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Associations between long-term exposure to ambient particulate air pollution and type 2 diabetes prevalence, blood glucose and glycosylated hemoglobin levels in China

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Abstract

Background—The evidence for an association between particulate air pollution and type 2 diabetes mellitus (T2DM) in developing countries was very scarce.

Objective—To investigate the associations of long-term exposure to fine particulate matter ($PM_{2.5}$) with T2DM prevalence and with fasting glucose and glycosylated hemoglobin (HbA1c) levels in China.

Methods—This is a cross-sectional study based on a nation-wide baseline survey of 11,847 adults who participated in the China Health and Retirement Longitudinal Study from June 2011 to

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Appendix A. Supplementary data

Results of crude data on basic characteristics of the study participants (Table S1), results of the second sensitivity analysis (Table S2) and effect estimates of ozone (Table S3) are available.

March 2012. The average residential exposure to $PM_{2.5}$ for each participant in the same period was estimated using a satellite-based spatial statistical model. We determined the association between $PM_{2.5}$ and T2DM prevalence by multivariable logistic regression models. We also evaluated the association between $PM_{2.5}$ and fasting glucose and HbA1c levels using multivariable linear regression models. Stratification analyses were conducted to explore potential effect modification.

Results—We identified 1,760 cases of T2DM, corresponding to 14.9% of the study population. The average $PM_{2.5}$ exposure for all participants was 72.6 μg/m^3 during the study period. An interquartile range increase in $PM_{2.5}$ (41.1μg/m^3) was significantly associated with increased T2DM prevalence (prevalence ratio, PR=1.14), and elevated levels of fasting glucose (0.26 mmol/L) and HbA1c (0.08%). The associations of $PM_{2.5}$ with T2DM prevalence and with fasting glucose and HbA1c were stronger in several subgroups.

Conclusions—This nationwide cross-sectional study suggested that long-term exposure to $PM_{2.5}$ might increase the risk of T2DM in China.

Keywords

fine particulate matter; type 2 diabetes mellitus; fasting glucose; glycosylated hemoglobin; cross-sectional study

1. Introduction

Type 2 diabetes mellitus (T2DM) is a long-term metabolic disorder that is primarily characterized by insulin resistance, relative insulin deficiency, and hyperglycemia. A high fasting blood glucose level was ranked as the 7th risk factor for global disease burden and accounted for 3.4 million deaths (Lim and others 2012). It was estimated that 590 million people would be suffering from T2DM by the year 2035 (Guariguata and others 2014). It is also an important risk factor for cardiovascular diseases, leading to enormous health consequences. Furthermore, the development of these outcomes in people with diabetes may be exacerbated by exposure to exogenous toxic factors (Zanobetti and Schwartz 2001).

There is growing evidence from both human and animal studies suggesting that particulate matter (PM) air pollution is an important risk factor for T2DM (Balti and others 2014; Esposito and others 2016; Eze and others 2015; Liu and others 2013; Park and Wang 2014). Dozens of cross-sectional and cohort studies have reported a positive association between long-term exposure to ambient PM and risk for T2DM (Janghorbani and others 2014; Li and others 2014; Wang and others 2014), but some other studies did not find such a relationship. For example, using two large prospective cohorts, the Nurses' Health Study and the Health Professionals Follow-Up Study, Puett *et al.* failed to find strong evidence of an association between exposure to PM in the previous 12 months and incident diabetes (Puett and others 2011). Additionally, studies have focused on the effects of PM on the incidence, prevalence and mortality of T2DM, but few have explored its effects on glucose homeostatic measures, such as fasting glucose and glycosylated hemoglobin (HbA1c) levels (Rajagopalan and Brook 2012). HbA1c is a well-acknowledged marker for measuring the average plasma glucose concentration over prolonged periods, and an elevated HbA1c level denotes an

increased risk of developing diabetes and its complications (Edelman and others 2004; Gillett 2009). Furthermore, most studies on the associations between PM and T2DM were conducted in North America and Europe, and the evidence has been very limited in developing countries, where a steep increase in T2DM was observed in the past few decades and where the air pollution level is much higher (Nicole 2015).

