Ambient air pollution in relation to diabetes and glucose-homoeostasis markers in China: a cross-sectional study with findings from the 33 Communities Chinese Health Study

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Summary

Background Health effects of air pollution on diabetes have been scarcely studied in developing countries. We aimed to explore the associations of long-term exposure to ambient particulate matter (PM) and gaseous pollutants with diabetes prevalence and glucose-homoeostasis markers in China.

Methods Between April 1 and Dec 31, 2009, we recruited a total of 15 477 participants aged 18–74 years using a random number generator and a four-staged, stratified and cluster sampling strategy from a large cross-sectional study (the 33 Communities Chinese Health Study) from three cities in Liaoning province, northeastern China. Fasting and 2 h insulin and glucose concentrations and the homoeostasis model assessment of insulin resistance index and β-cell function were used as glucose-homoeostasis markers. Diabetes was defined according to the American Diabetes Association's recommendations. We calculated exposure to air pollutants using data from monitoring stations (PM with an aerodynamic diameter of 10 μm or less [PM_{10}], sulphur dioxide, nitrogen dioxide, and ozone) and a spatial statistical model (PM with an aerodynamic diameter of 1 μm or less [PM_1] and 2·5 μm or less [$PM_{2·5}$]). We used two-level logistic regression and linear regression analyses to assess associations between exposure and outcomes, controlling for confounders.

Findings All the studied pollutants were significantly associated with increased diabetes prevalence (eg, the adjusted odds ratios associated with an increase in IQR for PM_1, $PM_{2·5}$, and PM_{10} were 1·13, 95% CI 1·04–1·22; 1·14, 1·03–1·25; and 1·20, 1·12–1·28, respectively). These air pollutants were also associated with higher concentrations of fasting glucose (0·04–0·09 mmol/L), 2 h glucose (0·10–0·19 mmol/L), and 2 h insulin (0·70–2·74 μU/L). No association was observed for the remaining biomarkers. Stratified analyses indicated greater effects on the individuals who were younger (<50 years) or overweight or obese.

Interpretation Long-term exposure to air pollution was associated with increased risk of diabetes in a Chinese population, particularly in individuals who were younger or overweight or obese.

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Introduction

Diabetes is a metabolic disorder distinguished by hyperglycaemia and insulin resistance, and has been considered one of the major contributors to the global burden of diseases and premature death.[1] Meanwhile, air pollution has been ranked as the leading environmental health threat worldwide, particularly in developing countries.[2] Accumulation of evidence suggests that ambient air pollution increases the risks of diabetes.[3,4] The possible biological pathways might include autonomic nervous system imbalances,[5] oxidative stress, adipose inflammation,[6,7] endothelial dysfunction, and alterations in insulin sensitivity, glucose metabolism, and glycosylated haemoglobin metabolism.[5,8]

Several human studies[3,9,10] have explored potential associations between exposure to ambient air pollutants and diabetes. A 2015 review[4] summarised these studies and concluded that air pollution might be associated with diabetes, but more critical analysis is warranted. Some studies[11,12] reported an increase in the risk of diabetes, but others did not detect a significant association. Additionally, most studies[3,4] were done in North America and Europe. Only a few studies[3,9,10] have been done in developing countries, where both diabetes prevalence and

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Research in context

Evidence before this study

We systematically searched seven databases (PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure, Chongqing VIP Chinese Science and Technology Periodical, Wanfang, and China Biological Medicine) using the search terms "air pollution", "air pollutants", "particulate matter (PM)", "PM with an aerodynamic diameter of 10 μm or less (PM_{10})", "PM with an aerodynamic diameter of 2·5 μm or less ($PM_{2·5}$)", "PM with an aerodynamic diameter of 1 μm or less (PM_1)", "nitrogen oxides", "nitrogen dioxide", "sulfur dioxide", "ozone", "type 2 diabetes", "diabetes mellitus", "insulin", and "glucose" for studies published up to Oct 25, 2017. We found that several human epidemiological studies have assessed the associations of ambient air pollution with diabetes and glucose-homoeostasis markers, and most of them are summarised in three reviews and meta-analyses. One systematic review concluded that available evidence suggests an association between air pollution exposure and diabetes, but more critical analysis is needed. A meta-analysis reviewed 17 studies worldwide and found significant associations between diabetes and six air pollutants (PM_{10}, $PM_{2·5}$, nitrogen dioxide [NO_2], ozone [O_3], sulphate, and sulphur dioxide [SO_2]), with pooled risk ratios or mortality risk ratios ranging from 1·01/10 μg/m³ to 1·07/10 μg/m³ increase in air pollutants. Another meta-analysis included 13 studies originating from North America and Europe, and reported that the risk of type 2 diabetes increased by 10% per 10 μg/m³ increase in $PM_{2·5}$ and by 8% per 10 μg/m³ for NO_2.

However, most of these studies were done in developed countries in North America and Europe. Data are scarce for developing countries, where the diabetes burden is greater and air pollution is severe, such as China. Additionally, prevalence, incidence, and mortality for diabetes in most published studies were based on self-reports, administrative databases, or hospital discharge records, which were not validated by doctors. Few studies considered glucose and insulin homoeostatic markers (such as glucose and insulin concentrations). Furthermore, PM_1 is a major component of $PM_{2·5}$, but no study has assessed its effects on diabetes and diabetes-related traits.

Added value of this study

To the best of our knowledge, this is the largest epidemiological study on the associations of ambient air pollution with diabetes and glucose-homoeostasis markers in a developing country. In addition, this is the first ever study to explore the diabetogenic effects of PM_1. We comprehensively measured six air pollutants (PM_1, $PM_{2·5}$, PM_{10}, SO_2, NO_2, and O_3) and six glucose-homoeostasis markers (fasting and 2 h insulin and glucose concentrations, the homoeostasis model assessment of insulin resistance index, and β-cell function), and adopted a strict definition of diabetes according to the American Diabetes Association's recommendations. We found that long-term exposure to air pollution was positively associated with diabetes prevalence, as well as higher glucose and insulin concentrations. Furthermore, younger study participants and the overweight or obese participants appeared to be more susceptible to the diabetogenic effects of air pollution than older study participants and participants with normal bodyweight.

Implications of all the available evidence

The results of previous studies and our present study suggest that long-term exposure to ambient air pollution might be associated with an increased risk of developing diabetes. In the future, additional studies should explore the effects of multiple-pollutant interactions and differentiate air pollution sources and chemical components, particularly in middle-income and low-income countries. Considering the coexistence of a diabetes epidemic and severe air pollution worldwide, the positive associations observed in our study and previous studies indicate an urgent need for governments to develop effective prevention and intervention policies, to protect people from the adverse health effects of ambient air pollution.

air pollution concentrations were reported to be much higher.[13,14] Evidence also showed that east Asian populations (eg, China) were different in their risk profile for diabetes compared with American and European populations.[15,16] Furthermore, in most published studies, the prevalence, incidence, and mortality for diabetes were based on self-reports, administrative databases, or hospital discharge records, and these were not validated by doctors. Also, glucose and insulin homoeostatic markers (such as glucose and insulin concentrations) were only reported in a few studies,[8,17,18] which were often based on a single fasting measure. Therefore, further studies are needed to assess the associations between air pollution and diabetes, particularly in developing countries.

