Impact of PM2.5 exposure in old age and its interactive effect with smoking on incidence of diabetes

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Impact of $PM_{2.5}$ exposure in old age and its interactive effect with smoking on incidence of diabetes

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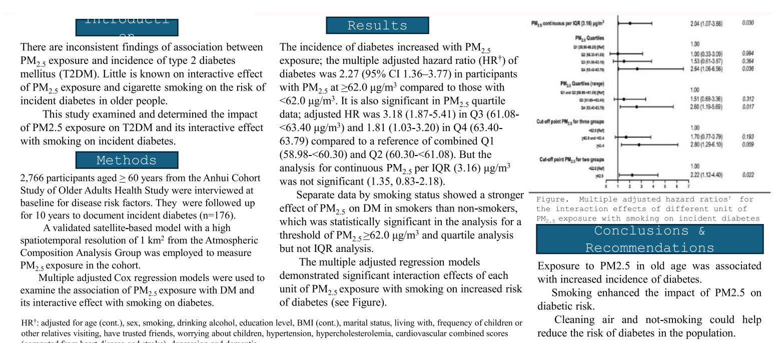
HIGHLIGHTS

- $PM_{2.5}$ exposure in old age is associated with an increased risk of diabetes.
- Exposure to $PM_{2.5}$ levels ≥62.0 μg/m^3 may double the risk of diabetes.
- Cigarette smoking enhances the adverse effect of $PM_{2.5}$ on diabetes.
- Clean air and no smoking would reduce the incidence of diabetes.

GRAPHICAL ABSTRACT



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ABSTRACT

Purpose: To determine the impact of $PM_{2.5}$ exposure in old age and its interactive effect with smoking on incident diabetes.

Methods: A total of 2766 participants aged ≥60 years in China were interviewed at baseline for disease risk factors in 2001–03 and were then followed up for 10 years to document incident diabetes. They were assessed for daily $PM_{2.5}$ exposure in 2005. Multivariate Cox regression models were used to examine the association of $PM_{2.5}$ exposure with incident diabetes and interactive effect between $PM_{2.5}$ and smoking on incident diabetes.

Results: During the cohort follow-up, 176 participants developed diabetes. The incidence of diabetes increased with $PM_{2.5}$ exposure; the multiple-adjusted hazard ratio (HR) of diabetes was 2.27 (95 % CI 1.36–3.77) in participants with $PM_{2.5}$ at ≥62.0 μg/m^3 compared to those at <62.0 μg/m^3. There was a significant interaction effect of $PM_{2.5}$ with smoking on increased risk of diabetes. The adjusted HR for participants exposed to $PM_{2.5}$

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levels ≥62.0 μg/m^3 who smoked was 4.39 (95 % CI 1.72–11.21), while for non-smokers it was 1.65 (95 % CI 0.88–3.09), compared to those at <62.0 μg/m^3.

Conclusions: Exposure to $PM_{2.5}$ in old age was associated with an increased incidence of diabetes and smoking enhanced the impact of $PM_{2.5}$ on diabetic risk. These findings underscore the urgent need for air quality improvement measures and smoking cessation programs to mitigate the risk of diabetes in aging populations.

1. Introduction

Exposure to ambient particulate matter ($PM_{2.5}$), consisting of fine inhalable particles with diameters of 2.5 μm or smaller, has been associated with heightened risks of cardiovascular diseases (Shah et al., 2013; Shah et al., 2015), respiratory diseases (Jiang et al., 2016), and mental disorders (Buoli et al., 2018; Kioumourtzoglou et al., 2017). Over the past decade, there has been a proliferation of studies examining the impact of $PM_{2.5}$ exposure on the incidence of type 2 diabetes mellitus (T2DM) (Chen et al., 2013; Hansen et al., 2016; Liu et al., 2019; Yang et al., 2020). However, the findings of current studies are inconsistent; some have shown a positive and significant association between $PM_{2.5}$ exposure and incident T2DM (Chen et al., 2013; Hansen et al., 2016; Bowe et al., 2018; Qiu et al., 2018; Clark et al., 2017), while others have found no significant association (Weinmayr et al., 2015; Puett et al., 2011; Park et al., 2015), and some have even reported a non-significant inverse association (Coogan et al., 2016; Renzi et al., 2018). These inconsistencies may be due to methodological issues in the studies, including inadequate adjustment for confounders and analysing only one unit of $PM_{2.5}$ exposure. Furthermore, most of previous studies have focused on young and middle-aged populations with $PM_{2.5}$ exposure (Yang et al., 2020), where disparities in diabetic risk attributed to risk factors profiles exist between young/middle and old aged groups (Wang et al., 2021). The majority of published cohort studies were undertaken in high income countries or regions (HICs), mainly from Europe and North America (Yang et al., 2020). The findings of these HICs studies may not be generalisable to those in low- and middle-income countries (LMICs), where there are high levels of Diabetes Mellitus (DM) (Wang et al., 2021) and $PM_{2.5}$, as well as other risk factors such as smoking, which may interact with $PM_{2.5}$ exposure to influence incident T2DM. Previous studies have shown that cigarette smoking increases the risk of T2DM in older people (Pan et al., 2015; Akter et al., 2017). However, it is unclear whether smoking had an interactive effect with ambient $PM_{2.5}$ exposure in old age on incident T2DM. In this paper, we examined the data from a population-based cohort of older people in China to assess the association of $PM_{2.5}$ exposure in old age with incident T2DM and investigate any interactive effects of ambient $PM_{2.5}$ exposure and smoking on the risk of T2DM.

