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Research Article

Frailty Risk in Older Adults Associated With Long-Term Exposure to Ambient $PM_{2.5}$ in 6 Middle-Income Countries

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Abstract

Background: A series of studies have explored the health effects of long-term exposure to ambient $PM_{2.5}$ among older adults. However, few studies have investigated the adverse effect of long-term exposure to ambient $PM_{2.5}$ on frailty, and the results are inconclusive. This study sought to investigate the associations between long-term exposure to ambient $PM_{2.5}$ and frailty in 6 low- and middle-income countries.
Methods: We included an analytical sample of 34 138 individuals aged 50 and older from the Study on global AGEing and adult health Wave 1 (2007/2010). Air pollution estimates were generated using a standard methodology derived from Moderate Resolution Imaging Spectroradiometer observations and Multiangle Imaging Spectroradiometer instruments from the Terra satellite, along with simulations from the GEOS-Chem chemical transport model. A 3-level hierarchical logistic model was used to evaluate the association between frailty index and long-term $PM_{2.5}$ exposure at 3 levels (individual, province, and country).
Results: In rural areas, each 10 μg/m³ increase in ambient $PM_{2.5}$ was associated with a 30% increase in the odds of frailty (OR = 1.30, 95% CI: 1.21–1.39) after adjusting for various potential confounding factors. The gender-stratified analysis showed that the association seemed to be slightly stronger in men (OR = 1.31, 95% CI: 1.18–1.46) than in women (OR = 1.21, 95% CI: 1.07–1.36) in rural areas.
Conclusion: In a large sample of community-based older adults from 6 middle-income countries, we found evidence that long-term $PM_{2.5}$ exposure was associated with frailty in rural areas.

Keywords: Air pollution, Ambient $PM_{2.5}$, Frailty, Older adults

A growing body of literature supports the adverse effect of long-term ambient air pollution exposure on lung function and other health outcomes (1,2). In older adults and susceptible individuals, short- and long-term exposures to air pollution have been associated with poor lung function, mortality, and cancer (3,4). Compared to other age groups, older adults are more susceptible to the impact of air pollution. At the same time, this population is also more susceptible to increased vulnerability to risk factors leading to frailty (5).

Given the current global trends of demographic aging, economic development, and urbanization, air pollution and frailty among older people have become emerging and intertwined public health issues. For example, individuals with compromised lung function do not have sufficient normal pulmonary defense mechanisms to respond to air pollution and particulate matter (6,7). Consequently, when the individuals experience an exacerbation of chronic obstructive pulmonary diseases due to pneumonia comorbid, they might become transiently frail or become frailer

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for those with existing frailty due to their inability to cope with the additional stress posed by air pollution. The situation can lead to poorer health outcomes and manifest as cardiovascular diseases or depression (8,9).

While a series of studies have explored the health effects of long-term exposure to ambient fine particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) among older adults, these studies generally assess the association between exposure to $PM_{2.5}$ with a single disease endpoint, such as the incidence of acute coronary event (10) or cognitive performance (11), rather than a complex outcome such as frailty that is usually measured as an index generated from multiple indicators. Though no single-standard assessment tool of frailty is available, the frailty index has been well tested in several populations (12). To the best of our knowledge, only one study has specifically investigated the relationship between air pollution and the incidence of frailty assessed by the frailty index (9). The study reported that $PM_{2.5}$ exposure was associated with an increased risk of developing frailty among patients suffering from myocardial infarction (OR = 1.53; 95% CI: 1.22–1.91, when comparing the 75th vs 25th percentiles of the exposure distribution), after adjusting for sociodemographic and clinical variables. However, a similar association has not been reported in a population-based study.

This article aims to examine the association between long-term exposure to $PM_{2.5}$ and frailty among older adults in 6 middle-income countries (MICs) who participated in the Study on global AGEing and adult health (SAGE) during 2007–2010. We further evaluate the dose–response association between $PM_{2.5}$ concentrations and frailty stratified by urban/rural settings.

