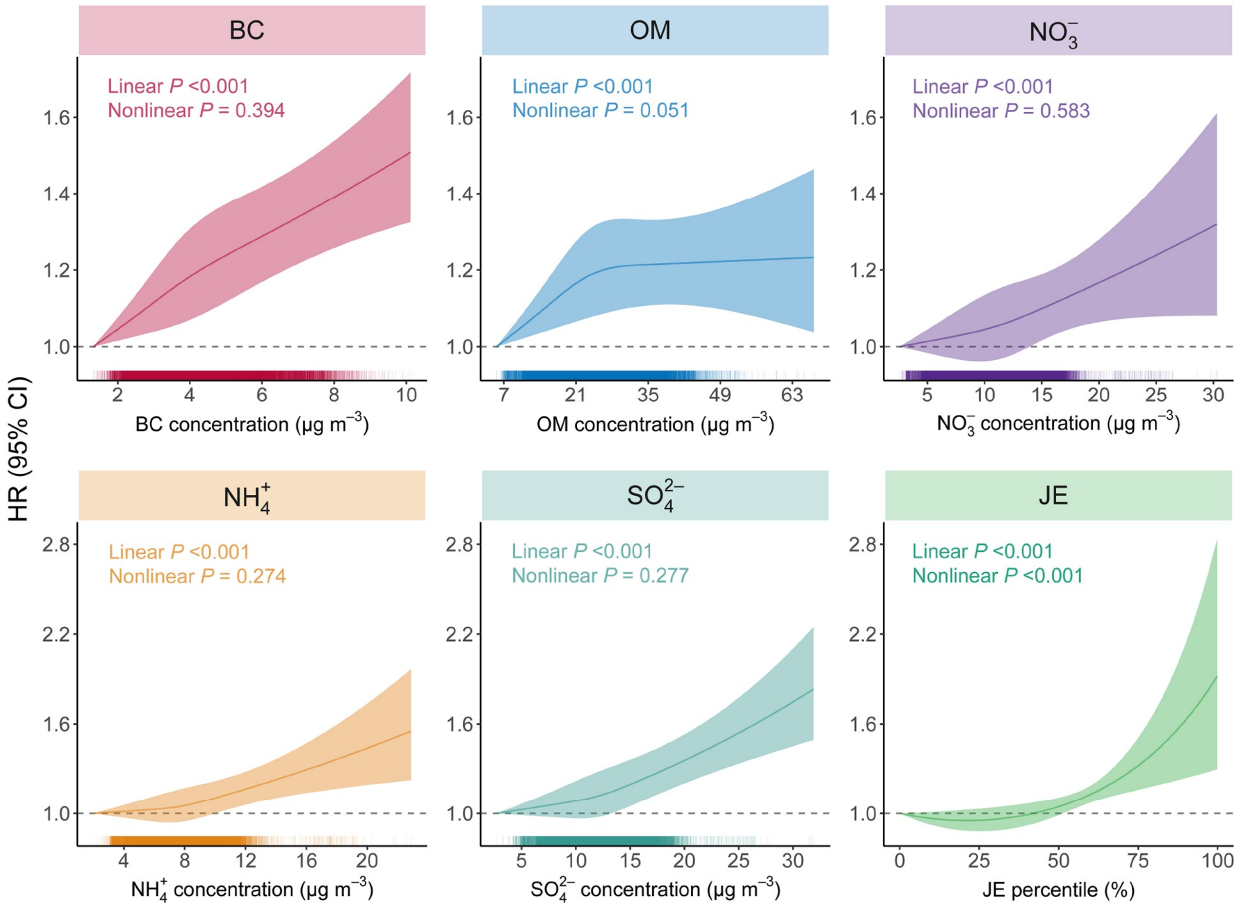

Figure 3. Concentration-response associations of all-cause mortality with individual and joint exposures to $PM_{2.5}$ constituents. HR, hazard ratio; CI, confidence interval; BC, black carbon; OM, organic matter; NO_3^-, nitrate; NH_4^+, ammonium; SO_4^{2-}, sulfate; JE, joint exposure.

