Ecotoxicology and Environmental Safety 274 (2024) 116212

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: www.elsevier.com/locate/ecoenv

Unveiling causal connections: Long-term particulate matter exposure and type 2 diabetes mellitus mortality in Southern China

Tong Guo [a,1], Xi Cheng [a,1], Jing Wei [b,1], Shirui Chen [a], Yuqin Zhang [a], Shao Lin [c], Xinlei Deng [d], Yanji Qu [e], Ziqiang Lin [f], Shimin Chen [a], Zhiqiang Li [a], Jie Sun [a], Xudan Chen [a], Zhibing Chen [a], Xurui Sun [a], Dan Chen [a], Xingling Ruan [a], Shaniduhaxi Tuohetasen [a], Xinyue Li [a], Man Zhang [g], Yongqing Sun [h], Shuming Zhu [a], Xueqing Deng [a], Yuantao Hao [i,*], Qinlong Jing [j,*], Wangjian Zhang [a,*]

[a] Department of Medical Statistics, School of Public Health & Research Center for Health Information & Sun Yat-sen Global Health Institute, Sun Yat-sen University, Guangzhou, Guangdong 510080, China
[b] Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, College Park, Maryland 20740, USA
[c] Department of Environmental Health Sciences, University at Albany, State University of New York, Rensselaer, NY, USA
[d] Epidemiology Branch, National Institute of Environmental Health Sciences, NIH, Research Triangle Park, NC, USA
[e] Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangdong, China
[f] Department of Public Health and Preventive Medicine, School of Medicine, Jinan University, Guangzhou, Guangdong, China
[g] Department of nosocomial infection management, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, China
[h] Department of Ultrasound, Beijing Obstetrics and Gynecology Hospital, Capital Medical University. Beijing Maternal and Child Health Care Hospital, Beijing 100026, China
[i] Peking University Center for Public Health and Epidemic Preparedness & Response, Peking, China
[j] Guangzhou Municipal Health Commission, Guangzhou, China

ARTICLE INFO

Edited by Dr. Renjie Chen

Keywords:
T2DM
long-term PM exposure
causal modeling
large cohort
effect modification

ABSTRACT

Evidence of the potential causal links between long-term exposure to particulate matters (PM, i.e., PM_1, $PM_{2.5}$, and $PM_{1-2.5}$) and T2DM mortality based on large cohorts is limited. In contrast, the existing evidence usually suffers from inherent bias with the traditional association assessment.

A prospective cohort of 580,757 participants in the southern region of China were recruited during 2009 and 2015 and followed up through December 2020. PM exposure at each residential address was estimated by linking to the well-established high-resolution simulation dataset. Hazard ratios (*HRs*) were calculated using time-varying marginal structural Cox models, an established causal inference approach, after adjusting for potential confounders.

During follow-up, a total of 717 subjects died from T2DM. For every 1 $\mu g/m^3$ increase in $PM_{2.5}$, the adjusted *HRs* and 95% confidence interval (*CI*) for T2DM mortality was 1.036 (1.019–1.053). Similarly, for every 1 $\mu g/m^3$ increase in PM_1 and $PM_{1-2.5}$, the adjusted *HRs* and 95% *CIs* were 1.032 (1.003–1.062) and 1.085 (1.054–1.116), respectively. Additionally, we observed a generally more pronounced impact among individuals with lower levels of education or lower residential greenness which as measured by the Normalized Difference Vegetation Index (NDVI). We identified substantial interactions between NDVI and PM_1 (*P*-interaction = 0.003), NDVI and $PM_{2.5}$ (*P*-interaction = 0.019), as well as education levels and PM_1 (*P*-interaction = 0.049).

List of abbreviations: BMI, body mass index; CI, confidence interval; DAG, directed acyclic graph; GEE, generalized estimating equation; GEE-IPW, inverse probability weight weighting by GPS using a generalized estimating equation; GPS, generalized propensity scores; HBV, Hepatitis B virus; HR, hazard ratio; IPW, inverse probability weight; LM, linear model; LM-IPW, inverse probability weight weighting by GPS using a linear model; ML, machine learning; ML-IPW, inverse probability weight weighting by GPS using a machine learning; NDVI, normalized difference vegetation index; PM, particulate matter; PM_1, particulate matter with an aerodynamic diameter $\leq$ 1 μm; $PM_{2.5}$, particulate matter with an aerodynamic diameter $\leq$ 2.5 μm; $PM_{1-2.5}$, particulate matter with an aerodynamic diameter greater than 1 μm and less than 2.5 μm; SD, standard deviation; T2DM, type 2 diabetes mellitus.

* Corresponding authors.
E-mail addresses: haoyt@bjmu.edu.cn (Y. Hao), jingqinlong@126.com (Q. Jing), zhangwj227@mail.sysu.edu.cn (W. Zhang).

[1] The authors contributed equally to this work.

https://doi.org/10.1016/j.ecoenv.2024.116212
Received 7 December 2023; Received in revised form 9 March 2024; Accepted 11 March 2024
Available online 14 March 2024

The study emphasizes the need to consider environmental and socio-economic factors in strategies to reduce T2DM mortality. We found that PM_1, $PM_{2.5}$, and $PM_{1-2.5}$ heighten the peril of T2DM mortality, with education and green space exposure roles in modifying it.

1. Introduction

Diabetes mellitus is a highly prevalent chronic disease worldwide, with a heavy burden of morbidity and mortality (Yuan et al., 2018). In 2021, it was responsible for 6.7 million deaths globally, resulting in one death every five seconds, with China accounting for 1.4 million of these deaths (Li et al., 2021b). Of all the diabetes cases, more than 90% fall into the category of type 2 diabetes mellitus (T2DM) (Zheng et al., 2018). In 2019, T2DM accounted for 2.6% of global deaths (Collaborators, 2020), including 170,000 from China, highlighting its significance as a severe public health issue, particularly within the Chinese population.

Known risk factors for T2DM incidence include genetics, aging, high body mass index (BMI), and poor dietary habits (Burkart et al., 2022; Eze et al., 2015). Contemporary studies also suggested that air pollution might significantly contribute to its development and prognosis (Liu et al., 2019a; Liu et al., 2019c). Immune system activation, inflammation within the central nervous system, endoplasmic reticulum stress, and oxidative stress represent some of the molecular factors contributing to the health impacts of air pollution (Gorini et al., 2021). Particulate matter (PM) is one of the dominant pollutants in the ambient air. In China, $PM_{2.5}$ was listed as the fourth major cause of disease burden, responsible for more than 0.9 million premature deaths yearly (Forouzanfar et al., 2015). Recent research has delved into possible links between exposure to PM and the onset of diabetes. For example, in a meta-analysis which encompassed 17 cohort studies, it was reported that the risk of T2DM mortality increased by a 10% (95% confidence interval (*CI*): 4-17%) for every 10 $\mu g/m^3$ increment in $PM_{2.5}$ and 11% (95% *CI*: 0-22%) for PM_{10}, respectively (Yang et al., 2020a). Similarly, a Chinese cohort study demonstrated a 27% increase in the risk of T2DM-related mortality with every 10 $\mu g/m^3$ increment in annual $PM_{2.5}$ concentration (95% *CI*: 17-38%) (Lao et al., 2019). These existing studies provide important insights regarding the detrimental effects of PM exposure on the mortality risk of T2DM (Chilian-Herrera et al., 2021; Liu et al., 2019b).

