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The influence of socioeconomic status on the association between residential greenness and gestational diabetes mellitus in an urban setting: a multicenter study

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Abstract

Background Inconsistencies were found between residential greenness and the risk of gestational diabetes mellitus (GDM), possibly due to variations in susceptibility among populations with different characteristics. However, little is known about whether this association could be modified by population characteristics like socioeconomic status (SES). This multicenter study conducted in a dense megacity aims to clarify these associations and explore the modification effects of demographic and socioeconomic factors.

Methods The study included 19,618 pregnant women in 20 hospitals throughout Shanghai, China, between 2015 and 2017. Multivariable logistic regression models were utilized to assess the associations of satellite-based greenness indicators [normalized difference vegetation index (NDVI) within 500 m- and 1000 m buffers] with GDM and whether demographic and socioeconomic factors modified the associations. Potential mediation effects of fine particulate matter ($PM_{2.5}$) on the associations between greenness and GDM were also explored.

Results During the first two trimesters of pregnancy, an increase in NDVI-500 m or NDVI-1000 m interquartile range was consistently associated with lower GDM risks, with adjusted odds ratios (aORs) and 95% confidence interval (CI) ranging from 0.82 (0.76, 0.88) to 0.90 (0.85, 0.96). Stratified analyses revealed that the health benefits of residential greenness are more pronounced during the first two trimesters among unemployed women (aOR = 0.70; 95%CI: 0.60, 0.82), those with lower education levels (aOR = 0.72; 95%CI: 0.63, 0.82), and those without medical insurance (aOR = 0.76; 95%CI: 0.69, 0.84). Mediation analysis shows that $PM_{2.5}$ reduction by greenness may explain 16.4% of the inverse association between the NDVI-500 m during early pregnancy and the risk of GDM.

†Tian Zhang and Wen Jiang contributed equally to this work and were thus considered as co-first authors.

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Conclusions Our research indicates that elevated residential greenness was associated with reduced GDM risks, partly attributed to decreased $PM_{2.5}$ levels. Women with lower SES experience amplified benefits from greenness. These findings highlight the significance of bolstering urban green infrastructure, particularly in communities confronting socioeconomic challenges and areas with high levels of air pollution.

Keywords Effect modification, Gestational diabetes mellitus, Residential greenness, Socioeconomic status, Urban setting

Background

Gestational diabetes mellitus (GDM), characterized by maternal glucose intolerance that first occurs during pregnancy, affects about 17% of pregnant women worldwide [1, 2]. It is associated with various short- and long-term adverse health outcomes, including elevated risks of adverse pregnancy outcomes, postpartum chronic diseases (e.g., type 2 diabetes), and future metabolic disorders in offspring [3, 4]. The etiology of GDM is multifactorial, including genetic, physiological, and lifestyle factors [5–7]. Accumulating evidence suggests that environmental factors like insufficient residential green space might also contribute to the pathogenesis of GDM [8].

Rapid urbanization in the past decades has led to a sharp increase in population density and environmental pressure worldwide, especially in developing countries [9]. In China, the urbanization rate surged from 17.9% in 1978 to 60.6% by 2019 [10]. Shanghai, one of the most remarkable examples of urban development in China over recent decades, has developed into the largest city in China and ranks among the world's largest urban areas. It has a total population exceeding 24 million and an average population density of 3926 inhabitants per square kilometer (km^2) [11]. The accelerated urbanization and industrialization in Shanghai have also led to increased environmental challenges, such as diminishing natural green spaces and deteriorating air quality [12]. Emerging evidence has revealed that greenness may provide health benefits through the diminution of harmful exposures (e.g., air pollution, noise, and heat), the facilitation of psychological well-being, and the promotion of physical activity [13, 14], which collectively hold significant implications for metabolic well-being.

Although some epidemiological studies have linked greenness to metabolic disorders like type 2 diabetes mellitus, the relationship between residential greenness and GDM remains inconclusive in pregnant women with high metabolic rates. In previous studies from China, residential greenness showed potential protection against GDM [15–17]. However, research from developed countries, such as the United States (U.S.) and Europe, found null associations [18–20]. The heterogeneity in findings across studies may be attributed to the differential susceptibility to greenness among populations with distinct socioeconomic characteristics. Identifying these characteristics can enhance the development of health protection initiatives targeted at vulnerable populations. Nevertheless, how various demographic and socioeconomic characteristics may affect the relationship between greenness and GDM have been rarely investigated. Due to the limited sample size and the availability of individual-level socioeconomic status information, the only two existing studies did not identify any significant effect modification by socioeconomic status indicators [15, 21]. In addition, previous studies suggest that air pollution, particularly fine particulate matter ($PM_{2.5}$), could increase the risk of GDM [22], while greenness might play a role in reducing air pollution levels [23]. However, the evidence remains limited whether and to what extent the potential benefits of green spaces on GDM are mediated by the reduction of $PM_{2.5}$.

Utilizing multicenter data from Shanghai, China, a densely populated urban setting, we aim to investigate the association between residential greenness and the risk of GDM, as well as the potential mediating role of $PM_{2.5}$. Furthermore, we intend to examine the impact of demographic and socioeconomic characteristics on this association.

Methods

Study design and population

The maternal information utilized in this study was obtained from a stratified, cluster-randomized field trial in 2015–2017. This trial was designed to investigate the impact of a package intervention in reducing unnecessary cesarean sections (CS) across 20 hospitals, which collectively covered approximately 50% of all childbirths in Shanghai, China. Trained research staff randomly retrieved electronic medical records (EMRs) of all the deliveries within the hospitals that participated from both the baseline and evaluation stages and extracted data on residential addresses, maternal characteristics, pregnancy complications, and perinatal outcomes. The trial reported no significant effects on the CS rate by the intervention. Therefore, data before and after the intervention were combined. A detailed description of this trial has been described elsewhere [24].

