

Original Article



Overweight Modified the Associations Between Long-Term Exposure to Ambient Fine Particulate Matter and Its Constituent and the Risk of Type 2 Diabetes in Rural China

Donghui Yang^{1,&}, Yun Chen^{2,&}, Xia Meng^{1,&}, Xiaolian Dong³, Haidong Kan^{1,#}, and Chaowei Fu^{1,#}

1. School of Public Health; NHC Key Laboratory of Health Technology Assessment; Key Laboratory of Public Health Safety, Fudan University, Shanghai 200032, China; 2. Yale School of Nursing, Orange, CT 06477, United States; 3. Deqing County Center for Disease Prevention and Control, Zhejiang Province, China

Abstract

Objective To investigate the association between long-term exposure to ambient fine particulate matter (PM_{2.5}) and its constituents and the risk of incident type 2 diabetes mellitus (T2DM), and to examine the modification roles of overweight status.

Methods This prospective study included 27,507 adults living in rural China. The annual mean residential exposure to PM_{2.5} and its constituents was estimated using a satellite-based statistical model. Cox models were used to estimate the risk of T2DM associated with PM_{2.5} and its constituents. Stratified analysis quantified the role of overweight status in the association between PM_{2.5} constituents and T2DM.

Results Over a median follow-up of 9.4 years, 3,001 new T2DM cases were identified. The hazard ratio (HR) for a 10 µg/m³ increase in ambient PM_{2.5} was 1.30 (95% confidence interval [CI]: 1.17, 1.45). Among the constituents, the strongest association was observed with black carbon. Being overweight significantly modified the association between certain constituents and the risk of T2DM. Participants exposed to the highest quartile of PM_{2.5} constituents and those who were overweight had the highest risk of T2DM (HR: 2.46, 95%CI: 2.04, 2.97).

Conclusions Our findings indicate that PM_{2.5} was associated with an increased risk of T2DM, with black carbon potentially being the primary contributor. Being overweight appeared to enhance the association between PM_{2.5} and T2DM. This suggests that controlling both PM_{2.5} exposure and overweight status may reduce the burden of T2DM.

Key words: PM_{2.5}; Constituents; Overweight; T2DM; Cohort study

Biomed Environ Sci, 2025; 38(11): 1-10

doi: [10.3967/bes2025.000](https://doi.org/10.3967/bes2025.000)

ISSN: 0895-3988

www.besjournal.com (full text)

CN: 11-2816/Q

Copyright ©2025 by China CDC

INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) has increased steadily in recent decades, with the global age-standardized

prevalence projected to reach 9.8% by 2050^[1]. As a leading cause of cardiovascular disease and mortality^[2], T2DM imposes substantial health^[3] and economic^[4] burdens. Established modified risk factors, such as physical inactivity^[5] and unhealthy

[&]These authors contributed equally to this work.

[#]Correspondence should be addressed to Haidong Kan, E-mail: kanhd@fudan.edu.cn; Chaowei Fu, E-mail: fcw@fudan.edu.cn

Biographical notes of the first authors: Donghui Yang, PhD candidate, chronic diseases epidemiology, E-mail: 22111020046@m.fudan.edu.cn; Yun Chen, PhD, chronic diseases epidemiology, E-mail: yun.chen@yale.edu; Xia Meng, Associate Professor, Environmental Epidemiology, E-mail: mengxia@fudan.edu.cn

diet^[6], contribute significantly to its development. Enhancing our understanding of the modifiable T2DM risk factors is crucial for developing effective prevention and control strategies.

Long-term exposure to ambient fine particulate matter (PM_{2.5}) has emerged as a significant risk factor for T2DM^[7-13]. According to the Global Burden of Disease study, ambient PM_{2.5} exposure may be responsible for approximately 13.4% of T2DM-related deaths and 13.6% of the associated disability-adjusted life years (DALYs)^[14]. A previous meta-analysis of studies from Europe and North America reported an 8–10% increase in T2DM risk per 10 µg/m³ increment in PM_{2.5} concentration^[12]. PM_{2.5} is a complex mixture containing constituents, such as black carbon (BC), ammonium (NH₄⁺), nitrate (NO₃⁻), organic carbon (OC), sulfate (SO₄²⁻), and soil dust, each with a distinct toxicological profile^[15]. While limited cross-sectional studies have explored the associations between individual PM_{2.5} constituents and T2DM,^[16-18] their long-term impacts remain unclear^[19,20]. Prospective investigations are warranted to identify key hazardous constituents and guide targeted strategies to reduce the PM_{2.5}-attributable T2DM burden.

Previous studies have shown that air pollution can lead to adverse health effects via inflammation and oxidative stress^[21,22]. Moreover, being overweight increases the risk of developing diabetes through inflammation^[23]. Therefore, air pollution and overweight status may contribute to diabetes via shared mechanisms. We hypothesize that overweight status may play a role in the PM_{2.5}–T2DM relationship. However, findings regarding the modifying effect of overweight status on this association are inconsistent^[24-26]. Whether overweight acts as an effect modifier is essential for identifying populations susceptible to PM_{2.5}-related T2DM.

Therefore, this study aims to (1) investigate the association between long-term exposure to ambient PM_{2.5} mass and its chemical constituents and the risk of T2DM incidence, and (2) determine whether being overweight modifies this association.

