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Short-term associations of particulate matter with different aerodynamic diameters with mortality due to mental disorders and dementia in Ningde, China

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ABSTRACT

Limited evidence is available regarding the impact of ambient inhalable particulate matter (PM) on mental disorder (MD) or dementia-related deaths, particularly PM_1, $PM_{1-2.5}$, and coarse particles ($PM_{2.5-10}$). Moreover, individual confounders have rarely been considered. In addition, evidence from low-pollution areas is needed but is inadequate. Using death records from the Death Registration System during 2015–2021 in Ningde, a coastal city in southeast China, we combined a conditional quasi-Poisson model with a distributed lag nonlinear model to estimate the nonlinear and lagged associations of PM exposure with MD or dementia-related deaths in Ningde, China, comprehensively controlling for individual time-invariant confounders using a time-stratified case-crossover design. The attributable fraction and number were calculated to quantify the burden of MD or dementia-related deaths that were related to PMs. We found J-shaped relationships between MD or dementia-related deaths and PMs, with different thresholds of 13, 9, 19, 33 and 12 μg/m^3 for PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$. An inter-quartile range increase for PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ above the thresholds led to an increase of 31.8% (95% confidence interval, 14.3–51.9%), 53.7% (22.4–93.1%), 32.6% (15.0–53.0%), 35.1% (17.7–55.0%) and 25.9% (13.0–40.3%) in MD-related deaths at lag 0–3 days, respectively. The associations were significant in the cool season rather than in the warm season and were significantly greater among people aged 75–84 years than in others. The fractions of MD-related deaths attributable to PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ were 5.55%, 6.49%, 7.68%, 10.66%, and 15.11%, respectively; however, only some of them could be protected by the concentrations recommended by the World Health Organisation or China grade I standard. Smaller associations and similar patterns were observed between PMs and dementia-related death. These findings suggest stricter standards, and provide evidence for the development of relevant policies and measures.

1. Introduction

Mental disorders (MDs) are among the top ten global disease burdens, accounting for 4.9% of global disability-adjusted life years by 2019 (Collaborators, 2022). In 2016, 8 million people died from MD-related causes, accounting for 14.3% of the worldwide mortality rate (Walker et al., 2015). Dementia is a subtype of MD. Globally, 50 million people live with dementia, which places a heavy social and economic burden (WHO, 2023). Identifying the risk factors for MD or dementia-related mortality is critical for developing proactive and preventive interventions to prevent or slow the progression of disease deterioration; moreover, prevention is more cost-effective and efficient than treatment in reducing the burden on healthcare systems and society.

Particulate matter (PM) is the fourth leading cause of death in China (Zhou et al., 2019). Previous studies have observed that PM_{10} and $PM_{2.5}$ increase outpatient visits and hospitalisation rates for depression (Lu

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et al., 2020; Wang et al., 2018) and anxiety disorders (Yue et al., 2020) and also increase the risk of cognitive decline, MDs, and dementia (Chen et al., 2018a; Jung et al., 2015; Li et al., 2019a; Min et al., 2019). However, few studies have assessed the impact of PM on deaths due to MDs or dementia. Moreover, existing studies usually employ a time-series analysis that fails to comprehensively control for individual confounders (Chen et al., 2018a; Min et al., 2019), such as lifestyle, physical conditions, and socioeconomic status, which probably leads to a biased estimation. Although the latest revision of the World Health Organisation (WHO) pollutant standards lowers the concentration of PM (WHO, 2021), evidence regarding the effect of PM on MD or dementia-related deaths is limited to low-pollution areas. The attributable function and number (AF and AN, respectively) could be used to quantitatively evaluate the burden of MD or dementia-related deaths attributable to PM exposure and investigate the potential associations with the recommended standard concentrations; however, related evidence remains scarce.

PMs with different aerodynamic diameters affect different organs of the human body through various mechanisms (Guo et al., 2012; Shih et al., 2018; Thiankhaw et al., 2022), resulting in different toxicity profiles. However, existing population-based studies have focused on the association between $PM_{2.5}$ and PM_{10} and MD-related deaths (Ran et al., 2021; Tan et al., 2021; Yang et al., 2022). The effect of PM_1 on MD-related deaths has rarely been examined; however, it is suggested to cause neuronal atrophy and brain damage (Shih et al., 2018). In addition, $PM_{1\text{–}2.5}$ and $PM_{2.5\text{–}10}$ have shown different toxicological responses in previous studies (Happo et al., 2010; Jalava et al., 2006); however, the mechanism of their effects is still unclear. In 2006, the USA Environmental Protection Agency proposed replacing the PM_{10} standard with that of $PM_{2.5\text{–}10}$ (coarse particles), defined as the difference between PM_{10} and $PM_{2.5}$. Importantly, there is a need to understand the potential health effects of PMs of different sizes to provide a scientific basis for the development of standard concentrations.

