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Association Between Long-Term PM$_1$ Exposure and Cognition in Middle-Aged and Older Adults: Evidence from China and the United Kingdom

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ABSTRACT

Early risk detection and management are essential for cognitive preservation. While particulate matter with a diameter smaller than 2.5 μm (PM$_{2.5}$) is considered harmful to cognition, the effect of smaller, more penetrative particulate matter with a diameter smaller than 1 μm (PM$_1$) requires further evidence and explicit safety thresholds. In this study, we explored the effects of long-term PM$_1$ exposure on early cognitive impairment and longitudinal cognitive changes in middle-aged and older populations. This study assessed data from two large-scale longitudinal surveys: the China Health and Retirement Longitudinal Study (CHARLS) and UK Biobank (UKB). Cross-sectional, longitudinal, and trajectory analyses were conducted to investigate the association between long-term PM$_1$ exposure and cognition. Additionally, the exposure–response curves were fitted to determine the customized thresholds. The findings indicated that sustained PM$_1$ exposure may lead to mild cognitive impairment, particularly at concentrations exceeding 30 and 5.6 μg·m^{-3} in CHARLS and UKB participants, respectively. Furthermore, we found that long-term PM$_1$ exposure can contribute to rapid cognitive decline at concentrations exceeding 23 and 5.5 μg·m^{-3} in CHARLS and UKB participants, respectively. In conclusion, reducing PM$_1$ exposure can improve the cognitive health of middle-aged and older adults.

1. Introduction

Cognitive function generally declines with age in middle-aged and older adults. However, some individuals experience cognitive impairment beyond the expected age-associated decline, including mild cognitive impairment (MCI) and rapid cognitive decline (RCD). Notably, MCI is a condition in which individuals experience a slight but noticeable decline in cognitive function, which is considered a transitional stage between normal aging and dementia [1]. Whereas, individuals experiencing RCD are at a higher risk of physical disability and mortality [2]. Furthermore, impaired cognitive function has become a major contributor to disability and dependence among middle-aged and older adults [3]. Considering that cognitive decline is an irreversible, progressive, and incurable process, identifying the risk factors associated with impaired cognitive function in its early stages is imperative.

Among the factors that can contribute to impaired cognitive function, including genetic predisposition, chronic diseases, and environmental pollutants [4–6], ambient particulate matter is recognized as a critical risk factor [7]. Many studies have suggested that exposure to particulate matter with a diameter smaller than 2.5 μm (PM$_{2.5}$) adversely affects cognitive function [8,9]. Compared to PM$_{2.5}$, the smaller diameter of PM$_1$ (particulate matter with a diameter of ≤ 1 μm) allows it to absorb harmful substances and linger in the atmosphere for longer periods [10]. Due to its smaller particle size, PM$_1$ has higher pulmonary deposition efficiency and easier vascular penetration, indicating stronger adverse effects [10]. Epidemiological evidence has shown that exposure to PM$_1$ can contribute to cardiovascular and metabolic diseases [11,12],

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which can affect cognition by altering the cerebral blood flow [5]. However, evidence of the effects of PM_1 exposure on cognitive function remains limited.

To date, two studies have explored the relationship between long-term PM_1 exposure and cognitive status at a single point in the Chinese population [13,14]; however, longitudinal cognitive changes, which are crucial for prognosis, also warrant consideration. Another study elucidated the relationship between PM_1 exposure and changes in cognitive performance before and after clean air action in China [15]. However, evidence from other regions is limited.

Owing to differences in exposure levels and population susceptibility, evidence derived from a single region has limitations in extrapolation. However, all the existing studies have only been conducted in China. Cognitive function has been reported to be associated with social-economic factors, and approximately 60% of individuals with impaired cognitive function reside in low and middle-income countries [16]. Moreover, low- and middle-income countries typically experience elevated levels of air pollution than high-income countries [15]. Considering that targeted approaches for PM_1 pollution control in areas with different pollution levels can yield greater health benefits, regional comparisons of the health effects of PM_1 exposure are extremely important for developing locally tailored regulatory policies.

Taking advantage of two large-scale longitudinal surveys from China and the United Kingdom (UK), we explored the effects of long-term PM_1 exposure on early cognitive impairment and longitudinal cognitive changes among middle-aged and older populations. Furthermore, we compared the differences in effects between China and the UK, and the exposure–response curves were fitted to guide the construction of tailored thresholds across regions with varying exposure levels.

2. Methods

2.1. Study design and participants

This study assessed data from two large-scale longitudinal surveys: the China Health and Retirement Longitudinal Study (CHARLS) [17] and UK Biobank (UKB). Details of the study design, recruitment, follow-up, attrition, and data collection in the two surveys are presented in Method S1 in Appendix A. This study focused on participants aged higher than 45 years. We excluded participants who were unable to accurately evaluate long-term PM_1 exposure and those who did not complete all cognitive tests. Participants with dementia, brain damage, or mental disorders at enrollment were excluded. Ultimately, our analysis included 10 179 participants from the CHARLS and 32 861 from the UKB (Fig. 1(a)).