2. Methods

2.1. Study design and population

The studied population was drawn from individuals participating in the Anhui Cohort Study of Older People Health (Chen et al., 2021). The methods employed in the Anhui cohort study at baseline and follow-up have been fully described in previous studies (Chen et al., 2021; Chen et al., 2012; Han et al., 2017). In brief, we randomly recruited 3336 older residents in Anhui province, China, for a health survey (1736 aged ≥65 years old in Yiming sub-district of Hefei city in 2001, and 1600 in Tangdian District of Yingshang County in 2003; Fig. 1 shows the distribution of participants in Anhui province) (Chen et al., 2021; Chen et al., 2012; Han et al., 2017). Participants were interviewed at home using a standard method, including the Geriatric Mental Status (GMS) – a comprehensive semi-structured mental state interview (Chen et al., 2012) and a health record questionnaire. The questionnaire collected information on sociodemographic data, smoking status, alcohol drinking, social networks and support, psychosocial aspects, cardiovascular disease (CVD), diabetes and other chronic diseases, and risk factors for each participant (Han et al., 2017). Smoking status was recorded as either having smoked or not over the last two years. Diabetes was defined based on a recorded doctor-diagnosis in the questionnaire interview for those who answered "*Yes*" to the question, "*Have you ever been told by a doctor that you have diabetes?*". The GMS questionnaire data was read by the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) to diagnose depression and dementia cases for each participant. Blood pressure and anthropometric measurements according to standard procedures (Han et al., 2017; Chen et al., 2022).

2.2. Assessment of $PM_{2.5}$ exposure

We employed a valid satellite-based model with high spatiotemporal resolution of 1 km^2 from the Atmospheric Composition Analysis Group (Meng et al., 2021) to measure $PM_{2.5}$ exposure in the cohort. In China, satellite data including aerosol optical depth (AOD) with wide temporal and spatial coverage have been increasingly used, in combination with advanced modelling strategies, to predict the ground $PM_{2.5}$ levels (Meng et al., 2021). In this study, the Multi-Angle Implementation of Atmospheric Correction (MAIAC) AOD data with a spatial resolution of 1-km was used. High resolution AOD was retrieved based on the MAIAC algorithm of the Moderate Resolution Imaging Spectroradiometer (MODIS) aboard the Terra and Aqua satellites. Gridded MAIAC AOD data were downloaded from the Earth Data portal (https://search.earthdata.nasa.gov) and values with quality assurance flags indicating cloud contaminated or covered by snow/water were cleaned. The 1-km resolution modelling grid based on MAIAC AOD was used to integrate all parameters. $PM_{2.5}$ monitoring sites were spatially matched to the 1-km grid cells. Model development and $PM_{2.5}$ predictions were done at the grid level. This model is recognised for its high accuracy in measuring air pollution levels, providing reliable and precise data for analysis (Meng et al., 2021). The model predicts the earliest year $PM_{2.5}$ concentrations from 2005. Based on the participants' residential address, daily $PM_{2.5}$ exposure concentrations were assessed using the satellite-based model. For the exposure window, we calculated the annual average $PM_{2.5}$ for each participant over the 365 days (one year) prior to the interview day. We used the average daily $PM_{2.5}$ concentration in 2005 for analysis.

2.3. Follow-up of the cohort and outcome identification

The participants were followed up with three additional survey interviews of surviving cohort members: one year after the baseline survey (*wave 2*), in 2007 to 2009 (*wave 3*), and in 2010–2011 (*wave 4*) (Chen et al., 2014). Similar questionnaires to those used at baseline were administered at each follow-up wave. At each follow-up interview, however, we recorded smoking status as "never, former or current smoker". We used the data of wave 1 smoking status, being combined with data of wave 2, wave 3, and wave 4 surveys to divide participants into two groups of smokers and never-smokers (if "yes" to any follow-up