Method

Study Population

The study population was drawn from the SAGE Wave 1 (2007–2010), a longitudinal cohort survey of aging and older adults in 6 MICs: China, Ghana, India, Mexico, Russian Federation, and South Africa. SAGE employed multistage cluster sampling strategies in all countries (13). The strata selected were defined by provinces/states and locality (urban/rural). Enumeration areas constituted the primary sampling units and were selected using the probability proportional to size method. Finally, household enumerations were randomly selected as the final sampling unit. The sampling design in Mexico was similar to the other 5 countries but included a supplementary, random sample from urban and rural households to compensate for the overrepresentation of metropolitan strata. Face-to-face interviews were used to complete the questionnaires. The response rates ranged from 51% in Mexico to 93% in China (India 68%, Ghana 80%, Russia 83%, and South Africa 77%).

Ethics and Consent

WHO's Ethical Review Committee approved SAGE (RPC146). Additionally, each country obtained ethical clearance through their respective review bodies, and SAGE obtained written informed consent from each respondent.

Study Variables

Outcome variable—the frailty index

Frailty was defined as the accumulation of deficits (14). In this study, the frailty index was constructed as the proportion of deficits present in 40 variables (15). The index included variables on medical symptoms, medically diagnosed conditions, activities of daily living, and performance tests (walking speed and grip strength). The likelihood of frailty increases with more decrements in health (16). The complete list of variables and the coding is presented in Supplementary Table 3. The individual frailty scores ranged from 0 (no deficits) to 1 (highest level of deficits in all variables). A cutoff value of 0.2 has been recognized as a threshold for approaching a frail state (17,18). Hence, we classified individuals into not frail (0 to less than 0.2) and frail (0.2–1.0) groups.

Exposure variable—air pollution assessment

This study estimated the ambient $PM_{2.5}$ levels using remotely sensed data. These estimates were derived from a combination of observations from the Moderate Resolution Imaging Spectroradiometer (19) and Multiangle Imaging Spectroradiometer instruments from the Terra satellite, along with simulations from the GEOS-Chem chemical transport model (www.geos-chem.org). The analysis resulted in estimates of the average long-term level of exposure to $PM_{2.5}$ at an approximate resolution of 10 km × 10 km. According to a previous validation study, the estimated $PM_{2.5}$ data had an expected 1-sigma uncertainty of 1 μg/m^3 + 25% (20).

The location of respondents was geocoded using coordinates from the SAGE data sets and mapped to Google Earth at the community level. We refer to these as community addresses to indicate the varying size and meaning of the aerial unit to which each address was geocoded. A corresponding $PM_{2.5}$ concentration estimate was assigned and used in the regression models. The "community" in our study refers to the township in China, enumeration block in Ghana and South Africa, village and enumeration block in India, a geostatistic area in Mexico, and atenum in Russia. We obtained the 1–5 years averaged $PM_{2.5}$ concentration estimate before SAGE Wave 1 with this method. We used the 3-year averaged $PM_{2.5}$ concentration in the main models. Considering the effect of temperature and humidity on the length of time people are exposed to $PM_{2.5}$ outdoors, we also collected the 1–5 years averaged temperature and humidity for each "community."

Other covariates

Other variables used in the analyses included age, gender, education, wealth quintiles, tobacco use, vegetable and fruit intake, and physical activity levels. According to the International Standard Classification of Education, education was divided into 5 levels. Wealth quintiles were derived from the household ownership of durable goods, dwelling characteristics (floor, wall, and stove), and access to services such as clean water, sanitation, and cooking fuel. Tobacco use was assessed by self-reported questions and categorized into never smokers, noncurrent smokers, current nondaily smokers, and current daily smokers. We used the average number of daily servings consumed in a typical day to assess fruit and vegetable consumption. Five or more servings of fruits and/or vegetables were defined as sufficient daily intake (equivalent to at least 400 g/day). Fewer than 5 servings were categorized as insufficient. We generated a categorical indicator of physical activity (low, moderate, and high levels) from the self-reported total time spent on physical activity, the number of days, and the intensity of physical activity (21). The study asked fuel types for domestic cooking and usage of ventilation to assess indoor air pollution. It categorized them as clean fuels (electricity and natural gas) and unclean fuels (coal, wood, dung, and agricultural residues).