MATERIALS and METHODS

Study Design and Population

The Rural Deqing Cohort Study (RDCS) is a prospective cohort established in Deqing County, Zhejiang Province, China. Between 2006–2008, 2011–2012, and 2013–2014, a total of 29,229

residents aged ≥ 18 years were recruited from 65 villages across eight rural townships. The detailed study design and participant inclusion criteria have been published previously.^[27] The study protocol was approved by the Institutional Review Board of the School of Public Health, Fudan University (Approval Nos. #07-06-0099, #2011-03-0624, #2014-03-480, #2022-04-0956). All participants provided written informed consent at enrollment.

In the current analysis, we excluded participants who were lost to follow-up ($n = 295$), those younger than 18 years ($n = 76$), those diagnosed with T2DM at baseline ($n = 1,317$), and those with missing information on sex ($n = 23$) or detailed address ($n = 11$). Consequently, 27,507 eligible participants were included in the final analysis (Supplementary Figure S1).

Assessment of Ambient PM_{2.5}

The PM_{2.5} mass and six main chemical constituents, namely BC, OC, NH₄⁺, NO₃⁻, SO₄²⁻, and soil dust, were assessed using a Combined Geoscience Statistical Method (CGSM) developed by the Atmospheric Composition Analysis Group at Dalhousie University^[28]. The CGSM methodology has been previously documented^[29]. The annual average ground-level concentrations of PM_{2.5} and constituents were derived from a satellite-based prediction model, which offered estimates at a spatial resolution of 1 km × 1 km for the Deqing County region. Subsequently, these estimates were mapped to the geocoded residential addresses corresponding to the year of enrollment. Detailed information regarding the PM_{2.5} mass estimate in Deqing County has been provided in an earlier study^[30].

Assessment of Outcome

All participants were followed up annually for incident T2DM from enrollment to October 31st, 2021, via linkage to the Deqing electronic health records system. T2DM was defined if participants met either of the following criteria: (1) self-reported physician diagnosis of diabetes or use of anti-diabetic medications; and/or (2) fasting plasma glucose ≥ 7.0 mmol/L.^[31]

Assessment of Overweight Status and Other Covariates

Data on overweight status and other covariates were collected at baseline. Trained health professionals collected anthropometric data, including body weight and height, to calculate the

body mass index (BMI) as weight in kilograms divided by height in meters squared (kg/m^2). BMI was categorized according to the Chinese standard (non-overweight: $\text{BMI} < 24.0 \text{ kg/m}^2$, overweight: $\text{BMI} \geq 24.0 \text{ kg/m}^2$)^[32]. Baseline data on demographic characteristics (age, sex, educational attainment, occupation, household income, and residential address), lifestyle (smoking, alcohol consumption, physical activity, diet, and tea consumption), family history of T2DM, and history of chronic diseases were collected using a structured questionnaire. Ever smokers (including former or current smokers) were defined as having smoked at least one cigarette daily for over six months in life^[33]. Alcohol consumption was defined as drinking any alcohol at least once per week^[33]. Regular physical activity was defined as engaging in at least 30 min of exercise once a week^[33]. Tea consumption was defined as daily consumption of any type of tea. Comorbid chronic diseases were defined as having been diagnosed in any secondary or tertiary hospital with at least one of the following diseases: hypertension, asthma, stroke, coronary heart disease, chronic obstructive pulmonary disease, or malignant tumors.

Statistical Analyses

Baseline characteristics were summarized according to outcome status. Differences among groups were assessed using the Student's t-test for continuous variables and the chi-square test for categorical variables. Spearman correlations were used to evaluate associations with air pollutants. The person-years (PYs) were calculated from the date of enrollment to the earliest occurrence of the first diagnosis of T2DM, death, or the end of the current follow-up (October 31st, 2021). Cox proportional hazard regression models were employed to estimate the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for the associations between PM_{2.5} and its constituents, and risk of T2DM incidence. The proportional hazards assumption was tested, and all models were met. Based on previous studies and data accessibility, the following potential confounders were adjusted in Model 1: age (<40, 40–50, 50–60, 60–70, and ≥ 70 years), sex, and stratified by baseline year (2006–2008, 2011–2012, and 2013–2014). In Model 2, we further included education attainment (< 9 or ≥ 9 years), occupation (farmer, other, and missing), household income (low, middle, high), smoking status (never or ever), alcohol consumption (yes or no), regular physical activity (yes, no, and missing), diet (vegetable mainly, meat mainly, and equally),

tea consumption (yes or no), family history of diabetes (yes or no), and history of chronic diseases (yes or no). For PM_{2.5} and individual constituents, HRs were estimated using both continuous (per $10 \mu\text{g/m}^3$ increase for PM_{2.5}, per interquartile range [IQR] increase for individual constituents) and categorical (in quartiles) approaches with single-constituent models.

To examine the potential nonlinear exposure-response relationship, we fitted a multivariable Cox model incorporating restricted cubic splines with four knots at the 5th, 35th, 65th, and 95th percentiles of each pollutant. The minimum pollutant concentrations were set as the reference values.

We also performed subgroup analyses by overweight status to evaluate its modifying effect and included the cross-product term in the overall model to test for interactions on a multiplicative scale. Additionally, we estimated the joint association of PM_{2.5}, its constituents (in quartiles), and overweight on the risk of T2DM incidence. The relative excess risk due to interaction (RERI) was used to calculate the interaction on an additive scale, with an interaction unequal to zero indicating significance.