As the largest developing country, China is facing a growing prevalence of diabetes and severe air pollution problems (Yang and others 2013). Given the vast population affected by diabetes and the ubiquitous exposure to air pollution, it is of increasing public health significance to examine the impacts of PM on diabetes. Therefore, the objective of this study was to evaluate the association of long-term exposure to PM with T2DM and with fasting blood glucose and HbA1c levels in China. This study was based on a nationally representative survey of the China Health and Retirement Longitudinal Study (CHARLS) project (Zhao and others 2014), which aimed to provide a high-quality public database with a wide range of information to facilitate needs of scientific and policy research on ageing-related issues.

2. Materials and Methods

2.1 Study population and health data

This is a cross-sectional study based on a national baseline survey within the CHARLS project. This baseline survey was conducted from June 2011 to March 2012 and included 17,708 middle-aged and elderly participants (≥45 years old) (Zhao and others 2014). Briefly, these participants were selected from 150 counties or districts from 28 provinces using a four-staged, stratified and cluster sampling method. Individual information on sociodemographic characteristics, behaviors, indoor air pollution and chronic diseases (T2DM, etc.) was obtained using a standardized questionnaire. Sociodemographic information included home address, location of residence (rural or urban according to China's administrative divisions), age, sex, education level (low, ≤ 5 years; medium, 6-9 years; high, ≥10 years) and body mass index (BMI). Behavioral variables included smoking status (current; former: quitted smoking ≥3 years; never), pack years of smoking (packs per day multiplied by the years of smoking) and alcohol drinking (>1/month; <1/month; none). Indoor air pollution levels were represented by the type of energy used for heating (central heating; clean; unclean; others) and cooking (clean; unclean; others). The response rate of the survey was 80.5%. The reasons for nonresponse included recusal (8.8%), loss of contact (8.2%) and others (2.5%).

A blood test was conducted to measure the fasting glucose and HbA1c levels of participants who were willing to donate venous blood samples. Blood bioassays were performed at the Youanmen Center for Clinical Laboratory of Capital Medical University. HbA1c levels were measured using the Boronate affinity HPLC method, with a variation coefficient of 1.90% within assays and 2.10% between assays. Glucose levels were tested using an enzymatic colorimetric method with a variation coefficient of 0.90% within assays and 1.80% between assays. In total, 92% of the subjects claimed to have fasted overnight and non-fasting samples were excluded from this analysis.

A total of 5,861 individuals in the nationwide survey were excluded from this analysis due to the refusal to blood donation; thus, we finally included 11,847 participants. The main definition of T2DM was self-reported diabetes, and/or fasting glucose ≥7 mmol/L, and/or HbA1c ≥ 6.5%, and/or insulin use according to the recommendations of the American Diabetes Association (American Diabetes Association 2014; Eze and others 2014; Yuan and others 2015). To ensure that the calculations would be representative of the overall Chinese population aged 45 years or older, weights were used to correct for household non-response in the initial sampling and separately for individual non-response in the blood sampling. In brief, corrections for non-response were created using a propensity score from a logit regression of the household being measured or the individual giving blood on numerous covariates. We then took the inverse probability for each observation and multiplied that by the regular sample weight (Zhao and others 2016).

2.2 Air pollution data

The geocoded residential addresses of 11,847 participants were linked to average $PM_{2.5}$ concentrations between June 2011 and March 2012, which were estimated from a satellite-based spatial statistical model developed by Ma *et al.* (Ma and others 2015). Briefly, this model was established using the Collection 6 aerosol optical depth (AOD) retrieved by the US National Aeronautics and Space Administration (NASA) Moderate Resolution Imaging Spectroradiometer (MODIS), assimilated meteorology data, land use data (fire spots, urban and forest cover, etc.) and $PM_{2.5}$ concentrations from China's ground monitoring network, which was established at the end of 2012. This model was validated to have little bias in the monthly and seasonal estimates on $PM_{2.5}$. For a certain grid cell, the model could not predict the $PM_{2.5}$ value if the AOD value was missing. A minimum of 6 data points of AOD in a month was shown to be sufficient to appropriately represent a monthly average (Ma and others 2015). To allow for the adjustment for atmospheric ozone (O_3), we obtained the O_3 exposure data during the study period from the database of the 2013 Global Burden of Disease (GBD) project, which was estimated using the global chemical transport model TM5 (Brauer and others 2015).