Statistical Methods

We used descriptive statistics to describe the sociodemographic characteristics and selected covariates for respondents in the 6 countries, including observations and weighted proportions for categorical variables. We generated country-specific frequency histograms to describe the 3-year averaged $PM_{2.5}$ concentration distribution. A 3-level hierarchical logistic model was used to evaluate the association between long-term 3-year $PM_{2.5}$ exposure and frailty, considering that individuals were nested within provinces, which were nested within countries. Covariates of interest at the individual level (Level 1) included age, gender, education, tobacco use, vegetable and fruit intake, and physical activity. All models were stratified by urban/rural setting. To avoid small regression coefficients, we set 10 μg/m^3 instead of 1 μg/m^3 as the minimum concentration unit. We also performed a stratified analysis to compare whether the associations varied by country, age group, or gender to identify the potential effect modifiers. We evaluated the dose–response association between $PM_{2.5}$ concentrations and frailty by modeling the $PM_{2.5}$ concentrations using restricted cubic splines with knots at the $PM_{2.5}$ concentration quartiles. We generated the plots separately for urban and rural areas.

We also conducted sensitivity tests to assess the robustness of the analyses to different $PM_{2.5}$ exposure duration and different scales of frailty as the outcome variable. First, in addition to the 3-year $PM_{2.5}$ exposure, we also tested for different exposure durations, including 1-year, 2-year, 4-year, and 5-year $PM_{2.5}$ exposures. Second, we repeated all the analyses and used the frailty index as a continuous variable in the model. All analyses were performed using Stata v16.0 (StataCorp, College Station, TX). We used the p value <.05 to determine statistical significance.

Role of the Funding Source

The funder had no role in the study design; collection, analysis, and interpretation of data; writing of the report; or the decision to submit the report for publication.

Results

A total of 38 670 individuals aged 50 and older participated in SAGE Wave 1, among which 4 532 individuals who could not complete or partially completed an interview or with missing sociodemographic variables were excluded from the analyses. China had the largest sample (N = 13 070), and Mexico (N = 2 249) had the smallest.

The demographic and socioeconomic characteristics of the respondents differed widely across the 6 countries (Table 1). The proportion of women was higher in China, Mexico, Russia, and South Africa and the 50–59 age group category was the largest proportion of respondents in all countries. More than two thirds of Indians resided in rural areas. Most older Mexicans, Russians, and South Africans lived in urban areas. Compared to other SAGE countries, participants in Ghana and India had lower educational levels, with 64.2% and 60.8%, respectively, of the older population having less than primary education. Men were more likely than women to use tobacco in all 6 countries. The prevalence of inadequate fruit and vegetable intake was high in all countries, particularly among India's older population. The prevalence of low physical activity level was highest in South Africa at 59.2%.

The 3-year averaged $PM_{2.5}$ concentration in the 6 countries was 22.6 μg/m^3. China and India had the highest average $PM_{2.5}$ concentrations (32.9 and 31.0 μg/m^3, respectively), while South Africa had the lowest level of $PM_{2.5}$ (6.0 μg/m^3; Figure 1).

The prevalence of frailty for each country and by age group, gender, and residential areas is displayed in Table 2. The prevalence of frailty was the highest in India, while China had the lowest prevalence at 14.5%. In all 6 countries, frailty prevalence was higher in older age groups, men, and rural residents.