All participants provided written informed consent before data collection. The CHARLS study was approved by the Biomedical Ethics Committee of Peking University (approval number: IRB00001052–11015), whereas the UKB study was approved by the NHS National Research Ethics Service (approval number: 11/ NW/0382).

2.2. Exposure assessment

Surface PM_1 concentrations were evaluated based on Modern-Era Retrospective analysis for Research and Applications version 2 reanalysis data [18], which is a state-of-the-art reanalysis project that combines global atmospheric observations and modeling outputs from 1980 to the present over a grid of $0.5°$ latitude by $0.625°$ longitude. Details about the sources, derivations, and preparations

for the exposure assessment are shown in Method S2 in Appendix A.

For privacy purposes, the home locations of participants in the CHARLS can only be geocoded to their regionalization code. Therefore, we aggregated exposure data at the city level by matching a regular grid to a map of the prefectures of China [19]. The coordinates presented in the UKB were derived from UK postcode information obtained from a variety of sources, including self-reports by the participants, and exposure assessments were assigned to each participant based on their home location. Long-term exposure was evaluated using 5-year averages of annual exposure estimates before the enrollment date [20].

2.3. Cognitive function assessment

Cognitive function was evaluated using cognitive tests covering two domains: memory and executive function. The follow-up period for cognitive assessment in the CHARLS cohort was approximately five years, whereas that in the UKB cohort ranged from 11 to 14 years. Cognitive function assessments were conducted at enrollment, followed by two repeated assessments (Fig. 1(b)). In the CHARLS, participants completed two cognitive tests: the CHARLS episodic memory test and questions from the Telephone Interview of Cognitive Status battery (Table S1 in Appendix A). Global cognitive scores in the CHARLS were calculated as the z-score of the sum of scores from the two tests [21]. In the UKB, the participants completed four cognitive tests: the UKB pairs matching, UKB reaction time, UKB fluid intelligence, and UKB numeric memory test (Table S1). The global cognitive scores in the UKB were constructed by taking the first component of the principal component analysis of the four tests [22]; details are shown in Method S3, Fig. S1, and Table S2 in Appendix A. Higher global cognitive scores in both the CHARLS and UKB indicated better cognitive function.
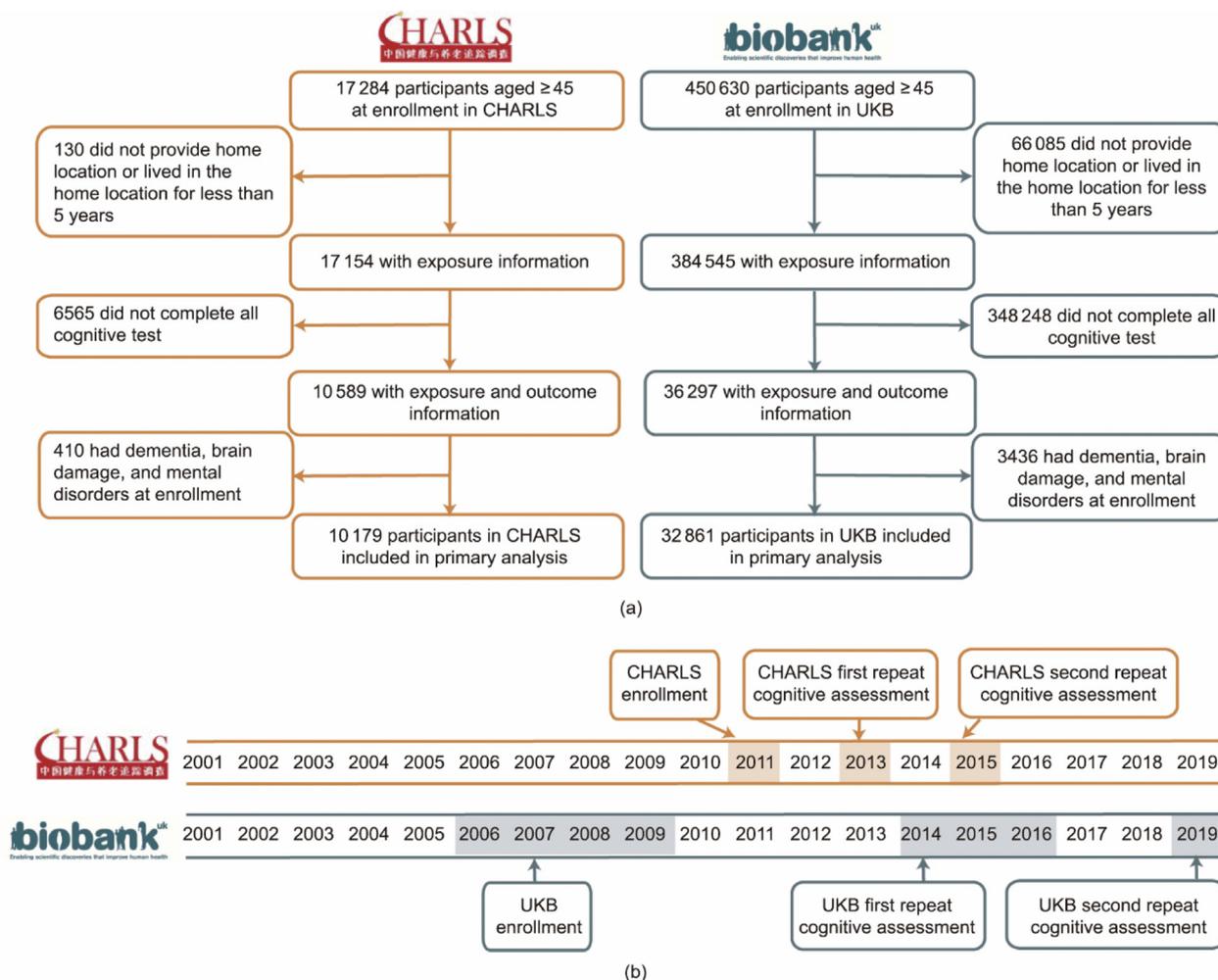
Following the criteria established by the National Institute on Aging-Alzheimer's Association workgroups, MCI was assigned to individuals who showed objective evidence of cognitive impairment based on cognitive function tests and did not meet the criteria for dementia [1]. In this study, dementia diagnosed based on self-reported questionnaires and medical records, and cognitive impairment was characterized as scoring 1.5 standard deviations (SDs) below age-specific means [23].