Sensitivity analyses highlighted consistent evidence for heightened mortality risks associated with long-term exposure to five $PM_{2.5}$ constituents (Table S1 in Supporting Information). The effect estimates were generally robust or mildly changed in analyses based on dwellers surviving more than six months and different covariates-adjusted strategies. For instance, the estimated mortality risk was increased by 8.8% (95% CI: 4.6%–13.2%) in the directed acyclic graph-based analysis versus 8.2% (95% CI: 4.0%–12.6%) in our multivariable-adjusted model, for an IQR-equivalent rise in joint exposure. Besides, highly comparable associations were seen before and after controlling for the effect of clean air actions (e.g., joint exposure HR [95% CI]: 1.082 [1.040–1.126] versus 1.081 [1.039–1.125]).

DISCUSSION

To the best of our knowledge, this is the first national dynamic cohort to investigate the relationship between long-term exposure to $PM_{2.5}$ constituents and mortality of the oldest-old, utilizing well-validated high-resolution spatiotemporal datasets developed specifically for China. By enrolling ~15,000 oldest-old adults from 23 provinces in China, this study found elevated mortality risk related to individual and joint exposures to $PM_{2.5}$ constituents, through multiple Cox analyses with time-varying exposures. We also observed evidently stronger exposure-mortality associations among octogenarians and those living in rural areas. Also, the weight analysis of mixture exposure identified the predominant role of SO_4^{2-} and BC in driving $PM_{2.5}$-related mortality, highlighting the priority to control emission activities associated with these constituents.

Data from North America (Chung et al., 2015; Wang et al., 2022b) and Western Europe (Hvidtfeldt et al., 2019; Nilsson Sommar et al., 2021) have provided robust evidence that chronic exposure to BC was a noticeable contributor to all-cause and cardiopulmonary mortality. In agreement with Chinese cohorts of national general population (Liu et al., 2022) and Hong Kong elderly (Yang et al., 2018), we associated raised mortality risk with long-term BC exposure in the oldest-old. The underlying biological mechanisms driving this adverse health effect remain unclear. However, experimental studies have indicated that exposure to BC may cause oxidative stress, inflammation (Niranjan and Thakur, 2017), and autonomic nervous system dysfunction (Zhao et al., 2014) to the circulatory system, which can lead to increased risk of hypertension, atherosclerosis and stroke. BC was considered as one of the specific markers for incomplete combustion of biomass used for cooking and heating in developing countries (Xiao et al., 2023). Therefore, to mitigate disease burden from BC exposure in polluted countries like China, a combination of health-oriented policies and individual-level interventions is urgently warranted to reduce emissions from solid fuels (e.g., coal and wood).