However, there are several challenges with the existing research evidence. First, existing studies focus on regularly monitored particles such as $PM_{2.5}$ and PM_{10} while ignoring the effect of smaller particles represented by PM_1. It has been reported that PM_1 poses a greater risk on human health compared to coarser PMs (e.g., $PM_{2.5}$ and PM_{10}), in part due to its more significant proportion of surface area to volume and an increased concentration of harmful chemical components (Chen et al., 2017; Hu et al., 2018). The smaller size of PM_1 particles enables them to penetrate more deeply into the lungs (Zhang et al., 2022), subsequently triggering a more significant adverse health effect. Secondly, evidence from prospective cohorts is still limited in China (Yang et al., 2020a). Much of the available evidence comes from Western countries, which may not apply to China, where the concentration and composition of particles and population vulnerability differ from those in Western countries.

In contrast, existing studies on PM_1 and T2DM in China tend to be cross-sectional, while high-quality cohort evidence is still lacking (Ao et al., 2022; Yang et al., 2018a). In addition, the available evidence was usually based on association assessment, which was susceptible to many confounding factors not included in the model (Higbee et al., 2020). Recently, causal inference methods have been devised to enhance control over confounding factors by simulating randomized controlled trials using observational data (Robins et al., 2000a; VanderWeele et al., 2016). However, reliable evidence based on causal inference is even more scarce.

Therefore, utilizing a community-based cohort comprising 0.6 million individuals from South China, this study was designed to employ casual inference to assess the potential connection of long-term PM_1, $PM_{2.5}$, and $PM_{1-2.5}$ exposure with T2DM mortality. In addition, we also evaluated the potential moderating impacts of multiple individual factors.

2. Methods

2.1. Study design and population

Our research stemmed from a project initially focused on studying the prevalence of Hepatitis B virus (HBV) and individuals infected with HBV in the southern regions of China, focusing on developing community-based preventive strategies. This longitudinal study was part of the Major Projects of Science Research for the 11th (2006–2010) and 12th (2012–2017) five-year plans of China (Ruan et al., 2019; Wang et al., 2023). We carried out the current study in Guangzhou, one of China's most densely populated areas, covering an area of $>$ 7000 square kilometers due to the availability of outcome data. We enrolled 654,115 participants from 35 communities randomly selected in the area from January 2009 to December 2015. Information on the existing diabetes condition was not adequately collected for the cohort. We did not exclude the participants who already had diabetes at baseline. Therefore, our study tended to capture the mortality impact of air pollution, which included both the risk of healthy individuals developing diabetes and subsequently dying during follow-up and the risk of people with diabetes at baseline having their condition exacerbated and dying. Figure S1 shows the flow chart for screening participants. We administered in-person questionnaire surveys and comprehensive health checks following standard protocols for each participant. The study received ethics clearance from the Human Ethics Committee at Sun Yat-sen University, and all participants gave written, voluntary agreements before taking part.

2.2. Outcome definition and covariates

Mortality data were sourced from the Death Registry of the Guangzhou Center for Disease Control and Prevention (GCDC). The cause of death would be confirmed by GCDC by cross-checking patient history and conducting a verbal autopsy if the information was not reported by medical centers. The causes of death were categorized following the ICD-10, the 10th revision of the International Classification of Diseases. This study mainly focused on T2DM mortality (ICD-10: E11) and the duration from enrollment to the specific event under consideration (or the last day of follow-up, 12/31/2020, or administrative censoring whichever came first). We gathered data regarding demographic attributes and lifestyle elements, including gender, age, ethnicity, marital status, education, medical insurance, smoking and drinking habits, exercise frequency, and BMI.

2.3. Evaluation of PM and associated environmental exposures

We retrieved the yearly PM_1, $PM_{2.5}$, and PM_{10} levels from the China High Air Pollutants (CHAP) dataset at a spatial resolution of 1 km^2 (Bai et al., 2022). These concentrations were determined using validated spatial-temporal models, which exhibited predictive solid performance. The models achieved R^2 values of 77% and 90% and root mean square errors of 14.6 $\mu g/m^3$ and 10.01 $\mu g/m^3$ for the daily calculations of PM_1 and $PM_{2.5}$, respectively. Detailed descriptions of the data simulation

process can be found in previous studies(Bai et al., 2022). Additionally, we included $PM_{1-2.5}$, calculated as the difference between $PM_{2.5}$ and PM_1 concentrations, with the exact spatial resolution of 1 km. The yearly mean PM levels were allocated to every participant based on their residential location, serving as the main in our study. The distribution of air pollutants conformed to a normal distribution as indicated by the Shapiro-Wilk test. Therefore, Pearson's correlation coefficients were computed to evaluate the correlation between the concentration of air pollutants. As previous research suggests an association between greenness, air pollution, and T2DM (Tsai et al., 2020), we also considered the potential confounding influence of greenness evaluated via the normalized difference vegetation index (NDVI). The NDVI data, obtained from the Moderate Resolution Imaging Spectroradiometer (MODIS) for the study period (2009–2020), was assigned to each participant within a 500-meter radial buffer centered around their residence.

2.4. Statistical analysis

We utilized a marginal structural Cox proportional hazards model to evaluate the association between long-term PM exposure and the risk of T2DM mortality, with hazard ratios (*HR*s) and their 95% confidence intervals (*CI*s) being calculated. Considering time-dependent variables, including yearly PM concentrations and NDVI, we specifically configured the models with time-varying covariates. We identified confounders using a directed acyclic graph (DAG) (Fig. 1), including demographic factors (age, gender, ethnic group, marital status, medical insurance, and education level), physical activity, and NDVI. Our dataset has a longitudinal structure, where each row represents the data of one participant at a specific follow-up point in time, and a participant with several years of follow-up means several rows of data for that participant. The primary parameters in our models include the *HR*s for PM exposure (β_1), baseline covariates (β_2), and time-varying potential confounders (β_3).