2.4. Covariates

We identified potential confounders based on a directed acyclic graph (Fig. S2 in Appendix A) [24]. These confounders included age, sex, smoking status (never vs former or current), household fuel (clean vs unclean fuel), education (lower than high school vs high school or higher), physical activity (low vs moderate vs high), long-term green space exposure, and long-term $PM_{2.5}$ exposure. The data collection process and categorizations of these covariates are described in Method S4 in Appendix A. The percentage of missing data for the covariates varied from 0 to 18.11%, and data imputation was performed using the random forest method. All analyses were performed using the imputed dataset.

2.5. Statistical analyses

We combined cross-sectional, longitudinal, and trajectory analyses to explore the association between long-term PM_1 exposure and cognitive function. The protocol for the main statistical analysis is shown in Fig. S3 in Appendix A. For the cross-sectional analysis, we first used linear regression models to examine the links between long-term PM_1 exposure and the global cognitive score at enrollment. We then used logistic regression models to assess the effect of prolonged PM_1 exposure on MCI at enrollment. We

Fig. 1. Flowchart of population selection and timeline of cognition assessments in this study. (a) Flowchart of population selection in this study; (b) timeline of enrollment and repeated assessments of cognitive function during follow-up.

performed a longitudinal analysis based on the three cognitive assessments conducted throughout the study. Participants with at least one repeat cognitive measurement were included in the longitudinal analysis. Generalized estimating equations (GEEs) were used to examine the association between exposure and repeated measures of cognitive function. The working correlation structure in the GEEs is presented in Table S3 in Appendix A [25]. To identify trajectories of cognitive function, latent class mixed models (LCMMs) were used (Method S5 in Appendix A) [9]. Next, we distinguished participants with RCD from those with normal cognitive aging and used logistic regression models to assess the association between prolonged PM_1 exposure and RCD. To examine the potential nonlinear relationships between exposure and response, restricted cubic spline functions were applied to the CHARLS, UKB, and all participants. The number of knots was determined based on the Akaike Information Criterion [26] (Table S4 in Appendix A). Results of the linear regressions and GEE (beta coefficient (β) and 95% confidence interval (CI)) were reported per SD change in cognitive outcomes for 1 $\mu g \cdot m^{-3}$ increase in PM_1 exposure, and risk ratios (RR) for 1 $\mu g \cdot m^{-3}$ increase in PM_1 exposure for dichotomous outcomes.

We conducted stratified analyses to assess potential modifications in the associations by age, sex, smoking status, household fuel, education, physical activity, long-term green space exposure, and long-term $PM_{2.5}$ exposure. To test these interactions, we added

cross-product terms to separate the models. In the CHARLS, we divided regions based on provinces, whereas in the UKB, we used cities where the recruitment centers were located. Based on the mean PM_1 exposure levels of the populations in different regions, we categorized all regions into six groups: 0–10 (very low), 10–20 (low), 20–30 (medium), 30–40 (high), 40–50 (very high), and higher than 50 $\mu g \cdot m^{-3}$ (extremely high). We then conducted stratified analyses based on these regions.

We conducted five sets of sensitivity analyses to assess the robustness of the findings. To account for potential regional influences, we used mixed-effects models including a random effect for regions [6,27]. Additionally, complete-case datasets were used to assess the sensitivity of the findings. Because depressive symptoms have been reported as potential mediators of the relationship between air pollution exposure and cognitive function, we repeated our analyses by excluding participants with depressive symptoms [7,28,29]. Given that individuals with MCI are more susceptible to RCD, we developed our main models by excluding participants with MCI at enrollment to evaluate the effects of long-term PM_1 exposure on RCD. To evaluate the robustness of our findings and adjust for potential short-term effects, we incorporated PM_1 exposure during the follow-up period into the model in a longitudinal analysis.