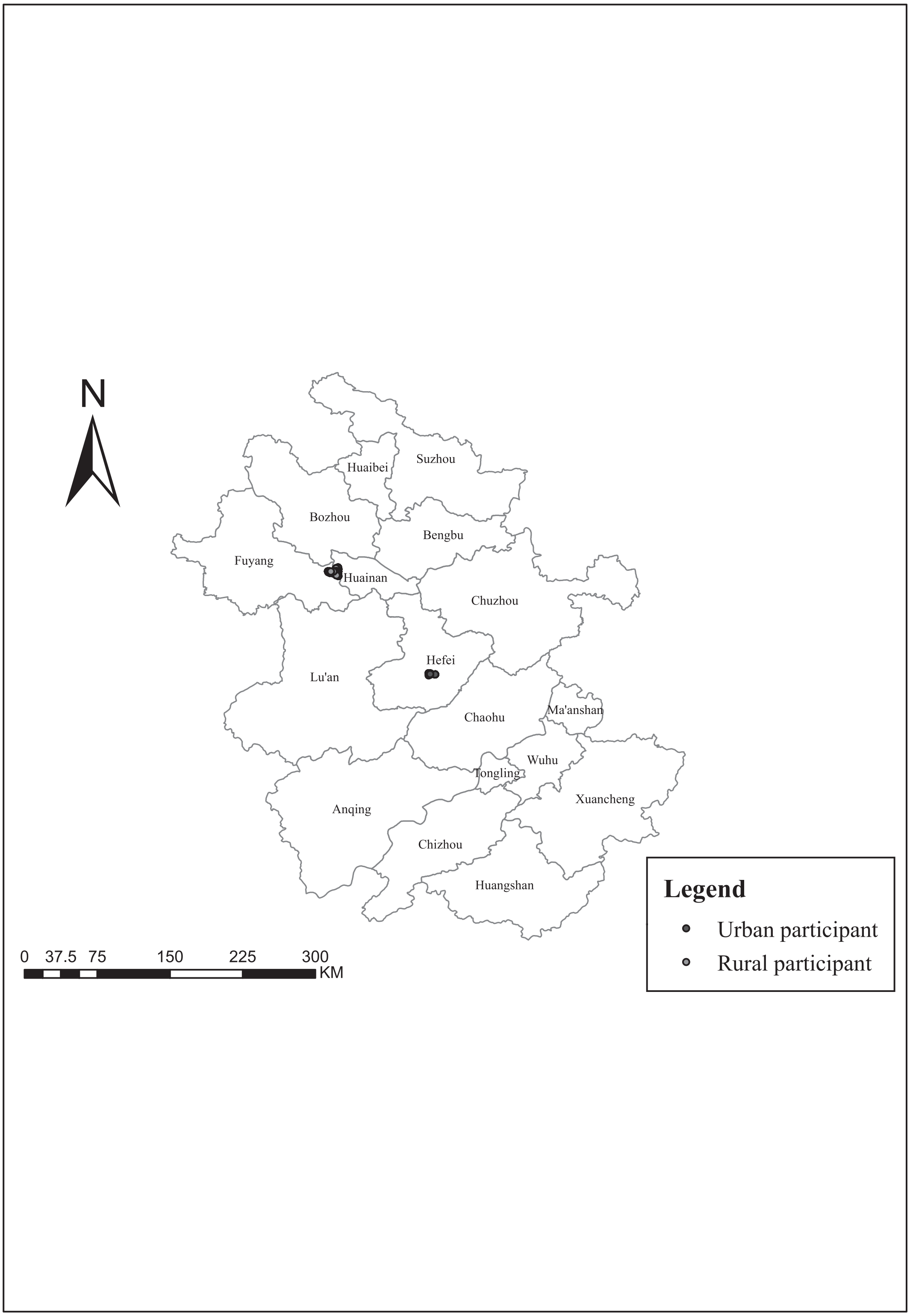

Fig. 1. Distribution of Participants in Anhui Province, China.

former smokers, one should be smokers). We documented incident diabetes cases based on doctor diagnoses recorded in the questionnaire, and incident diabetes were also identified from causes of deaths (Chen et al., 2021; Chen et al., 2022).

2.4. Data analysis

We examined differences in the distributions of baseline characteristics between participants who developed DM and those who did not develop DM using appropriate statistical tests: for continuous variables, a *t*-test was employed, while for categorical variables, a Chi-square test was used. Multiple adjusted Cox regression models were employed to assess the impact of $PM_{2.5}$ exposure on incident diabetes, calculating hazard ratio (HR) and 95 % confidence intervals (CIs). Firstly, we examined the association of continuous $PM_{2.5}$ in its interquartile range (IQR) as a unit with incident DM. Secondly, we assessed the association of $PM_{2.5}$ exposure categorized into quartiles [Q1 (58.98 - < 60.30 μg/m^3), Q2 (60.30 - < 61.08 μg/m^3), Q3 (61.08 - < 63.40 μg/m^3) and Q4 (63.40–63.79 μg/m^3)] with DM. Thirdly, following the quartile distribution of the Anhui cohort baseline $PM_{2.5}$ exposure and the China national mean of $PM_{2.5}$ (61 μg/m^3) (Zhang and Cao, 2015), we took $PM_{2.5}$ < 62.0 μg/m^3 as a reference group to examine the risk of DM in participants with $PM_{2.5}$ exposure at 62.0 - < 63.4 μg/m^3, and ≥ 63.4 μg/m^3 respectively, which were corresponding to exposure at Q3 and Q4 $PM_{2.5}$ levels respectively. Finally, we calculated the risk of incident DM in participants with $PM_{2.5} \geq 62.0$ compared to those with $PM_{2.5} < 62.0$ μg/m^3. The association of $PM_{2.5}$ with incident diabetes was examined through Cox proportional hazards regression models. A likelihood ratio (LR) test (with the interaction of time) was conducted to test the proportional hazards assumption, showing no violation in the proportional hazards assumption for air pollution ($p > 0.05$).

We investigated the interaction effect of $PM_{2.5}$ exposure and smoking on incident DM in the Cox regression models by including the interaction term of "$PM_{2.5}$ * smoking" in each analysis. Also, we stratified the data by smoking status for analysis to test for differences between smokers and non-smokers in the association of $PM_{2.5}$ with the incidence of DM. Smoking status differences in the associations were examined via two hazard ratios (Ratio of two hazard ratios, RHRs) using the method outlined in our previous studies (Chen et al., 2022). All analyses were performed using SPSS version 26.0 (IBM Co., Armonk, NY, USA).

2.5. Ethical approval

Ethical approvals for the Anhui cohort study were obtained from the Research Ethics Committees of University College London (UK), of Anhui Medical University (China), and of School of Health and Wellbeing at University of Wolverhampton (UK).