Among 116,910 pregnant women in the 20 hospitals in Shanghai from 2015 to 2017, we utilized systematic random sampling to select a representative sample of 21,360 women. Exclusions were made for the following reasons: unclear or non-Shanghai residential addresses during pregnancy ($n=1146$), maternal age at delivery younger than 15 or older than 50 years ($n=12$), gestational age ≤ 28 weeks or > 44 weeks ($n=22$), multiple pregnancies ($n=302$), stillbirth or unclear birth outcomes ($n=86$), diagnosis or missing data on pre-existing diabetes mellitus ($n=56$), missing values on GDM diagnosis ($n=11$), maternal or neonatal birth dates ($n=16$), and gestational age ($n=91$). The final analyses included 19,618 women (Figure S1). This research project obtained ethical approval from the Ethics Committee of the Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, and all the other collaborating hospitals (XHEC-C-2016-095).

Outcome definition

The GDM diagnosis was extracted from the medical record, which was defined according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria using a 75 g oral glucose tolerance test (OGTT) conducted between 24 and 28 weeks of pregnancy [25]. Specifically, GDM was identified if any of the following three criteria were met: (1) fasting plasma glucose (FPG) ≥ 5.1 mmol/L; (2) 1-h plasma glucose ≥ 10.0 mmol/L; or (3) 2-h plasma glucose ≥ 8.5 mmol/L.

Exposure assessment

To characterize the greenness of residential areas, the normalized difference vegetation index (NDVI) was utilized in this study (Figure S2). This indicator has been widely validated as a robust proxy for greenness exposure and is the most commonly used vegetation index in epidemiological studies. We employed gap-filled and smoothed composite satellite imagery from the Moderate-resolution Imaging Spectroradiometer (MODIS) with a spatial resolution of 250 × 250 m and a temporal resolution of 16 days, obtained through the National Aeronautics and Space Administration (NASA). The calculation of NDVI relies on the red and near-infrared light reflected by vegetation, as captured by satellite sensors [26]. NDVI values fall within the − 1 to 1 range, with higher positive values representing greater plant coverage, whereas values at or below 0 represent bare land or water bodies. Data preprocessing involved the application of an algorithm that identifies the optimal pixel value among the entirety of 16-day acquisitions, with specific criteria including a low viewing angle, minimal cloud coverage, and the highest NDVI value. The greenness exposure levels were determined by calculating the average NDVI within the 500 m and 1000 m buffers (abbreviated as NDVI-500 m and NDVI-1000 m) around the participants' residential addresses. Exposure windows for the main analyses included the 1st trimester (1–13 weeks of gestation), the 2nd trimester (14–27 weeks of gestation), and the combined 1st and 2nd trimesters (1–27 weeks of gestation). In supplementary analyses, exposures during the preconception period (i.e., 12 weeks before conception) and the extended periconceptional period (i.e., from preconception through the 2nd trimester) were also examined.

The $PM_{2.5}$ exposure during various trimesters was estimated from a satellite-based model. The model building and verification details have been elucidated elsewhere [27]. Briefly, everyday $PM_{2.5}$ concentrations were predicted using random forest algorithms that integrated satellite aerosol optical depth (AOD), visibility data, meteorological factors, population demographics, and land use characteristics at a resolution of 1 km × 1 km. The daily R^2 [root-mean-square error (RMSE)] value for full-coverage predictions derived from 10-fold cross-validation (CV) was 0.81 (18.5 μg/m^3), which signifies the model's high accuracy in predicting $PM_{2.5}$ concentrations. Daily temperature and relative humidity data throughout the study period were obtained from the China National Weather Data Sharing System, accessible at https://data.cma.cn. The mean values of ambient temp erature and relative humidity throughout the gestational period were then estimated based on data from the closest meteorological station to the residential address. The measurements of $PM_{2.5}$ and greenness indexes beyond 3 standard deviations (SD) of means were excluded to reduce the influence of outliers on the analyses.

Ambient concentrations of PM_{10}, nitrogen dioxide (NO_2), and carbon monoxide (CO) were obtained from the ChinaHighAirPollutants (CHAP) dataset (https://weijing-rs.github.io/product.html), which provides high-res olution exposure estimates using an extended space-time extremely randomized trees (STET) model. The model integrates satellite remote sensing, meteorological data, emission inventories, and land-use information to estimate concentrations of PM_{10} (1-km resolution) and NO_2/CO (10-km resolution) across China. The R^2 for PM_{10}, NO_2, and CO were 0.86, 0.84, and 0.80 [28, 29]. Daily concentrations of PM_{10}, NO_2 and CO were matched to geocoded residential addresses and averaged over gestational exposure windows.

Covariates

Covariates were selected based on the directed acyclic graph (Figure S3) and data availability. Maternal age at delivery was grouped as < 25, 25–34, ≥ 35 years; occupation was categorized into workers and farmers, unemployed, and other (e.g., military personnel, teachers, performing artists, and students); maternal education level was classified as middle school or below, high school, college graduate and above. Health insurance status was based on the payment method derived from electronic medical records and categorized as yes (with coverage through any public or employer-sponsored plan, including Urban Employee Basic Medical Insurance (UEBMI), Urban-Rural Resident Basic Medical Insurance (URRBMI), New Rural Cooperative Medical Scheme (NRCMS), commercial insurance, or other social insurance programs) or no (fully self-paid). Other covariates included parity (nulliparous, multiparous), body mass index [BMI, defined as weight in kilograms divided by the square of height in meters (kg/m^2), < 18.5, 18.5–24.0, ≥ 24.0] at the initial prenatal visit, year of conception (2015, 2016, 2017), season of conception (spring: March-May; summer: June-August; autumn: September-November; winter: December-February), infant sex (male, female), ambient temperature (continuous variable), and humidity (continuous variable). Data on maternal demographics, anthropometric measurements, last menstrual period (LMP), and infant sex were extracted from hospital EMRs. Year and season of conception were derived from LMP dates. The multivariate imputation with chained equations (MICE) algorithm was used to impute the covariates with missing values before regression analyses. Ten imputed datasets were analyzed independently and results were pooled following Rubin's rule to obtain the final estimates [30].

Statistical analyses

Descriptive statistics were summarized using the mean ± SD for continuous variables and frequencies (proportions) for categorical variables. Student t-tests or Chi-square tests were employed to compare the characteristic differences between the GDM and non-GDM groups when appropriate. The Spearman's correlation coefficients were assessed among the average NDVI and $PM_{2.5}$ during the 1st and 2nd trimesters of pregnancy.