Table 3 presents the associations between the prevalence of frailty and ambient $PM_{2.5}$ exposure and the separate stratified analyses. Overall, for rural residence, each 10 μg/m^3 increase in ambient $PM_{2.5}$ was associated with a 29.7% increase in the odds of frailty (OR = 1.297, 95% CI: 1.211–1.388) after adjusting for various potential confounding factors including age, sex, education, wealth index, tobacco use, physical activity levels, temperature, and humidity. We did not observe significant associations in urban areas. In China, though, higher ambient $PM_{2.5}$ was associated with lower odds of frailty in urban areas. But in South Africa, there was a significant positive association between ambient $PM_{2.5}$ and frailty in both urban and rural areas. The gender-stratified association between ambient $PM_{2.5}$ and frailty showed that the association seems to be slightly stronger in men (OR = 1.314, 95% CI: 1.182–1.460) than in women (OR = 1.207, 95% CI: 1.071–1.359) in rural areas. In spline regression models (Figure 2), the dose–response relationship was progressive over the range of ambient $PM_{2.5}$ concentrations in rural areas.

The sensitivity analyses suggested that the length of exposure had little effect on the association between $PM_{2.5}$ and frailty in rural areas. Similarly, the association remains unchanged significantly after including the frailty index as a continuous variable in the model (Supplementary Tables 1 and 2).

Discussion

In a large sample of community-based adults aged 50 years and older from 6 MICs, we found strong evidence that long-term $PM_{2.5}$ exposure was associated with frailty in rural areas. The association was robust, remaining significant when using the average concentrations of 1-year, 2-year, 4-year, and 5-year $PM_{2.5}$ exposure before the survey after adjusting for demographic characteristics, behavioral risk factors, and indoor air pollution. To our best knowledge, this is the first study to investigate the association between ambient $PM_{2.5}$ exposure and frailty as measured using a frailty index among community-dwelling older adults in MICs.

Numerous epidemiological studies have demonstrated a positive correlation between exposure to ambient $PM_{2.5}$ and risk of cardiovascular disease (22,23), the incidence of acute coronary events, and cerebrovascular events (10,24). Some studies have also highlighted an association between exposure to ambient $PM_{2.5}$ and depression in low-income countries and MICs (8). Very few studies have investigated the effect of long-term exposure to ambient $PM_{2.5}$ on frailty. In a nationwide analysis of 28 million individuals 55 years and older across 3 034 counties in the United States, higher levels of $PM_{2.5}$ air pollution were associated with lower population-based probabilities of exceptional aging, defined as reaching age 85 years (25). Another study found increased odds of developing frailty as measured using a frailty index associated with exposure to $PM_{2.5}$ among postmyocardial infarction patients (9). Our study has for the first time described the association between long-term exposure to ambient $PM_{2.5}$ and frailty among the general population aged 50 and older in middle-income settings. We also found an approximately linear dose–response relationship in rural areas in each country.

Air pollution, including long-term exposure to ambient $PM_{2.5}$, induces chronic systemic oxidative stress, inflammation, hormonal changes, and genetic and epigenetic modifications (26,27), all of which can cause damage to cellular and molecular structures. This damage may promote cumulative decline in multiple physiological systems like the endocrine, immune, and skeletal muscle. Abnormal results in 3 or more systems are a significant predictor of frailty (28). This suggested the onset of frailty when physiological decline reaches an aggregate critical mass. However, while markers of inflammation related to air pollution were not predictive of the onset of frailty in one study (3), underlying environmental factors like long-term exposure to ambient $PM_{2.5}$ in combination with genetic factors may play an essential role

Table 1. Demographic Characteristics Among SAGE Respondents Aged 50 Years and Older (Weighted), by Country