The fundamental idea behind marginal structural Cox models is to construct a weighted pseudo-population to mimic a randomized controlled trial, ensuring that confounding effects are evenly distributed among exposure groups. As a result, the effect estimates are considered to reflect causal links. This procedure is performed by developing a generalized propensity score (GPS) and an inverse probability weight (IPW) following the methods described in previous studies (Austin, 2011). While traditional propensity scores are limited to dichotomous exposures, the GPS could accommodate multi-categorical and continuous exposure variables. IPW is a rigorous approach to establishing causality and is gaining popularity in observational studies (Robins et al., 2000b). We included IPW in our model to mitigate confounding effects and ensure a balanced distribution of covariates using a pseudo-population created by IPW, considering baseline and time-varying influences in the causal analysis framework. In this study, we generated weights based on three different methods (i.e., a linear model (LM), a generalized estimating equation (GEE), or a gradient-boosting machine learning approach (ML) (Nalluri et al., 2020). Subsequently, we assessed covariate balance within the weighted pseudo-population using the average absolute correlation (AC) (Wu et al., 2020). Values <0.1 indicated a high-fidelity level of mimicking randomized experiments. The GEE-IPWs method which achieved the optimal balance of confounders, as depicted in Figure S2, were employed in the final mode to estimate *HR* for T2DM mortality outcomes per 1 $\mu g/m^3$ increase in PM concentrations. We also fitted traditional Cox models using yearly PM concentrations and NDVI as the time-varying variables.

We constructed four models: (1) Model 0, which served as the crude model under the conventional Cox proportional hazards model. (2) Model 1, which adjusted for age and sex in addition to the variables in Model 0. 3) Model 2, which further included adjustments for ethnicity, education level, marital status, medical insurance, exercise frequency, smoking status, and NDVI (500 m) based on model 1. 4) Model 3: refitting Model 2 with the marginal structural Cox proportional hazards model. The results of Model 3 were reported as the main results in the present study.

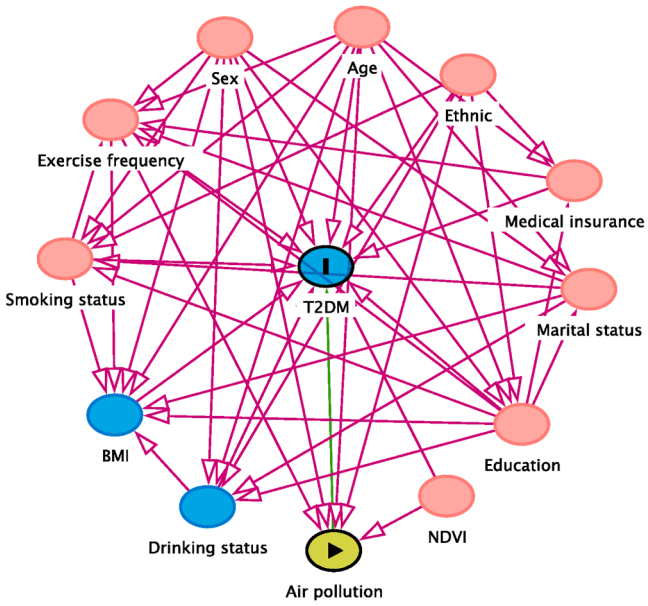

Fig. 1. Directed acyclic graph (DAG) for the association between air pollution and T2DM, created with the help of dagitty.net The DAG is a graphic representation of the assumption of how variables are causally related. Combined with the backdoor criterion, DAG can be used to determine the minimally sufficient confounders set that can eliminate all potential confounding. The green node at the bottom is the exposure variable, and the blue node with I in the center is the outcome variable. The pink nodes represent observed confounders, and the other blue nodes are ancestors of the outcome. The directed edges represent the causal relationship between pairs of variables, which start from the cause and end at the outcome. The green and pink lines represent the causal and biasing paths, respectively. More details on DAG can be found elsewhere. According to the final DAG and back door criteria, the minimal sufficient set of confounders includes sex (men or women), age (years), ethnicity (Han or Minority), education level (illiterate or semiliterate, elementary school, middle school, high school or college or above), marital status (never married, married, widowed or divorce), medical insurance (for urban workers, for urban residents, the new rural cooperative medical insurance, others), exercise frequency (very low, low, moderate, high), smoking status (never, ever or current), alcohol assumption (never, once a week, occasionally, daily).

Findings obtained using the final model (model 3) were also stratified by age (<65 years, ≥ 65 years), sex, marital status (unmarried, married, widowed/divorced), education level (elementary school and below, middle and high school, college degree or above), exercise frequency (never, moderate, every day), smoking status (never, ever, current), and NDVI. To address missing data in confounding variables, we employed multiple imputations by chained equations (MICE), an established method of disappeared imputations widely used in the literature (van Buuren, 2007; White et al., 2011). This approach sequentially imputes missing values based on other variables, creating multiple complete datasets for robust Analysis. We first constructed a predictive model for each variable with missing values using a subset of the entire data, considering the nonlinear relationships and interactions between the variables. We interpolated the variables in the order of their missing rates and expected dependencies. The variable with the highest missing rate, ethnicity, is filled first, and then the other variables are filled in turn. While this method assumes data are missing at random, we conducted sensitivity analyses to assess the impact of imputation on our results, ensuring the reliability of our findings (Van Buuren and Groothuis-Oudshoorn, 2011), shown in Table S2.

2.5. Sensitivity analyses

We performed multiple sensitivity analyses to assess the stability of our findings. First, we included additional explanatory variables of BMI and alcohol consumption, respectively, in the primary Analysis to account for the impact of these individual variables, even though they were not included in the minimal set of variables identified in the DAG plot. Second, we employed varying buffer sizes (250 m and 1000 m) to define NDVI exposure. Third, to assess the impact of missing data imputation, we conducted the Analysis exclusively on the complete subset before imputation. Last but not least, we calculated the E-values to assess the resilience of our results in the face of potential unmeasured confounders. The E-value is calculated as: E-value= $\sqrt{RR \times (RR-1)}+1$, where RR is the risk ratio for the association of interest. The E-value indicates the minimum strength of association an unmeasured confounder would need with both the exposure and the outcome to explain away the observed effect fully. A higher E-value suggests that our results are robust, requiring a substantial effect size of an unmeasured confounder to negate the observed association. This Analysis enhances our understanding of the robustness of our results against potential unmeasured confounding (Trinquart et al., 2019). We performed all statistical analyses using R (version 4.1.3, https://www.r-project.org/). Statistical significance was defined as a two-sided P-value < 0.05.

3. Result

Among the 580,757 participants [mean (SD) age = 48.3 (17.6) years; 275,676 (47.5%) men], a total of 717 mortality cases of T2DM were documented during an average follow-up time of 8.2 years (SD = 1.72 years). Summary statistics and participant demographics are presented in Table 1. Participants who experienced mortality due to T2DM were generally of advanced age (70.9 years old vs. 48.3 years old, P<0.01), the Han Chinese (99.7% vs. 0.3%, P<0.01), without a college degree (95.0% vs. 5.0%, P<0.01), married (78.2% vs. 21.8%, P<0.01), urban workers (63.0% vs. 37.0%, P<0.01), never smokers (82.6% vs. 17.4%, P<0.01), or having greater BMI (22.5 kg/m^2 vs. 22.1 kg/m^2, P<0.01). During the follow-up period, PM concentrations increased in 2013 and decreased over the years (Figure S3). The mean levels were 19.564 (SD: 4.482) μg/m^3 for PM_1, 38.753 (SD: 8.71) μg/m^3 for $PM_{2.5}$, and 19.189 (SD: 4.523) μg/m^3 for $PM_{1–2.5}$ (Table 2). Besides, Table S1 shows details of the entire dataset and the complete subset.