Multivariable logistics regression models that adjusted for covariates were constructed to evaluate the associations of residential greenness and $PM_{2.5}$ levels during each exposure window independently with the risk of GDM. Adjusted odds ratios (aORs) and corresponding 95% confidence intervals (CIs) were employed to demonstrate the GDM risk per interquartile range (IQR) increase in exposures. Quartiles of NDVI and $PM_{2.5}$ were also recoded as ordinal variables (1, 2, 3, and 4) and treated as continuous in regression models to assess potential linear trends across exposure levels, with "*P* for trend" derived from Wald tests. Then, the 3-df restricted cubic spline (RCS) models were also constructed to visualize the potential nonlinear relationship of NDVI and $PM_{2.5}$ exposures with GDM risk, utilizing the "rms" R package.

The stratified analyses by maternal age at delivery, occupation, education levels, health insurance status, parity, and BMI at an early stage of pregnancy were performed. The "*P* value for effect modification" was derived by including an interaction term between NDVI and the corresponding stratification variable in the multivariable logistic regression model and its significance was tested using the Wald test. The estimation of the potential mediating effect of $PM_{2.5}$ on the relationship between residential greenness and GDM was conducted using the "mediation" R package [31]. A quasi-Bayesian Monte Carlo approach, which contained 1000 simulations based on normal approximation, was used to account for uncertainty. The average causal mediation effect (ACME) represented the indirect effect of greenness on GDM through $PM_{2.5}$, and the average direct effect (ADE) reflected the effect of greenness on GDM not mediated by $PM_{2.5}$. The total effect was calculated as the sum of ACME and ADE, and the proportion mediated was defined as the ratio of ACME to the total effect.

Several supplementary analyses were conducted. First, we performed additional stratification based on the pairwise combinations of maternal health insurance status (Yes/No), occupation (Employed/Unemployed), and education levels (High/Low), creating twelve distinct categories. Second, $PM_{2.5}$ was further adjusted to evaluate the associations between residential greenness exposure during different gestational windows and the risk of GDM. Third, we assessed associations of exposure to residential greenness and $PM_{2.5}$ during the preconception period (12 weeks before pregnancy) and the extended periconceptional period (from preconception through the 2nd trimester) with the risk of GDM. Fourth, we conducted analyses on additional air pollutants (PM_{10}, NO_2, or CO) to: (1) examine the associations between maternal exposure to these air pollutants during pregnancy and the risk of GDM; (2) explore their potential mediating effects on the relationship between residential greenness exposure during pregnancy and GDM; and (3) account for potential confounding by individually adjusting for PM_{10}, NO_2, or CO in separate models.

R software (version 4.2.1) was used for all statistical analyses, with $\alpha = 0.05$ as the level of significance.

Results

Table 1 shows the demographic characteristics of 19,618 pregnant women in our study, of which 2924 (14.9%) were diagnosed with GDM. The average maternal age at delivery [± SD] was 30.5 ± 4.4 years. The average BMI at the early stage of pregnancy was 22.2 ± 3.2 kg/m^2. In comparison to women without GDM, those with GDM tended to have higher BMI and had a higher proportion of male offspring, low education levels, multipara, without health insurance, and conceptions during autumn and winter. No statistically significant differences in maternal occupation were identified across groups. Figure S4 shows the Spearman correlations among NDVI-500 m, NDVI-1000 m, $PM_{2.5}$ and additional air pollutants, as well as meteorological variables during the

Table 1 Sociodemographic characteristics of the study population ($N=19618$)

	Total	Non-GDM	GDM	*P*-value*
	***N*=19,618**	***n*=16,694**	***n*=2924**	
Maternal age at delivery (years)	30.5±4.4	30.8±4.4	29.1±4.6	**<0.001**
<25	2257 (11.5)	1701 (10.2)	556 (19.0)	
25–34	14,554 (74.2)	12,436 (74.5)	2118 (72.4)	
≥35	2807 (14.3)	2557 (15.3)	250 (8.5)	
Occupation, **n (%)**				0.224
Workers and farmers	10,138 (51.7)	8584 (51.4)	1554 (53.1)	
Unemployed	3415 (17.4)	2924 (17.5)	491 (16.8)	
Other	6065 (30.9)	5186 (31.1)	879 (30.1)	
Maternal education level, **n (%)**				**<0.001**
Middle school or below	3857 (19.7)	3259 (19.5)	598 (20.5)	
High school	2916 (14.9)	2413 (14.5)	503 (17.2)	
College graduate or higher	12,845 (65.5)	11,022 (66.0)	1823 (62.3)	
Health insurance status, **n (%)**				**<0.001**
Yes	11,318 (57.7)	9543 (57.2)	1775 (60.7)	
No	8300 (42.3)	7151 (42.8)	1149 (39.3)	
Parity, **n (%)**				**<0.001**
0	11,804 (60.2)	10,170 (60.9)	1634 (55.9)	
1+	7814 (39.8)	6524 (39.1)	1290 (44.1)	
BMI in early pregnancy (kg/m^2)	22.2±3.2	22.0±3.1	23.4±3.5	**<0.001**
<18.5	1785 (9.1)	1634 (9.8)	151 (5.2)	
18.5–23.9	12,980 (66.2)	11,340 (67.9)	1640 (56.1)	
≥24.0	4853 (24.7)	3720 (22.3)	1133 (38.7)	
Year of conception, **n (%)**				**<0.001**
2015	9877 (50.3)	8537 (51.1)	1340 (45.8)	
2016	8331 (42.5)	6991 (41.9)	1340 (45.8)	
2017	1410 (7.2)	1166 (7.0)	244 (8.3)	
Season of conception, **n (%)**				**<0.001**
Spring	3023 (15.4)	2623 (15.7)	400 (13.7)	
Summer	7113 (36.3)	6103 (36.6)	1010 (34.5)	
Autumn	6417 (32.7)	5399 (32.3)	1018 (34.8)	
Winter	3065 (15.6)	2569 (15.4)	496 (17.0)	
Infant sex, **n (%)**				**0.047**
Male	10,329 (52.7)	8740 (52.4)	1589 (54.3)	
Female	9289 (47.3)	7954 (47.6)	1335 (45.7)	