China has had a concerning rise in the incidence of diabetes during the past two decades.[19] Meanwhile, air pollution has become one of the most serious environmental health issues in China.[2] Given the grave public health implications of the diabetes epidemic and the ubiquitous nature of ambient air pollution, exploration of the association between air pollution and diabetes in China is crucial for development of preventive measures. Therefore, our main aim was to estimate the associations of long-term exposure to six air pollutants with diabetes prevalence and glucose-homoeostasis markers, using data from the 33 Communities Chinese Health Study (33 CCHS). The comprehensive panel of measured air pollutants and glucose-homoeostasis markers in the 33 CCHS, as well as its large sample size, provide a unique opportunity to determine associations between air pollution and diabetes.

Methods

Study population

The study population was from the 33 CCHS study, which was a large cross-sectional investigation carried out

between April 1 and Dec 31, 2009, in Liaoning province, northeastern China. Air pollution was severe in this province due to the high emissions from fossil fuel combustion and biomass burning, topographic features, and climate.[20] Additionally, the prevalence of cardiovascular diseases (such as stroke and coronary heart disease) and their risk factors (such as hypertension, diabetes, and dyslipidaemia) were reported to be high in Liaoning province.[21] The 33 CCHS study design and eligibility criteria have been previously described.[22] Briefly, using a random number generator, we adopted a four-stage, stratified and cluster sampling strategy to randomly recruit study participants. First, to maximise the inter-city and intra-city gradients of interest, and to minimise the correlation between pollutants, three (Shenyang, Anshan, and Jinzhou) out of 14 cities in Liaoning province were selected on the basis of 2006–08 air pollution measurements. Second, we randomly selected three communities, from each city district (five cities in Shenyang, three cities in Anshan, and three cities in Jinzhou) located within 1 km of the single district air quality monitoring station, generating a total of 33 communities. Third, we randomly identified 700–1000 households from each study community. Finally, we randomly selected one participant, aged 18–74 years, who had lived there for at least 5 years. Patients with cancer, people with severe diseases, and pregnant women were excluded.

We collected sociodemographics, socioeconomic status, behavioural habits, and other health information through completion of a standardised questionnaire. Sociodemographic information consisted of age, sex, nationality (Han or other), and home address. Variables on socioeconomic status included occupation (officials, workers, farmers, or others), household annual income (≤¥5000, ¥5001–10 000, ¥10 001–30 000, or ≥¥30 000), and highest educational attainment (no school, primary school [7–12 years old], middle school [13–15 years old], junior college, or higher [≥16 years old]). Behavioural variables included current smoking (yes or no), alcohol consumption (yes or no), exercise status (yes or no), low calorie and low fat controlled diet (yes or no), and sugar-sweetened soft drink consumption (≤1 day per week, 2–4 days per week, or ≥5 days per week). Other health information included current health problems and family history of diabetes.

We invited a total of 28 830 participants on the basis of the sampling frame. However, 3985 individuals did not complete the study questionnaire, leaving 24 845 participants, and reaching an overall response of 86·2%. We obtained written informed consent from all participants before data and sample collection. All study procedures and protocols were reviewed and approved by the Human Studies Committee of Sun Yat-sen University.

Glucose-homoeostasis markers and diabetes assessment

After an overnight fast, a 75 g oral glucose tolerance test was done in the morning on participants whose venous blood samples were available, with duplicate measurements of plasma glucose concentrations, and insulin concentrations at 0 h and 2 h after glucose intake. Blood bioassays were done in the institutional laboratory at local community health service centres. Plasma glucose concentrations were analysed by an enzymatic colorimetric method, with a hexokinase photometric assay. Insulin concentrations were determined via immunoassay. We estimated insulin resistance by the homoeostasis model assessment of insulin resistance index (HOMA-IR) as

$$\frac{[(\text{fasting insulin } (\mu U/L) \times \text{fasting glucose } (\text{mmol}/L)]}{22{\cdot}5}$$

β-cell function was indicated by the homoeostasis model assessment of β-cell function (HOMA-B) as[23]

$$\frac{[20 \times \text{fasting insulin } (\mu U/L)]}{(\text{fasting glucose } (\text{mmol}/L) - 3{\cdot}5}$$

We established the main definition of diabetes on the recommendations of the American Diabetes Association,[24] as fasting glucose of 7·0 mmol/L or higher or 2 h glucose of 11·1 mmol/L or higher, or intake of any antidiabetic medication (both insulin and oral antidiabetic drugs), or both. As 9368 individuals refused to provide a blood sample, glucose-homoeostasis markers were measured in a subsample of 15 477 participants (62·3% of the participants in 33 CCHS).

Air pollution assessment

We have previously described the exposure assessment in detail[22] and a detailed explanation can also be found in the appendix. Briefly, concentrations of particulate matter with an aerodynamic diameter of 10 μm or less (PM_{10}), sulphur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) from 11 air monitoring stations were assigned to each study participant for the evaluation of pollution exposure. In each