Thus, this study adopted a time-stratified case-crossover design to assess the short-term association between PM with different aerodynamic diameters and the death risk of MDs and dementia and used conditional quasi-Poisson regression combined with a distributed lag nonlinear model (DLNM) to consider the nonlinear and delayed effects of PMs. Then, we conducted stratified analyses to examine the effect of modification by age, sex, and season. In addition, we calculated the AF and AN of MD and dementia-related deaths to assess the disease burden related to PMs using different standards of PMs as baseline levels. These findings will contribute to the development of policies and standards regarding air pollution to reduce the burden of MD and dementia-related deaths.

2. Materials and methods

2.1. Study area and population

Ningde is a coastal city located in the southeastern region of China, covering an area of 13,500 km^2; it had a permanent population of 3.15 million in 2020. The city has a subtropical marine monsoon climate characterised by high temperature and humidity, with an annual mean temperature of 17.5 °C (Ningde Meteorological Bureau, 2023). The annual mean concentrations of $PM_{2.5}$ and PM_{10} in Ningde were 14 and 26 $\mu g/m^3$, respectively (Ningde City Ecological Environment Bureau, 2022), which exceeds the level 1 standard mentioned in the 2021 WHO Global Air Quality Guidelines (WHO, 2021).

2.2. Data sources

We collected death records from 2015 to 2021 in Ningde, China, from the Death Registration System, which included information on age, sex, cause of death, and date of death. The cause of death was coded according to the 10th Revision of the International Classification of Diseases (ICD-10). We selected MD-related deaths using codes F00–F99 and dementia-related deaths using codes F00–F03 and G30–G31. We considered three age subgroups (i.e., ≤74, 75–84, and ≥85 years) and two seasons (cool season from October to March and warm season from April to September). Data of PMs with aerodynamic diameters below 1, 2.5, or 10 μm in $\mu g/m^3$ (PM_1, $PM_{2.5}$, or $PM_{10,}$ respectively) at 1 km spatial resolution were estimated using spatial-time extremely randomised trees (STET) model based on remote sensing satellite observation data in our previous studies (Wei et al., 2019; Wei et al., 2021a; Wei et al., 2021b). The STET model considered meteorological variables, emissions, auxiliary data, and spatiotemporal information and performed well in estimating the daily mean gapless PM_1, $PM_{2.5}$, and PM_{10} concentrations in China, with average cross-validation coefficients of determination (CV-R^2) of 0.83, 0.86, and 0.86, respectively. Owing to the high proportion of individuals with imprecise addresses (35%), we assumed that each individual shared the citywide average PM exposure on the same day. Concentrations of $PM_{1\text{–}2.5}$ and $PM_{2.5\text{–}10}$ (particulate matter with an aerodynamic diameter between 1 and 2.5 μm and between 2.5 and 10 μm, respectively) were calculated by subtracting daily average concentrations of PM_1 from $PM_{2.5}$ and that of $PM_{2.5}$ from PM_{10}, respectively (Perez et al., 2012). The outliers of $PM_{2.5\text{–}10}$ exceeding the median by three times the interquartile range (IQR) were replaced with the mean of the two neighbouring days. Daily air pollution measured using the fixed monitor sites were collected from the China National Environmental Monitoring Center, including that of sulphur dioxide (SO_2), nitrogen dioxide (NO_2), carbon dioxide (CO), and ozone (O_3). Data of daily relative humidity (%) and mean temperature (°C) were obtained from the China National Meteorological Administration.

2.3. Statistical analysis

A time-stratified case-crossover design was adopted to control for the potential impact of known and unknown time-invariant confounders (e.g. lifestyle, physical conditions, and socioeconomic status) by matching each death to itself, which is extensively used in epidemiological studies (He et al., 2022; Wang et al., 2022). The *stratum* variable indicating the same year, month, and day of the week was used to select the control periods, which could also control for confounding temporal trends, including seasonality and long-term trends. We used a quasi-Poisson regression model conditioned on the *stratum* variable to analyse data from the time-stratified case-crossover design, as in previous studies (Armstrong et al., 2014; Lu and Zeger, 2007), which also allows for overdispersion of daily MD and dementia-related deaths. Further, we combined the basic model with the DLNM to investigate the nonlinear and lagged associations between PM exposure and MD or dementia-related deaths.

$$Log[E(Y_t)] = \beta Z_t + ns(temp, df = 3) + DOW + Holiday_t + \alpha \tag{1}$$

where t is the observation time; $E(Y_t)$ indicates the expected number of deaths due to MDs or dementia; Z_t represents PM concentration; *ns*() is a natural cubic spline smoothing function with the degree of freedom (*df*) of 3 to control the confounding effect of ambient temperature (Qiu et al., 2019); *DOW* and *Holiday* are categorical variables that indicate the day of the week and public holidays, respectively; and β and α are the relative coefficients.