The geocoding and exposure assignment was conducted in ArcMap (Version 10.2). Specifically, we merged the grid cells of modeled data over the study period with the boundaries of China's administrative divisions. Each grid cell had a spatial resolution of 10 km × 10 km, with individuals who resided in the same cell sharing the same exposure levels. The modeled exposures were recorded as monthly averages, and we calculated the average concentrations during our study period (June 2011 to March 2012) as indicators of the historical (long-term) exposure, assuming that the annual exposure varied little in recent years. For sensitivity analysis, we obtained another source of modeled $PM_{2.5}$ concentrations from the GBD database, which generated yearly average estimates by combining the satellite-based estimates, chemical transport model (TM5) simulations and ground measurements (Brauer and others 2015).

2.3 Statistical analysis

We evaluated the long-term associations of exposure to $PM_{2.5}$ with T2DM prevalence and glucose homeostatic measures (*i.e.,* fasting glucose and HbA1c levels) using the crude

(rather than weighted) data. For T2DM prevalence, we calculated odd ratios associated with an interquartile range (IQR) increase in $PM_{2.5}$ using multivariable logistic regression models. The odds ratio might overstate the relative risk in cross-sectional studies; thus, we further calculated the prevalence ratios (PRs) of T2DM using the formula $PR=OR/((1-P_0)+(P_0\times OR))$ (Zhang and Yu 1998), in which P_0 was the crude prevalence of T2DM in this analysis. For glucose homeostatic measures, we calculated changes in fasting glucose and HbA1c levels associated with an IQR increase in $PM_{2.5}$ using multivariable linear regression models.

We established a crude model and an adjusted model. Specifically, the crude model referred to the unadjusted analysis and crude effects were estimated. In the adjusted model, we controlled for sociodemographic characteristics (age, sex, BMI, educational level and location of residence), behavioral variable (smoking, drinking and indoor air pollution) and ambient O_3 as potential confounders according to previous studies in this area (Andersen and others 2012; Chen and others 2015; Ren and others 2010).

To test the possible effect modification, we conducted several stratification analyses by dichotomizing the age, sex, educational level, BMI, smoking status, drinking, type of household energy and location of residence.

To evaluate the robustness of our results, we conducted three sensitivity analyses. First, we introduced alternative $PM_{2.5}$ exposure data from the GBD database. Secondly, we used 7 different definitions of T2DM to calculate the diabetes prevalence, *i.e.,* a combination of self-reported T2DM, fasting glucose ≥ 7 mmol/L, HbA1c ≥ 6.5% and the use of insulin. Thirdly, we only included one person from each spouse pair (rather than both) in the main analysis to examine the possible influences related to the dependency of exposure between the spouses.

The statistical tests were two-sided, and the alpha level for statistical significance was set at 0.05. All statistical analyses were performed using SPSS statistical software (Version 19).

3. RESULTS

3.1 Descriptive statistics

The weighted descriptive statistics on sociodemographic characteristics, behaviors, and indoor air pollution of the study population (n=11,847) are summarized in Table 1. For example, the age range of the participants was 45 to 99, with an average of 59. There were similar proportions of males and females (48.0% VS 52.0%). According to the main definition, the prevalence of T2DM in the study population was 15.8%, which was comparable to that (11.6%) reported in another nationwide survey in 2010 (Xu and others 2013). The mean fasting glucose and HbA1c levels were 6.1 mmol/L and 5.2 %, respectively. The crude descriptive statistics are provided in Table S1 in the Supplemental Data.

Table 2 presents the average air pollution data at residential addresses over the study period (June 2011 to March 2012). The $PM_{2.5}$ exposure varied greatly in the population with a

mean of 72.6 μg/m^3, which was much higher than the air quality guideline issued by the World Health Organization (annual mean: 15 μg/m^3) (Krzyzanowski and Cohen 2008). On average, the $PM_{2.5}$ exposure level was 74.9 μg/m^3 among diabetes patients, slightly higher than that among non-diabetes patients (72.2 μg/m^3).The $PM_{2.5}$ concentrations derived from the GBD project were appreciably lower (50.4 μg/m^3) but were strongly correlated with those used in the main analyses (Pearson $r = 0.93$). The average concentration of O_3 estimated by the GBD project was 62.6 μg/m^3.