Long-term exposure to PM_1, $PM_{2.5}$, and $PM_{1–2.5}$ was significantly associated with an elevated risk of T2DM (Fig. 2). Specifically, we found a 3.6% (95% *CI*, 1.9–5.3%) rise in the risk of T2DM mortality following every 1 μg/m^3 rise in the concentration of $PM_{2.5}$. The same increment in the concentrations of PM_1 and $PM_{1–2.5}$ also corresponded to a significant elevation in the risk of T2DM death, with *HR*s of 1.032 (95% *CI*, 1.003–1.062) and 1.085 (95% *CI*, 1.054–1.116), respectively.

Fig. 3 illustrates the interaction effects of PM exposures with the demographic and lifestyle variables on the mortality risk of T2DM. We observed a statistically significant interaction between the education levels and PM_1 exposure ($P = 0.049$). Meanwhile, we also observed interactions between the NDVI and both exposures to PM_1 ($P = 0.003$) and $PM_{2.5}$ ($P = 0.019$). We did not monitor a statistically significant interaction between demographic variables and $PM_{1–2.5}$ exposure.

Specifically, subgroup analyses revealed that individuals with a lower education level experienced a significantly increased risk of T2DM mortality following PM_1 exposure (*HR*, 1.058; 95% *CI*, 1.009–1.107). In contrast, higher education presented a protective effect on the risk of T2DM mortality (*HR*, 0.915; 95% *CI*, 0.832–0.998). Although the impact of $PM_{2.5}$ and $PM_{1–2.5}$ was not statistically significant across different education levels, the trends were consistent with those observed for PM_1.

We observed different risk patterns across the NDVI quartiles following PM_1 and $PM_{2.5}$ exposures. Specifically, the impact of PM_1 exposure tended to be more pronounced among the residents in the first (*HR*, 1.014; 95% *CI*, 0.965–1.065) quartile of NDVI relative to the rest of participants (*HR* ranges 0.952–1.010), although the estimates in each stratum were not statistically significant. For $PM_{2.5}$, we detected a considerable effect estimate among the participants in the first (*HR*, 1.037; 95% *CI*, 1.010–1.065) quartile of NDVI but not in other quartiles, displaying a significant disparity in the vulnerability of participants across the NDVI levels. For $PM_{1–2.5}$ exposure, we observed the most pronounced effect estimates in participants within the lowest NDVI quartile (*HR*, 1.095; 95% *CI*, 1.048–1.146). As the NDVI quartile increased, the magnitude of the effect estimates diminished, though the interactions did not achieve statistical significance.

However, the impact of PM exposures showed a consistent pattern across the subgroups stratified by other demographic and lifestyle factors, including age, sex, marital status, physical activity, and smoking status.

Sensitivity analyses showed similar effect estimates when we incorporated additional factors such as BMI and alcohol consumption, which were not identified in the DAG. The results remained similar when we

Table 1
Descriptive characteristics of the participants according to the presence of mortality due to T2DM.

	Died from T2DM	Others	*P*
N	717	580040	
Demographics			
Age (mean (SD), years)	70.898(12.234)	48.297 (17.533)	<0.001
Sex= Men (%)	334 (46.583)	275342 (47.469)	0.671
Ethnic = Minority (%)	2 (0.279)	10951 (1.888)	<0.001
Education level (%)			<0.001
Illiterate or semiliterate	39 (5.439)	6564 (1.132)	
Elementary school	219 (30.544)	67028 (11.556)	
Middle school	203 (28.312)	131191 (22.618)	
High school	220 (30.683)	266247 (45.901)	
College or above	36 (5.021)	109010 (18.794)	
Marital status (%)			<0.001
Never Married	40 (5.579)	108384 (18.686)	
Married	561 (78.243)	447577 (77.163)	
Widowed	101 (14.086)	17161 (2.959)	
Divorce	15 (2.092)	6918 (1.193)	
Medical insurance (%)			<0.001
For urban workers	452 (63.040)	353944 (61.021)	
For urban residents	227 (31.660)	163986 (28.271)	
The new rural cooperative medical insurance	3 (0.418)	6436 (1.110)	
Others	35 (4.881)	55674 (9.598)	
Lifestyle behaviors			
Exercise frequency (%)			<0.001
Very low	386 (53.835)	321839 (55.486)	
Low	101 (14.086)	73002 (12.586)	
Moderate	73 (10.181)	68762 (11.855)	
High	157 (21.897)	116437 (20.074)	
Smoking status (%)			<0.001
Never	592 (82.566)	504793 (87.027)	
Ever	30 (4.184)	6686 (1.153)	
Current	95 (13.250)	68561 (11.820)	
Alcohol consumption (%)			0.07
Never	629 (87.727)	514576 (88.714)	
Once a week	15 (2.092)	18853 (3.250)	
Occasionally	8 (1.116)	5836 (1.006)	
Daily	65 (9.066)	40775 (7.030)	
Clinical characteristics			
BMI (mean (SD), kg/m^2)	22.510 (2.549)	22.067 (2.452)	<0.001
Land-use variables			
NDVI (mean (SD))	0.214 (0.038)	0.214 (0.040)	0.247

Abbreviations: SD, standard deviation; PM_1, particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 μm; $PM_{1–2.5}$, particulate matter with an aerodynamic diameter greater than 1μm and less than 2.5 μm; BMI, body mass index; NDVI, normalized difference vegetation index.

Table 2
Descriptive characteristics for PMs at individuals' residential addresses of cohort baseline and Pearson's correlation coefficients between them.

Pollutants	Mean±SD	Interquartile range	Min	Max	Pearson's correlation coefficients (ρ)		
					PM_1	$PM_{2.5}$	$PM_{1–2.5}$
PM_1, μg/m^3	19.56 ± 4.48	6.72	10.70	30.63	1	-	-
$PM_{2.5}$, μg/m^3	38.75 ± 8.71	13.3	22	57.2	0.97	1	-
$PM_{1–2.5}$, μg/m^3	19.19 ± 4.52	6.87	9.10	28.59	0.87	0.97	1

Abbreviations: SD, standard deviation; PM_1, particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 μm; $PM_{1–2.5}$, particulate matter with an aerodynamic diameter greater than 1μm and less than 2.5 μm.