3. Results

Out of the initial 3336 participants, 49 individuals did not have their house addresses clearly recorded, resulting in the inability to measure their $PM_{2.5}$ exposure. Additionally, 187 participants who had baseline diabetes were excluded in order to estimate the incidence of DM. During the cohort follow-up, 334 participants were lost to follow-up and therefore not included in the data analysis. As a result, the data of 2766 cohort members were analysed. Over 10 years follow-up (median 5.55 years), 176 new cases of diabetes were documented in the cohort.

Of the 2766 participants, the mean age at baseline was 71.68 years (SD 6.89) and 48.3 % were men. 52.2 % were illiterate, and 34.1 % of the participants were smoking, including formerly smoking. Table 1 displays the distribution of participant's baseline characteristics of other variables. 80.6 % of participants were not drinking alcohol in the last two years, 73.0 % were married, 89.3 % were living with others, 59.4 % were daily visited by their children or other relatives, 75.9 % got trusted friends, 24.8 % were worrying about something, 18.7 % worrying about children, 58.2 % were hypertensive, 6.4 % had increased hypercholesteronemia, 14.0 % had heart disease, 4.0 % had stroke, 4.1 % had depression and 7.7 % lived with dementia. Their average BMI was 23.53 kg/m^2 (SD 3.37). Compared to those who did not develop diabetes, participants with incident DM were more likely to have higher education levels, be married, live with others, obtain trusted friends, not have daily visits from their children or other relatives, express no worries about their children, have increased body mass index (BMI), and have uncontrolled hypertension and hypercholesterolemia. Other factors listed in Table 1 did not show significant differences between the two groups.

In the cohort, the mean annual $PM_{2.5}$ concentration measured at baseline was 61.80 (μg/m^3) (SD 1.64) and IQR was 3.16 μg/m^3. Participants who developed DM had increased $PM_{2.5}$ exposure (mean daily concentration 62.28 μg/m^3, SD 1.51) compared to those who did not develop diabetes (mean 61.77, SD 1.64), with a significant difference observed $p < 0.001$. Table 2 presents the numbers, rates, and hazards ratios of incident diabetes among participants with different levels of $PM_{2.5}$ exposure. Analysing $PM_{2.5}$ continuous variable per IQR of 3.16 μg/m^3 with adjustment for age, sex, smoking and drinking alcohol (Model 1) revealed a significantly increased HR of incident DM (2.16, 95 % CI 1.59–2.93). However, with additional adjustments for educational level, BMI, social network and psychosocial factors (Model 2) the HR was reduced to be 1.41 (0.88–2.26), and further adjustments for comorbidities (Model 3) resulted in an HR of 1.35 (0.83–2.18), both of which were not statistically significant.

Data analysis of quartile $PM_{2.5}$ revealed significant differences in the incident rates of DM across the four groups. Lower incidences of DM were in Q1 (7.94 per thousand person-years) and in Q2 (5.62), followed by increased incidences of DM in Q3 (24.05) and Q4 (13.75). After adjustment for age, sex, smoking and drinking alcohol, the HR of incident DM in Q2 was not significantly different from that in Q1, but it was significantly increased in Q3 and in Q4 respectively. In the analyses adjusting for more confounders (model 2 and model 3), the increased HR remained significant in Q3 but not in Q4 (Table 2). By combining Q1 and Q2 as a reference group (due to no differences in their HRs), the analysis demonstrated significantly increased HRs in both Q3 and in Q4 (Table 2).

In the analysis of $PM_{2.5}$ exposure categorized into three levels, Model 1 revealed a significantly increased HR of incident DM at $PM_{2.5}$ exposure levels of 62.0 - <63.4 μg/m^3 (3.52, 2.44–5.09) and at exposure levels ≥63.4 μg/m^3 (2.16, 1.48–3.14) compared to those with $PM_{2.5}$ exposure at <62.0 μg/m^3. Further adjustments in Models 2 and 3 led to reductions in the HRs. Specifically, the HR at $PM_{2.5}$ exposure ≥ 63.4 μg/m^3 became borderline significant in both Model 2 and Model 3 (Table 2). Analysing the data for two levels of $PM_{2.5}$ exposure at <62.0 μg/m^3 and ≥62.0 μg/m^3 demonstrated that participants with $PM_{2.5}$ exposure at ≥62.0 μg/m^3 had a significantly increased HR of incident DM (2.70, 2.37 and 2.26 in Models 1, 2 and 3 respectively) (Table 2).

In the Model 3 analyses, we further examined the interaction effect of $PM_{2.5}$ with smoking on incident DM. We found that each of the various units of $PM_{2.5}$ significantly interacted with smoking on incident DM (Fig. 2).

Table 3 presents the fully adjusted HRs of incident diabetes across various units of $PM_{2.5}$ between smokers and non-smoking participants, along with their differences. In the analysis of $PM_{2.5}$ as a continuous variable ($PM_{2.5}$ per IQR μg/m^3), there were no significant HRs observed for smokers and non-smokers, nor were there significant differences between them. However, in the $PM_{2.5}$ quartile analyses, smokers exhibited significantly increased HRs of DM in relation to $PM_{2.5}$ in Q3 and Q4, while non-smokers did not show any significant HRs. There were no significant differences in HRs between smokers and non-smokers across quartiles, while the RHR appeared to increase with the quartiles of $PM_{2.5}$ exposure. In the combined quartiles of $PM_{2.5}$ exposure analysis, smokers in $PM_{2.5}$ Q4 had a significantly increased HR compared to non-smokers; the RHR was significant (Table 3). Moreover, in the analysis of $PM_{2.5}$ exposure as a cut-off point into three level

Table 1
Characteristics of participants: Anhui cohort study, China.