To assess the robustness of the results, several sensitivity analyses were conducted. First, new T2DM cases diagnosed within the first two years of follow-up were excluded to account for potential reverse causality. Second, individuals with prevalent chronic diseases at baseline were excluded. Third, utilizing different exposure time windows: i) exposure level at the baseline year with a one-year lag, and ii) average concentration from 2006–2016. Participants enrolled in the cohort in 2006 were excluded from the one-year lag analysis when exposure was unavailable. Last, models were established after residual adjustment. The residuals were obtained from the linear model, where the dependent variable is the PM_{2.5} levels and the independent variables are the various components.

Analyses were performed in R software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria) using the “*survival*” package for the Cox regression and “*rms*” package for the restricted cubic spline. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

Study Participants

Table 1 presents the baseline characteristics of

the study population stratified by incident T2DM status. Among the 27,507 eligible participants (44.30% were men; mean age 56.79 ± 14.51 years), 3,001 new T2DM cases were identified during a median follow-up of 9.4 years. Compared with participants without T2DM, those who developed T2DM were older, had a higher household income, elevated BMI, greater prevalence of family history of diabetes, and history of chronic disease, and reported higher rates of regular physical activity at

baseline. Moreover, incident T2DM cases had lower educational attainment and were less likely to report a balanced diet.

The average baseline $PM_{2.5}$ mass concentration was $50.88 \mu\text{g}/\text{m}^3$. Among six chemical constituents, the highest concentration of $PM_{2.5}$ mass was observed in NO_3^- ($14.17 \mu\text{g}/\text{m}^3$), followed by SO_4^{2-} ($13.06 \mu\text{g}/\text{m}^3$), NH_4^+ ($8.91 \mu\text{g}/\text{m}^3$), OC ($8.90 \mu\text{g}/\text{m}^3$), BC ($3.23 \mu\text{g}/\text{m}^3$), and soil dust ($2.64 \mu\text{g}/\text{m}^3$) (Supplementary Table S1). Strong correlations were

Table 1. Baseline characteristics of the study population

Characteristic	Total (<i>N</i> = 27,507)	Non-T2DM (<i>n</i> = 24,506)	T2DM (<i>n</i> = 3,001)	<i>P</i> value
Age (years, SD)	56.79 $\pm$ 14.51	56.55 $\pm$ 14.80	58.70 $\pm$ 11.61	< 0.001
18.0–	3,275 (11.91)	3,114 (12.71)	161 (5.36)	< 0.001
40.0–	5,543 (20.15)	5,034 (20.54)	509 (16.96)	
50.0–	7,064 (25.68)	6,138 (25.05)	926 (30.86)	
60.0–	6,653 (24.19)	5,745 (23.44)	908 (30.26)	
≥ 70.0	4,972 (18.08)	4,475 (18.26)	497 (16.56)	
Men	12,185 (44.30)	10,884 (44.41)	1,301 (43.35)	0.278
Farmer ^a	20,501 (74.53)	18,235 (74.41)	2,266 (75.51)	0.327
Education >9 years	5,619 (20.43)	5,136 (20.96)	483 (16.09)	< 0.001
Household income				0.008
Low	4,015 (14.60)	3,592 (14.66)	423 (14.10)	
Middle	21,336 (77.57)	19,036 (77.68)	2,300 (76.64)	
High	2,156 (7.84)	1,878 (7.66)	278 (9.26)	
Ever smoker	6,335 (23.03)	5,661 (23.10)	674 (22.46)	0.445
Alcohol consumption	5,197 (18.89)	4,643 (18.95)	554 (18.46)	0.537
Regular physical activity ^a	2,771 (10.07)	2,448 (9.99)	323 (10.76)	< 0.001
Diet				0.013
Vegetable mainly	3,737 (13.59)	3,318 (13.54)	419 (13.96)	
Meat mainly	3,357 (12.20)	2,944 (12.01)	413 (13.76)	
Equally	20,413 (74.21)	18,244 (74.45)	2,169 (72.28)	
Tea consumption	10,635 (38.66)	9,457 (38.59)	1,178 (39.25)	0.494
BMI (kg/m^2)	22.54 $\pm$ 2.96	22.42 $\pm$ 2.90	23.49 $\pm$ 3.29	< 0.001
< 18.5	1,829 (6.65)	1,693 (6.91)	136 (4.53)	< 0.001
18.5–	17,233 (62.65)	15,634 (63.80)	1,599 (53.28)	
24.0–	7,482 (27.20)	6,453 (26.33)	1,029 (34.29)	
≥ 28.0	963 (3.50)	726 (2.96)	237 (7.90)	
Family history of diabetes	379 (1.38)	312 (1.27)	67 (2.23)	< 0.001
History of chronic disease	10,195 (37.06)	8,693 (35.47)	1,502 (50.05)	< 0.001

Note. Descriptive statistics are presented as mean $\pm$ standard deviation for continuous variables and as *N* (%) for categorical variables. Student's *t*-test was used for continuous variables, and the chi-square test was used for categorical variables. ^a missing data. Abbreviation: T2DM, type 2 diabetes; BMI, body mass index.

observed between the total PM_{2.5} mass and six chemical constituents, with Spearman correlation coefficients ranging from 0.78 to 0.97 (Supplementary Table S2).