Compared with prior investigations from high-income coun-

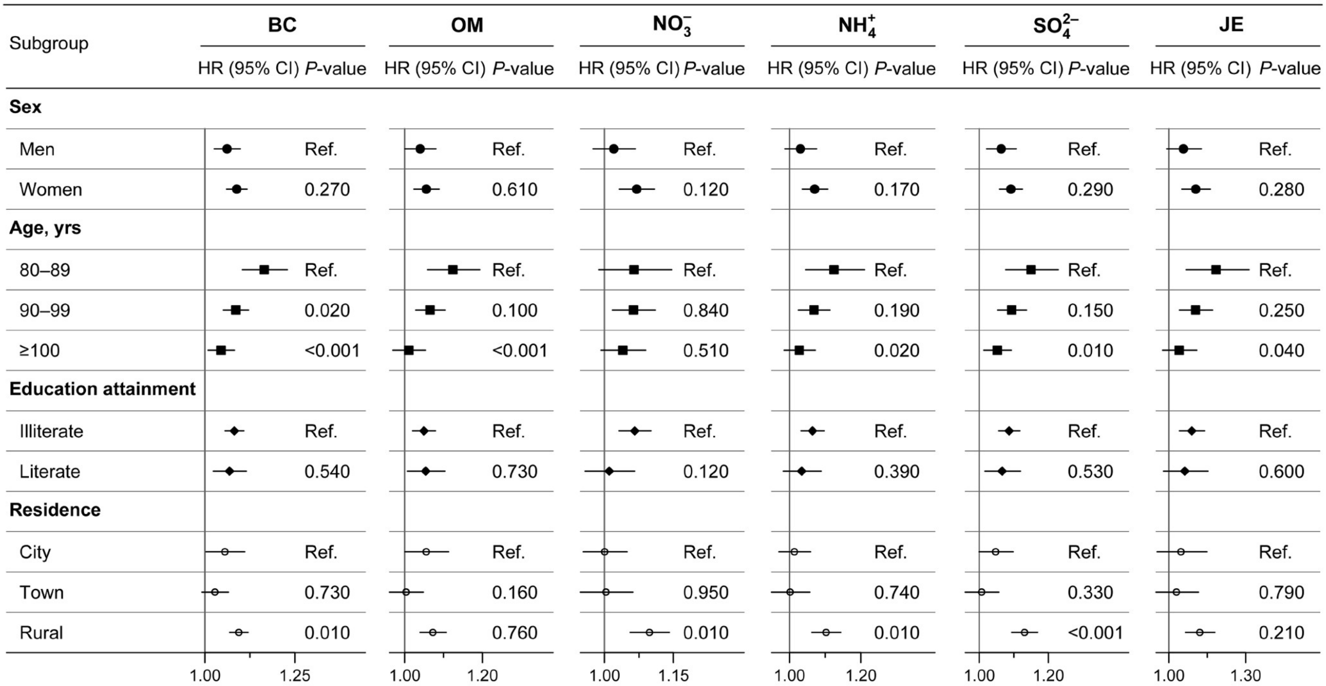

Figure 4. Estimated mortality risk associated with per IQR increase in individual exposure to $PM_{2.5}$ constituents or an IQR-equivalent rise in joint exposure. $P<0.05$ indicates the significant between-group effect heterogeneity. HR, hazard ratio; CI, confidence interval; IQR, interquartile range; BC, black carbon; OM, organic matter; NO_3^-, nitrate; NH_4^+, ammonium; SO_4^{2-}, sulfate; JE, joint exposure.

tries with lower $PM_{2.5}$ pollution levels (<20 μg m^{-3}) (Strak et al., 2021), only two national cohorts in China have investigated the association between mortality and long-term OM exposure in high-exposure scenarios. These studies linked a 10%–12% increase in the risk of all-cause (Liu et al., 2022) and cardiovascular (Liang et al., 2022) mortality per IQR (6.3–7.1 μg m^{-3}) rise in annual OM exposure in adults aged 16 years and older. In this study, we estimated a 4.9% (95% CI: 2.4%–7.4%) heightened mortality risk associated with per IQR (10.3 μg m^{-3}) rise in OM exposure among the oldest-old. Differences in effect magnitude may partially be attributed to great between-study heterogeneity in the surveyed population (e.g., age-related vulnerability and exposure pattern) and analytic strategies (e.g., exposure assessment and adjusted confounders) (Yang et al., 2022). Given the limited population-based evidence, large cohorts across diverse populations and countries are warranted to further elucidate underlying causal relationships between OM exposure and long-term survival.

In line with recent large-scale national cohorts in Danish (Hvidtfeldt et al., 2019) and China (Liu et al., 2022), excess mortality effects relating to long-term exposure to three major secondary inorganic aerosols (SIAs) were also observed in our CLHLS study. Linear C-R curves without thresholds were observed in associations of all-cause mortality with individual exposure to NO_3^-, NH_4^+, and SO_4^{2-}. Using a quantile-based g-computation approach with 1,000 Monte Carlo simulations and 500 bootstraps, we exploratively fitted a nearly J-shaped association in mixture exposure of both carbon fractions and SIAs. However, given high correlations (Figure S1 in Supporting Information), shared sources (e.g., fossil fuel combustion and traffic exhaust emissions) (Wang et al., 2022b), and inter-conversion characteristics (Zhang et al., 2021), it should be methodologically difficult to separate their relative contributions and independent effects. To date, it is still of great challenge to differentiate individual health impacts of multiple co-pollutants (e.g., $PM_{2.5}$ constituents), and future environmental health advances should be devoted to developing sophisticated methods or quasi-experimental designs (e.g., randomized controlled exposure trials) to address this gap (Niu et al., 2022; Wang et al., 2022a).