Variable	All participants		Non-DM		DM		Differences[a]
	$N = 2766$ (%)		$n = 2590$ (%)		$n = 176$ (%)		P[*]
Age (years)							
Mean (SD)	71.68	*6.89*	71.71	*6.93*	71.12	*6.27*	0.272
Sex (n, %)							
Women[b]	1429	*51.7*	1337	*51.6*	92	*52.3*	0.867
Smoking status[c]							
Yes[b]	942	*34.1*	882	*34.1*	60	*34.1*	0.992
Alcohol drinking in the last 2 years							
Daily/often/occasionally[b]	536	*19.4*	506	*19.5*	30	*17.0*	0.655
Educational level (years)							
>High Secondary school (10–12)	624	*22.6*	572	22.1	52	29.5	0.001
Secondary school (7–9)	356	*12.9*	327	12.6	29	16.5	
Primary school (1–6)	333	12.0	305	11.8	28	15.9	
Illiterate	1453	52.5	1386	53.5	67	38.1	
Marital Status							
Married	2018	*73.0*	1875	*72.4*	143	*81.3*	0.038
Divorced/Never married	114	*4.1*	109	*4.2*	5	*2.8*	
Widow	634	*22.9*	606	*23.4*	28	*15.9*	
Living with							
No-one[b]	295	*10.7*	284	*11.0*	11	*6.3*	0.050
Frequency of visiting children or other relatives							
Daily	1643	*59.4*	1562	*60.3*	81	*46.0*	<0.001
At least weekly	705	*25.5*	640	*24.7*	65	*36.9*	
At least monthly or less often	323	*11.7*	303	*11.7*	20	*11.4*	
Never	95	*3.4*	85	*3.3*	10	*5.7*	
Psychosocial factors							
Get trusted friends							
Yes[b]	2099	*75.9*	1952	*75.4*	147	*83.5*	0.014
Worrying							
No	2075	*75.0*	1932	*74.6*	143	*81.3*	0.052
Yes	687	*24.8*	654	*25.3*	33	*18.8*	
Unknown[*]	4	*0.1*	4	*0.2*	0	*0.0*	
Worry about children							
Yes[b]	517	*18.7*	500	*19.3*	17	*9.7*	0.001
Cardiovascular risk factors							
Body mass index (BMI) (kg/m^2)							
Mean (SD)	23.53	*3.37*	23.46	*3.37*	24.60	*3.12*	<0.001
Hypertension status							
No hypertension (<140*90)	1156	*41.8*	1085	*41.9*	71	*40.3*	0.002
Undetected	901	*32.6*	855	*33.0*	46	*26.1*	
Untreated	157	*5.7*	152	*5.9*	5	*2.8*	
Uncontrolled	430	*15.5*	386	*14.9*	44	*25.0*	
Controlled	122	*4.4*	112	*4.3*	10	*5.7*	
Hypercholesteronemia							
No	2568	92.8	2417	*93.3*	151	*85.8*	<0.001
Yes	177	6.4	153	*5.9*	24	*13.6*	
Unknown[*]	21	0.8	20	*0.8*	1	*0.6*	
Comorbidities							
Heart disease							
No	2366	*85.5*	2223	*85.8*	143	*81.3*	0.094
Yes	386	*14.0*	354	*13.7*	32	*18.2*	
Unknown[*]	14	*0.5*	13	*0.5*	1	*0.6*	
Stroke							
No	2651	*95.8*	2482	*95.8*	169	*96.0*	0.698
Yes	110	*4.0*	104	*4.0*	104	*3.4*	
Unknown[*]	5	*0.2*	4	*0.2*	1	*0.6*	
GMS-AGECAT diagnosis for depression and dementia							
"Well"	2067	*74.7*	1928	*74.4*	139	*79.0*	0.460
Depression-subcase	93	*3.4*	87	*3.4*	6	*3.4*	
Depression-case	113	*4.1*	110	*4.2*	3	*1.7*	
Dementia-subcase	280	*10.1*	263	*10.2*	17	*9.7*	
Dementia-case	213	*7.7*	202	*7.8*	11	*6.3*	

[*] *P*-values in the chi-square test are calculated based on available data, not including "Unknown" data.
[a] Test differences between two groups using a t-test for continuous variables and a Chi-square test for categorical variables.
[b] Binary variables: **Sex** (Women vs Men), **Alcohol drinking in the last 2 years (**Daily/often/occasionally vs No), **Living with (**No-one vs Others), **Get trusted friends** (Yes vs No), and **Worry about children** (Yes vs No).
[c] Smokers were those who had smoked over the last 2 years in Wave 1 or were recorded as former smokers in Wave 2, Wave 3, or Wave 4 surveys.

Table 2
Number, rate and hazard ratio of incident diabetes in older people with $PM_{2.5}$ exposure: Anhui cohort study.