Associations of PM_{2.5} and Its Chemical Constituents with Risk of T2DM Incidence

Long-term exposure to ambient PM_{2.5} was significantly associated with an increased risk of incident, both at the continuous level (HR: 1.30; 95% CI: 1.17, 1.45; per 10 µg/m³ increase) and categorical level (HR_{Q4 vs. Q1}: 1.66; 95% CI: 1.42, 1.94) in the fully adjusted model (Table 2). Among the six chemical constituents, the strongest adverse association with T2DM was observed for BC, followed by SO₄²⁻, NO₃⁻, NH₄⁺, OC, and soil dust, with HRs ranging from 1.15 to 1.33 per IQR increase in concentration. Restricted cubic spline analysis revealed a significant nonlinear association between PM_{2.5} and the risk of T2DM incidence (overall $P < 0.001$, nonlinear $P = 0.005$; Figure 1). Similar nonlinear associations were observed for BC, NH₄⁺, and NO₃⁻ (overall and nonlinear $P < 0.05$), whereas OC and SO₄²⁻ exhibited linear associations (overall $P < 0.05$, nonlinear $P > 0.05$) (Supplementary Figure S2).

Associations of PM_{2.5} and Its Chemical Constituents and Overweight with Risk of T2DM Incidence

Stratified analyses revealed a marginal modification effect of BMI ($P_{\text{interaction}} = 0.060$), with the association appearing stronger among non-overweight participants (Supplementary Table S3). Notably, a significant joint association of PM_{2.5} and BMI with the risk of T2DM incidence was identified (Figure 2). Overweight participants exposed to the highest quartile of PM_{2.5} had the highest risk compared to their non-overweight counterparts exposed to the lowest quartile of PM_{2.5} (HR: 2.46; 95% CI: 2.04, 2.97; $P_{\text{trend}} < 0.001$). Similar patterns were observed for PM_{2.5} chemical constituents, with the highest risk of T2DM observed among overweight participants exposed to the highest quartile of pollutants (Supplementary Figure S3; all $P_{\text{trend}} < 0.001$).

Sensitivity Analyses

As shown in Supplementary Table S4, the adverse associations between long-term exposure to PM_{2.5} and its chemical constituents, and the risk of T2DM incidence were similar and remained robust after excluding new cases diagnosed within the first two years of follow-up, or those with chronic diseases at baseline. Sensitivity analyses further

showed that results using baseline exposure were similar to those using one-year lag exposure, although the associations were slightly attenuated using the average concentration. Notably, the association between NO₃⁻ and T2DM risk was not significant in the model after adjusting for residual.

DISCUSSIONS

In this large prospective cohort of rural adults in East China, long-term exposure to higher levels of ambient PM_{2.5} mass and its constituents was associated with an increased risk of T2DM incidence. Overweight individuals exposed to higher levels of PM_{2.5} appeared to have a higher risk of T2DM incidence than non-overweight individuals with lower exposure.

Ambient PM_{2.5} plays a significant role in the development of diabetes.^[16-18] A prior study among older Chinese adults indicated that long-term exposure to higher concentrations of PM_{2.5} was associated with elevated fasting glucose and HbA1c levels, as well as the prevalence and incidence of T2DM.^[34] Two Mendelian randomization studies have further demonstrated the causal effect of long-term exposure to PM_{2.5} on T2DM.^[35,36] In this study, we confirmed the significant positive associations between long-term exposure to ambient PM_{2.5} and risk of T2DM incidence among rural Chinese adults (HR: 1.30, 95% CI: 1.17-1.45, per 10 µg/m³ increase).

Evidence suggests that PM_{2.5} constituents may play various roles in the adverse health effects of PM_{2.5}.^[15] However, studies linking PM_{2.5} constituents with T2DM, have mostly been cross-sectional, and prospective studies in China are limited.^[16-18] A cross-sectional study involving 17,326 participants aged ≥ 45 years in mainland China found that exposure to high concentrations of PM_{2.5} and its constituents (BC, OC, NO₃⁻, and NH₄⁺) was associated with elevated glucose levels and increased prevalence of diabetes.^[16] Another cross-sectional study involving 69,210 adults in Southwest China from 2018 to 2019 identified positive associations between long-term exposure to BC, NO₃⁻, NH₄⁺, OC, and soil dust with diabetes.^[17] A more recent cross-sectional study conducted in rural China found that long-term exposure to BC, NO₃⁻, NH₄⁺, OC, SO₄²⁻, and soil dust was associated with altered glucose metabolism.^[18] To the best of our knowledge, only one prospective study, which included 19,884 participants (791 T2DM cases) in Northwest China, reported that BC, NO₃⁻, NH₄⁺, and OC, based on estimates of concentration at a 10 km × 10 km spatial resolution,

Table 2. Associations of long-term exposure to ambient PM_{2.5} mass and its chemical constituents with risk of T2DM incidence