See Online for appendix

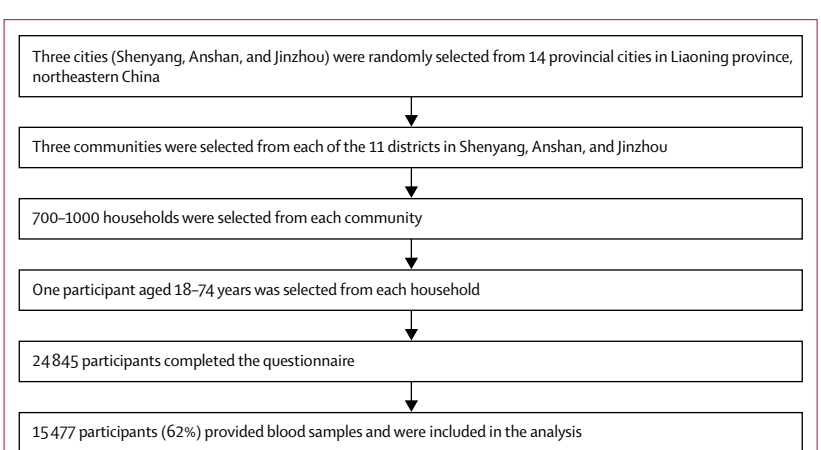

Figure: **Sampling process for the 33 Communities Chinese Health Study**

	Participants without diabetes (n=13 783)	Participants with diabetes (n=1694)	Total (n=15 477)	p value
Age (years)	43·9 (13·4)	53·7 (10·8)	45·0 (13·5)	<0·0001
Sex	..	..	..	<0·0001
Male	7070 (51·3%)	1086 (64·1%)	8156 (52·7%)	..
Female	6713 (48·7%)	608 (35·9%)	7321 (47·3%)	..
Nationality	..	..	..	0·0065
Han	12 936 (93·9%)	1618 (95·5%)	14 554 (94·0%)	..
Other	847 (6·1%)	76 (4·5%)	923 (6·0%)	..
Education	..	..	..	<0·0001
Junior college or higher (≥16 years)	3359 (24·4%)	220 (13·0%)	3579 (23·1%)	..
Middle school (13–15 years)	8479 (61·5%)	1075 (63·5%)	9554 (61·7%)	..
Primary school (7–12 years)	1564 (11·3%)	299 (17·7%)	1863 (12·0%)	..
No school	381 (2·8%)	100 (5·9%)	481 (3·1%)	..
Career	..	..	..	<0·0001
Official	2578 (18·7%)	322 (19·0%)	2900 (18·7%)	..
Worker	4432 (32·2%)	564 (33·3%)	4996 (32·3%)	..
Farmer	1907 (13·8%)	303 (17·9%)	2210 (14·3%)	..
Other	4866 (35·3%)	505 (29·8%)	5371 (34·7%)	..
Family income per year	..	..	..	<0·0001
≤¥5000	1016 (7·4%)	151 (8·9%)	1167 (7·5%)	..
¥5001–10 000	1657 (12·0%)	320 (18·9%)	1977 (12·8%)	..
¥10 001–30 000	7078 (51·4%)	791 (46·7%)	7869 (50·8%)	..
≥¥30 000	4032 (29·3%)	432 (25·5%)	4464 (28·8%)	..
Smoking status	..	..	..	0·1419
Non-smoker	9677 (70·2%)	1160 (68·5%)	10 837 (70·0%)	..
Smoker	4106 (29·8%)	534 (31·5%)	4640 (30·0%)	..
Alcohol consumption	..	..	..	0·0140
Non-consumer	10 432 (75·7%)	1236 (73·0%)	11 668 (75·4%)	..
Consumer	3351 (24·3%)	458 (27·0%)	3809 (24·6%)	..
Exercise (≥180 min/week)	..	..	..	<0·0001
No	9516 (69·0%)	1029 (60·7%)	10 545 (68·1%)	..
Yes	4267 (31·0%)	665 (39·3%)	4932 (31·9%)	..
Low calorie and low fat controlled diet	..	..	..	<0·0001
No	10 461 (75·9%)	1155 (68·2%)	11 616 (75·1%)	..
Yes	3322 (24·1%)	539 (31·8%)	3861 (24·9%)	..
Sugar-sweetened soft drink consumption (day per week)	..	..	..	<0·0001
≤1	8059 (58·5%)	683 (40·3%)	8742 (56·5%)	..
2–4	670 (4·9%)	234 (13·8%)	904 (5·8%)	..
≥5	5054 (36·7%)	777 (45·9%)	5831 (37·7%)	..
Body-mass index (kg/m²)	..	..	..	<0·0001
≤25	8546 (62·0%)	674 (39·8%)	9220 (59·6%)	..
26–30	4536 (32·9%)	882 (52·1%)	5418 (35·0%)	..
≥30	701 (5·1%)	138 (8·2%)	839 (5·4%)	..
Family history of diabetes	..	..	..	<0·0001
No	11 898 (86·3%)	1258 (74·3%)	13 156 (85·0%)	..
Yes	1885 (13·7%)	436 (25·7%)	2321 (15·0%)	..

Data are mean (SD) or n (%).

Table 1: **Characteristics of the study participants in the 11 districts of three Chinese cities**

district, one available air monitoring station (within 1 km distance from the study participants' residential address) generated ambient concentrations of PM_{10}, SO_2, NO_2, and O_3. These monitoring stations were mandated to be away from main traffic roads, industry sources, or residential sources of emissions, thus reflecting the background pollution concentration in a city. The monitoring strictly adhered to the procedures set by the State Environmental Protection Administration of China.[25] We calculated the measurements of PM_{10} using β-attenuation, SO_2 using ultraviolet fluorescence, NO_2 using chemiluminescence, and O_3 using ultraviolet photometry. These measurements were continuously collected and reported every hour. In the present study, we used 3 year (2006–08) average measurements of PM_{10}, SO_2, NO_2, and O_3 in the estimation of the long-term exposure.

We predicted daily PM with an aerodynamic diameter of 1 μm or less (PM_1) and 2·5 μm or less ($PM_{2·5}$) concentrations for the 33 communities during 2006–08 using ground-monitored data, satellite remote sensing, meteorology, and land use information, which was detailed in our previous paper.[26] Briefly, two types of Moderate Resolution Imaging Spectroradiometer, dark target and deep blue, collected aerosol optical depth data and were combined. A spatiotemporal model was developed to link ground-monitored PM_1 and $PM_{2·5}$ data (appendix) with aerosol optical depth data and other spatial and temporal predictors (eg, urban cover, forest cover, weather data, and calendar month). The results of 10-fold cross-validation showed that, R^2 and root-mean-square error for monthly PM_1 prediction were 71% and 13·0 μg/m³, respectively, and the R^2 and root-mean-squared error for monthly $PM_{2·5}$ prediction were 75% and 15·08 μg/m³, respectively. We assigned data from the 33 study communities to each study participant for the predicted concentrations of PM_1 and $PM_{2·5}$.

Statistical analysis

We used the Shapiro-Wilk test to assess the data for normality and the Bartlett test for unequal variance to assess homogeneity. We tested the contrasts in baseline characteristics in the diabetes and non-diabetes groups using Student's *t* test and χ^2 test. We also compared characteristics for study participants to those participants who were excluded, to evaluate the differences. We determined the association between diabetes and ambient air pollutants using a two-level binary logistic regression model in which participants were the first-level units and districts were the second-level units, as described previously[22] and as detailed in the appendix.