$PM_{2.5}$ (μg/m^3)	Total participants		DM		Model 1				Model 2				Model 3			
	Nos.	PYAR[a]	Yes	Rate[b]	HR[1]	95 % CI		P	HR[2]	95 % CI		p	HR[3]	95 % CI		p
Continuous $PM_{2.5}$ per IQR (3.16) μg/m^3	2766	14,897.82	176	11.81	2.16	1.59	2.93	<0.001	1.41	0.88	2.26	0.154	1.35	0.83	2.18	0.225
$PM_{2.5}$ Quartiles †																
Q1 (58.98- < 60.30)	703	4028.65	32	7.94	1.00				1.00				1.00			
Q2 (60.30- < 61.08)	697	4093.60	23	5.62	0.72	0.42	1.23	0.230	0.66	0.39	1.13	0.131	0.65	0.38	1.12	0.121
Q3 (61.08- < 63.40)	589	2702.83	65	24.05	3.15	2.04	4.85	<0.001	2.66	1.49	4.75	0.001	2.56	1.42	4.61	0.002
Q4 (63.40–63.79)	777	4072.74	56	13.75	1.93	1.24	3.01	0.004	1.50	0.81	2.77	0.201	1.45	0.78	2.71	0.241
$PM_{2.5}$ Quartiles (combined) †																
Q1 and Q2 (58.98- < 61.08)	1400	8122.25	55	6.77	1.00				1.00				1.00			
Q3 (61.08- < 63.40)	589	2702.83	65	24.05	3.66	2.53	5.30	<0.001	3.30	1.96	5.54	<0.001	3.18	1.87	5.41	<0.001
Q4 (63.40–63.79)	777	4072.74	56	13.75	2.25	1.54	3.29	<0.001	1.86	1.07	3.25	0.029	1.81	1.03	3.20	0.039
Cut-off point $PM_{2.5}$ for three groups†																
<62.0	1426	8247.9	58	7.0	1.00				1.00				1.00			
62.0- <63.4	563	2576.6	62	24.1	3.52	2.44	5.09	<0.001	3.05	1.82	5.12	<0.001	2.93	1.73	4.97	<0.001
≥63.4	777	4072.7	56	13.8	2.16	1.48	3.14	<0.001	1.71	0.98	2.96	0.057	1.66	0.95	2.90	0.076
Cut-off point $PM_{2.5}$ for two groups†																
<62.0	1426	8247.9	58	7.0	1.00				1.00				1.00			
≥62.0	1340	6649.4	118	17.7	2.70	1.95	3.74	<0.001	2.37	1.43	3.91	0.001	2.27	1.36	3.77	0.002

HR[1]: adjusted for age (cont.), sex, smoking, drinking alcohol.
HR[2]: adjusted for age (cont.), sex, smoking, drinking alcohol, education level, BMI (cont.), marital status, living with, frequency of children or other relatives visiting, have trusted friends, worrying about children.
HR[3]: adjusted for age (cont.), sex, smoking, drinking alcohol, education level, BMI (cont.), marital status, living with, frequency of children or other relatives visiting, have trusted friends, worrying about children, hypertension, hypercholesterolemia, cardiovascular combined scores (computed from heart disease and stroke), depression and dementia.
[a] Person-Years At Risk (PYAR)
[b] Per 1000 PYAR.
† Chi-square test, all p values <0.001.

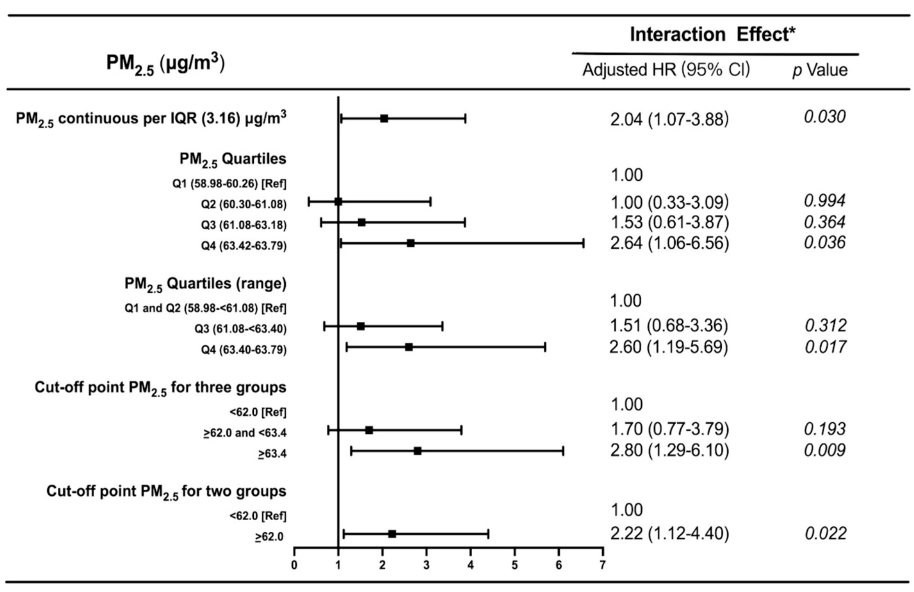

Fig. 2. Interaction effect of $PM_{2.5}$ with smoking on incident DM across different measurements of $PM_{2.5}$.

Table 3
Adjusted HRs of incident diabetes across different measurements of $PM_{2.5}$ by smoking status, and their differences.