Preliminary analysis incorporated the Z_t as a cross-basis derived from the DLNM, consisting of an *ns* function of PM with 4 *df* (knots at the 33rd and 66th percentiles) and *ns* of maximum lag time of 7 days with 4 *df* (knots at equally spaced log-values). Linear threshold models were adopted to simplify the models and increase their interpretability, and the smallest quasi-Akaike information criterion was used to select the thresholds by iterating various values in the potential interval. The associations between PM and MD and dementia-related deaths were expressed as relative risk (RR) with a 95% confidence interval (CI) for an IQR increase in concentration compared with the thresholds. We conducted a subgroup analyses using potential effect modifiers, including sex, age group, and season, to identify vulnerable populations. In addition, we tested the statistical significance of the differences between subgroups using the RR ratio (RRR) with a 95% CI:

$$(Q1 - Q2) \pm 1.96\sqrt{SE_1^2 + SE_2^2}$$

where $Q1$ and $Q2$ are the effect estimates for the subgroups, and SE_1 and SE_2 are the standard errors (Altman and Bland, 2003). A modifier significantly modified the association if the 95% CI of RRR did not include 1.

We further calculated the AF and AN to quantify the burden of MD and dementia-related deaths related to PMs. We calculated AF and AN based on the effect estimates obtained in the above analysis according to a previous study (Gasparrini and Leone, 2014); the formula used is as follows:

$$AF_t = 1 - \exp(-\beta * \Delta Z_{t-i}), \quad (2)$$

$$AN_t = n_t * AF_t \quad (3)$$

where AF_t and AN_t represent the fraction and the number of MD or dementia-related deaths attributable to exceeding PMs exposure on day t, respectively; n_t indicates the count of MD or dementia-related deaths on day t; the parameter β used in (2) represents the risk associated with the exposure derived from regression models adjusting for confounders; and ΔZ_{t-i} is the concentration difference between the observed of PMs on day t–i reference to the threshold concentration. The AF and AN were calculated for PMs with concentrations exceeding the thresholds in this study or the standard concentrations recommended by the WHO air quality guidelines and the China grade I standard.

2.4. Sensitivity analysis

Sensitivity analyses were conducted to evaluate the robustness of the results. We adjusted the natural cubic spline functions with 4 *df* for the lag 0–7 moving averages of SO_2, NO_2, CO, O_3 and relative humidity, separately. In addition, we changed the *df* of the temperature and alternatively chose different lag periods for the PMs.

All analyses were performed using the R software (version 4.2.0). The two-sided $P < 0.05$ was considered statistically significant.

3. Results

Table 1 shows the descriptive statistics of the daily deaths related to MDs or dementia, air pollutants, and meteorological conditions in Ningde from 2015 to 2021. There were 1685 MD-related deaths and 1199 dementia-related deaths during the study period. The proportions were higher among people aged over 75 years, males, and in cool seasons, at 75.0%, 53.6%, and 59.7%, respectively. The average daily concentrations of PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$, SO_2, NO_2, CO and O_3 were 14.41 μg/m^3, 8.98 μg/m^3, 23.39 μg/m^3, 38.49 μg/m^3, 14.99 μg/m^3, 6.26 μg/m^3, 19.14 μg/m^3, 0.76 mg/m^3 and 55.18 μg/m^3, respectively, while the average daily temperature and relative humidity were 18.27 °C and 78.78%. Fig. S1 shows that both the averages and variations in PMs were greater during the cool season than during the warm season. Table S1 shows the Spearman's correlations between exposures. Only the coefficients between PMs were higher than 0.6, indicating a strong correlation between PMs.

Fig. 1 shows the exposure–response curves between PMs with different aerodynamic diameters and MD or dementia-related deaths accumulated over 0–7 lag days. There were J-shaped associations between MD and dementia-related deaths with PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$, with approximately linear growth trends when exposure exceeded potential thresholds. The best-fitting thresholds of 13, 9, 19, 33 and 12 μg/m^3 were selected from the possible interval for PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$, respectively (Table S2). These threshold values were lower than the standard concentrations recommended by the WHO Air Quality Guidelines and the Chinese Grade I standard.

Table 1

Descriptive statistics on daily death from mental disorders, concentration of air pollutants and meteorological variables in Ningde city from 2015 to 2021.