We applied linear regression models to assess the associations of ambient air pollutants with concentrations of fasting glucose, 2 h glucose, fasting insulin, 2 h insulin, HOMA-IR, and HOMA-B. In our main analysis, PM_1, $PM_{2·5}$, PM_{10}, SO_2, NO_2, and O_3 concentrations were included as the primary exposure variables. Analyses were

also adjusted for a priori selected confounders, which included age, sex, body-mass index (BMI), education, family income, smoking, alcohol consumption, exercise, low calorie and low fat controlled diet, sugar-sweetened soft drink consumption, family history of diabetes, and district (or community). Among them, district or community was incorporated as random effects, and the remaining variables were included as fixed effects. No values were missing for any participants. Because of high or moderate correlations among air pollutants (appendix), only single-pollutant models were used in our study to avoid collinearity. Furthermore, we did subgroup analyses according to sex, age, education, smoking, and BMI, and a cross-product term was added into the linear regression models to assess the significance of the interaction. To evaluate the robustness of our estimates, we did additional sensitivity analyses using different definitions of diabetes and by excluding participants with prediabetes. We did all analyses using the GLIMMIX procedure in SAS 9.2 with an a priori α level of 0·05 to determine statistical significance.

Role of the funding source

The funders had no role in the study design, data collection, analysis, interpretation, or writing of the report. The corresponding authors had full access to all the study data and had final responsibility for the decision to submit for publication.

Results

We recruited 15 477 (62·3%) participants to the study (figure, table 1). The population was composed of adult residents with an average age of 45·0 years (SD 13·5) and a roughly equal sex distribution. The prevalence of diabetes was 10·9%. All sociodemographic and behavioural variables differed between participants with diabetes and without diabetes, with the exception of smoking status. Additionally, we observed that the distribution of the baseline characteristics was similar between the participants and those individuals who were excluded from the present study (appendix).

Regarding the annual average concentrations of the six air pollutants in the 11 residential districts, the concentrations varied greatly across the different districts, with ranges of 50–82 μg/m³ for PM_1, 64–104 μg/m³ for $PM_{2·5}$, 93–145 μg/m³ for PM_{10}, 36–78 μg/m³ for SO_2, 27–45 μg/m³ for NO_2, and 27–71 μg/m³ for O_3 (table 2). The $PM_{2·5}$, PM_{10}, and SO_2 concentrations in all 11 districts were higher than WHO guidelines.[27]

For diabetes per IQR increase in pollutants, we observed positive associations of diabetes with all six pollutants (table 3). The associations appeared to be strongest for PM_{10} and NO_2. Additional sensitivity analyses based on six different definitions for diabetes generated similar odds ratios (ORs) for all pollutants (table 4). After we excluded participants with prediabetes and those individuals taking antidiabetic drugs simultaneously, the estimated ORs did not change significantly for the six air pollutants (appendix). Stratified analysis by sex, education level, and smoking status showed that the increase in diabetes risk seemed to be greater for men, individuals who were less educated, and current smokers (except for the associated risks among women for higher PM_1 and $PM_{2·5}$; table 3, appendix). When stratified by age and BMI, significant associations for all the six pollutants were mainly apparent for the young age group (<50 years of age) and for those individuals who were overweight or obese (table 3, appendix).

We further estimated the associations of air pollutants with glucose and insulin homoeostasis markers (table 5). All six air pollutants were associated with concentrations of fasting glucose (0·04–0·09 mmol/L), 2 h glucose (0·10–0·19 mmol/L), fasting insulin (0·16–0·54 μU/L), 2 h insulin (0·70–2·74 μU/L), and HOMA-IR (0·05–0·24), although not statistically significant for most air pollutants with concentrations of fasting insulin and HOMA-IR (table 5). The associations between air pollutants and glucose and insulin homoeostasis markers appeared to be generally stronger for PM_{10} and NO_2 (table 5). We additionally excluded participants with prediabetes in a sensitivity analysis and the outcomes were similar (appendix). Stratified analyses showed that the effect estimates were generally greater in men, younger participants, those individuals who were less educated, current smokers, and participants who were overweight or

	PM_1 (μg/m³)*	$PM_{2·5}$ (μg/m³)*	PM_{10} (μg/m³)†	SO_2 (μg/m³)†	NO_2 (μg/m³)†	O_3 (μg/m³)†
Shenyang						
District 1	74	95	133	51	32	49
District 2	78	99	123	44	36	34
District 3	74	94	116	42	42	42
District 4	82	104	145	78	45	65
District 5	75	96	135	58	38	63
Anshan						
District 1	63	73	126	78	31	71
District 2	63	73	137	64	40	58
District 3	62	73	120	48	32	50
Jinzhou						
District 1	53	66	104	39	29	30
District 2	50	64	110	36	33	41
District 3	53	67	93	47	27	27
Mean (SD)	66·0 (10·7)	82·0 (14·8)	123·1 (14·6)	54·4 (14·3)	35·3 (4·5)	49·4 (14·1)
Median (IQR)‡	62 (61–76)	73 (71–97)	123 (116–135)	48 (44–64)	33 (31–40)	50 (41–63)
WHO guideline§	None	10	20	20	40	100
% of >WHO guideline	None	100	100	100	18·2	0

PM_1=particle with aerodynamic diameter of 1 μm or less. $PM_{2·5}$=particle with aerodynamic diameter of 2·5 μm or less. PM_{10}=particle with aerodynamic diameter of 10 μm or less. SO_2=sulphur dioxide. NO_2=nitrogen dioxide. O_3=ozone. *Based on values from 33 communities. †Based on values from 11 districts. ‡IQR was computed by subtracting the 25th percentile from the 75th percentile. For each pollutant, IQR was 15 μg/m³ for PM_1, 26 μg/m³ for $PM_{2·5}$, 19 μg/m³ for PM_{10}, 20 μg/m³ for SO_2, 9 μg/m³ for NO_2, and 22 μg/m³ for O_3. §WHO air quality guidelines (2005).[27]

Table 2: **Distributions of 3-year average concentrations of air pollutants in 11 districts**

obese (appendix). However, there was an exception in that increases in 2 h glucose concentrations were generally greater in non-smokers than in smokers (appendix).

Discussion

To our knowledge, this was the largest epidemiological study to date to investigate the associations of ambient air pollution with diabetes in a developing country and to explore the diabetogenic effects of PM_1. We found positive associations of long-term exposure to air pollution with diabetes prevalence and concentrations of glucose and insulin. Additionally, we observed that the diabetogenic effects of PM_{10} and NO_2 appeared to be stronger than other air pollutants and that younger participants and overweight or obese participants appeared to be more susceptible to the diabetogenic effects of air pollutants than the older subgroups and participants with normal bodyweight.