3.2 Regression results

As shown in Table 3, we found significant positive associations between $PM_{2.5}$ exposure and T2DM. The association was slightly stronger when we adjusted for all the covariates. For an IQR increase in $PM_{2.5}$, the PR of T2DM was 1.14 [95% confidence interval (CI): 1.08, 1.20] in the adjusted model.

The associations between $PM_{2.5}$ and fasting glucose and HbA1c levels were also statistically significant and positive in both the unadjusted model and the adjusted model (Table 4). The effect estimate increased slightly when all covariates were controlled. In the adjusted model, an IQR increase in $PM_{2.5}$ was associated with elevated levels of fasting glucose (0.26 [95% CI: 0.19, 0.32], mmol/L) and HbA1c (0.08 [95% CI: 0.06, 0.10], %). The associations of O_3 with T2DM prevalence, fasting glucose and HbA1c levels were inverse but not statistically significant in both single-pollutant and two-pollutant models (Table S3 in the Supplemental Data).

According to the results of stratification analyses (Table 5), the PRs of T2DM were 22%-135% higher among patients who were male, were less educated, had higher BMI, were currently smoking, were using unclean heating energy sources, or were living in rural areas. The increments of fasting glucose and HbA1c were 20%-82% higher among those with older age and less attainment of education. The differences were small (<20%) or inconsistent for the remaining sub-categories.

In the first sensitivity analysis, the estimates of the T2DM prevalence and the fasting glucose and HbA1c levels per an IQR increase in $PM_{2.5}$ were attenuated slightly but were still statistically significant for the alternative exposure data from the GBD project (see Table 3 and Table 4). As shown in Table S2 in the Supplement Data, although the T2DM prevalence and PRs varied appreciably with the various definitions of T2DM, the estimated PRs remained statistically significant; the definition used in the main analysis generated the smallest PR estimates. In the last sensitivity analysis, after exclusion of one person from each spouse pair from the analysis, an IQR increase in $PM_{2.5}$ was associated with a prevalence ratio of 1.12 (95% CI: 1.03, 1.21) in T2DM, a 0.26 (95% CI: 0.18, 0.34) mmol/L increase in fasting glucose and a 0.09 (95% CI: 0.05, 0.12) % increase in HbA1c, which were very similar to the estimates from the main analyses.

4. Discussion

To our knowledge, this was the largest epidemiological study to explore the association between long-term $PM_{2.5}$ exposure and T2DM in a developing country. Our findings showed

that long-term exposure to $PM_{2.5}$ was positively associated with significant increases in diabetes prevalence, fasting glucose and HbA1c levels. These associations were robust to different definitions of diabetes, exposure modeling methods and the exclusion of one person from each spouse pair.

The number of studies on the associations between PM and risk of T2DM has increased in the past few years. A recent review based on 21 published studies concluded that exposure to air pollutants was significantly associated with insulin resistance and increased incidence of T2DM (Meo and others 2015). However, few epidemiological studies explored the association between $PM_{2.5}$ and T2DM in developing countries, such as China where air pollution levels are much higher than in developed countries. This analysis found a PR of 1.17 (95% CI : 1.09, 1.25) in T2DM associated with an IQR increase (41.1μg/m^3) in $PM_{2.5}$ concentration, which was consistent with previous studies in North America and Western Europe. For example, in the Canadian National Breast Screening Study, the investigators estimated a PR of 1.10 per IQR increase (3.8 μg/m^3) in $PM_{2.5}$ (To and others 2015). In the baseline survey of the Multi-Ethnic Study of Atherosclerosis, Park *et al.* found significant associations of T2DM prevalence with $PM_{2.5}$ (odds ratio = 1.09) per each IQR increase (2.4 μg/m^3) in $PM_{2.5}$ (Park and others 2015).