	China (*N* = 13 070)	Ghana (*N* = 4 271)	India (*N* = 6 415)	Mexico (*N* = 2 249)	Russian Federation (*N* = 3 751)	South Africa (*N* = 3 796)
	Weighted Percentages					
Age group						
50–59	45.1	40	49.2	48.5	44.9	50
60–69	31.9	27.5	31	25.7	26.8	30.7
70–79	18.5	22.9	15.7	17.6	21	13.8
80+	4.5	9.6	4.2	8.2	7.3	5.5
Gender						
Men	49.8	52.6	51.5	47	42.1	44
Women	50.2	47.4	48.5	53	57.9	56
Residence						
Urban	47.3	40.9	29.0	79	70.7	64.8
Rural	52.7	59.1	71.0	21	29.3	35.2
Education						
Less than primary	42	64.2	60.8	55.2	1.5	49.2
Primary school completed	21	11	14.9	24.1	5.3	22.3
Secondary school completed	19.8	4	10.3	10	17.6	14.3
High school completed	12.6	17.2	8.7	2.4	54.6	8.5
College completed and above	4.5	3.6	5.2	8.2	21	5.8
Wealth quintile						
Q1 (lowest)	16.2	18.3	18	15	13.2	20.8
Q2	18.1	19.1	19.5	24.8	16.9	19.9
Q3	20.4	20.4	18.6	16.7	19.2	18.2
Q4	23.4	20.7	19.8	16.7	22.3	19.7
Q5 (highest)	21.8	21.5	24.1	26.8	28.4	21.4
Fruit and vegetable intake						
Sufficient	64.4	31.1	9.4	18.6	19.1	31.3
Insufficient	35.6	68.9	90.6	81.4	80.9	68.7
Tobacco use						
Never smoker	64.1	75.4	45.4	60.5	65	67.6
Noncurrent smokers	6.6	14.3	4.6	19.2	13.4	9.6
Current nondaily smokers	2.5	2.6	2.9	7	2.1	3.4
Current daily smokers	26.9	7.7	47.1	13.3	19.5	19.4
Physical activity						
High level	44.6	62	52.7	40	62.6	28.5
Moderate level	27.4	12.5	23	22.5	15.7	12.3
Low level	28.1	25.5	24.3	37.5	21.7	59.2

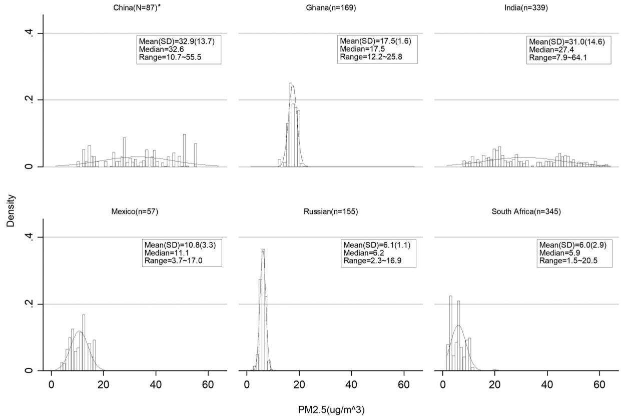

Figure 1. The 3-year averaged $PM_{2.5}$ concentration across 6 middle-income countries. *Unique value of $PM_{2.5}$ concentration.

in this process. In this study, physiological decline and genetic factors might be underlying mechanisms contributing to the observed association between long-term exposure to ambient $PM_{2.5}$ and frailty.

The country-stratified analyses showed that the association between ambient $PM_{2.5}$ and frailty is quite different in urban China and South Africa; the reason for the difference is poorly understood. Still, there are significant differences in $PM_{2.5}$ exposure and sample size between the 2 countries. That is why we further used pooled data to analyze the association between $PM_{2.5}$ and frailty after adjusting for the impact at the national level. The gender-stratified analysis also showed that the association seems to be slightly stronger in men than in women in rural areas. This result is consistent with a Danish cohort study that showed higher hazard ratios for all-cause and cardiovascular disease mortality in men than in women for $PM_{2.5}$ and PM_{10} (29).