All analyses were performed using R software (version 4.2.2), with a significance threshold set at $P < 0.05$.

3. Results

3.1. Descriptive statistics

The basic characteristics of the participants according to their geographical locations are shown in Table 1. At enrollment, the participants in the CHARLS (58.37 years old) were younger than those in the UKB (58.60 years old). The ratios of women, smoking, having a high school or higher education, using clean household fuel, and performing moderate or intense exercise in the CHARLS were lower than those in the UKB. For long-term green space exposure, the mean (SD) normalized difference vegetation index (NDVI) of the home location with a buffer size of 500 m in CHARLS (range: 0–1) was 0.74 (0.10), whereas the mean (SD) green space percentage of the home location with a buffer size of 300 m in UKB (range: 0–100) was 41.51 (26.29). The long-term $PM_{2.5}$ exposure of participants in the CHARLS (mean (SD): 50.62 (17.19) $\mu g \cdot m^{-3}$) was higher than that in the UKB (mean (SD): 12.32 (1.82) $\mu g \cdot m^{-3}$).

During the follow-up period, 6404 and 2950 participants in the CHARLS and UKB, respectively, underwent at least one repeat cognitive measurement and were included in the longitudinal analysis. Among them, 4777 and 2876 participants in the CHARLS and UKB, respectively, underwent the first repeat cognitive assessment and 5028 and 470 participants in the CHARLS and UKB, respectively, underwent the second repeat cognitive assessment. The differences in basic characteristics between the participants who underwent the second cognitive assessment and the total population are shown in Tables S5–S8 in Appendix A.

Fig. S4 in Appendix A shows the average PM_1 concentrations in China and the UK between 2001 and 2011. The distribution of long-term PM_1 exposure in the CHARLS and UKB participants is shown in Table S9 in Appendix A. The participants in the CHARLS had an average long-term PM_1 exposure level of 38.77 $\mu g \cdot m^{-3}$, ranging from 7.75 to 82.98 $\mu g \cdot m^{-3}$. Whereas, the average exposure levels in the UKB study was 4.54 $\mu g \cdot m^{-3}$, ranging from 3.86 to 5.73 $\mu g \cdot m^{-3}$.

3.2. Association between long-term PM_1 exposure and cognitive function at enrollment

Next, we investigated the association between long-term PM_1 exposure and cognitive function at enrollment. Among participants in the CHARLS, for each 1 $\mu g \cdot m^{-3}$ increase in PM_1 exposure, a 0.012 SD decrease was observed in global cognitive performance (Fig. 2(a); $\beta = -0.012$, 95% CI: -0.014–-0.009). However, the association was not significant among participants in the UKB (Fig. 2(a); $\beta = -0.016$, 95% CI: -0.040–-0.008). We then investigated the association between long-term PM_1 exposure and MCI at enrollment. A rise of 1 $\mu g \cdot m^{-3}$ in PM_1 exposure was found to be significantly associated with a 3.6% and 19.3% increase in the incidence of MCI among participants in the CHARLS and UKB, respectively (Fig. 2(b)). Similar results were obtained when analyzing the changes caused by each interquartile range (IQR) increase in PM_1 exposure (Fig. S5 in Appendix A). Exposure–response curves between prolonged PM_1 exposure and MCI are shown in Fig. 2(c). In the CHARLS, the harmful effects appeared when the concentrations exceeded 30 $\mu g \cdot m^{-3}$ and the slopes were steeper at concentrations higher than 68 $\mu g \cdot m^{-3}$. In the UKB, although the exposure levels were significantly lower, PM_1 exposure exhibited detrimental effects when the concentration surpassed 5.6 $\mu g \cdot m^{-3}$.

3.3. Association between long-term PM_1 exposure and longitudinal changes of cognitive function in the follow-up period

Using GEEs, we identified an inverse association between long-term PM_1 exposure and cognitive function measured repeatedly

Table 1
Basic characteristics of included participants at enrollment.

Item	N	Age, mean (SD), year[a]	Sex, participants, N (%)			Smoking status, participants, N (%)			Education, participants, N (%)			Physical activity, participants, N (%)				Household fuel, participants, N (%)			Green space, mean (SD)[b]	$PM_{2.5}$, mean (SD), $\mu g \cdot m^{-3}$
			Men	Women	Missing	Never	Former or current	Missing	Lower than high school	High school or higher	Missing	Low	Moderate	High	Missing	Clean fuel	Unclean fuel	Missing		
CHARLS	10 179	58.37 (9.18)	5389 (52.94)	4784 (47.00)	6 (0.06)	5846 (57.43)	4332 (42.56)	1 (0.01)	8448 (82.99)	1727 (16.97)	4 (0.04)	7396 (72.66)	1359 (13.35)	1424 (13.99)	0 (0)	2682 (61.53)	6263 (26.35)	1234 (12.12)	0.74 (0.10)	50.62 (17.19)
UKB	32 861	58.60 (6.69)	14 669 (44.60)	18 192 (55.40)	0 (0)	19 279 (58.67)	13 477 (41.01)	105 (0.32)	12 703 (38.66)	14 895 (45.33)	5263 (16.01)	4339 (13.21)	10 782 (32.81)	11 788 (35.87)	5952 (18.11)	25 323 (77.06)	1620 (4.93)	5918 (18.01)	41.51 (26.29)	12.32 (1.82)
P-value		0.005	<0.001			0.012			<0.001			<0.001				<0.001			–	<0.001

