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SHORT REPORT

Long-term fine particular exposure and incidence of frailty in older adults: findings from the Chinese Longitudinal Healthy Longevity Survey

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Abstract

Background: The association between fine particular matter ($PM_{2.5}$) and frailty is less studied, and the national burden of $PM_{2.5}$-related frailty in China is unknown.
Objective: To explore the association between $PM_{2.5}$ exposure and incident frailty in older adults, and estimate the corresponding disease burden.
Design: Chinese Longitudinal Healthy Longevity Survey from 1998 to 2014.
Setting: Twenty-three provinces in China.
Subjects: A total of 25,047 participants aged ≥65-year-old.
Methods: Cox proportional hazards models were performed to evaluate the association between $PM_{2.5}$ and frailty in older adults. A method adapted from the Global Burden of Disease Study was used to calculate the $PM_{2.5}$-related frailty disease burden.
Results: A total of 5,733 incidents of frailty were observed during 107,814.8 person-years follow-up. A 10 $\mu g/m^3$ increment of $PM_{2.5}$ was associated with a 5.0% increase in the risk of frailty (Hazard Ratio = 1.05, 95% confidence interval = [1.03–1.07]). Monotonic, but non-linear exposure-response, relationships of $PM_{2.5}$ with risk of frailty were observed, and slopes were steeper at concentrations >50 $\mu g/m^3$. Considering the interaction between population ageing and mitigation of $PM_{2.5}$,

the $PM_{2.5}$-related frailty cases were almost unchanged in 2010, 2020 and 2030, with estimations of 664,097, 730,858 and 665,169, respectively.

Conclusions: This nation-wide prospective cohort study showed a positive association between long-term $PM_{2.5}$ exposure and frailty incidence. The estimated disease burden indicated that implementing clean air actions may prevent frailty and substantially offset the burden of population ageing worldwide.

Keywords: fine particular matter ($PM_{2.5}$), frailty, older adults, Chinese Longitudinal Healthy Longevity Survey (CLHLS), disease burden, older people

Key Points

- This nation-wide prospective cohort study showed a positive association between long-term fine particular matter ($PM_{2.5}$) exposure and frailty.
- Monotonic, but non-linear exposure-response associations were observed, and slopes were steeper at concentrations $\geq 50\ \mu g/m^3$.
- Considering rapid population ageing and significant decrease in fine particular matter ($PM_{2.5}$), the disease burden was almost unchanged in 2010–2030.

Introduction

Frailty is an emerging global disease burden that has a significant impact on clinical practice and public health [1]. With the rapid ageing population, the prevalence of frailty is expected to increase [2]. More studies are required to provide suggestions on modifiable factors and develop effective strategies that target the prevention and management of frailty in the ageing population [3].

Fine particular matter ($PM_{2.5}$) is an environmental exposure leading to ageing-related health outcomes [4–7]. Three studies in China have concluded that $PM_{2.5}$ may increase the incidence of frailty [8–10]. Due to the cross-sectional nature and the lack of individualized $PM_{2.5}$ exposure, current evidence was insufficient to support the casual relationship between $PM_{2.5}$ and frailty. Furthermore, no study has been conducted to estimate the national burden of $PM_{2.5}$-related frailty in China.

We conducted a comprehensive investigation on the longitudinal association between $PM_{2.5}$ and incident frailty among older adults using detailed personal $PM_{2.5}$ at 1 km × 1 km, and estimated the national burden of $PM_{2.5}$-related frailty at 2010, 2020 and 2030 in consideration of different scenarios of $PM_{2.5}$ pollution and population ageing in China [11–13].

Methods

Study design and participants

The Chinese Longitudinal Healthy Longevity Survey (CLHLS) was conducted from 1998 to 2014 [14] with 3–5 years' follow-up intervals. Recruited were 42,037 participants aged ≥65-year-old. We excluded participants who lost-to-follow-up in the first follow-up survey ($n = 6{,}324$), with < 50% indicators to calculate Frailty Index (FI) ($n = 702$), with prevalent frailty at baseline ($n = 6{,}210$), and with uncertain addresses ($n = 3{,}754$). Finally, 25,047 participants were included in the analysis (Supplementary Figure 1). The study was approved by the Biomedical Ethics Committee of Peking University (IRB00001052–13074).