	N	Mean	SD	Minimum	Maximum
Mental disorders	1685	0.71	0.92	0	6
Age (years)					
0–74	422	0.18	0.42	0	3
75–84	554	0.23	0.51	0	4
≥ 85	709	0.30	0.57	0	4
Gender					
Male	904	0.38	0.63	0	4
Female	781	0.33	0.60	0	4
Season					
Cool	1007	0.42	0.83	0	6
Warm	678	0.29	0.63	0	4
Dementia	1199	0.51	0.75	0	4
Age (years)					
0–74	225	0.09	0.31	0	2
75–84	426	0.18	0.43	0	3
≥ 85	548	0.23	0.49	0	3
Gender					
Male	639	0.27	0.53	0	3
Female	560	0.24	0.50	0	4
Season					
Cool	695	0.29	0.64	0	4
Warm	504	0.21	0.52	0	4
Air pollutants					
PM_1(μg/m^3)	-	14.41	6.42	4.31	42.31
$PM_{1-2.5}$ (μg/m^3)	-	8.98	2.27	4.17	22.47
$PM_{2.5}$ (μg/m^3)	-	23.39	8.60	8.95	61.00
PM_{10} (μg/m^3)	-	38.49	12.87	14.83	92.83
$PM_{2.5-10}$ (μg/m^3)	-	14.99	5.06	3.52	35.96
SO_2 (μg/m^3)	-	6.26	2.76	1.17	32.83
NO_2 (μg/m^3)	-	19.14	8.90	2.63	60.65
CO (mg/m^3)	-	0.76	0.27	0.26	2.81
O_3 (μg/m^3)	-	55.18	24.56	1.63	163.98
Meteorological variables					
Temperature (℃)	-	18.27	7.05	-0.72	30.28
Relative humidity (%)	-	78.78	11.58	0.00	99.96

N is the number of deaths, SD is standard deviation, and cool and warm seasons are from October to March and from April to September, respectively.

Fig. 2 shows the lagged associations of PMs with different aerodynamic diameters on MD or dementia-related deaths over 7 lag days. Adverse associations of PMs occurred on the current day, and significant associations of PMs lasted for lags of 0–3 days. The RRs over lag 0–3 days of an IQR increase from the thresholds in PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ on MD-related deaths were 1.318 (95% CI, 1.143–1.519), 1.537 (95% CI, 1.224–1.931), 1.326 (95% CI, 1.150–1.530), 1.351 (95% CI, 1.177–1.550), and 1.259 (95% CI, 1.130–1.403), respectively. The RRs were slightly smaller for dementia-related deaths than for MD-related deaths (Table 2).

Table 2 illustrates the RRs of PMs for MD or dementia-related deaths modified by age group, sex, and season. All PMs significantly increased the number of MD and dementia-related deaths. There were differences in the RRs between the PMs; however, the differences were not significant. PMs had the largest RRs for deaths from MDs and dementia among people aged 75–84 years old, which were significantly higher than the RR for people aged at least 85 years. There was a difference in the number of MD and dementia-related deaths in females than in males; however, the difference was not statistically significant. In addition, the RRs of all PMs for MD and dementia-related deaths were more significant during the cool season than during the warm season.

Table 3 summarises the fraction and number of MD and dementia-related deaths attributable to PM exposure exceeding the thresholds and standard concentrations recommended by the WHO air quality guidelines and the China grade I standard. There were 5.55%, 6.49%,