Pollutants	Model 1		Model 2	
	HR (95% CI)	P value	HR (95% CI)	P value
PM_{2.5}^a	1.32 (1.19, 1.46)	<0.001	1.30 (1.17, 1.45)	<0.001
Q1	1.00		1.00	
Q2	1.25 (1.13, 1.39)	<0.001	1.23 (1.10, 1.37)	<0.001
Q3	1.16 (1.03, 1.31)	0.02	1.17 (1.03, 1.33)	0.02
Q4	1.72 (1.48, 2.01)	<0.001	1.66 (1.42, 1.94)	<0.001
BC^b	1.35 (1.22, 1.50)	<0.001	1.33 (1.19, 1.48)	<0.001
Q1	1.00		1.00	
Q2	1.12 (1.00, 1.25)	0.045	1.10 (0.98, 1.23)	0.097
Q3	1.13 (0.99, 1.28)	0.06	1.14 (1.00, 1.30)	0.049
Q4	1.66 (1.42, 1.93)	<0.001	1.59 (1.36, 1.87)	<0.001
OC^b	1.19 (1.08, 1.31)	0.001	1.19 (1.08, 1.32)	<0.001
Q1	1.00		1.00	
Q2	1.23 (1.07, 1.41)	0.004	1.19 (1.03, 1.37)	0.015
Q3	1.27 (1.09, 1.47)	0.002	1.28 (1.10, 1.49)	0.002
Q4	1.48 (1.27, 1.74)	<0.001	1.42 (1.20, 1.67)	<0.001
NH₄⁺^b	1.24 (1.15, 1.33)	<0.001	1.22 (1.13, 1.31)	<0.001
Q1	1.00		1.00	
Q2	1.01 (0.91, 1.13)	0.83	1.02 (0.92, 1.14)	0.719
Q3	1.06 (0.95, 1.19)	0.29	1.07 (0.96, 1.21)	0.223
Q4	1.65 (1.42, 1.90)	<0.001	1.60 (1.38, 1.85)	<0.001
NO₃⁻^b	1.26 (1.14, 1.39)	<0.001	1.24 (1.12, 1.37)	<0.001
Q1	1.00		1.00	
Q2	1.06 (0.90, 1.24)	0.51	1.09 (0.93, 1.28)	0.271
Q3	1.04 (0.88, 1.23)	0.64	1.08 (0.91, 1.28)	0.369
Q4	1.56 (1.31, 1.84)	<0.001	1.53 (1.29, 1.82)	<0.001
SO₄²⁻^b	1.30 (1.20, 1.42)	<0.001	1.27 (1.16, 1.39)	<0.001
Q1	1.00		1.00	
Q2	1.16 (1.03, 1.30)	0.01	1.16 (1.03, 1.30)	0.014
Q3	1.15 (0.98, 1.34)	0.09	1.15 (0.98, 1.35)	0.091
Q4	1.47 (1.25, 1.73)	<0.001	1.41 (1.19, 1.67)	<0.001
Soil dust^b	1.14 (1.02, 1.28)	0.02	1.15 (1.02, 1.29)	0.03
Q1	1.00		1.00	
Q2	0.93 (0.82, 1.07)	0.31	0.93 (0.81, 1.07)	0.294
Q3	1.18 (1.03, 1.35)	0.02	1.18 (1.02, 1.35)	0.024
Q4	1.11 (0.93, 1.33)	0.25	1.09 (0.91, 1.31)	0.367

Note. ^a per 10 µg/m³ increase; ^b per IQR increase (BC, 0.65 µg/m³; OC, 1.72 µg/m³; NH₄⁺, 1.28 µg/m³; NO₃⁻, 2.79 µg/m³; SO₄²⁻, 2.43 µg/m³; Soil dust: 1.03 µg/m³). Model 1: adjusted for age, sex, stratified by baseline year. Model 2: Model 1 plus education level, occupation, household income, smoking status, alcohol consumption, regular physical activity, tea consumption, diet, family history of T2DM, and history of chronic disease. HR, hazard ratio; 95% CI, 95% confidence interval; PM_{2.5}, fine particulate matter with an aerodynamic diameter of 2.5 µm or less; BC, black carbon; OC, organic carbon; NH₄⁺, ammonium; NO₃⁻, nitrate; SO₄²⁻, sulfate.

were positively associated with the incidence of T2DM.^[19] Another prospective study found significant associations between several constituents and T2DM risk.^[20] However, few prospective studies have investigated the associations between PM_{2.5} constituents and T2DM in China, especially in rural areas, using a higher spatial resolution. Based on a large prospective cohort study with 1 × 1 km spatial resolution, we found that BC, NO₃⁻, NH₄⁺, OC, SO₄²⁻, and soil dust were positively associated with an increased risk of T2DM incidence. Our findings provide additional evidence that PM_{2.5} constituents, particularly BC, plays a dual role in increasing the risk of T2DM incidence. Mechanisms such as oxidative stress and inflammatory responses may partially explain how black carbon exposure leads to diabetes^[37]. The BC emissions in rural China mainly originate from solid fuel combustion^[38], highlighting the importance of targeted air pollution control measures to effectively reduce T2DM risk.

While several previous studies have investigated the modification effect of BMI on the associations

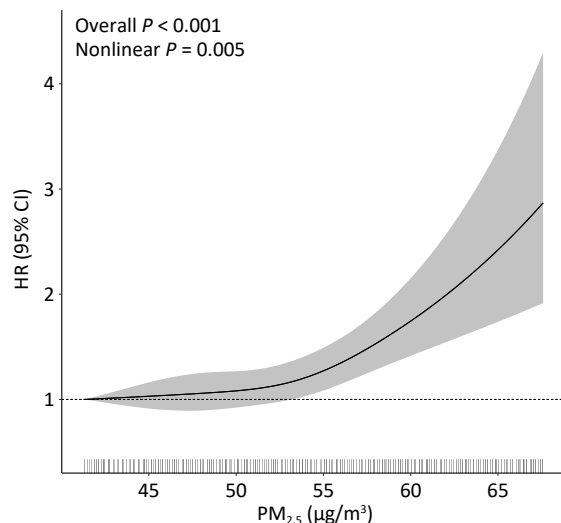


Figure 1. Exposure-response relation between ambient PM_{2.5} concentrations at baseline and risk of T2DM incidence. Multivariable Cox proportional hazard regression with restricted cubic splines adjusted for age, sex, education level, occupation, household income, smoking status, alcohol consumption, regular physical activity, tea consumption, diet, family history of T2DM, and history of chronic disease, stratified by baseline year. Abbreviations: PM_{2.5}, fine particulate matter with an aerodynamic diameter of 2.5 µm or less; HR, hazard ratio; 95% CI, 95% confidence interval.