Individualized ambient $PM_{2.5}$ exposure

Estimates of ground-level concentrations of $PM_{2.5}$ at 1 km × 1 km resolution were obtained from the Atmospheric Composition Analysis Group [15], which were highly consistent ($R^2 = 0.81$) with out-of-sample cross-validated $PM_{2.5}$ concentrations from monitors [16]. We calculated personal exposures of $PM_{2.5}$ by linking residential locations to the nearest $PM_{2.5}$ grids.

Frailty assessment

Frailty status were measured by FI including multiple dimensions of cumulative health deficits such as body functions and other physiological systems [17]. As previously reported [17], the FI which was calculated using 39 health-related deficits of various dimensions collected from baseline and follow-up surveys by self-report and physical measurements (Supplementary Table 1).

Covariates

We categorised the education level as illiterate and literate; categorised residence as rural or urban; categorised marital status as married or unmarried, divorced, or widowed; categorised income as pension or other; categorised occupation before 60-year-old as intellectual, labour or others; categorised living arrangement as living with family members, alone or in a nursing home; divided the current statuses of regular exercising, smoking, and alcohol drinking into yes or no.

Statistical analysis

The missing data (<2%) were imputed using multiple imputation methods ($N_{\text{imputation}} = 5$) [18]. Cox proportional hazards models were performed to evaluate the association

Fine Particular Pollutants ($PM_{2.5}$)	Events	Participants	Baseline exposure [HR (95%CI)]
Each 10 μg/m³ increase in $PM_{2.5}$	5733	25047	1.05(1.03~1.07)
$PM_{2.5}$ as categorical variable			
First quartile (8.3-40.2 μg/m³)	1389	6258	1.00 Reference
Second quartile (40.2-49.9 ug/m³)	1408	6186	1.03 (0.95~1.11)
Third quartile (49.9-59.5 μg/m³)	1449	6262	1.21 (1.12~1.31)
Forth quartile (59.5-118.0 μg/m³)	1487	6341	1.20 (1.11~1.30)
P-value for trend			<0.001
$PM_{2.5}$ categorized by Chinese guidelines			
<35 μg/m³	776	3485	1.00 Reference
35-75 μg/m³	4753	20812	1.10 (1.01~1.19)
>75 μg/m³	204	750	1.24 (1.05~1.47)
P-value for trend			<0.001

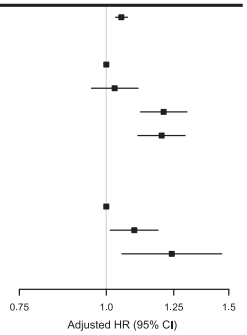

Figure 1. Long-term personal fine particular pollutants ($PM_{2.5}$) exposure and incident frailty in Chinese older adults. Model adjusted for age, sex, education level, residence, marital, income, previous occupation and living status, current smoking, current drinking and regular exercising.

between $PM_{2.5}$ exposure and incident frailty with controlling for potential covariates. We modelled $PM_{2.5}$ as (i) a simple continuous variable [with hazard ratios (HRs) and 95% confidence intervals (CIs) estimated for each 10 $\mu g/m^3$ increment]; (ii) ordinal variables by quartiles; (iii) categorical variables according to Chinese guidelines (<35, 35–75 and ≥ 75 $\mu g/m^3$).

We used the HR estimates from the Cox proportional hazards models to calculate the $PM_{2.5}$-related disease burden in China, using a method adapted from the Global Burden of Disease Study [19]. On the hypothesis that the frailty rate would remain stable if $PM_{2.5}$ concentrations were reduced to 10 $\mu g/m^3$. We calculated, for each county (*i*), the frailty (*Fi*) in the population aged ≥65-year-old that is attributable to ambient $PM_{2.5}$ (Supplementary Formulae 1A and 1B, Supplementary Tables 2 and 3).