It has been hypothesized that sex may modify the health effect of particulate air pollution, while findings were less consistent in population-based investigations (Clougherty, 2010). Our sex-stratified results were echoed by an Australian quasi-experiment study (Yu et al., 2020), showing higher mortality risks associated with long-term exposure to $PM_{2.5}$ mass or its constituents in women. Compared to men, women typically possess smaller lungs and narrower airways, which may predispose them to cumulative adverse effects of air pollution on health (Yunginger et al., 1992). In our age-stratified analysis, participants aged 80−89 years were found to have higher $PM_{2.5}$-related risks of death in both individual and joint exposures. Given distinct $PM_{2.5}$ concentration between indoor and outdoor environments (Long et al., 2001), the observed attenuated susceptibility in the nonagenarians (90–99) and centenarians (⩾100) may be related to potential bias in exposure assessment using ambient outdoor $PM_{2.5}$ estimates, because these super-aged groups are more likely to be staying indoors due to restricted mobility (Zeng et al., 2017). In the future, life-course epidemiologic studies are needed for in-depth understanding of sex- and age-inequality in the $PM_{2.5}$-mortality association to achieve superior health and well-being throughout the whole life cycle.

Mounting evidence reported increased vulnerability to short-term $PM_{2.5}$-related health risks in persons with low socio-economic status (SES) (Bell et al., 2013). Using formal school education as a proxy of SES, we found that the illiterate oldest-old were possibly at higher death risks from long-term exposure to $PM_{2.5}$ constituents compared to the educated counterparts. Considering that measuring SES based solely on education attainment may be insufficient, analyses integrating multiple SES indicators (e.g., employment, education, and income) are likely to provide a more accurate representation of real-world conditions. As also reported in prior investigations (Li et al., 2018; Liang et al., 2020), our analysis suggested that rural participants were more strongly affected by ambient exposure to $PM_{2.5}$ constituents. Increased susceptibility in rural oldest-old adults could be partially attributed to inadequate access to medical services and healthcare (Chen et al., 2020), relatively poor physical and nutritional conditions (Dent et al., 2023), and more frequent parallel exposure to indoor emission of pollutants (Snider et al., 2018). These findings emphasize the high priority of health policies or projects aiming at mitigating SES-related and rural-urban inequalities due to particulate air pollution, for pursuing a shared vision of "One Health" and "Healthy Ageing".

Several limitations should be noted in the current study. First, using ambient concentrations of $PM_{2.5}$ components as proxies of air pollution exposures may inevitably lead to exposure misclassification owing to the lack of time-activity details. Also, our $PM_{2.5}$-mortality association analyses failed to consider the influence of some unmeasured factors (e.g., genetic susceptibility and traffic-related noise) due to data unavailability. However, our E-value analyses (Table S2 in Supporting Information, 1.26–1.41) suggested that the observed associations were unlikely to be largely biased by unmeasured confounders. Second, while the effects of individual components remained largely robust across multiple models, completely separating their health effects from $PM_{2.5}$ mass is challenging in cohort studies due to their natural co-exposure and shared emission sources. Third, the collection of time-dependent covariates relied on self-reported questionnaire in each survey wave, which may possibly introduce to-some-extent recall bias. Fourth, this cohort study was conducted in a unique oldest-old population, cautioning against overgeneralizing these findings to other populations.

In conclusion, this large-scale population-based cohort study added compelling evidence that later-life exposure to $PM_{2.5}$ major constituents (i.e., BC, OM, NO_3^-, NH_4^+, and SO_4^{2-}) may curtail long-term survival of the Chinese oldest-old. Our individual and joint analyses revealed consistently greater exposure-associated risks among octogenarians (aged 80–89 years) and rural dwellers in China. The present study identified the predominant role of SO_4^{2-} and BC in triggering $PM_{2.5}$-associated deaths, underscoring their importance as priority pollutants for mitigating particulate matter pollution and protecting vulnerable population, for the sake of building environment-friendly society and achieving healthy longevity in LMICs.

MATERIALS AND METHODS

Study population

We designed a dynamic cohort study base on five waves (2005-, 2008-, 2011-, 2014-, and 2018-wave) of the CLHLS, a nationwide representative survey of oldest-old adults (aged 80+). Details on cohort design and sampling procedure have been presented in prior literatures (Yao et al., 2022; Zeng et al., 2017). Briefly, the CLHLS has randomly selected samples of elderly residents from half of the counties or cities in 23 provincial administrative regions of China since 1998, and traced them every 2–4 years. New participants were recruited during each wave of CLHLS to offset attrition from death or loss to follow-up, amounting to a total enrollment of 27,585 subjects from 2005 to 2014 (Figure S2 in Supporting Information).