Our findings suggested that $PM_{2.5}$ exposure was associated with an increased risk of frailty in rural-dwelling older adults, but no consistent associations were observed in urban areas. The differences between urban and rural areas are unknown, especially with the widespread media coverage of urban pollution in Beijing and New Delhi, for example, but could be related to the type of employment. Public health and policy measures would be crucial in preventing air pollution. Differences in how the policy is implemented and monitored in urban and rural areas may contribute to the differences. Health care access and supply often differ between urban and rural areas and may play a role in compensating for health loss caused by environmental pollution. Even though association estimates were generally inconsistent in urban areas, we noted a more robust association among males, older respondents, and those with lower education levels. Our findings warrant further investigation of location-specific mechanisms and other community or individual characteristics that may play a role in the onset of frailty.

Our study was based on a large population-based sample of respondents with relatively high response rates across the 6 MICs. Furthermore, we included vital risk factors that may have affected the results, including socioeconomic status, behavioral risk factors, indoor air pollution, and other factors, for potential confounding. The inclusion should help to improve the study's ability to detect any real associations. There are also limitations to acknowledge. This study can only state associations between long-term $PM_{2.5}$ and frailty but cannot infer causality, in part because of the cross-sectional data used in this study SAGE Wave 1. The use of remote sensing data in estimating $PM_{2.5}$ in grid cell of 100 km^2 in our study resulted

Table 2. The Prevalence of Frailty* Among Older Men and Women, by Country

	China		India		Mexico		Russian Federation		South Africa		Ghana	
	Weighted Percent (%)	Number	Weighted Percent (%)	Number	Weighted Percent (%)	Number	Weighted Percent (%)	Number	Weighted Percent (%)	Number	Weighted Percent (%)	Number
Total	14.5	13 028	51.6	6 377	34.3	2 257	39.9	3 751	41.3	3 780	39.2	4 266
Age group												
50–59	7.8	5 687	40.2	2 919	24.5	430	19.9	1 427	35.8	1 681	22.0	1 686
60–69	15.0	3 900	55.3	2 187	34.6	924	42.9	1 026	41.5	1 221	37.2	1 194
70–79	24.5	2 733	70.4	1 017	49.2	600	63.4	971	49.2	650	56.8	973
80+	41.2	750	87.0	292	59.2	302	86.6	327	67.8	245	74.5	418
Gender												
Men	11.9	6 124	41.2	3 250	29.5	894	35.7	1 334	36.2	1 618	34.1	2 237
Women	17.4	6 946	62.6	3 165	38.5	1 355	43.2	2 417	45.0	2 179	44.8	2 034
Residence												
Urban	13.7	6 362	47.1	1 657	31.9	1 657	38.1	2 894	40.7	2 532	38.6	1 741
Rural	15.6	6 709	53.4	4 758	43.2	604	44.3	862	42.0	1 264	39.6	2 530

*Frailty was defined as the accumulation of deficits using the frailty index approach. Index values of 0 to less than 0.2 were categorized as not frail, index values of 0.2–1.0 were categorized as frail.

Table 3. Results From Stratified Analyses Examining the Association Between Ambient $PM_{2.5}$ Exposure and Frailty

		Urban		Rural	
$PM_{2.5}$ (per 10 μg/m³ increase)		OR	95% CI	OR	95% CI
Overall		1.030	0.717–1.480	1.297**	1.211–1.388
Country	China	0.835*	0.705–0.991	0.926	0.761–1.126
	Ghana	1.358	0.109–16.943	2.337	0.457–11.958
	India	1.069	0.845–1.353	0.988	0.906–1.078
	Mexico	1.693	0.483–5.931	5.195*	1.056–25.555
	Russian Federation	0.309	0.018–5.442	0.180	0.001–54.057
	South Africa	10.473**	3.616–30.332	4.780**	1.625–14.060
Age group	50–59	1.101	0.644–1.882	1.231**	1.145–1.325
	60–69	0.925	0.632–1.354	1.335**	1.111–1.603
	70–79	0.767**	0.702–0.838	1.016	0.841–1.227
	80+	0.868	0.752–1.001	0.885	0.572–1.368
Gender	Men	0.947	0.711–1.260	1.314**	1.182–1.460
	Women	0.925	0.608–1.406	1.207**	1.071–1.359