Our results have certain public health significance because of the increasing number of T2DM cases and the ubiquitous exposure to high air pollution levels in China. In the present analysis, we speculated that 11.3% of diabetes cases could be attributed to exposure to excess $PM_{2.5}$ beyond the guidelines of the World Health Organization (annual mean: 15 μg/m^3). Furthermore, 2970 cases of diabetes would be avoided if the annual mean exposure levels were reduced to this recommended level.

Fasting glucose and HbA1c levels are both classic measures of homeostatic glucose levels. The associations between long-term exposure to PM and the two indicators have rarely been investigated in previous epidemiological studies. Our findings were consistent with a prior study of 1,023 participants from the Social Environment and Biomarkers of Aging Study in Taiwan, which suggested increments of 1.9 mmol/L (95% CI: 0.9, 2.9) in fasting glucose and 2.1% (95% CI: 1.5%, 2.7%) in HbA1c in association with an IQR increase (20.42 μg/m^3) in $PM_{2.5}$ (Chuang and others 2011). The positive associations between $PM_{2.5}$ and homeostatic glucose levels provided solid support for the increased diabetes risk observed in our study. These associations are biologically plausible (Sun and others 2005; Sun and others 2009). The oxidative stress and adipose tissue inflammation induced by PM exposure might result in endoplasmic reticulum stress, insulin signaling abnormalities and apoptosis (Andersen and others 2012; Fleisch and others 2014), which might further lead to insulin resistance and metabolic disturbances (Fantuzzi 2005). Thereafter, high blood glucose levels for a prolonged period can enhance the formation of HbA1c in red blood cells.

Exposure assessment is crucial in air pollution epidemiological studies, and different models for assigning concentrations to participants can lead to different estimates on the effects of PM. The exposure misclassification was large in some previous studies that simply used central monitors (Gehring and others 2006; Zeger and Diggle 2001). In contrast, we used spatially resolved concentrations of $PM_{2.5}$ from satellite-originated data, assimilated

meteorology data, land use data, and ground $PM_{2.5}$ measurements of the newly established national monitoring network. This model was validated to have little bias in predicting historical $PM_{2.5}$, and was thus believed to have advantages over other models (Ma and others 2015). Furthermore, the estimates were generated as monthly average, which could better capture the study period of this analysis. The exposure estimation from GBD was based on a chemical transport model (TM5), satellite data and some ground measurements. This approach predicted $PM_{2.5}$ concentrations only on a yearly average basis, which could not completely cover our study period (Brauer and others 2015). Nevertheless, despite the difference in exposure assessment, we still estimated significant associations of $PM_{2.5}$ with diabetes prevalence and indicators of homeostatic glucose using the GBD-originated exposure data.

This study may have several strengths. First, this is the first study examining the long-term association between air pollution and diabetes in China, and thus contributed to the very limited evidence on the association between PM and diabetes (or metrics of glucose) in populations that suffer from exposure to very high levels of air pollution. Second, this analysis is based on a large nationwide cohort in China, ensuring the sufficient statistical power and generalizability of our results. Third, we used a newly-developed exposure model with high spatial resolution and little bias in predicting historical $PM_{2.5}$, thus substantially reducing the potential exposure misclassification.

Several limitations for our study should be also recognized. First, we could not completely exclude exposure measurement errors because the spatial resolution of the $PM_{2.5}$ data was still not very high, and individual information on time-location activity patterns was not available. Second, it would have been far more informative to have long-term $PM_{2.5}$ measurements before the survey for several years. However, we were investigating the spatial contrasts of air pollution which may change only very slowly over time. Air pollution control measures usually affect the whole region (Cesaroni and others 2012; Gulliver and others 2013). Thus, we assumed that our exposure models might be also valid predictors of the historic spatial contrasts. Third, we failed to acquire the information in the field survey about how long the individuals had already experienced T2DM. Fourth, we were unable to control the potential confounding factors from physical activity in our models due to unavailability of this information for most of the participants. Fifth, we did not evaluate medication as a possible effect modifier because we failed to collect the exact categories of medication use in the baseline survey. Sixth, a change in residence would add uncertainty to the exposure assessment. However, only 21 of all the participants had just moved to the present residence 2 years ago; thus migration might not induce appreciable influences on our results. Overall, the cross-sectional study design is limiting our study findings in a way that we had one-time-measurements giving no indication of the sequence of health events. Since health outcomes were determined concurrently to the air pollution exposure in this study, based on our associations it is not possible to infer causation. Further longitudinal work of either retrospective or prospective design is needed to confirm the causal association between $PM_{2.5}$ exposure and increased diabetes risk.