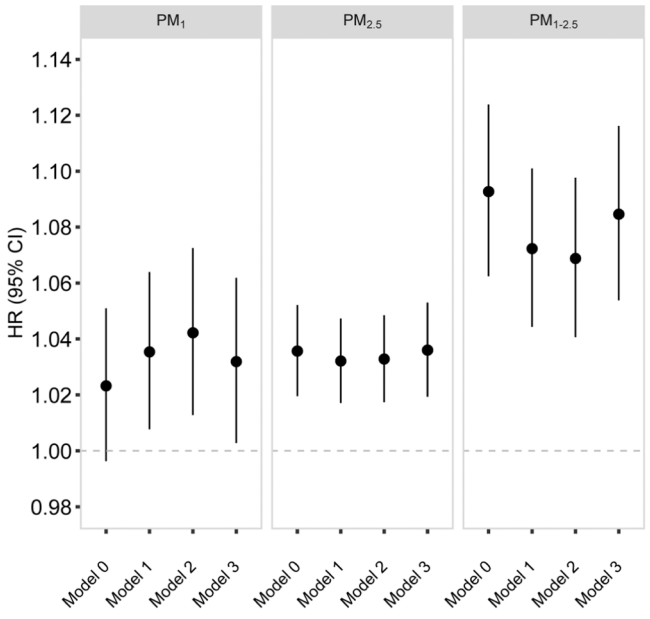

Fig. 2. *HRs* (95% *CIs*) of the mortality risk due to T2DM with each 1 μg/m^3 increase in exposure to PMs. Abbreviations: Model 0: A model with only air pollution exposure. Model 1: A model with air pollution exposure, age, and gender; Model 2: A model with air pollution exposure and all potential confounders. Model 3: A model with air pollution exposure and potential confounders using IPWs with a generalized estimating equation. *HR*, hazard ratio; PM_1, particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 μm; $PM_{1–2.5}$, particulate matter with an aerodynamic diameter greater than 1μm and less than 2.5 μm.

used the complete subset or adjusted the radius of NDVI buffers to 250 m and 1000 m (Table S2). The findings remained robust with three distinct marginal structural Cox models employing IPWs based on LM, ML, or GEE (Figure S4). Our conclusions were considered relatively sturdy against the potential unmeasured confounding bias, as indicated by the E values (Table S3).

4. Discussion

This large-scale cohort study investigated the potential causal associations between prolonged exposure to different PMs and T2DM mortality among over 600,000 individuals in South China. We found that prolonged exposure to PM heightened the risk of T2DM-related mortality in the study population. Additionally, individuals with lower educational levels or lower NDVI tended to have higher effect estimates. This study provides the first prospective evidence of a causal link between prolonged exposure to PM and T2DM mortality in China, with potential implications for environmental and social policies to protect human health.

4.1. PM exposure and T2DM mortality outcomes

Our findings reveal that $PM_{2.5}$, PM_1, and $PM_{1–2.5}$ increases are linked to higher risks of T2DM mortality. Although previous research on the relationship of PM_1 and $PM_{1–2.5}$ with diabetes is limited, the existing evidence for $PM_{2.5}$ aligns with our discoveries (Eze et al., 2015; Rajagopalan and Brook, 2012; Yang et al., 2020a). To illustrate, a meta-analysis in 2020 revealed that every 10 μg/m^3 elevation in $PM_{2.5}$ showed a connection with a 6–49% rise in the risk of diabetes-related mortality by summarizing 11 cohort studies (Yang et al., 2020a). Compared to previous research(Yang et al., 2018b), our findings suggest a higher estimated mortality risk associated with exposure to $PM_{1–2.5}$ and $PM_{2.5}$. This discrepancy may be partly attributed to the distinct characteristics of air pollutants. Our study was conducted in the heart of the Pearl River Delta region, characterized by its dense manufacturing and chemical industries and significant traffic congestion, all of which contribute to the emission of pollutants with heightened toxicity levels. For instance, a comprehensive study across China indicated that the mortality risk of PM exposure in Guangzhou was approximately 2–3 times higher than that reported in other cities, highlighting the increased particle toxicity in this region (Chen et al., 2012). Moreover, the favorable climate in Guangzhou encourages a higher rate of outdoor activities among its residents, potentially leading to greater exposure to ambient air pollution.

Notably, the effect of PM_1 on T2DM mortality appears to be less pronounced than that of $PM_{2.5}$ and $PM_{1–2.5}$. One study showed that for every 1 μg/m^3 increase in $PM_{2.5}$ and PM_1, the odds of developing type 2 diabetes increased by 6.8% and 4.0%, respectively. This difference may stem from their different sources and chemical compositions, which may influence the relative impact of different particle sizes on the development of T2DM (Liang et al., 2019). $PM_{1–2.5}$ had the most significant effect associated with T2DM in this study, but it represents the transition region between the fine and coarse particle size ranges (Kozákovác et al., 2018). Due to this property, $PM_{1–2.5}$ may contain particles from both modes. A longitudinal study from China showed that a 10 μg/m^3 increase in PM_1 and $PM_{1–2.5}$ was associated with 1.11 (95% *CI*: 1.01–1.23) and 1.23 (95% *CI*: 1.06–1.43) times higher dyslipidemia risk, respectively (Hu et al., 2023). According to an analysis in the Czech Republic, $PM_{1–2.5}$ was influenced by the source of the coarse particle fraction during all events (Kozákovác et al., 2018), which may account for its most significant effect on outcome. At the same time, further studies on its chemical composition or toxic substances are still needed for follow-up.

Understanding the potential mechanisms underlying these associations is crucial. Several mechanisms have been proposed to explain how PM exposure influences T2DM mortality. Oxidative stress, induced by PM exposure, may contribute to cellular damage and disrupt insulin signaling pathways, leading to insulin resistance (Rajagopalan and Brook, 2012). Inflammation, triggered by PM exposure, is a known factor in the development of T2DM and may exacerbate metabolic dysfunction (Li et al., 2019; Rajagopalan and Brook, 2012). Furthermore, the size of particulate matter is a critical factor influencing its health implications. Smaller particles, notably PM_1, exhibit a greater surface area relative to their volume than larger particles such as $PM_{2.5}$. This characteristic enhances their potential for detrimental interactions