For the present study, a total of 14,884 eligible respondents were included for analysis after excluding those who were lost to follow-up in subsequent waves (n=5,214), with missing residential information (n=1,714), younger than 80 years old at baseline (n=5,708), and with invalid or incomplete date of death (n=65). After signing written informed consent, the interviewees completed a structured questionnaire on demographic, behavioral and health characteristics in the form of face-to-face household interview. For the deceased during follow-up, death information was collected by family members or community doctors. Therefore, loss to follow-up in this study was defined as being alive but not participating in any subsequent surveys. Given the causes of death were largely unknown or inconclusive, our analyses were limited to all-cause mortality outcome in this study. The Biomedical Ethics Committee of Peking University in Beijing, China granted approval to CLHLS (IRB00001052–13074).

Exposure assessment

Estimates of $PM_{2.5}$ constituents at a 1×1-km resolution from 2005 through 2018 (Wei et al., 2023) were derived from ChinaHighAirPollutants dataset, which has been widely applied to air pollution epidemiology in recent years (Huang et al., 2023; Wu et al., 2022; Zhang et al., 2022). The daily estimates of spatiotemporal $PM_{2.5}$ chemical constituents were simulated using a four-dimensional spatiotemporal deep forest (4D-STDF) model, which integrated measurements of $PM_{2.5}$ species from a high-density observation network, satellite $PM_{2.5}$ retrievals, and atmospheric reanalysis. The 4D-STDF model demonstrated excellent predictive performance for daily estimates during 2013–2020 across China, as evidenced by high cross-validated coefficients of determination (CV-R^2, 0.71–0.75) and low average root-mean-square errors (RMSE, 4.3–6.6 μg m^{-3}). Modeling details for $PM_{2.5}$ chemical components could be found in the prior publication (Wei et al., 2023).

To capture temporal and spatial variations of $PM_{2.5}$ constituents, we assigned time-dependent exposures to each participant based on the residential address for each calendar year during follow-up period. For the year being analyzed, address information obtained from the most recent survey wave was used to account for residential migrations. Due to its strong ability of penetrating into indoor environments effectively (Bousiotis et al., 2023), outdoor concentrations of $PM_{2.5}$ and its constituents could generally reflect indoor exposure levels to some extent. Given limited mobility of the oldest-old in CLHLS cohort, residential exposure assessment at a 1×1-km resolution could minimize the exposure misclassification from complex time-activity patterns.

Covariates

Several sets of covariables gleaned at baseline and sequential survey waves were considered according to their associations with both exposures and mortality, as specified in existing literature (Chen and Hoek, 2020). These covariates included (1) demographic characteristics: age, sex (men or women), ethnicity (minority or Han), marital status (married or unmarried), educational attainment (illiterate or literate), per capita gross domestic product, and hospital beds per thousand population; (2) behavioral factors: smoking or drinking status (current, former, or never), physical activity (yes or no), night sleep duration (<6, 6–8, or>8 h); (3) chronic diseases: diabetes (yes or no), hypertension (yes or no), stroke (yes or no), heart disease (yes or no), and respiratory disease (yes or no); (4) geography: region (north, midwest, or southeast) and residence (city, town, or village). Specifically, we extracted county-level estimates of per capita gross domestic product and hospital beds per thousand population from the China Statistical Yearbook, and chose them as proxies of SES and healthcare access to account for potential area-level confounders. We considered above-mentioned common illnesses to as much as possible capture the influence of a wide range of pre-existing chronic diseases on the exposure-mortality association.

Details for the included covariates were described in Table A1. Given the relatively low missing proportion of each individual covariate (<5%, Figure S3 in Supporting Information), we utilized predictive mean matching to impute continuous variables and mode interpolation for categorical variables, aiming to minimize sample loss. By comparing summary statistics of study participants from the imputed dataset with complete-case data (excluding participants with missing variables), we did not identify great differences in basic characteristics between these two groups of population (Table S3 in Supporting Information). All analyses were thus performed based on the imputed dataset.

Statistical analysis

The baseline characteristics of the study participants were reported using counts and percentages (%) for categorical variables and mean (SD) for continuous variables. We calculated the person-years of follow-up for each subject as the interval from enrollment to the last follow-up interviews, or the dates of death, or the end of CLHLS 2018, whichever came first. Spearman's correlation coefficients were applied to measure correlations between $PM_{2.5}$ constituents. Cox proportional hazards models with time-varying exposures and covariates were employed to assess individual and joint associations of long-term exposure to $PM_{2.5}$ constituents with mortality risk. All statistical analyses were conducted in R software (Version 4.0.3, R Foundation for Statistical Computing, Vienna, Austria), and two-tailed $P<0.05$ was considered statistically significant.