5. Conclusions

In conclusion, this nationwide cross-sectional study suggested that long-term exposure to $PM_{2.5}$ might increase the risk of T2DM in China. Our findings demonstrated that particulate air pollution was an important modifiable environmental factor contributing to the development and prevalence of diabetes in China. Therefore, there is an urgent need to reduce particulate air pollution in this country where the prevalence of diabetes was growing rapidly.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Highlights

- Limited evidence on the $PM_{2.5}$-diabetes association in developing countries.
- A nationwide cross-sectional study based on a representative cohort in China.
- $PM_{2.5}$ was associated with increased diabetes prevalence.
- $PM_{2.5}$ was associated with increased levels of fasting glucose and HbA1c.

Table 1

The weighted descriptive statistics of the study participants (n=11847)

Variables	Value
Sociodemographic characteristics	
Age (years, mean ± SD)	59.3±10.6
Sex (%)	
Male	48.0
Female	52.0
Educational level (%)	
Low	63.5
Medium	22.3
High	14.2
BMI (kg/m^2, mean ± SD)	21.5±2.1
Smoking status (%)	
Current	27.2
Former	9.0
Never	63.8
Pack-years of cigarette for current smokers	32.3 ± 24.1
Drinking frequency (%)	
>1/month	24.5
<1/month	7.8
Never	67.7
Residence (%)	
Urban	32.4
Rural	67.6
Type of heating energy (%)	
Central heating	11.6
Clean (solar energy, electricity, natural gas)	24.3
Unclean (coal or biomass)	46.3
Other	17.9
Type of cooking energy (%)	
Clean (solar energy, electricity, natural gas)	53.7
Unclean (coal or biomass)	45.7
Other	0.6
Diabetes	
Prevalence of T2DM (%)	15.8
Fasting glucose (mmol/L, mean ± SD)	6.1±2.0
HbA1c (%, mean ± SD)	5.2±0.8

Abbreviations: SD, standard deviation; BMI, body mass index; HbA1c, glycosylated hemoglobin, %.

All numbers were weighted with the inverse probability weights, which were constructed by estimating a logic regression of whether the individual participated in the blood drawn.

Table 2

Summary statistics of air pollution data

Pollutants (μg/m^3)	Mean ± SD	Percentiles					IQR
		Min	25th	50th	75th	Max	
$PM_{2.5}$ [a]	72.6 ± 27.3	25.5	53.8	70.4	94.9	127.9	41.1
$PM_{2.5}$ [b]	50.4 ± 20.2	6.9	35.5	51.7	67.5	89.2	32.0
O_3 [c]	62.6 ± 5.9	26.3	60.9	63.0	65.0	78.6	4.1

Abbreviation: IQR, Interquartile range; SD, standard deviation; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; O_3, ozone.

Note:

[a] data derived from a study by Ma *et al.* and used in the main analyses.

[b] data derived from the database of the 2013 Global Burden of Disease project.

[c] data derived from the database of the 2013 Global Burden of Disease project.

Table 3

Prevalence ratio (and its 95% confidence interval) of T2DM associated with an interquartile range increase in $PM_{2.5}$

Source of $PM_{2.5}$	Model	PR	95%CI
Ma *et al.*	Unadjusted	1.12	1.06,1.19
	Adjusted	1.14	1.08,1.20
GBD	Unadjusted	1.11	1.04,1.18
	Adjusted	1.12	1.05,1.19

Abbreviation: PR, prevalence ratio; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; GBD, 2013 Global Burden of Disease project.

Note: Covariates in the adjusted models include: location of residence (urban or rural), age, sex, educational level (low, medium, high), body mass index, smoking status (current smoker, ex-smoker and non-smoker), pack years for current smokers, drinking (>1/month,<1/month, never), type of heating energy: central heating, clean, unclean ,other; type of cooking energy: clean, unclean, other) and ozone (estimated by the GBD project).