Abbreviations: BMI, body mass index; SD, standard deviation

*Student t-test for continuous variables and Chi-square test for categorical variables

first two trimesters of pregnancy. There are strong positive correlations among NDVI-500 m and NDVI-1000 m with an estimate of 0.89 ($P<0.001$). Strong positive correlations were also observed among air pollutants, particularly between $PM_{2.5}$ and PM_{10} ($r=0.88$), CO ($r=0.76$), and NO_2 ($r=0.69$), all with $P<0.001$. Moderate negative correlations were found between greenness indicators and the $PM_{2.5}$ concentration, and the coefficients ranged from −0.33 to -0.35 ($P<0.01$). The medians (IQR) were 0.27 (0.09) and 0.28 (0.09) for NDVI-500 m and NDVI-1000 m; 45.03 (8.49) μg/m^3, 69.56 (11.46) μg/m^3, 45.75 (8.31) μg/m^3, 0.83 (0.08) mg/m^3 for $PM_{2.5}$, PM_{10}, NO_2, and CO; 17.77 (7.91) °C for ambient temperature; and 74.38 (2.84) % for relative humidity (Table S1).

Table 2 presents the relationships between NDVI levels and GDM risks. An increase in NDVI-500 m by one interquartile range during the 1st, 2nd, and the combined first two trimesters of pregnancy was associated with a 12% (aOR=0.88, 95%CI: 0.82, 0.94), 10% (aOR=0.90, 95%CI: 0.84, 0.97), and 10% (aOR=0.90, 95%CI: 0.85, 0.96) decreased risk of GDM, accordingly. Likewise, per IQR increase of NDVI-1000 m was associated with decreased risks of GDM, with aORs (95%CI) ranging from 0.82 (0.76, 0.88) to 0.86 (0.81, 0.91) in corresponding trimesters of pregnancy. When treating the greenness indicators as categorical variables, NDVI-500 m and NDVI-1000 m exhibited a dose-dependent relationship with GDM (adjusted *P* for trend<0.005). For $PM_{2.5}$ exposures, an increased risk of GDM was observed exclusively

Table 2 Associations of exposure to NDVI-based residential greenness during different gestational windows and GDM risk*

	Gestational windows		
	1st trimester	**2nd trimester**	**1st + 2nd trimester**
	aOR (95%CI)	**aOR (95%CI)**	**aOR (95%CI)**
$NDVI_{500\ m}$, continuous (with IQR increment)	**0.88 (0.82, 0.94)**	**0.90 (0.84, 0.97)**	**0.90 (0.85, 0.96)**
$NDVI_{500\ m}$, quartiles			
Q1	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2	**0.88 (0.79, 0.99)**	0.91 (0.81, 1.02)	**0.85 (0.76, 0.95)**
Q3	**0.82 (0.73, 0.94)**	**0.88 (0.78, 0.99)**	**0.83 (0.74, 0.94)**
Q4	**0.77 (0.68, 0.89)**	**0.81 (0.70, 0.93)**	**0.79 (0.70, 0.90)**
P for trend	**< 0.001**	**0.003**	**< 0.001**
$NDVI_{1000\ m}$, continuous (with IQR increment)	**0.82 (0.76, 0.88)**	**0.86 (0.80, 0.93)**	**0.86 (0.81, 0.91)**
$NDVI_{1000\ m}$, quartiles			
Q1	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q2	**0.89 (0.79, 0.99)**	**0.88 (0.78, 0.99)**	**0.84 (0.75, 0.94)**
Q3	**0.80 (0.70, 0.91)**	**0.81 (0.72, 0.92)**	**0.79 (0.70, 0.89)**
Q4	**0.71 (0.61, 0.82)**	**0.74 (0.64, 0.86)**	**0.72 (0.63, 0.81)**
P for trend	**< 0.001**	**< 0.001**	**< 0.001**

Abbreviations: $NDVI_{500m}$, normalized difference vegetation index with a buffer of 500 m; $NDVI_{1000m}$, normalized difference vegetation index with a buffer of 1000 m; GDM, gestational diabetes mellitus; aOR, the adjusted odds ratio; CI, confidence interval; IQR, interquartile range; Q1, 1st quartile; Q2, 2nd quartile; Q3, 3rd quartile; Q4, 4th quartile

* Multivariable logistic regression models were applied, adjusting for maternal age at delivery, BMI in early pregnancy, occupation, education level, health insurance status, parity, year of conception, season of conception, infant sex, ambient temperature and humidity

during the 1st trimester (aOR = 1.27, 95%CI: 1.09, 1.48) (Table S2).

No non-linear association was observed between residential greenness exposure and the risk of GDM across different gestational windows. The exposure-response (E-R) curves were approximately linear and tended to flatten at higher levels of residential greenness (Fig. 1). Exposure to $PM_{2.5}$ during the 1st trimester also showed no non-linearity with GDM risks (*P* for non-linearity > 0.05) (Figure S5).

We detected the profound effect modification by socioeconomic factors in stratified analyses. During the first two trimesters, the association between NDVI-500 m and reduced GDM risk was more pronounced among unemployed women (aOR = 0.70, 95%CI: 0.60, 0.82) than among those who were employed as workers and farmers (aOR = 0.98, 95%CI: 0.90, 1.06). This association was also stronger among women with lower education levels, with aORs (95% CI) of 0.72 (0.63, 0.82) for middle school education or below, 0.83 (0.72, 0.97) for high school education, and 0.99 (0.91, 1.07) for college education or above. Similarly, women without health insurance showed a stronger negative association (aOR = 0.76, 95% CI: 0.69, 0.84) compared to those with health insurance (aOR = 1.01, 95% CI: 0.94, 1.10) (Table 3). Consistent trends were identified in NDVI-1000 m (Table 4). Although only a marginally significant effect modification by maternal BMI at early stage of pregnancy was observed, the protective effect of NDVI-500 m against GDM seems to be stronger in overweight/obese women (aOR = 0.84, 95%CI: 0.76, 0.93) compared to women of normal weight (aOR = 0.94, 95%CI: 0.87, 1.02). No other significant between-group differences were identified for maternal age at delivery and parity.