In the UKB cohort, long-term green space exposure was evaluated using the green space percentage of the home location buffered at 300 m, with a range of 0–100; 0 indicates the lowest green space exposure and 100 indicates the highest green space exposure.
[a] Age at enrollment.
[b] In the CHARLS cohort, long-term green space exposure was evaluated with NDVI of the home location buffered at 500 m, with a range of 0–1; higher scores indicate higher green space exposure.

within a 5-year period among participants in the CHARLS (β = −0.013, 95% CI: −0.015–−0.011); however, this association was not significant among participants in the UKB (β = −0.017, 95% CI: −0.042–−0.008; Fig. 3(a)).

3.4. Association between long-term PM$_1$ exposure and cognitive trajectories in the follow-up period

For the CHARLS participants, the LCMM with two latent classes met our criteria for the optimal number of latent classes, and 9.53% of them were assigned to the RCD group (Fig. 3(b) and Table S10 in Appendix A). Whereas, the LCMM with three latent classes fit best in the UKB cohort. Among participants in the UKB group, 1.49% were identified as the RCD group, and participants with RCD had poorer cognitive function at baseline than those in the normal group (Fig. 3(b) and Table S11 in Appendix A). Each increment of 1 µg·m^{-3} in PM$_1$ concentration was associated with a 2.4% and 47.7% elevated risk of RCD among participants in the CHARLS and UKB, respectively (Fig. 3(c)). The exposure–response curves revealed that harmful effects were observed at concentrations higher than 23 µg·m^{-3} among the CHARLS participants, whereas the harmful effects appeared at concentrations higher than 5.5 µg·m^{-3} among the UKB participants (Fig. 3(d)).

3.5. Interaction and stratified analyses

Next, we performed stratified analyses based on participant characteristics (age, sex, smoking status, household fuel, education, physical activity, green space, and PM$_{2.5}$) on the association between long-term PM$_1$ exposure and cognitive scores, MCI at recruitment and during follow-up, and RCD during follow-up (Figs. S6–S9 in Appendix A). Generally, the results of the stratified analyses were robust. We found an effect modification of smoking status and education in the UKB cohort, where the never-smokers and lower-educated population was more susceptible to cognitive decline after PM$_1$ exposure (Figs. S6–S9). In the CHARLS, we found that the effects of modification of long-term PM$_{2.5}$ exposure, and

the harmful effects were strongest in populations with relatively high PM$_{2.5}$ exposure levels (range: 48.84–63.64 µg·m^{-3}; Figs. S6–S9). In the CHARLS participants, we found that increased green space exposure mitigated the detrimental effects of PM$_1$ exposure on cognition, and this trend was robust in both the cross-sectional and longitudinal analyses (Figs. S6–S9). As shown in Fig. S10 in Appendix A, all the UKB participants resided in areas with very low PM$_1$ exposure. The CHARLS participants were distributed across a wide range of PM$_1$ exposure levels, with a significant number of regions identified as medium, high, and very high. Further stratified analyses revealed that in regions with extremely high PM$_1$ concentrations, the detrimental effects of PM$_1$ exposure on cognition were consistently significant (Fig. S11 in Appendix A).

3.6. Sensitivity analyses

We found robust results in the mixed-effects model, including the random effect for regions, in the sensitivity analyses using datasets without imputation, and in the analyses excluding participants with depressive symptoms (Tables S12–S14 in Appendix A). After excluding participants with MCI at recruitment, we found significant associations between long-term PM$_1$ exposure and RCD in the follow-up period among participants in the CHARLS (RR = 1.021, 95% CI: 1.012–1.030) (Table S15 in Appendix A).