Results

During 107,814.8 person-years follow-up, 5,733 incidents of frailty were observed. In the fully adjusted cox proportional hazards model, each 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 5.0% increase in the risk of frailty (HR = 1.05, 95% CI = [1.03–1.07]). Compared with the lowest quartile of $PM_{2.5}$, the HRs (95% CI) of the second, third and fourth quartiles were 1.03 (0.95–1.11), 1.21 (1.12–1.31) and 1.20 (1.11–1.30), respectively. Categorised by Chinese guidelines, adjusted HRs (95% CI) were 1.10 (1.01–1.19) and 1.24 (1.05–1.47) for participants with $PM_{2.5}$ concentrations at 35–75 and ≥ 75 $\mu g/m^3$, respectively, compared with those <35 $\mu g/m^3$ (Figure 1). Monotonic, but non-linear exposure-response relationships of long-term $PM_{2.5}$ exposure with risk of frailty were observed, and slopes were steeper at concentrations ≥50 $\mu g/m^3$ (Supplementary Figures 4A and 5B). Results remained stable in sensitive analyses (Supplementary Figure S5).

Considering the interaction between population ageing and mitigation of $PM_{2.5}$, the cases of $PM_{2.5}$-related frailty were 664,097, 730,858 and 665,169 for 2010, 2020 and 2030, respectively. With the population ageing and unimproved air quality, the $PM_{2.5}$-related incident frailty cases were estimated to be 1,041,760 in 2020 and 1,341,428 in 2030. As the population ageing is usually irreversible, compared with the disease burden without considering improved air quality, the significant decreases of $PM_{2.5}$-related frailty incidents (310,902 in 2020 and 676,259 in 2030) in the scenario with improved air quality were primarily benefited from the substantial mitigation of $PM_{2.5}$ (Figure 2).

Discussion

Through this nation-wide prospective cohort study, we found a stable positive association between long-term $PM_{2.5}$ exposure and frailty in Chinese older adults. As the population ageing is usually irreversible, the significant decreases of $PM_{2.5}$-related frailty burden were primarily benefited from the mitigation of $PM_{2.5}$.

This study shared several common findings with the previous two studies on the association between air quality and frailty. Compared to Hu et al.'s study [10] using city-level air pollution data without individualized $PM_{2.5}$, our study established the association between $PM_{2.5}$ and frailty with personal exposure at 1 km × 1 km, and further explored the non-linear dose–response relationship between them. Lee et al. reported the relationship between $PM_{2.5}$ and frailty in Asians [9], but limited by the lack of national representative samples. Therefore, our findings provided new hints for larger-scale epidemiological studies to uncover the landscape of air pollution's impact on healthy ageing.

We further estimated the $PM_{2.5}$-related frailty disease burden in China. The ageing population increased more than 50% in 2020 compared with 2010, while the incident frailty cases attributable to $PM_{2.5}$ in older adults increased by <3%. The plausible explanation may be that $PM_{2.5}$ levels in China decreased (from 49.9 to 33.1 $\mu g/m^3$) over the decade for the stringent air quality control policy since 2013. The interaction between population ageing and mitigation of $PM_{2.5}$ in this study emphasised that the importance of taking actions to reduce air pollution.