As a significant association of $PM_{2.5}$ exposure with GDM risk was only identified in the 1st trimester, we limited our mediation analysis to this gestational period. We also found that $PM_{2.5}$ suggestively mediated 16.4% (95%CI: 2.2 – 42.5%) of the association between NDVI-500 m exposure and the risk of GDM in the 1st trimester (Fig. 2). Specifically, the ADE of per IQR increase in NDVI-500 m on GDM was – 0.015 (95%CI: -0.028, -0.004, adjusted *P* = 0.008), and the indirect effect (mediated by $PM_{2.5}$) was – 0.003 (95%CI: -0.006, -0.0004, adjusted *P* = 0.032). No significant mediation effects of $PM_{2.5}$ exposure were observed between NDVI-1000 m exposure and GDM in the 1st trimester (Table S3).

In stratification based on the combinations of maternal health insurance status, occupation, and education level, the protective effect of NDVI-500 m-based residential greenness on GDM was most pronounced among women without health insurance and unemployed, unemployed with low education levels, and women without health insurance and with low education levels, with aORs (95%CI) across different gestational windows ranged from 0.59 (0.49, 0.71) to 0.64 (0.55, 0.76), 0.59 (0.49, 0.72) to 0.65 (0.55, 0.77), and 0.69 (0.60, 0.78) to 0.72 (0.64, 0.81), respectively (Table S4). Similar patterns were observed when examining NDVI-1000 m (Table S5). Upon additional control for $PM_{2.5}$ exposure during each trimester in the models, the relationships between residential greenness and the risk of GDM remained robust

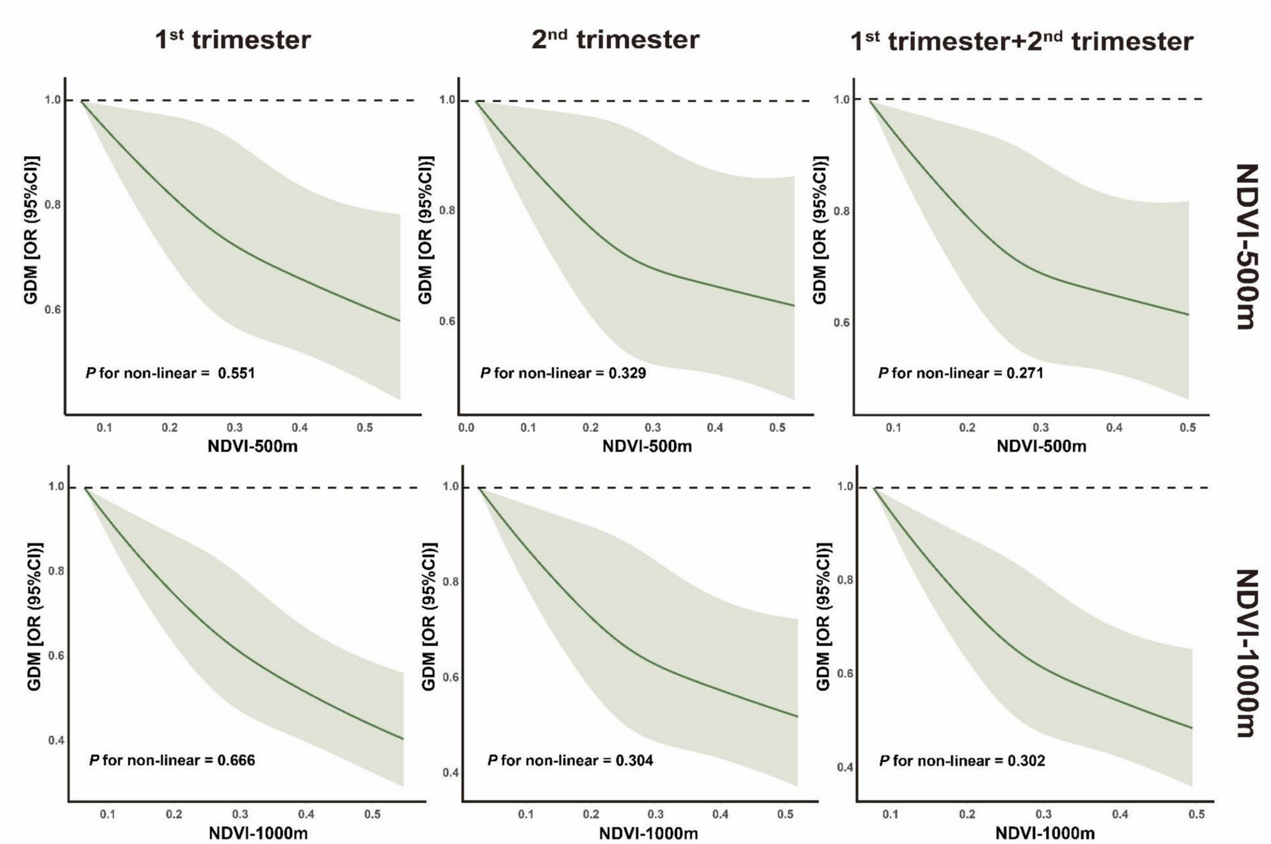

Fig. 1 Exposure-response curves for the association of NDVI-based residential greenness during the first two trimesters of pregnancy with odds of GDM. GDM, gestational diabetes mellitus; OR, the odds ratio; NDVI, normalized difference vegetation index. All models were adjusted for maternal age at delivery, BMI at an early stage of pregnancy, occupation, educational level, health insurance status, parity, year of conception, season of conception, infant sex, ambient temperature, and humidity

in both the 500 m and 1000 m buffers (Table S6). During both the preconception and extended periconceptional periods, residential greenness was consistently associated with a reduced risk of GDM, whereas $PM_{2.5}$ exposure was not significantly associated with GDM during either period (Tables S7-S8). Additional air pollutants (PM_{10}, NO_2, and CO) exhibited generally similar associations with GDM as $PM_{2.5}$ across various exposure windows (Table S9). Notably, NO_2 and CO also demonstrated significant mediating effects on the association between residential greenness and GDM, particularly during early pregnancy (Table S10). After further adjustment for these air pollutants, the protective association between residential greenness exposure and GDM remained robust (Table S11).