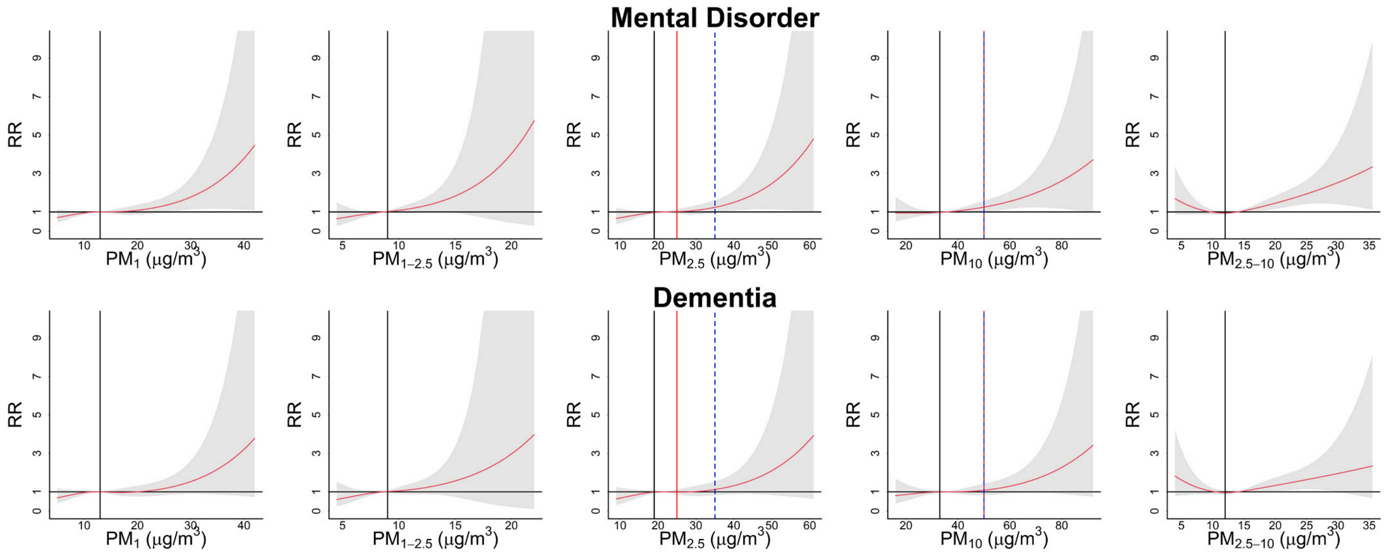

Fig. 1. Exposure-response curves between particulate matters with different aerodynamic diameters and mental disorders/dementia deaths. Black solid vertical line indicates the threshold concentration; Red solid line and blue dashed line indicate the standard concentration recommended by the WHO's air quality guidelines and the China grade I standard, respectively.

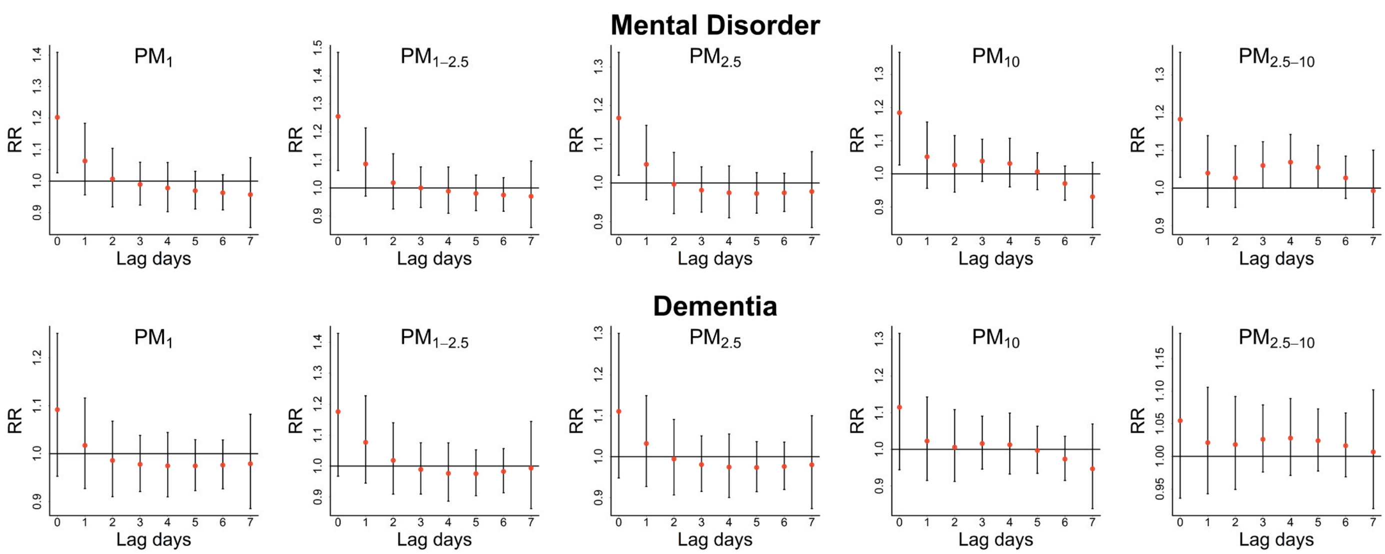

Fig. 2. Lagged effects of particulate matters with different aerodynamic diameters on death risk of mental disorders/dementia along lag days. The relative risk was calculated for an interquartile range increase in exposure compared to the thresholds.

7.68%, 10.66%, and 15.11% of MD-related deaths attributable to PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$, respectively, exceeding the thresholds, and 2.72%, 4.81%, 4.51%, 5.40%, and 11.77% of dementia-related deaths, respectively. Moreover, the fractions attributable to $PM_{2.5}$ and PM_{10} levels exceeding the WHO's air quality guidelines or the China Grade I standard were smaller than those exceeding the thresholds. In addition, we calculated the attributable fraction at the reference values of median concentrations that ensures the same number of exposure days (Tables S3), which shows similar results.