4. Discussion

To the best of our knowledge, this study represents the first attempt to integrate cross-sectional, longitudinal, and trajectory analyses to investigate the connection between long-term PM$_1$ exposure and cognition in middle-aged and older individuals. Furthermore, a regional comparative research was conducted to create tailored thresholds across regions with varying exposure levels. We found that long-term PM$_1$ exposure could contribute to cognitive impairment and abnormal cognitive trajectories and that the effects differed between participants from China and the UK. This study provides comprehensive evidence of the health effects of
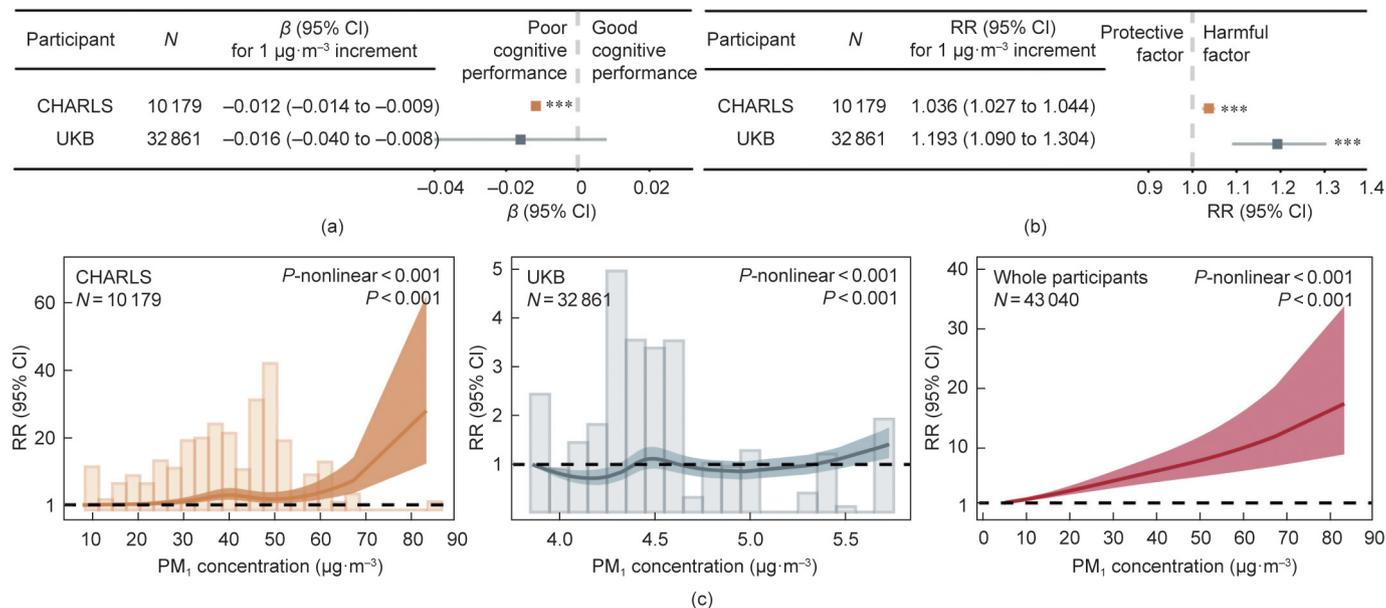

Fig. 2. Results of associations between long-term PM$_1$ exposure and cognitive function at enrollment. (a) Results of the linear regression models for the association between long-term PM$_1$ exposure and global cognitive scores at enrollment; (b) results of logistic regression models for the association between long-term PM$_1$ exposure and incidence of MCI at enrollment; (c) results of restricted cubic spline functions for the exposure–response relationship between long-term PM$_1$ exposure and the incidence of MCI at enrollment. All linear regression models, logistic regression models, and restricted cubic spline functions were adjusted for age, sex, smoking status, household fuel, education, physical activity, long-term green space exposure, and long-term PM$_{2.5}$ exposure. *** P < 0.001. RR: risk ratio.
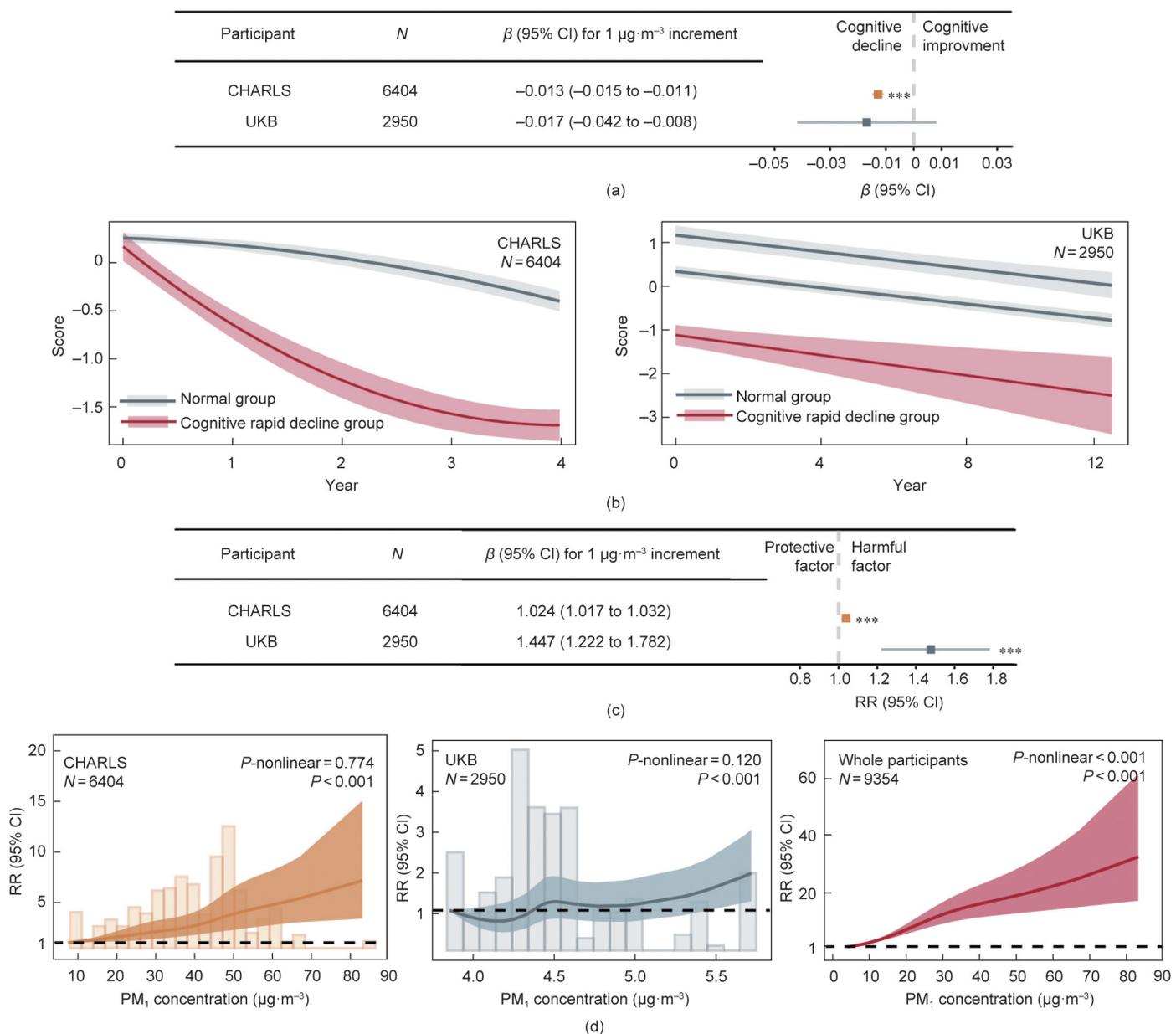
long-term PM$_1$ exposure and highlights the adequacy of current air quality guidelines.