Discussion

In this multicenter study in Shanghai, we identified a notable inverse association between residential greenness and GDM risk. Furthermore, our analysis revealed that the protective effect of urban greenness on the risk of GDM was particularly pronounced among socioeconomically disadvantaged women, highlighting the amplified benefits of green spaces for these vulnerable populations. Additionally, we found that the reduction in $PM_{2.5}$ levels mediates 16.4% of the negative association between NDVI-500 m during the 1st trimester of gestation and GDM, suggesting one potential pathway through which greenness may exert its protective effect.

Recently, the influence of greenness on GDM has increasingly garnered attention, but the results remain inconclusive. In line with our findings, three previous studies in China suggest that greenness may protect against GDM [15, 17, 21]. For example, a multicenter study with 5237 pregnant women from Guangdong Province, China, identified that interquartile increases in NDVI within 250 m, 500 m, and 1000 m buffers were associated with decreases in GDM risk by 13%, 8% and 3% [15]. However, some other studies, mainly conducted in the U.S. and Europe, have reported null results [18–20]. Young et al. estimated the total square kilometers of recreational green spaces roughly using residential ZIP codes and reported no significant association with

Table 3 Associations between NDVI-500 m and GDM risk stratified by maternal demographic and socioeconomic factors*

	Gestational windows		
	1st trimester	**2nd trimester**	**1st + 2nd trimester**
	aOR (95%CI)	**aOR (95%CI)**	**aOR (95%CI)**
Maternal age at delivery			
<25	1.01 (0.85, 1.19)	1.09 (0.92, 1.30)	1.05 (0.90, 1.22)
25–34	**0.88 (0.81, 0.96)**	**0.89 (0.82, 0.97)**	**0.90 (0.83, 0.96)**
≥35	**0.71 (0.57, 0.88)**	**0.72 (0.57, 0.91)**	**0.73 (0.60, 0.89)**
P value for effect modification	0.610	0.526	0.498
Occupation			
Workers and farmers	0.98 (0.89, 1.07)	1.00 (0.90, 1.10)	0.98 (0.90, 1.06)
Unemployed	**0.71 (0.60, 0.84)**	**0.65 (0.54, 0.77)**	**0.70 (0.60, 0.82)**
Other	**0.83 (0.73, 0.95)**	0.91 (0.80, 1.04)	0.90 (0.80, 1.00)
P value for effect modification	**0.028**	**0.054**	**0.013**
Maternal education level			
Middle school or below	**0.67 (0.58, 0.78)**	**0.71 (0.60, 0.83)**	**0.72 (0.63, 0.82)**
High school	**0.78 (0.66, 0.93)**	**0.81 (0.68, 0.97)**	**0.83 (0.72, 0.97)**
College graduate or higher	1.00 (0.91, 1.09)	1.00 (0.91, 1.10)	0.99 (0.91, 1.07)
P value for effect modification	**0.001**	**< 0.001**	**< 0.001**
Health insurance status			
Yes	1.00 (0.91, 1.09)	1.05 (0.96, 1.15)	1.01 (0.94, 1.10)
No	**0.74 (0.67, 0.83)**	**0.72 (0.65, 0.81)**	**0.76 (0.69, 0.84)**
P value for effect modification	**0.005**	**< 0.001**	**< 0.001**
Parity			
0	**0.91 (0.83, 1.00)**	**0.90 (0.82, 0.99)**	**0.91 (0.84, 0.99)**
1+	**0.84 (0.76, 0.93)**	**0.90 (0.81, 1.00)**	**0.88 (0.80, 0.97)**
P value for effect modification	0.525	0.808	0.601
BMI in early pregnancy			
<18.5	0.90 (0.66, 1.22)	0.80 (0.59, 1.10)	0.87 (0.66, 1.14)
18.5–23.9	0.93 (0.85, 1.02)	0.95 (0.87, 1.04)	0.94 (0.87, 1.02)
≥24.0	**0.81 (0.73, 0.92)**	**0.83 (0.74, 0.94)**	**0.84 (0.76, 0.93)**
P value for effect modification	0.051	0.345	0.089

Abbreviations: aOR, the adjusted odds ratio of per interquartile range increase in NDVI-500 m; CI, confidence interval; NDVI, normalized difference vegetation index; BMI, body mass index; GDM, gestational diabetes mellitus

* Multivariable logistic regression models were applied. All models were adjusted for the same covariates as the main analysis except for stratification factors

GDM [20]. Among 61,640 women in the U.S., Choe et al. likewise reported no correlation between residential NDVI-500 m and 4884 GDM cases [18]. The heterogeneity between studies may be ascribed to differences in study designs, population characteristics, sample sizes, greenness coverage, and exposure assessment methods. The exposure-response (E-R) curves appear to suggest a flattening trend at higher greenness levels, potentially indicating diminishing health benefits beyond a specific NDVI level. Nonetheless, the nonlinearity was not statistically significant (*P* for non-linear > 0.05). The E-R curves might help explain that in regions with high greenness levels (e.g., the U.S. and Europe), no significant health impacts of greenness were found [18–20], whereas in areas with lower levels of greenness, such as China, more pronounced health benefits are observed [15, 17, 21]. SES may partly account for these differences, as our stratified analysis showed stronger protective effects of greenness among lower SES populations. This can be explained by the potential differences in residential greenness accessibility, healthcare resource availability, and other factors associated with SES. More studies in the future are warrant to validate the difference in the effects of greenness between western countries and China, as well as between different SES subgroups. Different buffers of greenness used in studies might be another source of heterogeneity. A smaller buffer is believed to reflect the mitigating impact of vegetation, such as trees, alongside residential roadways against traffic-related air pollution and noise. Similarly, it may represent the visible greenery in the immediate vicinity, potentially alleviating stress through mood enhancement, thereby possibly better representing restorative influences [23, 32]. In contrast, a larger buffer encompasses a more extensive walkable greenery range around the residence, potentially offering a more accurate representation of the impact of greenspace on physical activities [23, 32].