Table S4 shows the results of the sensitivity analyses of the associations between PM and MD or dementia-related deaths. The dual-pollutant model showed that the associations of PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ did not change considerably, indicating that PMs is likely to be an independent risk factor for SO_2, NO_2, CO, and O_3. In addition, the results remained robust when considering the confounding effect of relative humidity, using alternative *df* values of the meteorological and air pollution variables and different lag periods.

4. Discussion

This study has filled the gaps in evidence on the association between MD or dementia-related deaths and PM with different aerodynamic diameters, especially PM_1, after controlling for unknown or unmeasured time-invariant confounders using a time-stratified case-crossover design. We found similar J-shaped associations between MD or dementia-related deaths and PMs with different aerodynamic diameters, indicating that the risks increased rapidly and linearly because of the potential thresholds. PMs are an independent risk factor of MD or dementia-related deaths; significant associations with PMs lasted for 0–3 days. People aged 75–84 years were found to be more susceptible to PMs than other age group people. The associations of all PMs with MD and dementia-related deaths were more significant during the cool season than during the warm season. There were 5.55%, 6.49%, 7.68%, 10.66%, and 15.11% of MD-related deaths attributable to PM_1, $PM_{1-2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$, respectively, exceeding the thresholds, and

Table 2
Relative risk (95% CI) of MDs/dementia deaths associated with an inter-quartile range increase in particulate matter at lag 0–3 days by age, gender, and season.

	PM_1	$PM_{1\text{-}2.5}$	$PM_{2.5}$	PM_{10}	$PM_{2.5\text{-}10}$
Mental disorders	**1.318 (1.143, 1.519)**	**1.537 (1.224, 1.931)**	**1.326 (1.150, 1.530)**	**1.351 (1.177, 1.550)**	**1.259 (1.130, 1.403)**
Age (years)					
0–74	**1.348 (1.075, 1.689)**	**1.694 (1.180, 2.431)**	**1.356 (1.083, 1.697)**	**1.424 (1.154, 1.757)**	**1.271 (1.081, 1.493)**
75–84	**1.688 (1.378, 2.067)***	**2.053 (1.475, 2.858)***	**1.649 (1.343, 2.025)***	**1.709 (1.395, 2.094)***	**1.447 (1.232, 1.701)***
≥ 85	1.093 (0.906, 1.318)	1.228 (0.913, 1.653)	1.128 (0.935, 1.361)	1.133 (0.946, 1.356)	1.148 (0.996, 1.323)
Gender					
Male	1.194 (1.004, 1.420)	**1.430 (1.080, 1.895)**	**1.195 (1.003, 1.423)**	**1.246 (1.052, 1.475)**	**1.205 (1.054, 1.377)**
Female	**1.483 (1.225, 1.794)**	**1.691 (1.250, 2.288)**	**1.501 (1.240, 1.817)**	**1.475 (1.228, 1.772)**	**1.315 (1.138, 1.519)**
Season					
Cool	**1.337 (1.197, 1.494)**	**1.597 (1.330, 1.917)**	**1.344 (1.200, 1.506)**	**1.388 (1.240, 1.553)**	**1.287 (1.173, 1.412)**
Warm	1.024 (0.771, 1.361)	1.079 (0.726, 1.604)	1.036 (0.800, 1.342)	1.095 (0.877, 1.367)	1.196 (1.032, 1.385)
Dementia	**1.203 (1.019, 1.421)**	**1.334 (1.019, 1.747)**	**1.220 (1.031, 1.445)**	**1.206 (1.027, 1.416)**	**1.144 (1.008, 1.299)**
Age (years)					
0–74	1.178 (0.920, 1.507)	1.468 (0.984, 2.192)	1.185 (0.926, 1.516)	1.213 (0.958, 1.535)	1.102 (0.914, 1.329)
75–84	**1.583 (1.266, 1.980)***	**1.891 (1.313, 2.724)***	**1.599 (1.273, 2.010)***	**1.604 (1.284, 2.003)***	**1.357 (1.140, 1.616)***
≥ 85	1.001 (0.816, 1.228)	1.043 (0.752, 1.446)	1.027 (0.836, 1.263)	1.007 (0.829, 1.222)	1.031 (0.885, 1.200)
Gender					
Male	1.107 (0.909, 1.350)	1.238 (0.896, 1.711)	1.092 (0.892, 1.335)	1.149 (0.949, 1.392)	1.119 (0.962, 1.303)
Female	**1.320 (1.068, 1.630)**	**1.462 (1.041, 2.052)**	**1.386 (1.119, 1.717)**	**1.262 (1.029, 1.548)**	1.156 (0.984, 1.359)
Season					
Cool	**1.224 (1.075, 1.394)**	**1.367 (1.101, 1.698)**	**1.234 (1.081, 1.415)**	**1.264 (1.109, 1.441)**	**1.179 (1.058, 1.315)**
Warm	1.169 (0.838, 1.631)	1.024 (0.644, 1.628)	1.071 (0.793, 1.445)	1.174 (0.895, 1.540)	1.026 (0.857, 1.228)