We adopted Cox proportional hazards models with attained age as the underlying time scale to examine individual associations of exposure to $PM_{2.5}$ constituents with all-cause mortality. To evaluate the robustness of the associations, a stepwise approach was adopted to construct three models with covariates being adjusted sequentially. Unadjusted model was developed to include the exposure variable of interest only. Age- and sex-adjusted model, where age groups were divided into 5-year intervals (i.e., 80–84, 85–89, 90–94, 95–99, and ⩾100), was established to allow for flexible stratum-specific mortality risks (Cologne et al., 2012; Griffin et al., 2012). Multivariable-adjusted model was additionally adjusted for the aforementioned time-dependent covariates (i.e., demographic, behavioral, health, and geography) that were acquired from the most recent wave of survey. Effect estimates were presented as the HR and its 95% CI for all-cause mortality associated with per IQR increase in exposure. To depict the C-R relationships between long-term exposure to $PM_{2.5}$ constituents and all-cause mortality, we adopted restricted cubic spline function with three knots at the 10th, 50th and 90th percentiles to smooth the exposure of interest in the multivariable-adjusted model (Inoue et al., 2020). Nonlinearity of the C-R relationship was examined via the likelihood ratio tests (Zhang, 2021).

Multivariable-adjusted Cox analysis incorporated with quantile-based g-computation approach was performed to estimate the joint effect of $PM_{2.5}$ constituents on mortality (Keil et al., 2020). In this study, we used quartiles to create indicators representing all $PM_{2.5}$ constituents (e.g., 0, 1, 2, and 3), equivalent to exposure ranges falling into the 0–25th, 25th–50th, 50th–75th, or 75th–100th percentile, and reported the mortality risk of an IQR-equivalent increase in joint exposure to five $PM_{2.5}$ constituents. We estimated the index weight of each constituent in the mixture exposure to quantify its relative contribution in joint association. The quantile-based g-computation method allows for flexibility in direction and magnitude of effect, so as to control for mutual confounding across $PM_{2.5}$ components (Zhang et al., 2022). We used cubic B-spline function with 1,000 Monte Carlo simulations and 500 bootstraps to fit C-R curve of joint exposure (Huang et al., 2023; Ramachandran et al., 2012).

We did *E*-value analyses to investigate the impact of possible residual confounding on relationships between $PM_{2.5}$ constituents and long-term survival of the oldest-old, where large *E*-values suggest that substantial unmeasured confounding would be required to nullify the observed associations, bolstering the likelihood of the argument for a genuine effect (VanderWeele and Ding, 2017). Several stratified analyses were performed to investigate underlying effect modification by sex, age, education attainment, and residence. In age-specific analysis, respondents were divided into octogenarians (80–89), nonagenarians (90–99), and centenarians (⩾100). Effect heterogeneity between subgroups was examined through a fixed effect meta-regression method (Ye et al., 2022), where the effect size was treated as the dependent variable and the stratum variable (e.g., age group) was included as an independent predictor.

Multiple sensitivity analyses were conducted to check the robustness of the results. First, to reduce the potential of reverse causality (Garcia Iii et al., 2021), we repeated our main analysis by excluding individuals who died within 6 months after the baseline survey. Second, to eliminate the underlying effect of clean air actions, we re-ran the multivariable-adjusted model via additionally adjusting for a binary variable (e.g., 1 for 2013–2018 and 0 for other years) indicating whether national policies for controlling air pollution were implemented in each year. Third, we incorporated the calendar year of cohort enrollment as a stratification factor in the multivariable-adjusted model to account for potential temporal variations in survival trends of CLHLS participants from multiple survey waves. Fourth, to avoid over-adjustment in association analyses, we utilized a directed acyclic graph, as an alternative approach for covariate selection, to determine a minimal sufficient adjustment covariate set (age, sex, education attainment, ethnicity, residence, and region, Figure S4 in Supporting Information). In addition, we re-ran the analysis through excluding participants with pre-existing chronic diseases to eliminate the potential confounding bias from bad health status in the oldest-old.

Compliance and ethics

The authors confirm that there are no known competing financial interests or personal relationships that could have influenced the integrity of the work presented in this paper.

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