between PM_{2.5} and T2DM, the results were inconsistent due to differences in study design, source population, sample size, and exposure duration.^[24-26,39,40] A few prospective studies have reported that the association between long-term exposure to PM_{2.5} and the risk of T2DM incidence was significantly modified by BMI, with adults with lower BMI appearing more susceptible to the adverse effects of PM_{2.5} exposure^[26,40]. However, studies from Western countries suggested that the association between PM_{2.5} and diabetes was stronger among adults with higher BMI^[24,41]. Interestingly, our study found that overweight adults exposed to the highest levels of PM_{2.5} had the highest risk of T2DM incidence compared to non-overweight individuals exposed to the lowest levels of PM_{2.5}, which is consistent with a previous study among rural Chinese^[25]. However, in the subgroup analysis, the adverse association of PM_{2.5} with risk of T2DM incidence, was stronger among non-overweight participants than their overweight counterparts, although the interaction was borderline significant ($P_{\text{interaction}}=0.060$). Similar additive patterns of PM_{2.5} constituents with overweight were observed, with significant interactions for BC, OC, and NO₃⁻. These findings suggest a potential synergistic effect between PM_{2.5} and overweight. PM_{2.5} may emerge as a major contributor to PM_{2.5}/overweight-related T2DM

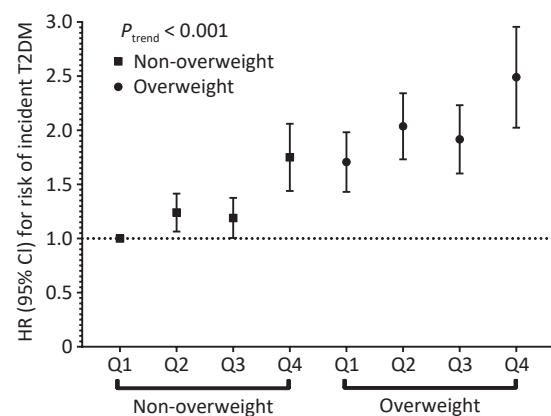


Figure 2. Joint effect of ambient PM_{2.5} mass exposure and overweight with risk of T2DM incidence. Multivariable Cox proportional hazard regression adjusted for age, sex, education level, occupation, household income, smoking status, alcohol consumption, regular physical activity, tea consumption, diet, family history of T2DM, and history of chronic disease stratified by baseline year. HR, hazard ratio; 95% CI, 95% confidence interval.

among non-overweight participants, while BMI plays a more significant role among overweight individuals. Biologically, the joint effect of PM_{2.5} and overweight on T2DM development is plausible. Being overweight may enhance the inflammatory response to PM_{2.5} and influence several hormones that accentuate the adverse effects of PM_{2.5}^[42-45]. A previous study showed that overweight individuals inhaled an average of 8.21 m³ more air than normal-weight individuals^[46] which might have led to a greater dose of inhaled PM_{2.5}. Changes in respiratory physiology among obese adults may also explain their increased susceptibility to PM_{2.5} exposure^[47].

This study had several strengths, including the use of a large prospective cohort of rural Chinese adults with a long follow-up duration, and a comprehensive assessment of ambient PM_{2.5} and its constituents in relation to T2DM development. In addition, the role of overweight in the association between PM_{2.5} and T2DM using stratified approaches was comprehensively studied. However, this study has several limitations. First, the findings may have been confounded by unmeasured factors, such as O₃ and NO₂ although typical T2DM related risk factors have been comprehensively considered. Second, the exposure level of PM_{2.5} was assessed based on the fixed addresses of participants, without considering their daily activity patterns, such as transport from home to office and other environmental pollutants, including indoor air pollution. Third, this analysis was conducted in one of the most developed regions of rural China, which may limit the generalizability of our results to urban Chinese populations with higher pollution levels. In addition, T2DM cases were predominantly identified through a single test for fasting plasma glucose or self-reporting in the baseline study, which could potentially increase the risk of underdiagnosis.

CONCLUSIONS

Based on this large prospective cohort in rural China, long-term exposure to ambient PM_{2.5} and its constituents was positively associated with the risk of T2DM incidence. Adults who were overweight and exposed to high concentrations of ambient PM_{2.5} had the highest risk of T2DM incidence, which further highlights the importance of controlling overweight status in reducing the effect of ambient PM_{2.5} on incident T2DM. The findings of this study suggest that government policies should implement measures targeting air pollution control and overweight prevention to help mitigate the burden

of T2DM.

Funding This work was supported by the National Nature Science Foundation of China (82173600) and Shanghai Leading Academic Project of Public Health, China (GWVI-8).

Competing Interests The authors declare that they have no competing financial interests or personal relationships that may have influenced the work reported in this study.

Ethics This study was approved by the Institutional Review Board of the School of Public Health, Fudan University (No. #07-06-0099, #2011-03-0624, #2014-03-480, #2022-04-0956). All participants provided written informed consent at enrollment.