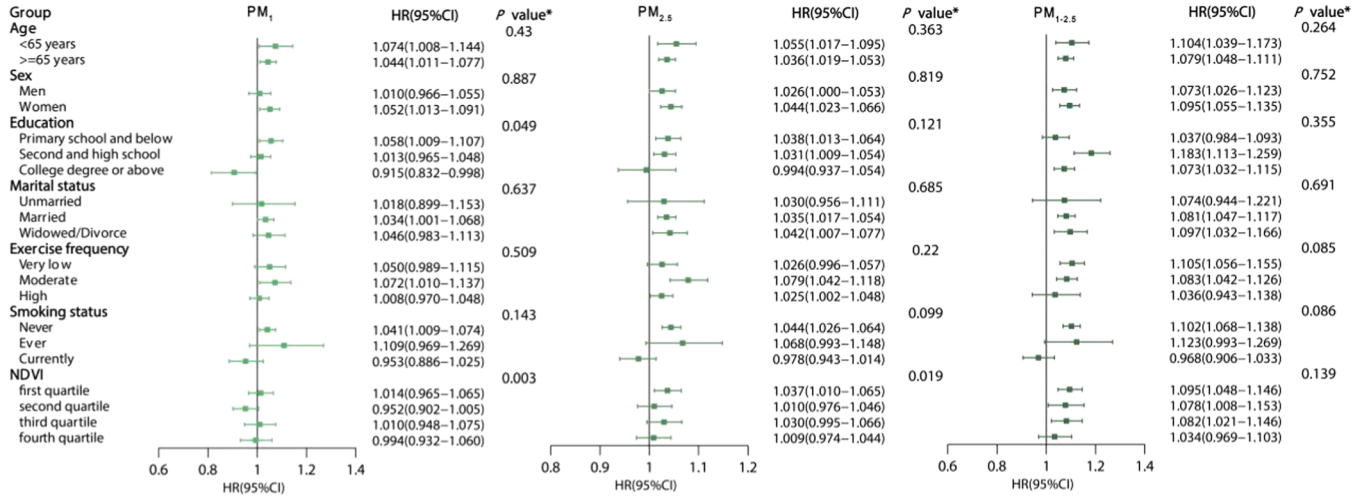

Fig. 3. Hazard ratios and 95% confidence interval of T2DM mortality risk associated with each 1 μg/m^3 in long-term exposure to ambient particulate matter, stratified by demographic and lifestyle factors. Note: The effects were estimated under the causal inference model with adjustment for age, sex, education, marital status, physical activity, smoke, and NDVI (500 m). All stratified estimates were adjusted for the remaining covariates. The interquartile range of NDVI is 0.0995–0.5328. The NDVI value is 0.0995–0.1875 for the first quartile, 0.0995–0.2112 for the second quartile, 0.0995–0.2449 for the third quartile, and 0.0995–0.5328 for the fourth quartile. Abbreviations: PM_1, particulate matter with an aerodynamic diameter $\leq$ 1 μm; $PM_{2.5}$, particulate matter with an aerodynamic diameter $\leq$ 2.5 μm; $PM_{1–2.5}$, particulate matter with an aerodynamic diameter greater than 1 μm and less than 2.5 μm; *HR*, hazard ratio; *CI*, confidence interval; NDVI, normalized difference vegetation index.

with the respiratory system (Yang et al., 2020b). However, the smaller size does not always equate to more significant harm; for instance, an experimental study exposing mature mice to different particulate matters (i.e., $PM_{0.49}$, $PM_{0.95}$, and $PM_{0.95–1.5}$) found that $PM_{0.95}$ had a more pronounced exacerbating effect on the development of asthma than $PM_{0.49}$, possibly due to the different types and proportions of toxic substances they carry (Mei et al., 2018). More studies should be conducted regarding the environmental health mechanism.

By shedding light on the association between PM exposure and T2DM mortality, our study emphasizes the importance of considering environmental factors in public health planning. Reducing PM exposure, especially PM_1 and $PM_{1–2.5}$, may be essential to lowering the risk of T2DM-related deaths. However, further research and public health interventions are necessary to elucidate and fully address the complexities of this association.

4.2. Stratified analysis

Our findings highlighted that both educational level and the extent of NDVI exposure play moderating roles in the PM-T2DM mortality relationship. Stratified Analysis by education indicated that individuals with a low education level, when exposed to PM over the long term, may face a heightened risk of T2DM mortality. This aligns with prior epidemiological research (Bowe et al., 2018; Brook et al., 2013), suggesting that individuals with a lower educational background are more vulnerable to PM exposure. One potential explanation is that those with lower educational attainment often face higher unemployment rates, lower incomes, and lack the financial resources for medical treatment, leading to a higher T2DM mortality rate (Brook et al., 2013).

Moreover, when categorizing NDVI into quartiles, there was a statistically significant role of NDVI in the effect of PM_1 and $PM_{2.5}$ exposure on diabetes mortality. Globally, an expanding body of studies documents the beneficial effects of greater exposure to green environments on diabetes (Yang et al., 2019). Elevated levels of greenness were significantly linked with reduced fasting and 2-hour glucose levels, as well as reduced 2-hour insulin levels, indicating decreased insulin resistance and enhanced β-cell function (Yang et al., 2018a).

The protective effects of green spaces against T2DM mortality can be attributed to several potential mechanisms. Green spaces can act as a buffer, reducing exposure to environmental pollutants, including PM (Li et al., 2021a). They also offer opportunities for physical activity, which reduces the risk of T2DM (Doubleday et al., 2022; Li et al., 2021a). Furthermore, green spaces can promote mental well-being by reducing stress linked to metabolic disturbances (Li et al., 2021a). Thus, urban green space development can be a strategic approach to mitigate T2DM risks.

4.3. Strength and limitation

Our study presents several notable strengths. Firstly, we assessed the potential causal association between T2DM mortality and chronic exposure to PM_1 and $PM_{1–2.5}$ exposure, often overlooked in conventional monitoring. Including participants from diverse socio-demographic backgrounds in the general population strengthens the applicability of our findings. The substantial sample size we employed bolstered our statistical power, enabling us to discern even subtle associations and evaluate variations across different subgroups. Our study is relevant for shaping health guidelines based on prolonged exposure effects by centering our research on long-term impacts. Furthermore, our analytical approach was rooted in the framework of causal inference. We adopted evidence-based strategies for selecting potential confounders and determining estimation methods using the DAG and causal inference methods like marginal structure models.

However, our study also has some limitations. First, our findings are based on a large sample from one province in China, which may limit the generalization of our findings to other regions. Although the diverse environmental and socio-economic dynamics in the study area contribute to the generalization of our results, future research covering multiple regions is still needed. Secondly, while we gauged individual PM exposure levels using residential addresses, the most commonly used in literature, exposure in the workplace may also play a role. However, this information was not collected.

Furthermore, we could not differentiate between the risk of healthy individuals developing diabetes and dying during the follow-up period and the risk of those with pre-existing diabetes at baseline deteriorating and dying. However, both situations of mortality are critically essential and warrant attention. Additionally, our findings might be biased by missing data. To address this issue, we employed multiple imputations

for the missing covariates. We conducted a sensitivity analysis to ensure that *HR*s remained consistent between the complete subset and the entire set. Besides, concerning other potential time-varying factors, due to data limitations, factors such as dietary habits, occupational exposure, and indoor air quality were not included in our Analysis. We recognize that these factors may modify the association between PM exposure and T2DM mortality and suggest that future studies should consider these additional variables. Lastly, although the causal inference methods we used could better adjust for confounding factors and contribute to the causal implication of our results, the observational nature of our study still limits the strength of the evidence. Therefore, our results still need to be interpreted cautiously, and the conclusion must be confirmed with future experimental studies. Considering the possibility of residual confounders, in our study, we measured the strength of the minimal association of unmeasured confounders with exposure and outcome by calculating E-values. The higher E-values indicate that our findings are robust and that unmeasured confounders with sizable effect sizes are needed to negate the observed associations.