Several previous human studies have explored the impact of ambient air pollutants on diabetes risk, and most of them have been summarised in reviews.[3,4,9] Despite some reported negative and null results, the overall meta-estimates support a positive association.[3,4,9] For example, Eze and colleagues included 13 studies originating from North America and Europe in their meta-analysis[3] and reported that the risk of type 2 diabetes increased by 10% and 8% per 10 μg/m³ increase in $PM_{2·5}$ and NO_2, respectively. The meta-analysis[9] by Janghorbani and colleagues reviewed 17 studies and found significant associations between diabetes and six air pollutants (PM_{10}, $PM_{2·5}$, NO_2, O_3, sulphate, and SO_2) with pooled risk ratios or mortality risk ratios ranging from 1·01/10 μg/m³ to 1·07/10 μg/m³ increases in air pollutants. In accordance with the results from these two meta-analyses, we also detected significant associations, the magnitudes of which were similar (except NO_2). Furthermore, we observed stronger diabetogenic effects for PM_{10} and NO_2, pollutants which more closely reflect local sources, thus suggesting that local pollution could have stronger effects. Overall, our results provide additional evidence in support of the diabetogenic effects of air pollution.

Elevated fasting and 2 h post-loaded glucose concentrations are both important indicators for diabetes. Several human epidemiological studies[8,17] have explored the effects of air pollutants on glucose concentrations and results generally suggested positive associations. For example, among 1023 participants from Taiwan, fasting glucose concentrations were positively associated with long-term exposure to PM_{10}, $PM_{2·5}$, NO_2 and O_3.[17] A study of 11 847 Chinese adults showed that an IQR (reported as 41·1 μg/m³) increase in long-term exposure to $PM_{2·5}$ was significantly associated with a 0·26 mmol/L increase in fasting glucose.[8] We detected significant 0·04–0·09 mmol/L increases in fasting glucose concentrations per IQR increment of air pollutants in this study, suggesting the possibility of chronic effects from air pollution on fasting glucose concentrations. Furthermore, we observed robust associations between higher air pollution concentrations and higher 2 h glucose concentrations. However, the only previously published study on this topic suggested that 2 h glucose concentrations were not significantly associated with short-term or long-term exposures to air pollutants.[28]

Reduced insulin sensitivity is a hallmark of diabetes. We detected associations between air pollutants and insulin concentrations and HOMA-IR, particularly for

	Total (n=15 477)	Men (n=8156)	Women (n=7321)	<50 years (n=9921)	≥50 years (n=5556)
PM_1	1·13 (1·04–1·22)	1·12 (1·02–1·23)	1·15 (1·01–1·32)	1·20 (1·11–1·35)	1·08 (0·99–1·17)
$PM_{2·5}$	1·14 (1·03–1·25)	1·12 (0·99–1·26)	1·18 (1·00–1·39)	1·23 (1·11–1·36)	1·07 (0·97–1·18)
PM_{10}	1·20 (1·12–1·28)	1·21 (1·10–1·33)	1·15 (1·01–1·30)	1·35 (1·21–1·51)	1·05 (0·96–1·15)
SO_2	1·12 (1·04–1·21)	1·14 (0·99–1·31)	1·09 (0·93–1·29)	1·25 (1·12–1·39)	1·02 (0·92–1·13)
NO_2	1·22 (1·12–1·33)	1·28 (1·11–1·47)	1·10 (0·94–1·30)	1·40 (1·23–1·60)	1·03 (0·92–1·16)
O_3	1·14 (1·05–1·25)	1·19 (1·02–1·39)	1·06 (0·89–1·27)	1·32 (1·16–1·51)	1·02 (0·91–1·14)

Data are OR (95% CI). OR was scaled to the IQR (computed by subtracting the 25th percentile from the 75th percentile and defined as the unit for OR) for each pollutant (15 μg/m³ for PM_1, 26 μg/m³ for $PM_{2·5}$, 19 μg/m³ for PM_{10}, 20 μg/m³ for SO_2, 9 μg/m³ for NO_2, and 22 μg/m³ for O_3). Data were adjusted for age, sex, body-mass index, education, family income, smoking, alcohol consumption, exercise, low calorie and low fat controlled diet, sugar-sweetened soft drink consumption, family history of diabetes, and district. OR=odds ratio. PM_1=particle with aerodynamic diameter of 1 μm or less. $PM_{2·5}$=particle with aerodynamic diameter of 2·5 μm or less. PM_{10}=particle with aerodynamic diameter of 10 μm or less. SO_2=sulphur dioxide. NO_2=nitrogen dioxide. O_3=ozone.

Table 3: **Adjusted OR for diabetes associated with an IQR increase of ambient air pollutants**

	PM_1	$PM_{2·5}$	PM_{10}	SO_2	NO_2	O_3
Antidiabetic medicine use	1·19 (1·05–1·35)	1·23 (1·05–1·45)	1·13 (1·02–1·26)	1·07 (0·96–1·20)	1·21 (1·06–1·37)	1·10 (0·97–1·25)
Fasting glucose ≥7 mmol/L	1·13 (1·03–1·24)	1·15 (1·02–1·29)	1·16 (1·06–1·26)	1·12 (1·02–1·22)	1·17 (1·05–1·30)	1·11 (1·00–1·24)
2 h glucose ≥11·1 mmol/L	1·12 (1·04–1·22)	1·13 (1·02–1·25)	1·20 (1·12–1·30)	1·13 (1·04–1·22)	1·23 (1·12–1·35)	1·15 (1·05–1·26)
Fasting glucose ≥7mmol/L or antidiabetic medicine use, or both	1·13 (1·03–1·23)	1·14 (1·02–1·28)	1·15 (1·06–1·24)	1·10 (1·01–1·20)	1·15 (1·04–1·27)	1·11 (1·01–1·23)
2 h glucose ≥11·1 mmol/L or antidiabetic medicine use, or both	1·13 (1·04–1·22)	1·13 (1·03–1·25)	1·22 (1·14–1·31)	1·16 (1·07–1·25)	1·26 (1·14–1·37)	1·17 (1·08–1·28)
Fasting glucose ≥7mmol/L or 2 h glucose ≥11·1 mmol/L, or both	1·13 (1·05–1·23)	1·15 (1·04–1·26)	1·20 (1·12–1·29)	1·12 (1·04–1·21)	1·23 (1·12–1·34)	1·14 (1·05–1·25)
Fasting glucose ≥7 mmol/L or 2 h glucose ≥11·1 mmol/L, or both, and antidiabetic medicine use (main definition in present study)	1·13 (1·04–1·22)	1·14 (1·03–1·25)	1·20 (1·12–1·28)	1·12 (1·04–1·21)	1·22 (1·12–1·33)	1·14 (1·05–1·25)

Data are OR (95% CI). OR was scaled to the IQR (computed by subtracting the 25th percentile from the 75th percentile and defined as the unit for OR) for each pollutant (15 μg/m³ for PM_1, 26 μg/m³ for $PM_{2·5}$, 19 μg/m³ for PM_{10}, 20 μg/m³ for SO_2, 9 μg/m³ for NO_2, and 22 μg/m³ for O_3). Data were adjusted for age, sex, body-mass index, education, family income, smoking, alcohol consumption, exercise, low calorie and low fat controlled diet, sugar-sweetened soft drink consumption, family history of diabetes, and district. PM_1=particle with aerodynamic diameter of 1 μm or less. $PM_{2·5}$=particle with aerodynamic diameter of 2·5 μm or less. PM_{10}=particle with aerodynamic diameter of 10 μm or less. SO_2=sulphur dioxide. NO_2=nitrogen dioxide. O_3=ozone. OR=odds ratio.