	Smokers[a]				Non-smokers				Differences in HRs	
$PM_{2.5}$ (μg/m^3)	HR[b]	95 % CI		p	HR[b]	95 % CI		p	RHR	P[c]
$PM_{2.5}$ continuous per IQR (3.16) μg/m^3	1.97	0.86	4.51	0.107	1.06	0.58	1.95	0.855	1.86	0.118
$PM_{2.5}$ Quartiles										
Q1 (58.98–60.26)	1.00				1.00					
Q2 (60.30–61.08)	0.60	0.24	1.51	0.276	0.64	0.33	1.26	0.199	0.94	0.456
Q3 (61.08–63.18)	3.72	1.26	10.99	0.018	2.07	0.99	4.31	0.052	1.80	0.190
Q4 (63.42–63.79)	2.89	1.02	8.20	0.046	1.01	0.46	2.23	0.974	2.56	0.057
$PM_{2.5}$ Quartiles (combined)										
Q1 and Q2 (58.98- < 61.08)	1.00				1.00					
Q3 (61.08- < 63.40)	4.78	1.74	13.06	0.002	2.60	1.35	5.03	0.004	1.83	0.161
Q4 (63.40–63.79)	3.72	1.42	9.72	0.007	1.28	0.62	2.61	0.501	2.91	0.040
Cut-off point $PM_{2.5}$ for three groups										
<62.0	1.00				1.00					
62.0- <63.4	5.34	1.90	14.97	0.001	2.21	1.16	4.12	0.015	2.42	0.077
≥63.4	3.98	1.51	10.49	0.005	1.09	0.54	2.19	0.806	3.65	0.017
Cut-off point $PM_{2.5}$ for two groups										
<62.0	1.00				1.00					
≥62.0	4.39	1.72	11.21	0.002	1.65	0.88	3.09	0.117	2.66	0.045

[a] Smoking over the last 2 years in Wave 1, plus those who were identified as former smokers in Wave 2, Wave 3, or Wave 4 surveys.
[b] ie, in Model 3 above, adjusted for age (cont.), sex, smoking, drinking alcohol, education level, BMI (cont.), marital status, living with, frequency of children or other relatives visiting, have trusted friends, worrying about children, hypertension, hypercholesterolemia, cardiovascular combined scores (computed from heart disease and stroke), depression and dementia.
[c] One-side p value.

groups, the adjusted HR at $PM_{2.5} \geq 63.4$ μg/m^3 was also significantly higher in smokers than in non-smokers ($p = 0.017$) (Table 3). Furthermore, the data analysis of dividing $PM_{2.5}$ levels at a cut-off point into two groups revealed a stronger effect of $PM_{2.5}$ on incident DM in smokers compared to non-smokers ($p = 0.045$) (Table 3).

4. Discussion

Our community-based cohort study examined the impact of ambient $PM_{2.5}$ exposure on the development of diabetes and its interaction effect with cigarette smoking. The data demonstrated that older people with increasing $PM_{2.5}$ exposure were at a higher risk of incident diabetes. We observed a significant interaction effect between $PM_{2.5}$ and smoking on the risk of T2DM. The impact of $PM_{2.5}$ exposure on T2DM was stronger in people who smoked than in those who did not smoke.

Previous studies in HICs have shown that exposure to air pollution, mainly $PM_{2.5}$ was significantly associated with an elevated risk of diabetes (Chen et al., 2013; Hansen et al., 2016; Valdez et al., 2022; Lee and Ohde, 2021). In 2013, Chen H et al. (Chen et al., 2013) carried out a cohort study of 62,012 non-diabetic adults aged ≥35 years in Canada and found a positive association between $PM_{2.5}$ exposure and incident diabetes. Since then, more cohort studies were conducted and published. In 2016, Hansen AB et al. (Hansen et al., 2016) examined the data of 24,147 nurses aged ≥44 years in the Danish Nurse Cohort and found that adjusted hazard ratio of diabetes was 1.11 (1.02–1.22) per interquartile range of 3.1 μg/m^3 in $PM_{2.5}$, but not significantly increased in PM_{10}, NO_2, and NOx. However, few studies have been undertaken in LMICs (Yang et al., 2020). China, the largest LMIC, has an aging population, including an 18 % population aged ≥60 years (Han et al., 2020) and had the largest number of patients with DM (Yongze et al., 2020). Over the last three decades, China has experienced rapid industrialisation, urbanization, and economic expansion. This has led to the frequent occurrence of smog or haze episodes characterized by high fine particulate matter level (Zhang and Cao, 2015; Kan et al., 2012), and thus it has a high level of air pollution (Xue et al., 2021). Also, there has been a high level of smoking in population in China (Zhang et al., 2022; Zhang et al., 2013). Our Anhui cohort study had an up to 10 years follow-up and employed different adjustment models, including adjustment for cigarette smoking, and the findings showed that $PM_{2.5}$ exposure was positively associated with incidence of DM, which was consistent with those in other studies (Chen et al., 2013; Hansen et al., 2016). It is not surprising to find out such a positive association between $PM_{2.5}$ exposure and incident DM in older people since the emerging evidence showed that $PM_{2.5}$ can lead to insulin resistance through oxidative damage, endothelial dysfunction, and inflammation (Rao et al., 2015; Faiz et al., 2013). Our study has generated new evidence for the impact of air pollution exposure in old age on incident diabetes – identifying a threshold of exposure to $PM_{2.5}$ ≥62.0 μg/m^3 which doubled the risk of diabetes in the population in China, and demnostrating that its impact may be more serious than previously thought.