Table 4

Increments (point estimates and 95% confidence intervals) in fasting glucose and HbA1c levels associated with an interquartile range increase in $PM_{2.5}$ in the adjusted model.

Analysis	Model	Fasting glucose (mmol/L)	HbA1c (%)
Ma *et al.*	Unadjusted	0.24 (0.19,0.30)	0.07 (0.05,0.10)
	Adjusted	0.26 (0.20,0.32)	0.08 (0.06,0.10)
GBD	Unadjusted	0.21 (0.15,0.27)	0.05 (0.02,0.07)
	Adjusted	0.22 (0.16,0.28)	0.05 (0.03,0.08)

Abbreviations: $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; HbA1c, glycosylated hemoglobin; GBD, 2013 Global Burden of Disease project.

Note: Covariates in the adjusted models include: location of residence (urban or rural), age, sex, educational level (low, medium, high), body mass index, smoking status (current smoker, ex-smoker and non-smoker), pack years for current smokers, drinking (>1/month,<1/month, never), type of heating energy: central heating, clean, unclean ,others; type of cooking energy: clean, unclean, other) and ozone (estimated by the GBD project)

Table 5

Prevalence ratios of T2DM and increments in fasting glucose and HbA1c levels (and their 95% confidence intervals) associated with an interquartile range (41.1μg/m^3) increase in $PM_{2.5}$ stratified by potential modifiers.

Variables	Categories	N	PRs	Fasting glucose(mmol/L)	HbA1c (%)
Age	≤Median	6057	1.14 (1.07,1.23)	0.22 (0.14,0.29)	0.06 (0.03,0.09)
	> Median	5766	1.14 (1.07,1.23)	0.30 (0.21,0.40)	0.11 (0.07,0.14)
Sex	Males	5502	1.17 (1.07,1.27)	0.27 (0.18,0.36)	0.08 (0.05,0.12)
	Females	6336	1.14 (1.03,1.20)	0.24 (0.16,0.32)	0.07 (0.04,0.11)
Educational level	Low	8175	1.17 (1.07,1.27)	0.30 (0.19,0.41)	0.08 (0.06,0.11)
	High	3653	1.07 (0.93,1.20)	0.23 (0.14,0.32)	0.07 (0.03,0.11)
BMI	≤Median	7037	1.14 (1.03,1.23)	0.29 (0.21,0.36)	0.07 (0.04,0.10)
	> Median	4810	1.17 (1.07,1.27)	0.22 (0.12,0.32)	0.09 (0.05,0.13)
Smoking status	Yes	3380	1.20 (1.07,1.33)	0.28 (0.18,0.39)	0.06 (0.02,0.10)
	No	8428	1.14 (1.03,1.20)	0.24 (0.17,0.32)	0.09 (0.06,0.12)
Drinking	Yes	3851	1.14 (1.03,1.27)	0.23 (0.13,0.33)	0.08 (0.05,0.12)
	No	7944	1.14 (1.07,1.23)	0.27 (0.15,0.34)	0.08 (0.05,0.11)
Heating energy	Clean	3145	1.07 (0.93,1.20)	0.30 (0.18,0.41)	0.05 (0.01,0.10)
	Unclean	8613	1.17 (1.10,1.23)	0.24 (0.18,0.31)	0.09 (0.06,0.12)
Cooking energy	Clean	5048	1.14 (1.03,1.23)	0.28 (0.19,0.37)	0.06 (0.02,0.09)
	Unclean	6724	1.14 (1.07,1.23)	0.25 (0.17,0.33)	0.10 (0.07,0.13)
Location	Rural	9557	1.17 (1.10,1.23)	0.25 (0.19,0.31)	0.08 (0.01,0.15)
	Urban	2275	1.07 (0.89,1.20)	0.29 (0.11,0.47)	0.08 (0.06,0.10)

Abbreviations: T2DM, type 2 diabetes mellitus; PR, prevalence ratio; CI, confidence interval; BMI: body mass index; HbA1c, glycosylated hemoglobin, %; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; IQR, interquartile range.

Note: Categories for variables were dichotomized: the median of age was 58; the median of BMI was 21.6; educational level (low ≤9years; high ≥10years); heating and cooking energy (clean: electricity, solar power or natural gas; unclean: coal or firewood).