5. Conclusions

In conclusion, our research offers compelling evidence that prolonged exposure to elevated PM_1, $PM_{2.5}$, and $PM_{1-2.5}$ contributes to T2DM mortality in southern China. Both a lower level of education and NDVI play pivotal roles in influencing T2DM mortality. Gaining a deeper understanding of how long-term PM exposure affects T2DM mortality will empower local and national governments to devise and implement effective environmental protection strategies to curb T2DM mortality.

Ethics approval and consent to participate

The study obtained ethics approval from the Human Ethics Committee at Sun Yat-sen University, and all study participants provided written, informed consent before participation.

Disclosure summary

The authors have nothing to disclose.

Consent for publication

Not applicable.

Fundings

This work was supported by National Natural Science Foundation of China (82204162, 81973150), Young Elite Scientist Sponsorship Program by China Association for Science and Technology (2023QNRC001), Guangdong Provincial Pearl River Talents Program (0920220207), Basic and Applied Basic Research Foundation of Guangdong Province (2022A1515010823), Guangzhou Municipal Science and Technology Bureau (2023A04J2072), Fundamental Research Funds for the Central Universities, Sun Yat-sen University (23qnpy108), and the Major Infectious Disease Prevention and Control of the National Science and Technique Major Project (2018ZX10715004).

CRediT authorship contribution statement

Shao Lin: Visualization, Validation, Supervision. **yuqin Zhang:** Visualization, Validation, Supervision, Methodology, Data curation, Conceptualization. **Shirui Chen:** Visualization, Validation, Supervision, Methodology, Data curation, Conceptualization. **Yongqing Sun:** Validation, Supervision. **Man Zhang:** Validation, Supervision. **Xinyue Li:** Validation, Supervision. **Shaniduhaxi Tuohetasen:** Validation, Supervision. **Jing Wei:** Visualization, Validation, Methodology, Conceptualization. **Yuantao Hao:** Validation, Supervision, Project administration, Funding acquisition. **Xi Cheng:** Writing – original draft, Visualization, Data curation. **Xueqing Deng:** Validation, Supervision. **Tong Guo:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Shuming Zhu:** Validation, Supervision. **Xingling Ruan:** Validation, Supervision. **Dan Chen:** Validation, Supervision. **Xurui Sun:** Validation, Supervision, Conceptualization. **Wangjian Zhang:** Writing – review & editing, Validation, Supervision, Software, Resources, Project administration, Funding acquisition, Data curation, Conceptualization. **shimin Chen:** Validation, Supervision. **Ziqiang Lin:** Validation, Supervision. **Yanji Qu:** Visualization, Validation, Supervision. **Qinlong Jing:** Validation, Supervision. **Xinlei Deng:** Visualization, Validation, Supervision. **zhibing Chen:** Validation, Supervision, Conceptualization. **xudan chen:** Validation, Supervision. **jie Sun:** Validation, Supervision. **Zhiqiang Li:** Validation, Supervision.

Declaration of Competing Interest

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

Data availability

Some or all datasets generated during and analyzed during the current study are not publicly available but are available from the corresponding author upon reasonable request.

Acknowledgments

Professor Yuantao Hao gratefully acknowledges the support of K.C. Wong Education Foundation. The authors declare no competing interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2024.116212.

References

Ao, L., et al., 2022. The joint effects of physical activity and air pollution on type 2 diabetes in older adults. BMC Geriatr. 22, 472. https://doi.org/10.1186/s12877-022-03139-8.

Austin, P.C., 2011. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivar. Behav. Res. 46, 399–424. https://doi.org/10.1080/00273171.2011.568786.

Bai, K., et al., 2022. LGHAP: the long-term gap-free high-resolution air pollutant concentration dataset, derived via tensor-flow-based multimodal data fusion. Earth Syst. Sci. Data 14, 907–927. https://doi.org/10.5194/essd-14-907-202.

Bowe, B., et al., 2018. The 2016 global and national burden of diabetes mellitus attributable to PM(2·5) air pollution. Lancet Planet Health 2, e301–e312. https://doi.org/10.1016/S2542-5196(18)30140-2.

Brook, R.D., et al., 2013. Long-term fine particulate matter exposure and mortality from diabetes in Canada. Diabetes Care 36, 3313–3320. https://doi.org/10.2337/dc12-2189.

Burkart, K., et al., 2022. Estimates, trends, and drivers of the global burden of type 2 diabetes attributable to PM2· 5 air pollution, 1990–2019: an analysis of data from the Global Burden of Disease Study 2019. Lancet Planet Heath 6, e586–e600. https://doi.org/10.1016/S2542-5196(22)00122-X.

van Buuren, S., 2007. Multiple imputation of discrete and continuous data by fully conditional specification. Stat. Methods Med Res 16, 219–242. https://doi.org/10.1177/0962280206074463.

Chen, G., et al., 2017. Effects of ambient PM1 air pollution on daily emergency hospital visits in China: an epidemiological study. Lancet Planet Health 1, e221–e229. https://doi.org/10.1016/S2542-5196(17)30100-6.

Chen, R., et al., 2012. Association of particulate air pollution with daily mortality: the China air pollution and health effects study. Am. J. Epidemiol. 175, 1173–1181. https://doi.org/10.1093/aje/kwr425.

Chilian-Herrera, O.L., et al., 2021. PM2. 5 exposure as a risk factor for type 2 diabetes mellitus in the Mexico City metropolitan area. BMC Public Health 21, 1–10. https://doi.org/10.1186/s12889-021-12112-w.

Collaborators, G.D. a I., 2020. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 396, 1204–1222. https://doi.org/10.1016/S0140-6736(20)30925-9.

Doubleday, A., et al., 2022. Neighborhood greenspace and risk of type 2 diabetes in a prospective cohort: the multi-ethncity study of Atherosclerosis. Environ. Health 21, 18 doi: 10.11 86/s12940-021-00824-w.

Eze, I.C., et al., 2015. Association between ambient air pollution and diabetes mellitus in Europe and North America: systematic review and meta-analysis. Environ. Health Perspect. 123, 381–389. https://doi.org/10.1289/ehp.1307823.

Forouzanfar, M.H., et al., 2015. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 386, 2287–2323. https://doi.org/10.1016/S0140-6736(16)31679-8.

Gorini, F., et al., 2021. Oxidative stress biomarkers in the relationship between Type 2 diabetes and air pollution. Antioxidants 10, 1234. https://doi.org/10.3390/antiox10081234.

Higbee, J.D., et al., 2020. Estimating long-term pollution exposure effects through inverse probability weighting methods with Cox proportional hazards models. Environ. Epidemiol. 4, e085 https://doi.org/10.1097/EE9.0000000000000085.

Hu, K., et al., 2018. Mortality burden attributable to PM1 in Zhejiang province, China. Environ. Int 121, 515–522. https://doi.org/10.1016/j.envint.2018.09.033.

Hu, M., et al., 2023. Long-term effect of submicronic particulate matter (PM1) and intermodal particulate matter (PM1-2.5) on incident dyslipidemia in China: a nationwide 5-year cohort study. Environ. Res 217, 114860. https://doi.org/10.1016/j.envres.2022.114860.