In our study, the concentration of PM$_1$ exposure in the Chinese population was generally higher than that in the UK population between 2001 and 2011. As previously reported, the average concentration of PM$_1$ exposure in China [14,30,31] and the UK [32] was approximately 40 and 4.3 μg·m^{-3}, respectively, which were consistent with the PM$_1$ exposure levels obtained in our study.

The cross-sectional analysis revealed a link between long-term PM$_1$ exposure and decreased global cognitive scores in Chinese participants. We also observed that prolonged PM$_1$ exposure led to MCI in China and the UK. Previous studies [13,14] reported that exposure to PM$_1$ could decrease cognitive function, and per 10 μg·m^{-3} increase in PM$_1$ exposure, the risk of MCI increased 8%. Another CHARLS study [15] concluded that a gradual decrease

exists in the prevalence of cognitive decline among a population experiencing improved air quality with regards to PM$_1$. These findings aligned with our findings.

According to the results of the GEEs, long-term PM$_1$ exposure was related to repeated measures of cognitive function in Chinese participants, which may be associated with the higher exposure levels in China. In both cohorts, trajectory analysis revealed a link between long-term PM$_1$ exposure and RCD. Considering that the follow-up period for cognitive assessment in the CHARLS cohort was approximately five years, while that in the UKB cohort ranged from 11 to 14 years, we deduced that long-term PM$_1$ exposure may lead to RCD over a span of more than a decade. After excluding participants with MCI during recruitment, this association remained robust in the Chinese population. To the best of our knowledge, no studies have explored the effects of PM$_1$ exposure on cognitive

Fig. 3. Results of regional comparison and exposure–response relationships among all participants. (a) Results of GEEs for the association between long-term PM$_1$ exposure and repeated measures of cognitive function during the follow-up period; (b) cognitive trajectories in the follow-up period; (c) results of logistic regression models for the association between long-term PM$_1$ exposure and the incidence of RCD during the follow-up period; (d) results of restricted cubic spline functions for the exposure–response relationship between long-term PM$_1$ exposure and the incidence of RCD during the follow-up period. All linear regression models, logistic regression models, restricted cubic spline functions, and GEEs were adjusted for age, sex, smoking status, household fuel, education, physical activity, long-term green space exposure, and long-term PM$_{2.5}$ exposure.

trajectories; however, some studies have explored the relationship between exposure to $PM_{2.5}$ and cognitive trajectories. Wang et al. [9] utilized the LCMM to identify episodic memory trajectories and found that exposure to $PM_{2.5}$, was associated with a faster decline in episodic memory. In 2020, Kulick et al. [33] found that participants residing in regions characterized by elevated levels of ambient air pollutants exhibited accelerated rates of cognitive decline over time. Our study revealed that prolonged exposure to PM_1 could contribute to RCD; however, this conclusion requires further confirmation.