Notes: OR = odds ratio; CI = confidence interval. Odds ratios are adjusted for age, education, gender, wealth index, fruit and vegetable intake, tobacco use, physical activity level, cooking fuel use, temperature, and humidity.
$^*p < .05$, $^{**}p < .01$.

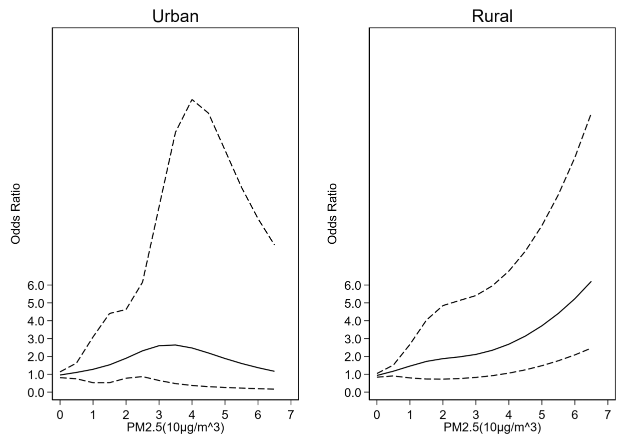

Figure 2. The concentration–response curves for $PM_{2.5}$ on frailty in urban and rural areas of 6 low- and middle-income countries. *Note:* Odds ratios (95% confidence intervals) of frailty according to $PM_{2.5}$ concentrations based on restricted cubic splines with knots at the quartiles. The reference value is set as the minimum value. Odds ratios are adjusted for age, education, gender, wealth index, fruit and vegetable intake, tobacco use, physical activity levels, cooking fuel use, temperature, and humidity. Lines represent the odds ratio (thick line) and 95% confidence interval (dashed lines).

in relatively small exposure contrast, contributing to measurement errors in $PM_{2.5}$ exposure. However, this method is widely applied to estimate the global burden of ambient $PM_{2.5}$ (20,30). A study in China during 2013–2015 also reported a high correlation between ground-based $PM_{2.5}$ concentrations and estimates from monitoring stations (23). In addition, due to the limited data, we only used the annual average $PM_{2.5}$ concentration values as the exposure variable. The use of annual concentration may result in less accurate results, especially in areas with high variable $PM_{2.5}$ concentrations over the year. However, as our health outcome, frailty index, reflects a more stable, chronic long-term situation collected at a one time point, we argue that higher resolution $PM_{2.5}$ concentrations and temperature data might not provide additional information to address our research question. Finally, we also did not consider the effect of population migration on $PM_{2.5}$ exposure assessment. The effect of population movement on effect estimation is more complex; the population in the exposed area can move out or in or both. If the population only moves out from the exposed area, the effect estimate is underestimated to a greater extent as the migration rate increases.

In summary, our study suggests that long-term exposure to ambient $PM_{2.5}$ is a significant risk factor of frailty in the rural-dwelling population aged 50 years and older in 6 MICs. More efforts are needed to protect older adults from ambient outdoor and indoor air pollution, especially in rural areas. In addition, more studies are needed with a particular focus on whether or how environmental pollutants affect frailty in older adult populations.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None declared.

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Author Contributions

All authors contributed to the study concept and design, acquisition, analysis, or interpretation of data. Y.F.G. and N.N. did the statistical analyses. Y.F.G. conducted the literature search and wrote the first draft of the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final version. F.W. obtained the funding.

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