Table 4: **Associations of ambient air pollutants with different definitions for diabetes**

	Total (n=15 477)	Men (n=8156)	Women (n=7321)	$p_{interaction}$	<50 years (n=9921)	≥50 years (n=5556)	$p_{interaction}$
Fasting glucose (mmol/L)							
PM_1	0·07 (0·04 to 0·10)	0·07 (0·03 to 0·12)	0·06 (0·01 to 0·10)	0·857	0·06 (0·02 to 0·09)	0·07 (0·01 to 0·13)	0·279
$PM_{2·5}$	0·08 (0·04 to 0·12)	0·08 (0·03 to 0·14)	0·07 (0·01 to 0·13)	0·779	0·06 (0·02 to 0·11)	0·09 (0·02 to 0·17)	0·382
PM_{10}	0·08 (0·05 to 0·11)	0·11 (0·07 to 0·15)	0·04 (–0·01 to 0·08)	0·013	0·10 (0·07 to 0·14)	0·03 (–0·03 to 0·08)	0·017
SO_2	0·04 (0·01 to 0·07)	0·10 (0·05 to 0·14)	–0·04 (–0·08 to 0·01)	<0·0001	0·08 (0·04 to 0·11)	–0·03 (–0·09 to 0·03)	0·0024
NO_2	0·09 (0·06 to 0·13)	0·16 (0·11 to 0·21)	0·01 (–0·04 to 0·06)	0·0001	0·12 (0·08–0·16)	0·02 (–0·05 to 0·09)	0·0081
O_3	0·04 (0·01 to 0·07)	0·10 (0·05 to 0·15)	–0·04 (–0·09 to 0·01)	0·0001	0·08 (0·04 to 0·12)	–0·03 (–0·10 to 0·03)	0·0022
2 h glucose (mmol/L)							
PM_1	0·10 (0·02 to 0·17)	0·01 (–0·10 to 0·11)	0·20 (0·08 to 0·31)	0·0024	0·07 (–0·02 to 0·15)	0·15 (0·00 to 0·29)	0·111
$PM_{2·5}$	0·11 (0·01 to 0·20)	0·00 (–0·13 to 0·13)	0·22 (0·08 to 0·36)	0·012	0·06 (–0·05 to 0·16)	0·19 (0·01 to 0·37)	0·207
PM_{10}	0·19 (0·12 to 0·26)	0·11 (0·02 to 0·21)	0·25 (0·15 to 0·34)	0·018	0·22 (0·15 to 0·30)	0·11 (–0·02 to 0·24)	0·091
SO_2	0·14 (0·07 to 0·21)	0·14 (0·04 to 0·24)	0·12 (0·02 to 0·23)	0·908	0·18 (0·10 to 0·27)	0·04 (–0·10 to 0·19)	0·093
NO_2	0·18 (0·09–0·26)	0·13 (0·01 to 0·25)	0·20 (0·08 to 0·32)	0·242	0·20 (0·11 to 0·30)	0·08 (–0·09 to 0·25)	0·141
O_3	0·13 (0·05 to 0·22)	0·12 (0·00 to 0·23)	0·12 (0·01 to 0·24)	0·730	0·20 (0·11 to 0·29)	0·02 (–0·14 to 0·18)	0·033
Fasting insulin (μU/L)							
PM_1	0·30 (–0·10 to 0·68)	0·73 (0·33 to 1·14)	–0·25 (–0·98 to 0·47)	0·113	0·43 (–0·09 to 0·95)	0·02 (–0·57 to 0·60)	0·843
$PM_{2·5}$	0·29 (–0·19 to 0·78)	0·85 (0·35 to 1·36)	0·34 (–1·23 to 0·53)	0·012	0·46 (–0·18 to 1·10)	–0·03 (–0·75 to 0·70)	0·335
PM_{10}	0·27 (–0·08 to 0·62)	0·84 (0·47 to 1·21)	–0·33 (–0·96 to 0·29)	0·0010	0·32 (–0·15 to 0·79)	0·19 (–0·32 to 0·70)	0·888
SO_2	0·16 (–0·23 to 0·54)	0·40 (0·00 to 0·81)	–0·10 (–0·79 to 0·60)	0·192	0·28 (–0·23 to 0·78)	–0·09 (–0·69 to 0·50)	0·542
NO_2	0·54 (0·09 to 0·99)	1·26 (0·78 to 1·74)	–0·19 (–0·97 to 0·60)	0·0014	0·65 (0·06 to 1·24)	0·32 (–0·35 to 0·99)	0·564
O_3	0·24 (–0·20 to 0·67)	0·69 (0·23 to 1·15)	–0·23 (–0·99 to 0·54)	0·035	0·28 (–0·29 to 0·85)	0·14 (–0·49 to 0·78)	0·942
2 h insulin (μU/L)							
PM_1	0·78 (–0·38 to 1·94)	1·40 (–0·26 to 3·06)	–0·55 (–2·15 to 1·06)	0·754	0·88 (–0·67 to 2·42)	0·28 (–1·39 to 1·95)	0·521
$PM_{2·5}$	0·70 (–0·74 to 2·13)	1·62 (–0·47 to 3·70)	–1·06 (–3·01 to 0·88)	0·105	0·88 (–1·03 to 2·79)	0·01 (–2·06 to 2·09)	0·604
PM_{10}	1·66 (0·63 to 2·70)	1·92 (0·38 to 2·70)	1·19 (–0·19 to 3·45)	0·529	1·77 (0·37 to 3·16)	1·27 (–0·19 to 2·73)	0·914
SO_2	1·91 (0·76 to 3·06)	2·21 (0·53 to 3·89)	1·42 (–0·13 to 2·96)	0·435	2·21 (0·70 to 3·72)	1·18 (–0·51 to 2·88)	0·734
NO_2	2·74 (1·42 to 4·06)	2·86 (0·87 to 4·85)	2·51 (0·77 to 4·24)	0·787	2·91 (1·16 to 4·67)	2·00 (0·08 to 3·92)	0·744
O_3	1·43 (0·15 to 2·71)	1·41 (–0·48 to 3·31)	1·39 (–0·30 to 3·08)	0·921	1·65 (–0·07 to 3·36)	0·93 (–0·88 to 2·74)	0·871
HOMA-IR							
PM_1	0·12 (–0·06 to 0·29)	0·28 (–0·01 to 0·57)	–0·05 (–0·22 to 0·11)	0·231	0·14 (0·03 to 0·26)	0·04 (–0·39 to 0·48)	0·938
$PM_{2·5}$	0·13 (–0·09 to 0·34)	0·33 (–0·03 to 0·69)	–0·07 (–0·27 to 0·12)	0·071	0·15 (0·01 to 0·29)	0·04 (–0·50 to 0·58)	0·586
PM_{10}	0·13 (–0·02 to 0·29)	0·34 (0·08 to 0·61)	–0·05 (–0·19 to 0·10)	0·010	0·15 (0·05 to 0·26)	0·11 (–0·27 to 0·49)	0·989
SO_2	0·05 (–0·12 to 0·22)	0·13 (–0·16 to 0·41)	–0·02 (–0·17 to 0·14)	0·327	0·13 (0·02 to 0·25)	–0·08 (–0·52 to 0·36)	0·379
NO_2	0·24 (0·04 to 0·44)	0·52 (0·18 to 0·87)	–0·01 (–0·19 to 0·17)	0·0087	0·25 (0·12 to 0·38)	0·22 (–0·28 to 0·72)	0·913
O_3	0·09 (–0·10 to 0·28)	0·26 (–0·07 to 0·58)	–0·05 (–0·22 to 0·12)	0·098	0·13 (0·01 to 0·26)	0·05 (–0·43 to 0·52)	0·822
HOMA-B							
PM_1	–4·19 (–13·64 to 5·27)	–1·17 (–14·42 to 12·09)	–8·80 (–22·36 to 4·77)	0·366	–3·10 (–13·69 to 7·48)	–4·94 (–23·28 to 13·40)	0·624
$PM_{2·5}$	–4·79 (–16·49 to 6·92)	–1·16 (–17·79 to 15·46)	–9·91 (–26·36 to 6·54)	0·450	–3·00 (–16·07 to –22·25)	–7·10 (–29·90 to 15·70)	0·609
PM_{10}	–8·11 (–16·56 to 0·34)	–1·97 (–14·28 to 10·34)	–15·32 (–27·00 to –3·65)	0·120	–10·24 (–19·79 to –0·68)	–2·14 (–18·22 to 13·94)	0·395
SO_2	–3·62 (–13·00 to 5·76)	–0·65 (–14·04 to 12·74)	–7·48 (–20·54 to 5·57)	0·427	–9·52 (–19·86 to 0·81)	10·24 (–8·39 to 28·88)	0·048
NO_2	–6·09 (–16·88 to 4·69)	1·82 (–14·05 to 17·69)	–14·91 (–29·55 to –0·27)	0·139	–7·21 (–19·23 to 4·81)	0·09 (–20·99 to 21·16)	0·681
O_3	–6·72 (–14·14 to 3·70)	–3·24 (–18·41 to 11·93)	–10·95 (–25·23 to 3·33)	0·460	–10·64 (–22·38 to 1·10)	2·32 (–17·59 to 22·24)	0·258