Table 4 Associations between NDVI-1000 m and GDM risk stratified by maternal demographic and socioeconomic factors*

	Gestational windows		
	1st trimester	**2nd trimester**	**1st + 2nd trimester**
	aOR (95%CI)	**aOR (95%CI)**	**aOR (95%CI)**
Maternal age at delivery			
<25	0.90 (0.75, 1.07)	1.04 (0.86, 1.25)	0.97 (0.83, 1.13)
25–34	**0.81 (0.75, 0.88)**	**0.85 (0.78, 0.93)**	**0.85 (0.79, 0.91)**
≥35	**0.74 (0.59, 0.92)**	**0.75 (0.58, 0.96)**	**0.78 (0.64, 0.95)**
P value for effect modification	0.923	0.814	0.914
Occupation			
Workers and farmers	**0.87 (0.79, 0.96)**	0.92 (0.83, 1.02)	**0.89 (0.82, 0.97)**
Unemployed	**0.73 (0.61, 0.86)**	**0.78 (0.65, 0.94)**	**0.80 (0.69, 0.93)**
Other	**0.78 (0.68, 0.89)**	**0.82 (0.71, 0.94)**	**0.83 (0.74, 0.92)**
P value for effect modification	0.177	0.869	0.454
Maternal education level			
Middle school or below	**0.64 (0.55, 0.75)**	**0.66 (0.56, 0.78)**	**0.70 (0.61, 0.80)**
High school	**0.80 (0.67, 0.95)**	0.91 (0.76, 1.09)	0.88 (0.75, 1.02)
College graduate or higher	**0.89 (0.82, 0.98)**	0.93 (0.85, 1.03)	0.92 (0.85, 1.00)
P value for effect modification	**0.047**	**< 0.001**	**0.001**
Health insurance status			
Yes	0.95 (0.86, 1.04)	1.04 (0.95, 1.15)	0.99 (0.91, 1.07)
No	**0.67 (0.60, 0.75)**	**0.66 (0.58, 0.74)**	**0.71 (0.64, 0.78)**
P value for effect modification	**0.001**	**< 0.001**	**< 0.001**
Parity			
0	**0.86 (0.78, 0.95)**	**0.88 (0.80, 0.98)**	**0.89 (0.82, 0.96)**
1+	**0.76 (0.68, 0.85)**	**0.84 (0.75, 0.94)**	**0.82 (0.75, 0.90)**
P value for effect modification	0.326	0.411	0.258
BMI in early pregnancy			
<18.5	0.74 (0.54, 1.02)	0.74 (0.53, 1.03)	0.78 (0.60, 1.03)
18.5–23.9	**0.83 (0.76, 0.91)**	0.91 (0.83, 1.01)	**0.88 (0.81, 0.95)**
≥24.0	**0.81 (0.72, 0.91)**	**0.81 (0.71, 0.91)**	**0.84 (0.76, 0.93)**
P value for effect modification	0.595	0.531	0.508

Abbreviations: aOR, the adjusted odds ratio of per interquartile range increase in NDVI-1000 m; CI, confidence interval; NDVI, normalized difference vegetation index; BMI, body mass index; GDM, gestational diabetes mellitus

* Multivariable logistic regression models were applied. All models were adjusted for the same covariates as the main analysis except for stratification factors

The distinct exposure-outcome patterns observed for residential greenness and $PM_{2.5}$ may reflect their different mechanisms and timeframes of impact on GDM risk. Regarding $PM_{2.5}$, its association with GDM was limited to the first trimester, suggesting that early pregnancy represents a critical window of vulnerability. This finding is consistent with many previous studies [33–35], which suggested $PM_{2.5}$ induces biological responses predominantly in early gestation. Exposure to $PM_{2.5}$ during early pregnancy has been linked to increased systemic inflammation [36, 37], altered placental global DNA methylation [38], and activated oxidative stress [39, 40], which ultimately contribute to β-cell dysfunction and insulin resistance and a higher risk of GDM [41]. Further investigations on molecular mechanisms are warranted to elucidate the biological association between $PM_{2.5}$ and GDM. For residential greenness, it was consistently associated with a reduced risk of GDM across all exposure windows, indicating a more sustained and cumulative effect. Although the underlying biopsychosocial mechanisms remain unclarified, they may involve encouraging physical activities, strengthening social cohesion and interactions, and alleviating psychological stress, and improving air quality, thereby providing potential benefits extending throughout pregnancy [14, 42]. Studies have also indicated that vegetation may serve as a natural air pollutant filter by effectively blocking airborne particles and facilitating their retention on leaf surfaces or tree absorption [17, 43]. Mediation analyses in our study revealed that the reduction in maternal $PM_{2.5}$ exposure mediated 16.4% of the protective effects of residential greenness on GDM during the 1st trimester of pregnancy, and supported the pathway to some extent. Prior literature on the mediation by $PM_{2.5}$ is scant, with only two previous studies reporting mediation proportions ranging from 2.5 to 24.1%, which align with our findings [17, 21]. Other potential pathways, such as the emotional alleviation effects of greenness, may also play a role in the impact of