Authors' Contributions D.Y., Y.C., and X.M. are co-first author who contributed equally to this study. Conceptualization, Methodology, Formal analysis, Validation, Writing-original draft, Visualization: D.Y., Y.C., and X.M.; Conceptualization, Methodology, Data curation, Writing-review & editing: X.D.; Conceptualization, Methodology, Supervision, Funding acquisition, Resource, Writing-review & editing: H.K.; Conceptualization, Methodology, Supervision, Funding acquisition, Resource, Writing-review & editing: C.F.

Acknowledgements We would like to thank all the participants enrolled in this study and all the health workers of the Deqing County Center for Disease Control and Prevention for contributing to this study.

Data Sharing The supplementary materials will be available in www.besjournal.com.

Received:

REFERENCES

1. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*, 2023; 402, 203–34.
2. Dal Canto E, Ceriello A, Rydén L, et al. Diabetes as a cardiovascular risk factor: an overview of global trends of macro and micro vascular complications. *Eur J Prev Cardiol*, 2019; 26, 25–32.
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol*, 2018; 14, 88–98.
4. Chen HY, Kuo S, Su PF, et al. Health care costs associated with macrovascular, microvascular, and metabolic complications of type 2 diabetes across time: estimates from a population-based cohort of more than 0.8 million individuals with up to 15 years of follow-up. *Diabetes Care*, 2020; 43, 1732–40.
5. Katzmarzyk PT, Friedenreich C, Shiroma EJ, et al. Physical inactivity and non-communicable disease burden in low-