Data are β (95% CI). β indicates partial regression coefficient. Estimates were scaled to the IQR (computed by subtracting the 25th percentile from the 75th percentile and defined as the unit for OR) for each pollutant (15 μg/m³ for PM_1, 26 μg/m³ for $PM_{2·5}$, 19 μg/m³ for PM_{10}, 20 μg/m³ for SO_2, 9 μg/m³ for NO_2, and 22 μg/m³ for O_3). Data were adjusted for age, sex, body-mass index, education, family income, smoking, alcohol consumption, exercise, low calorie and low fat controlled diet, sugar-sweetened soft drink consumption, family history of diabetes, and district. PM_1=particle with aerodynamic diameter of 1 μm or less. $PM_{2·5}$=particle with aerodynamic diameter of 2·5 μm or less. PM_{10}=particle with aerodynamic diameter of 10 μm or less. SO_2=sulphur dioxide. NO_2=nitrogen dioxide. O_3=ozone. HOMA-IR=homoeostasis model assessment of insulin resistance index. HOMA-B=homoeostasis model assessment of β-cell function. OR=odds ratio.

Table 5: **Adjusted estimates for measurements per IQR increase of ambient air pollutants**

NO_2 in the present study. Compared with our analysis, other epidemiological studies[18,28,29] have reported positive associations between air pollutants (eg, NO_2, NO_x, PM_{10}, and $PM_{2·5}$) and insulin resistance. However, many of these studies estimated only short-term effects or focused only on children, which limited a direct comparison to our findings. At present, we have identified only two studies[28,30] that examined the association between

long-term air pollution exposure and insulin resistance. Wolf and colleagues'[30] study reported on associations of long-term exposure to each of six standard ambient air pollutants (PM_{10}, PM_{coarse}, $PM_{2·5}$, $PM_{absorbance}$, NO_2, and NO_x) with higher HOMA-IR (% change 13·2–21·2) and fasting insulin concentrations (13·2–20·0), except for $PM_{2·5}$. Chen and colleagues'[28] study reported that higher long-term exposure to $PM_{2·5}$ was associated with higher HOMA-IR in 1023 Mexican Americans. The findings from these two studies are similar to our results.

Dysfunction of pancreatic β-cells is also an important defect in the pathogenesis of diabetes. We observed no associations between the six air pollutants and HOMA-B, although effect estimates were in a negative direction as expected. Our findings were in line with the study by Chen and colleagues[28] in which a disposition index was used to reflect β-cell function instead of HOMA-B, and no correlations were found with $PM_{2·5}$ or NO_2. In general, their findings, along with our results, did not indicate whether air pollution exposure had a hazardous effect on β-cell function, and thus more studies are needed to verify the present findings.

Although the exact biological mechanisms whereby air pollutants cause diabetes are not entirely clear, several plausible mechanisms have been proposed. One hypothesis is that air pollutants could lead to greater oxidative stress and adipose tissue inflammation, which further results in endoplasmic reticulum stress, insulin signalling abnormalities, and apoptosis. These processes might affect insulin resistance and metabolic disturbance.[6,7] Air pollutants could also cause autonomic nervous system imbalance and, as a result, directly affect insulin resistance.[5,8] The positive associations of air pollutants with insulin and glucose concentrations in our study support these mechanisms and provide solid support for the diabetic effects of air pollutants.

In an age-stratified analysis, we observed stronger effects for the younger subgroup (<50 years), in contrast to previous studies[31] that reported more effects in older groups. One plausible explanation for the discrepancy with our results might be that ageing individuals have a decreased sensitivity to autonomic and sympathetic nervous systems stimuli,[32] which has been reported to be closely related to diabetes and insulin resistance.[33] Additionally, older subjects are more likely to use antidiabetes medication, which might attenuate the glycaemic effect of air pollutants.[30] It is also possible that other diabetes risk factors, accumulating with advancing age, might obscure the effect of air pollution in ageing participants. The time-activity patterns between older and younger age groups might also have a key role in the observed difference. Ageing individuals are more likely to spend more time at home, thus they might be less affected by ambient air pollution.[34] Furthermore, because of survivor effects, if they were likely to have diabetes, younger people would develop diabetes before they advanced in age. With the exception of these survivor effects, young people are generally at low risk for diabetes because of competing risks, and thus one risk factor (eg, air pollution) might have a greater relative impact compared with the same risk factor in an older person who might have several other risk factors.