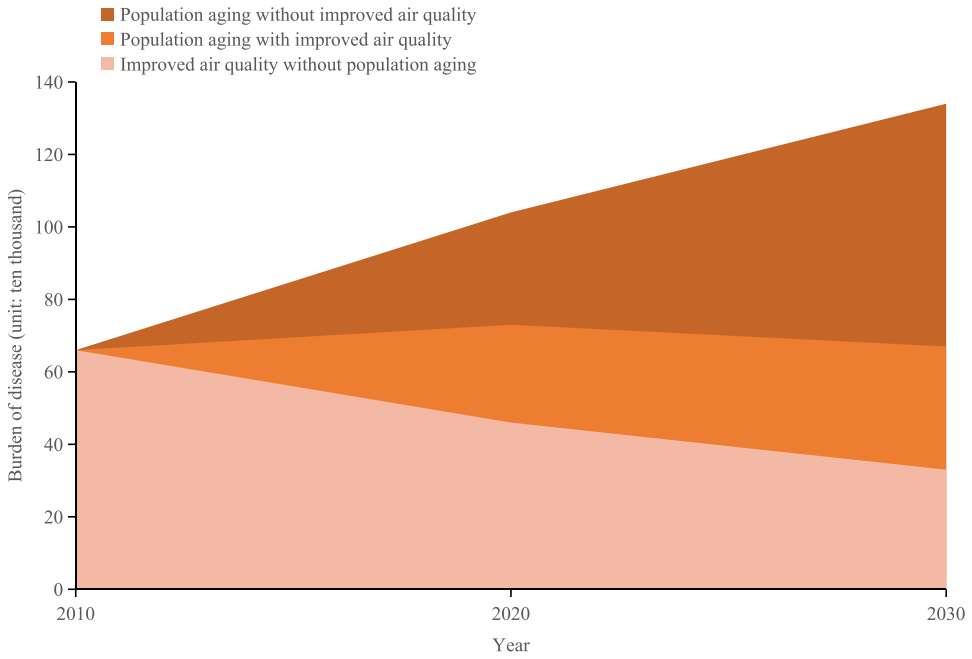

Figure 2. Estimated incident frailty related to $PM_{2.5}$ exposure in adults aged ≥65-year-old in China in 2010, 2020 and 2030 with respect to the interaction between population ageing and air quality improvement

Frailty is an emergent state of dysregulations in a compromised complex dynamical system that consists of the musculoskeletal system, metabolic system and stress-response system. Previous epidemiological and animal-based studies have shown that $PM_{2.5}$ and other air pollutants could manifest such age-related biological vulnerability to stressors and harmed physiological reserves [20]. In mice studies, long-term exposure to $PM_{2.5}$ impaired the function of brown adipose tissue and changed the gene expression from brown to white adipocyte specific patterns [21, 22], which are specialised for fatty acid metabolism, energy expenditure and heat generation. Also, long-term exposure to $PM_{2.5}$ could cause inflammatory reaction [23, 24]. We thus speculate that the arguments of systemic inflammation, insulin resistance and oxidative stress resulting from $PM_{2.5}$ would first cause mild disorders of the three systems to incubate frailty [25].

The major strengths of this study include the following: (i) it is the first long-term cohort study to investigate the causal association between $PM_{2.5}$ and frailty; (ii) we first estimated the national-wide burden of $PM_{2.5}$-related frailty among Chinese older adults under several different scenarios. The study also has limitations. Although we estimated individualized ambient $PM_{2.5}$ exposures at 1 km × 1 km for all participants, the unmeasured exposures and time spend indoors might still limit us to generate the real-world exposures. Participants in our study were Chinese older adults, which limits the generalisation of the results to other ethnic groups.

Conclusion

In conclusion, we added evidence to the relationship between $PM_{2.5}$ exposure and frailty incidence in a nation-wide prospective cohort study at community setting. We provided reliable risk estimations with the accurate individualized ambient $PM_{2.5}$ exposures and inclusion of numerous covariates. Although faced with a rapid ageing in recent decades, China's actions on air clean significantly decreased the concentration of $PM_{2.5}$ and correspondingly contributed to the reduction of frailty related disease burdens. Considering population ageing and mitigation of $PM_{2.5}$, the $PM_{2.5}$-related frailty cases were almost unchanged in 2010, 2020 and 2030. Evidence suggested that the benefit of air quality improvement was likely to offset the frailty-related disease burden aggravated by population ageing.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

Declaration of Conflicts of Interest: None.

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Data Availability: The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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