- income, middle-income and high-income countries. *Br J Sports Med*, 2022; 56, 101–6.
6. Forouhi NG, Misra A, Mohan V, et al. Dietary and nutritional approaches for prevention and management of type 2 diabetes. *BMJ*, 2018; 361, k2234.
 7. Chen ZH, Salam MT, Toledo-Corral C, et al. Ambient air pollutants have adverse effects on insulin and glucose homeostasis in Mexican Americans. *Diabetes Care*, 2016; 39, 547–54.
 8. Liu C, Yang CY, Zhao YH, et al. Associations between long-term exposure to ambient particulate air pollution and type 2 diabetes prevalence, blood glucose and glycosylated hemoglobin levels in China. *Environ Int*, 2016; 92–93, 416–21.
 9. Hansen AB, Ravnskjær L, Loft S, et al. Long-term exposure to fine particulate matter and incidence of diabetes in the Danish Nurse Cohort. *Environ Int*, 2016; 91, 243–50.
 10. Coogan PF, White LF, Jerrett M, et al. Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles. *Circulation*, 2012; 125, 767–72.
 11. Shin MK, Kim KN. Association between long-term air pollution exposure and development of diabetes among community-dwelling adults: modification of the associations by dietary nutrients. *Environ Int*, 2023; 174, 107908.
 12. Eze IC, Hemkens LG, Bucher HC, et al. Association between ambient air pollution and diabetes mellitus in Europe and North America: systematic review and meta-analysis. *Environ Health Perspect*, 2015; 123, 381–9.
 13. Wang B, Xu DH, Jing ZH, et al. MECHANISMS IN ENDOCRINOLOGY: effect of long-term exposure to air pollution on type 2 diabetes mellitus risk: a systemic review and meta-analysis of cohort studies. *Eur J Endocrinol*, 2014; 171, R173–82.
 14. GBD 2019 Diabetes and Air Pollution Collaborators. Estimates, trends, and drivers of the global burden of type 2 diabetes attributable to PM_{2.5} air pollution, 1990–2019: an analysis of data from the Global Burden of Disease Study 2019. *Lancet Planet Health*, 2022; 6, e586–600.
 15. Harrison RM, Yin JX. Particulate matter in the atmosphere: which particle properties are important for its effects on health?. *Sci Total Environ*, 2000; 249, 85–101.
 16. Zhou PX, Mo SC, Peng MJ, et al. Long-term exposure to PM_{2.5} constituents in relation to glucose levels and diabetes in middle-aged and older Chinese. *Ecotoxicol Environ Saf*, 2022; 245, 114096.
 17. Li SC, Guo B, Jiang Y, et al. Long-term exposure to ambient PM_{2.5} and its components associated with diabetes: evidence from a large population-based cohort from China. *Diabetes Care*, 2023; 46, 111–9.
 18. Kang N, Wu RY, Liao W, et al. Association of long-term exposure to PM_{2.5} constituents with glucose metabolism in Chinese rural population. *Sci Total Environ*, 2023; 859, 160364.
 19. Wang MZ, He YQ, Zhao YN, et al. Exposure to PM_{2.5} and its five constituents is associated with the incidence of type 2 diabetes mellitus: a prospective cohort study in northwest China. *Environ Geochem Health*, 2024; 46, 34.
 20. Zhou HW, Hong F, Wang LL, et al. Air pollution and risk of 32 health conditions: outcome-wide analyses in a population-based prospective cohort in Southwest China. *BMC Med*, 2024; 22, 370.
 21. Gangwar RS, Bevan GH, Palanivel R, et al. Oxidative stress pathways of air pollution mediated toxicity: recent insights. *Redox Biol*, 2020; 34, 101545.
 22. Li YZ, Xu L, Shan ZY, et al. Association between air pollution and type 2 diabetes: an updated review of the literature. *Ther Adv Endocrinol Metab*, 2019; 10, 2042018819897046.
 23. Rohm TV, Meier DT, Olefsky JM, et al. Inflammation in obesity, diabetes, and related disorders. *Immunity*, 2022; 55, 31–55.
 24. Li X, Wang MY, Song YZ, et al. Obesity and the relation between joint exposure to ambient air pollutants and incident type 2 diabetes: a cohort study in UK Biobank. *PLoS Med*, 2021; 18, e1003767.
 25. Kang N, Chen GB, Tu RQ, et al. Adverse associations of different obesity measures and the interactions with long-term exposure to air pollutants with prevalent type 2 diabetes mellitus: the Henan Rural Cohort study. *Environ Res*, 2022; 207, 112640.
 26. Lao XQ, Guo C, Chang LY, et al. Long-term exposure to ambient fine particulate matter (PM_{2.5}) and incident type 2 diabetes: a longitudinal cohort study. *Diabetologia*, 2019; 62, 759–69.
 27. Chen X, Wu Z, Chen Y, et al. Risk score model of type 2 diabetes prediction for rural Chinese adults: the Rural Deqing Cohort Study. *J Endocrinol Invest*, 2017; 40, 1115–23.
 28. Van Donkelaar A, Martin RV, Brauer M, et al. Global estimates of fine particulate matter using a combined geophysical-statistical method with information from satellites, models, and monitors. *Environ Sci Technol*, 2016; 50, 3762–72.
 29. van Donkelaar A, Martin RV, Li C, et al. Regional estimates of chemical composition of fine particulate matter using a combined geoscience-statistical method with information from satellites, models, and monitors. *Environ Sci Technol*, 2019; 53, 2595–611.
 30. Chen Y, Chen RJ, Chen Y, et al. The prospective effects of long-term exposure to ambient PM_{2.5} and constituents on mortality in rural East China. *Chemosphere*, 2021; 280, 130740.
 31. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*, 2014; 37 Suppl 1, S81–90.
 32. Chen CM, Lu FC, Department of Disease Control Ministry of Health, PR China. The guidelines for prevention and control of overweight and obesity in Chinese adults. *Biomed Environ Sci*, 2004; 17 Suppl, 1–36.
 33. Dong XL, Wang YZ, Chen Y, et al. Poor sleep quality and influencing factors among rural adults in Deqing, China. *Sleep Breath*, 2018; 22, 1213–20.
 34. Liu FF, Zhang K, Chen GB, et al. Sustained air pollution exposures, fasting plasma glucose, glycated haemoglobin, prevalence and incidence of diabetes: a nationwide study in China. *Int J Epidemiol*, 2022; 51, 1862–73.
 35. Kim JM, Kim E, Song DK, et al. Causal relationship between particulate matter 2.5 and diabetes: two sample Mendelian randomization. *Front Public Health*, 2023; 11, 1164647.
 36. Liu CX, Liu YB, Peng Y, et al. Causal effect of air pollution on the risk of cardiovascular and metabolic diseases and potential mediation by gut microbiota. *Sci Total Environ*, 2024; 912, 169418.
 37. Rajagopalan S, Brook RD. Air pollution and type 2 diabetes: mechanistic insights. *Diabetes*, 2012; 61, 3037–45.
 38. Shen XB, Wang PR, Zhang X, et al. Real-time measurements of black carbon and other pollutant emissions from residential biofuel stoves in rural China. *Sci Total Environ*, 2020; 727, 138649.
 39. Yang BY, Qian ZM, Li SS, et al. Ambient air pollution in relation to diabetes and glucose-homeostasis markers in China: a cross-sectional study with findings from the 33 Communities Chinese Health Study. *Lancet Planet Health*, 2018; 2, e64–73.
 40. Li YL, Wu JJ, Tang HB, et al. Long-term PM_{2.5} exposure and early-onset diabetes: does BMI link this risk?. *Sci Total Environ*, 2024; 913, 169791.
 41. Weinmayr G, Hennig F, Fuks K, et al. Long-term exposure to fine particulate matter and incidence of type 2 diabetes mellitus in a cohort study: effects of total and traffic-specific air pollution. *Environ Health*, 2015; 14, 53.

42. Li WY, Dorans KS, Wilker EH, et al. Residential proximity to major roadways, fine particulate matter, and adiposity: the framingham heart study. [Obesity](#), 2016; 24, 2593–9.
43. Dubowsky SD, Suh H, Schwartz J, et al. Diabetes, obesity, and hypertension may enhance associations between air pollution and markers of systemic inflammation. [Environ Health Perspect](#), 2006; 114, 992–8.
44. Chen W, Han YQ, Wang YW, et al. Associations between changes in adipokines and exposure to fine and ultrafine particulate matter in ambient air in Beijing residents with and without pre-diabetes. [BMJ Open Diabetes Res Care](#), 2020; 8, e001215.
45. Wolf K, Popp A, Schneider A, et al. Association between long-term exposure to air pollution and biomarkers related to insulin resistance, subclinical inflammation, and adipokines. [Diabetes](#), 2016; 65, 3314–26.
46. Brochu P, Bouchard M, Haddad S. Physiological daily inhalation rates for health risk assessment in overweight/obese children, adults, and elderly. [Risk Anal](#), 2014; 34, 567–82.
47. Sebastian J C. Respiratory physiology and pulmonary complications in obesity. [Best Pract Res Clin Endocrinol Metab](#), 2013; 27, 157–61.