The associations of air pollution with diabetes and several glucose-homoeostasis markers were stronger among overweight or obese participants compared with normal weight participants in a stratified analysis. These findings are generally consistent with the scarce epidemiological evidence that explores the effect of BMI on air pollution and diabetes.[6,8,35,36] For example, a large Chinese cross-sectional study[8] reported that the prevalence ratio of diabetes was higher in participants with higher BMI than in those participants with lower BMI. Another large Chinese cross-sectional study[35] reported similar results, in that associations for SO_2, NO_2, and PM_{10}, were stronger in overweight people than in underweight people. Additionally, in a cohort study[36] of 3607 Germans, Weinmayr and colleagues identified stronger effects for long-term PM_{10} and $PM_{2·5}$ exposure among individuals with a BMI above 30 kg/m². Although the underlying mechanism for the effect of BMI on the diabetogenic effects of air pollutants is not well understood, the role of systemic inflammation has emerged as a candidate.[37] Evidence shows that both air pollution and overweight or obesity are associated with higher amounts of systemic inflammation.[5,37] Therefore, overweight or obese individuals could be more vulnerable to additional stressors, such as air pollution, that act through the inflammation pathway.

The associations for air pollutants with diabetes were also generally stronger in men than in women, for those individuals who were less educated rather than more highly educated, and for current smokers than for former or non-smokers, in stratified analyses. Although these results raise the possibility of vulnerable subpopulations, these findings should be interpreted with caution, as stratum-specific effect estimates differed only modestly and 95% CIs overlapped. Additionally, several previous studies[3,6,8,35,36,38] have explored the modifications of sex, education (or socioeconomic status), and smoking status on the association of air pollution with diabetes, but the results of these previous studies were inconsistent.

The present study has several strengths. First, to our knowledge no other studies have comprehensively explored the associations of long-term exposure to ambient air pollutants with diabetes prevalence, along with glucose-homoeostasis markers, particularly 2 h glucose and 2 h insulin concentrations and β-cell function. Second, in addition to commonly studied air pollutants such as $PM_{2·5}$, PM_{10}, SO_2, NO_2, and O_3, we evaluated the diabetogenic effects of PM_1, which contributes novel epidemiological knowledge on the hazardous effects of ambient air pollution. Third, we implemented oral glucose tolerance testing, a more accurate approach than the frequently used

fasting plasma glucose test.[39] In addition, we adopted a strict definition of diabetes, according to the recommendations of the American Diabetes Association. Finally, our analysis was based on a large, population-based sample of adults who lived in urban areas recruited from 33 communities in three Chinese cities, to ensure sufficient statistical power to detect modest effects with high precision.

This study also has several limitations. First, air pollutants assessments were based on data from central study district monitoring stations (PM_{10}, SO_2, NO_2, and O_3) or communities ($PM_{2.5}$ and PM_1). We only included 11 air monitoring stations and 33 communities, and these stations mainly reflected the background air pollution concentrations. Thus, our measurements are susceptible to misclassification. Second, although we adjusted for many potential confounders, including district or community as random effects in our model, the observed associations were likely to have been affected in part by residual confounding from underlying differences between districts or communities (including economic status, health-care condition, available green space, and temperature). Third, we used a cross-sectional study design, in which glucose-homoeostasis markers were measured at a single timepoint, and prevalent diabetes cases were captured. Thus, we were unable to establish a clear temporal association between exposure and outcomes, despite having used estimates of air pollutant concentrations from 2006–08 as exposures, and having measured glucose-homoeostasis markers in 2009 as outcomes. Fourth, a selection bias is possible, because not all participants from 33 CCHS consented to provide blood samples. However, we found that the participants who were excluded were similar to the participants who were included, with respect to demographic and social characteristics, and thus any effect is likely to have been modest. Fifth, we adopted a questionnaire to compile information related to exposure such as smoking, drinking, physical activity, and dietary habits; thus, recall bias cannot be avoided and misclassification might have occurred. Additionally, these factors are temporally unstable and might have been modified by participants with diabetes as non-pharmacological approaches to control disease progression. However, when we removed these variables from the model, the main findings did not change significantly (appendix). Moreover, we included two diet variables and so we were unable to capture and adjust some potentially important items, such as fruit and vegetables. Sixth, data for some potential confounders, such as wind, temperature, noise, green space, and indoor air pollution, were also not collected. Seventh, we assessed associations for exposure to six individual air pollutants with diabetes and six glucose-homoeostasis markers as outcomes, leading to a large number of statistical tests. This assessment might have inflated the amount of type I errors, leading to false-positive results, or results by chance. However, to maximise our ability to detect and confirm modest effects by future investigations, we did not correct for multiple testing. Eighth, air pollution is very severe in China, thus our results might not be generalisable to populations from high-income countries, such as North America and parts of Europe, where the air quality is relatively good. However, our results provide valuable references for many middle-income countries, such as India, where air quality is decreasing with rapid industrialisation and the increase in motor-driven vehicles.[40] Finally, high to moderate correlations among air pollutants restricted our ability to assess the health effects of multiple pollutants.

In summary, our study indicates that exposure to PM_1, $PM_{2.5}$, PM_{10}, SO_2, NO_2, and O_3 might adversely affect glucose homoeostasis, including elevated concentrations of glucose and insulin, and consequently increases the risk of developing diabetes in China. Furthermore, young individuals and those individuals who are overweight or obese might be more vulnerable to the diabetogenic effects of air pollution. Given the coexistence of high air pollution and a diabetes pandemic in China, as in other middle-income countries, our results are of significance to public health. If the associations observed in our study are causal, policy makers should prioritise the rapid development and implementation of air quality improvement interventions to decrease air pollution-induced risks of diabetes. However, considering the limitations of our study, future prospective studies with more precise air pollution measurement, which also incorporate effects of wind and temperature, are warranted to confirm our findings.

Contributors

B-YY and G-HD analysed the data and wrote the manuscript. ZQ, SL, GC, MSB, ME, KWS, JH, IM, S-QW, DC, HM, D-HC, YL, MK, AL, K-KL, X-WZ, and L-WH contributed to the design of the study and reviewed and edited the manuscript. YG and G-HD interpreted the data, conceived the research, provided overall supervision, and reviewed and edited the manuscript. G-HD is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of interests

We declare no competing interests.

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