A comparison of the effects between participants from China and the UK revealed that long-term PM_1 exposure in participants from the UK was lower; however, the effect was much stronger when the PM_1 concentration increased at the same concentrations. A possible adaptive response to PM_1 has been previously reported in studies investigating the health effects of $PM_{2.5}$ and PM_{10}, which may be associated with long-term air pollution levels, the chemical composition of PM_1, population susceptibility, and the age distribution of the population [34–36]. Therefore, estimating exposure–response relationships is crucial for establishing tailored thresholds for pollution control across different regions. As the concentration of long-term PM_1 exposure increased, the risks of MCI and RCD increased. These findings led to the establishment of thresholds in countries with varying levels of air pollution exposure. In areas with high exposure levels, reducing the exposure levels is crucial for alleviating the disease burden. Combined with concentration–response curves, when the concentration surpasses approximately 23 $\mu g \cdot m^{-3}$ extra caution is warranted. In areas with low exposure levels, a small increase in exposure poses considerable risks; therefore, maintaining current exposure levels has immense public health significance. According to the exposure–response curves, maintaining exposures to lower than 5.5 $\mu g \cdot m^{-3}$ may be a relatively ideal state.

In the stratified analysis, we found that higher green space exposure mitigated the harmful effects of pollutant exposure in the CHARLS participants, and similar findings have been reported in previous study [12]. However, we did not observe a significant trend among the UKB participants. This discrepancy suggests that increasing green space exposure in high PM_1 exposure regions could provide greater cognitive health benefits for middle-aged and older individuals. Moreover, this study provides the first report on the interaction effects of $PM_{2.5}$ exposure in the relationships between PM_1 exposure and cognitive function, and highlights the need for further research to explore these relationships in greater detail.

The results of the sensitivity analysis suggested that the findings were generally robust. After incorporating region as a random effect, results for the Chinese population were consistent with the main findings. In the UK population, although the significance of the effects disappeared, the consistency in the direction of the effects indicated that the fundamental relationships remained intact even after adjusting for regional variability.

The mechanisms underlying these associations may involve oxidative stress, neuroinflammation, and vascular damage [29]. Owing to its small particle size, PM_1 can adsorb various neurotoxic substances such as lead, manganese, and polycyclic aromatic hydrocarbons [10]. Once it reaches the brain, PM_1 can induce the chronic release of pro-inflammatory factors and reactive oxygen species through activation of the resident innate immune response, ultimately leading to nervous system injury [29]. Some animal experiments revealed that higher particulate matter concentrations were associated with brain amyloid-β plaques, which is a feature of Alzheimer's disease [37]. Overall, these findings suggest that the biological mechanisms linking PM_1 exposure and cognitive decline are complex and multifaceted, and further research is required to fully understand this relationship.

This study has several strengths. First, we used two national prospective cohorts, the CHARLS and UKB, with large study samples covering a wide range of PM_1 exposure levels. Second, we combined cross-sectional, longitudinal, and trajectory analyses to investigate the relationship between prolonged PM_1 exposure and long-term cognitive function. Third, we conducted a regional comparative study and fitted exposure–response curves to establish tailored thresholds for pollution control across different regions.

However, our study has some limitations. First, missing data during the follow-up period in the UKB cohort are a concern for longitudinal data. Given the large sample size of our study, we maintained a sufficient number of participants. Second, we evaluated long-term PM_1 exposure based on the residential address at enrollment, which might have led to potential exposure misclassification. To mitigate exposure misclassification, we excluded individuals who had resided at their current address for less than five years. Finally, some unmeasured confounders may exist, such as cognitive-related, lifestyle, and other environmental factors.

5. Conclusions

In conclusion, long-term PM_1 exposure was associated with cognitive impairment and abnormal cognitive trajectories in middle-aged and older populations. Guided by exposure–response curves, this study provides recommendations for establishing region-specific pollution control thresholds based on diverse exposure levels. In high-exposure regions, lowering exposure levels is of utmost importance, necessitating caution when concentrations surpass 23 $\mu g \cdot m^{-3}$. In regions with low exposure, even slight increases in PM_1 exposure levels increases risks, warranting the recommendation to maintain levels below 5.5 $\mu g \cdot m^{-3}$. Compared to low-exposure regions, increasing green space exposure in high-exposure regions could provide greater cognitive health benefits for middle-aged and older individuals.

CRediT authorship contribution statement

Qiurun Yu: Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Hongcheng Wei:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Mingzhi Zhang:** Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition. **Xiaochen Zhang:** Writing – review & editing, Methodology, Conceptualization. **Francis Manyori Bigambo:** Writing – review & editing. **Danrong Chen:** Writing – review & editing, Data curation. **Quanquan Guan:** Writing – review & editing, Validation, Supervision. **Bo Hang:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Antoine M. Snijders:** Writing – review & editing, Supervision, Funding acquisition. **Yankai Xia:** Writing – review & editing, Supervision, Funding acquisition, Data curation, Conceptualization.

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.

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eng.2024.09.006.

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