Cool and warm seasons are from October to March and from April to September, respectively; The IQR increase of PM_1, $PM_{1\text{-}2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5\text{-}10}$ were 7.65, 3.37, 10.94, 16.41 and 6.02 $\mu g/m^3$, respectively; * indicates the 95% CI of RRR did not include 1, when the subgroups compared to ≥ 85 years old, male and cool season, respectively.

Table 3
The attributable fraction (AF, %) and attributable number (AN, counts) of MDs/dementia deaths due to exceeding PM concentrations in Ningde city, 2015–2021.

Cause	PM_1 AF (AN)	$PM_{1\text{-}2.5}$ AF (AN)	$PM_{2.5}$ AF (AN)	PM_{10} AF (AN)	$PM_{2.5\text{-}10}$ AF (AN)
Mental Disorder					
Threshold	**5.55 (93)**	**6.49 (109)**	**7.68 (129)**	**10.66 (180)**	**15.11 (255)**
WHO's air quality guideline	-	-	**6.92 (117)**	**6.99 (118)**	-
China grade I standard	-	-	**3.99 (67)**	**6.99 (118)**	-
Dementia					
Threshold	**2.72 (33)**	**4.81 (58)**	**4.51 (54)**	**5.40 (65)**	**11.77 (141)**
WHO's air quality guideline	-	-	**4.21 (50)**	**4.43 (53)**	-
China grade I standard	-	-	**3.01 (36)**	**4.43 (53)**	-

Thresholds in this study are 13, 9, 19, 33 and 12 $\mu g/m^3$ for PM_1, $PM_{1\text{-}2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5\text{-}10}$; The standard concentration recommended by the WHO's air quality guidelines are 25 $\mu g/m^3$ and 50 $\mu g/m^3$ for 24-h mean $PM_{2.5}$ and PM_{10}, while those recommended by the China grade I standard are 35 $\mu g/m^3$ and 50 $\mu g/m^3$ for 24-h mean $PM_{2.5}$ and PM_{10}. No standard concentration recommended for PM_1, $PM_{1\text{-}2.5}$ and $PM_{2.5\text{-}10}$.

2.72%, 4.81%, 4.51%, 5.40%, and 11.77% of dementia deaths, respectively.

We found similar J-shaped associations between MD or dementia-related deaths and PMs of different aerodynamic diameters, with the death risks related to MDs or dementia increasing rapidly and linearly above the potential thresholds, which is inconclusive in existing evidence. Previous studies showed similar results in that the relationship between $PM_{2.5}$ and all-cause mortality was J-shaped in eastern China (Chen et al., 2017). However, some researchers have assumed a linear relationship between PMs and MD outpatient visits and hospitalisations without considering nonlinearity (Lowe et al., 2021; Qiu et al., 2019), which may underestimate the risk of PMs exposure. Cohort studies have consistently observed that high $PM_{2.5}$ concentrations increase the risk of Alzheimer's disease-related deaths in Taiwan (Jung et al., 2015; Li et al., 2019b). We also found that the effect of PM on MD or dementia-related deaths was significant from lag 0 to 3 days, which was not different from that reported in previous studies (Hwang et al., 2022; Qiu et al., 2019; Yue et al., 2020). In addition, the adverse associations of PMs changed slightly after controlling for other air pollutants and meteorological conditions in this study, indicating that PMs were probably independent risk factors for MD or dementia-related deaths.

In this study, exposure to all PMs with different aerodynamic diameters significantly increased the risk of MD and dementia-related deaths; however, the differences between PMs were statistically insignificant. A study in Shanghai found that PM with a smaller aerodynamic diameter had a greater effect on the onset of autism (Chen et al., 2018b). There are two possible explanations for this discrepancy. Smaller particles, such as PM_1, can activate microglia in the brain and induce microglial cytotoxicity, lipid peroxidation, activation, and inflammatory responses (Bai et al., 2019). Besides, smaller particles enter organs through the blood circulation more easily and accumulate, adsorb, or condense on the cell surface in the body, thus greatly promoting toxicity (Natusch and Wallace, 1974). This study also found that the thresholds for PMs increased with the aerodynamic diameter, which might explain why PMs with a larger aerodynamic diameter have a larger mass than PMs with smaller aerodynamic diameters. However, evidence on the thresholds of the association between MD or dementia-related deaths and PMs of different sizes is limited. Further research is required to explore the thresholds of different PMs.