Kozákovác, J., et al., 2018. Chemical characterization of PM1-2.5 and its associations with PM1, PM2. 5-10 and meteorology in urban and suburban environments. Aerosol Air Qual. Res. 18, 1684–1697. https://doi.org/10.4209/aaqr.2017.11.0479.

Lao, X.Q., et al., 2019. Long-term exposure to ambient fine particulate matter (PM 2.5) and incident type 2 diabetes: a longitudinal cohort study. Diabetologia 62, 759–769. https://doi.org/10.1007/s00125-019-4825-1.

Li, R., et al., 2021a. Residential green and blue spaces and Type 2 diabetes mellitus: a population-based health study in China. Toxics 9, 11. https://doi.org/10.3390/toxics9010011.

Li, Y., et al., 2019. Association between air pollution and type 2 diabetes: an updated review of the literature, 2042018819897046 Ther. Adv. Endocrinol. Metab. 10. https://doi.org/10.1177/2042018819897046.

Li, Y., et al., 2021b. Secular incidence trends and effect of population aging on mortality due to type 1 and type 2 diabetes mellitus in China from 1990 to 2019: findings from the Global Burden of Disease Study 2019. BMJ Open Diabetes Res Care 9. https://doi.org/10.1136/bmjdrc-2021-002529.

Liang, X., et al., 2019. Chemical composition and source apportionment of PM1 and PM2. 5 in a national coal chemical industrial base of the Golden Energy Triangle, Northwest China. Sci. Total Environ. 659, 188–199. https://doi.org/10.1016/j.scitotenv.2018.12.335.

Liu, F., et al., 2019c. Associations of long-term exposure to PM1, PM2.5, NO2 with type 2 diabetes mellitus prevalence and fasting blood glucose levels in Chinese rural populations. Environ. Int 133, 105213. https://doi.org/10.1016/j.envint.2019.105213.

Liu, F., et al., 2019b. Associations of long-term exposure to PM1, PM2. 5, NO2 with type 2 diabetes mellitus prevalence and fasting blood glucose levels in Chinese rural populations. Environ. Int 133, 105213. https://doi.org/10.1016/j.envint.2019.105213.

Liu, F., et al., 2019a. Associations between long-term exposure to ambient air pollution and risk of type 2 diabetes mellitus: A systematic review and meta-analysis. Environ. Pollut. 252, 1235–1245. https://doi.org/10.1016/j.envpol.2019.06.033.

Mei, M., et al., 2018. Early-life exposure to three size-fractionated ultrafine and fine atmospheric particulates in Beijing exacerbates asthma development in mature mice. Part Fibre Toxicol. 15, 1–16. https://doi.org/10.1186/s12989-018-0249-1.

Nalluri, M., et al., 2020. A scalable tree boosting system: XG boost. Int. J. Res. Stud. Sci. Eng. Technol. 7, 36–51. https://doi.org/10.22259/2349-476X.0712005.

Rajagopalan, S., Brook, R.D., 2012. Air pollution and type 2 diabetes: mechanistic insights. Diabetes 61, 3037–3045. https://doi.org/10.2337/db12-0190.

Robins, J.M., et al., 2000a. Marginal structural models and causal inference in epidemiology. Epidemiology 550–560. https://doi.org/10.1097/00001648-200009000-00011.

Robins, J.M., et al., 2000b. Marginal structural models and causal inference in epidemiology. Epidemiology 11, 550–560. https://doi.org/10.1097/00001648-200009000-00011.

Ruan, B., et al., 2019. Establishment and development of national community-based collaborative innovation demonstration areas to achieve the control target of hepatitis B in China. BMC Infect. Dis. 19, 617. https://doi.org/10.1186/s12879-019-4150-9.

Trinquart, L., et al., 2019. Applying the E value to assess the robustness of epidemiologic fields of inquiry to unmeasured confounding. Am. J. Epidemiol. 188, 1174–1180. https://doi.org/10.1093/aje/kwz063.

Tsai, H.J., et al., 2020. The effect of surrounding greenness on Type 2 diabetes mellitus: a nationwide population-based cohort in Taiwan. Int J. Environ. Res Public Health 18, 267. https://doi.org/10.3390/ijerph18010267.

Van Buuren, S., Groothuis-Oudshoorn, K., 2011. mice: multivariate imputation by chained equations in R. J. Stat. Softw. 45, 1–67. https://doi.org/10.18637/jss.v045.i03.

VanderWeele, T.J., et al., 2016. Causal inference and longitudinal data: a case study of religion and mental health. Soc. Psychiatry Psychiatr. Epidemiol. 51, 1457–1466. https://doi.org/10.1007/s00127-016-1281-9.

Wang, Y., et al., 2023. Estimating causal links of long-term exposure to particulate matters with all-cause mortality in South China. Environ. Int 171, 107726. https://doi.org/10.1016/j.envint.2022.107726.

White, I.R., et al., 2011. Multiple imputation using chained equations: Issues and guidance for practice. Stat. Med 30, 377–399. https://doi.org/10.1002/sim.4067.

Wu, X., et al., 2020. Evaluating the impact of long-term exposure to fine particulate matter on mortality among the elderly. Sci. Adv. 6, eaba5692 https://doi.org/10.1126/sciadv.aba5692.

Yang, B.-Y., et al., 2018b. Long-term exposure to ambient air pollution (including PM1) and metabolic syndrome: The 33 Communities Chinese Health Study (33CCHS). Environ. Res 164, 204–211. https://doi.org/10.1016/j.envres.2018.02.029.

Yang, B.-Y., et al., 2018a. 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. Lancet Planet Health 2, e64–e73. https://doi.org/10.1016/S2542-5196(18)30001-9.

Yang, B.-Y., et al., 2019. Associations of greenness with diabetes mellitus and glucose-homeostasis markers: the 33 Communities Chinese Health Study. Int J. Hyg. Environ. Health 222, 283–290. https://doi.org/10.1016/j.ijheh.2018.12.001.

Yang, B.-Y., et al., 2020a. Ambient air pollution and diabetes: a systematic review and meta-analysis. Environ. Res 180, 108817. https://doi.org/10.1016/j.envres.2019.108817.

Yang, M., et al., 2020b. Is PM1 similar to PM2. 5? A new insight into the association of PM1 and PM2. 5 with children's lung function. Environ. Int 145, 106092. https://doi.org/10.1016/j.envint.2020.106092.

Yuan, H., et al., 2018. Type 2 diabetes epidemic in East Asia: a 35-year systematic trend analysis. Oncotarget 9, 6718–6727. https://doi.org/10.18632/oncotarget.22961.

Zhang, W., et al., 2022. Long-term PM0. 1 exposure and human blood lipid metabolism: new insight from the 33-community study in China. Environ. Pollut. 303, 119171 https://doi.org/10.1016/j.envpol.2022.119171.

Zheng, Y., et al., 2018. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat. Rev. Endocrinol. 14, 88–98. https://doi.org/10.1038/nrendo.2017.151.