$PM_{2.5}$ interaction with smoking on incident diabetes

Cigarette smoking is a risk factor for T2DM (Pan et al., 2015; Akter et al., 2017). Cigarette smoke contains many chemical toxins, including free radicals, and this is in addition to the well-known compounds such as carbon monoxide, tar, arsenic, lead and nicotine, leading to multiple pathways that may be involved in the pathogenesis, e.g., through increasing insulin resistance, reducing insulin secretion, leading to an inflammatory response, dyslipidaemia, destroying the exocrine part of the pancreas and chronic pancreatitis (Sliwinska-Mosson and Milnerowicz, 2017). It could interact with ambient $PM_{2.5}$ exposure on development of T2DM through its pathologic pathways and might enhance the impact of ambient $PM_{2.5}$ exposure on incident T2DM. However, few study has examined interactive effect of $PM_{2.5}$ with cigarette smoking on the risk of incident T2DM. Only one study from Denmark was published (Hansen et al., 2016), showing that adjusted hazard ratio of DM in $PM_{2.5}$ per interquartile range was 1.24 (1.09–1.42) in never smokers, 1.19 (1.03–1.36) in former smokers, and 0.97 (0.86–1.10) in current smokers. Their findings suggested that there was a significantly stronger impact of $PM_{2.5}$ exposure on incident diabetes in never smokers and in former smokers than in current smokers. Our community-based cohort study in China showed that people who were exposed to $PM_{2.5}$ and smoked had a higher risk of the development of DM than those who were exposed to $PM_{2.5}$ but did not smoke, which is different from their findings in the Danish Nurse Cohort (Hansen et al., 2016). The reasons for it could be: (1) the Danish Nurse Cohort is not a community-based cohort, which included nursing professionals, of which the health behaviours may be different from the general population, (2) it included female participants only, and (3) there are differences in confounding adjustment (e.g., adjusted for depression and other psychosocial factors in the Anhui cohort, but not in the Danish Nurse cohort).

Strengths and weaknesses of the study

To the best of our knowledge, this study is the first population-based research to examine the interactive effect of air pollution exposure in old age with cigarette smoking on incident DM and identify a stronger impact of $PM_{2.5}$ on increased risk of DM in smokers than non-smokers. Our study used various units of $PM_{2.5}$ for analysis, identifying specific exposure level $\geq$62.0 μg/m^3 which significantly increased the risk of DM in older people. Our study included many important confounders for adjustment, such as depression, which has been associated with both air pollution exposure and diabetes, thereby minimising residual effects, and the findings are robust. The study has limitations. First, our study did not measure all other air pollutants, such as NO_2 and O_3 to examine their interaction effects with smoking on T2DM. However, the significant association of air pollution exposure with incident T2DM was mainly observed in previous studies from $PM_{2.5}$ exposure (Hansen et al., 2016; Liu et al., 2019). Nevertheless, the interaction effects of other air pollutants with smoking on the risk of T2DM need to be investigated in future. Second, in this study the data of $PM_{2.5}$ measurement in the earliest year were only available in 2005 (i.e., in the middle time of the cohort). This would reduce our ability to establish a causal-response relationship between $PM_{2.5}$ exposure and DM within the cohort. However, in a sensitivity analysis excluding those DM cases identified prior to 2005, we found that the patterns of increased HRs in relation to $PM_{2.5}$ exposure (Supplement Table 1) were similar to those in the full data analysis (Table 2), suggesting the possible causal-response relationship between $PM_{2.5}$ exposure and DM in older people.

Implications

$PM_{2.5}$ is an air pollutant that causes many health problems (Shah et al., 2013; Shah et al., 2015; Jiang et al., 2016; Buoli et al., 2018; Kioumourtzoglou et al., 2017; Tang et al., 2023). Major sources of $PM_{2.5}$ can be found in outdoor sources such as from the emissions of gasoline combustion, oil, diesel fuel or wood. According to the WHO development indicators (Brauer, 2017), 91 % of the world's population is exposed to unhealthy levels of $PM_{2.5}$ pollution. The majority of these populations live in LMICs, such as China, South Asia having the highest level of pollution (The World Bank, 2019). Our study has shown that $PM_{2.5}$ exposure in old age was associated with increased risk of incident diabetes. The risk for incident diabetes was higher in those who smoked than those who did not smoke. This highlights the importance of clean air and not smoking in the population. Together with the findings of this study and our previous studies on air pollution associated with dementia (Tang et al., 2023), we recommend that individuals and local governments take actions such as promoting the use of public transportation, implementing stricter regulations on vehicle emissions, investing in renewable energy sources, and advocating for policies that reduce fossil fuel consumption to lower $PM_{2.5}$ levels in the air. People should give up smoking, no matter how old they are, to reduce the impact of $PM_{2.5}$ exposure on developing diabetes.

Conclusions

Our study has shown that $PM_{2.5}$ exposure in old age increased the incidence of diabetes and smoking could enhance the impact of ambient air pollution on the risk of DM. It is important to make the air cleaner to lower $PM_{2.5}$ levels and not smoke to reduce the risk of DM in the population.

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CRediT authorship contribution statement

Anthony Chen: Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Jiaqian Yin:** Writing – review & editing, Writing – original draft, Formal analysis. **Ying Ma:** Writing – review & editing, Investigation. **Jian Hou:** Writing – review & editing, Investigation. **Weiju Zhou:** Investigation, Formal analysis. **Zhongliang Bai:** Investigation, Data curation. **Xia Qin:** Investigation, Data curation. **Zhi Hu:** Project administration, Data curation. **Yuntao Chen:** Writing – review & editing. **Eric J. Brunner:** Writing – review & editing. **Haidong Kan:** Writing – review & editing, $PM_{2.5}$ measurments, Methology, Data curation. **Ruoling Chen:** Writing – review & editing, Conceptualization, Supervision, Funding acquisition, 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

The data that has been used is confidential.

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