We found that people aged 75–84 years old were more susceptible than people of other age groups to the association between MD-related deaths and PMs with different aerodynamic diameters. Consistently, a study in Shijiazhuang, China, reported that the risk for MD-related hospitalisations associated with PMs was greater among older people than among younger people (Song et al., 2018). A possible explanation for this is that older people have poorer physical conditions and more underlying diseases than younger people, which may make them more sensitive to the external environment. The RRs of PMs for MD and dementia-related deaths were not significant among people aged 85 years or older in this study. Previous studies have not focused on a subgroup of people aged > 85 years old (Lu et al., 2020; Zhang et al., 2014); hence, information on this age group remains unclear. One possible explanation for this is that people who have lived for at least 85 years may have fewer chronic conditions than those who die earlier, making them less vulnerable to PM exposure. Future studies are urgently needed to provide more insightful evidence on this aspect as the global population is rapidly aging.

In this study, we found an apparent seasonal pattern in the association between PM and MD or dementia-related deaths, with significant associations in the cool season rather than in the warm season, which is consistent with the results of previous studies in Chengdu and Tianjing, China (Qiu et al., 2019; Tong et al., 2016). A possible explanation for this result is that higher concentrations of ambient PMs occur during cool seasons than during warm seasons. Moreover, a higher frequency of using air conditioners and heavy rains during summer would improve air quality in Ningde. In addition, the varied impact of PMs in different seasons implies an interactive effect between PMs and temperature on MD or dementia-related deaths, which should be confirmed in further studies.

We found that 5.55%, 6.49%, 7.68%, 10.66%, and 15.11% of MD-related deaths attributable to PM_1, $PM_{1–2.5}$, $PM_{2.5}$, PM_{10} and $PM_{2.5–10}$ exceeding the thresholds, respectively. Previous studies found that the AF of MD-related hospitalisations caused by $PM_{2.5}$ and PM_{10} concentrations exceeding those recommended by the WHO air quality guidelines were 9.53% and 9.17%, respectively (Qiu et al., 2019). In addition, we found that the standard concentrations recommended by the WHO air quality guidelines and the China Grade I standard exceeded the thresholds, indicating that the existing recommended concentrations are not sufficiently strict to provide better protection. For instance, 4.00% and 7.20% of MD-related deaths attributable to $PM_{2.5}$ and PM_{10} exceeded the concentrations recommended by the China grade I standard, which means that 5.02% and 2.82% of MD-related deaths would not be protected by the standard concentrations. Meanwhile, 10.75% and 4.96% of deaths due to dementia were not protected against standard concentrations. Thus, these findings suggest that more stringent air quality standards need to be considered and advocated for awareness of the adverse impact of environmental PMs.

This study had some limitations. First, data on environmental exposure were from fixed monitoring stations or simulated data, not from individual and exact exposure of each resident, which inevitably led to underestimated associations of PMs with MD or dementia-related deaths. Second, an insufficient sample size may have resulted in lower statistical power with a wider CI and limited the analyses of more specific subtypes of MDs. There may be differences in the effects of PMs on deaths due to other subtypes. Third, although PM is a mixture containing a variety of trace metallic elements and organic components (Daellenbach et al., 2020), this study did not distinguish between the different sources of PMs. Finally, caution should be taken when generalising the findings of this single-city study from a subtropical region with low concentrations of PMs to other regions, particularly heavily polluted and non-subtropical regions.

5. Conclusions

In this study, we found a similar J-shaped association between MD or dementia-related deaths and PMs of different aerodynamic diameters with different thresholds, and the delayed associations lasted for a lag of 0–3 days. The females and people aged 75–84 years suffer more from PMs than males and other age group people, respectively. The associations with PM were more significant during the cool season than during the warm season. Stricter air quality standards should be considered to reduce the potential impacts of PM contamination on human health. These findings are essential for developing environmental protection policies and measures to reduce the health burden of MDs.

CRediT authorship contribution statement

Xu Xin-Ying: Writing – review & editing, Writing – original draft, Formal analysis. **Zhan Zhi-Ying:** Writing – review & editing, Writing – original draft, Funding acquisition, Data curation, Conceptualization. **Liu Mao-Lin:** Data curation. **Zhong Xue:** Data curation. **Fang Hai-Yin:** Methodology. **Wei Jing:** Resources, Data curation. **He Fei:** Writing – review & editing, Resources, Funding acquisition, Data curation, Conceptualization. **Ye Wei-Min:** Writing – review & editing. **Chen Zi-Shan:** Data curation.

Declaration of Competing Interest

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

Data availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2024.115931.

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