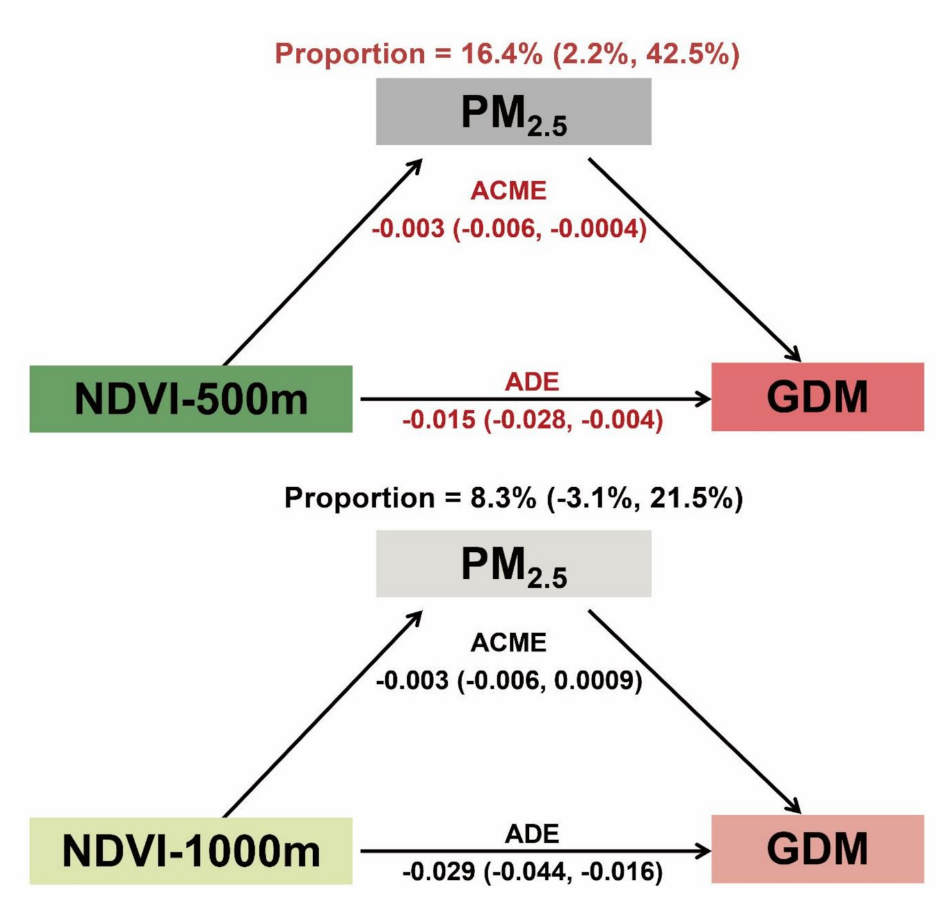

Fig. 2 The mediating role of $PM_{2.5}$ in the association between NDVI-based residential greenness during the first trimester of pregnancy and GDM. NDVI, normalized difference vegetation index; $PM_{2.5}$, particular matter with aerodynamic diameter ≤ 2.5 μm; GDM, gestational diabetes mellitus; ACME, average causal mediation effect; ADE, average direct effect

greenness on GDM. However, their specific mechanisms remain unclear and require further elucidation.

Socioeconomic status (SES) was found to modify the residential greenness exposure-GDM relationship. In stratified analyses, we observed a stronger negative association between green spaces and the risk of GDM among women without health insurance, those who were unemployed, and those with lower education levels. Moreover, upon further stratification based on the combination of maternal health insurance status, occupation, and education levels, it becomes evident that greenness exhibited the most substantial protective effect against GDM risk for unemployed women without health insurance, unemployed women with low education levels, as well as women without health insurance and with low education levels, followed by employed women without health insurance. In China, these women predominantly belong to lower SES groups [44]. Unemployment often leads to economic instability [45], which is frequently accompanied by a lack of health insurance. Women who are employed but lack insurance often work in informal employment sectors characterized by lower wages, where they typically do not receive comprehensive benefits, including health insurance. In line with our findings, a prior study conducted in Guangdong province observed a suggestive more pronounced protective impact of green spaces on GDM in women with lower levels of education or income [15]. However, it did not identify a significant effect modification of SES on the relationship, possibly due to its modest sample size (157 GDM cases). Another study conducted in Henan province [21], which used regional economic levels as a proxy of socioeconomic indicators due to the absence of individual-level variables, found no modification effects of socioeconomic status. One plausible explanation for a stronger protective effect of green space among pregnant women from lower socioeconomic backgrounds is that these women tend to make more use of green spaces near their residences, and are more likely to benefit from the greenery situated close to their homes [46]. Another potential reason is their limited access to nutritional supplements and healthcare provisions during pregnancy [47], as well as their likelihood to reside in areas with elevated pollution levels [23]. These circumstances may increase their susceptibility to the unfavorable environmental factors, which, in turn, might enhance their benefits from exposure to greenness [32]. Our finding underscores a stronger protective effect of greenness among socioeconomically disadvantaged women, highlighting the potential of residential greenness as a targeted intervention to mitigate health disparities and promote equity among those vulnerable populations. Notably, our study provided first-hand evidence suggesting that residential greenness may confer greater benefits against GDM for overweight or obese women in the early stage of pregnancy, although only a marginally significant modification effect was observed. The reason remains unclear and is worth further exploration. One possible explanation is that greenness may provide more opportunities for outdoor activities, aiding in improving insulin sensitivity during pregnancy, which is especially vital for overweight or obese women [48].

Our study has several strengths. Firstly, the study has a relatively large sample size, which was selected through random sampling to represent the larger, broader population's features accurately. This strategy not only strengthens the statistical robustness of our findings but also enhances the generalizability of our research outcomes. Secondly, we examined the residential greenness across different buffers of 500 m and 1000 m, and the consistent results strengthen our findings' reliability. Thirdly, the study explores the potential mediating role of $PM_{2.5}$ in the association between greenness and GDM, offering novel insights into how greenness may mitigate GDM risk.

Our study still has several limitations. First, as data on residential mobility during pregnancy is unavailable, the exposure evaluation relied on the residential addresses recorded during the first prenatal visit. Thus, exposure misclassification may be inevitable. However, prior research indicates that only a tiny proportion (fewer than 3%) of the population in China experienced changes in residential address during pregnancy [49], which is unlikely to result in significant bias in our results. Second, NDVI is merely a general measure of greenness, lacking precision in characterizing the diversity and quality of vegetation [23]. Future research should consider more refined metrics, such as tree canopy coverage, vegetation type, and accessibility to green spaces [50], to better capture the potential health benefits of residential greenness. Third, due to the lack of accessible neighborhood-level data in China (such as median household income, median educational attainment, and population density), as well as the lack of data regarding participants' lifestyle habits (such as drinking, smoking, dietary patterns, and physical activities) during the gestational period, there may be uncontrolled confounding factors that could potentially affect the accuracy and validity of our findings. Lastly, while our study primarily focused on $PM_{2.5}$ as a mediating pathway for the health benefits of greenness, it did not address other potential pathways, such as stress relief and promoted physical health. Future studies need to explore these additional mediating mechanisms to better understand the comprehensive benefits of greenness on maternal and fetal health.

Conclusions

This multicenter study added supporting evidence for the protective role of residential greenness against GDM. Notably, we found women with lower SES experience amplified benefits from greenness. In addition, the benefits of residential greenness may be partly mediated by reducing $PM_{2.5}$ level. These findings emphasize the significance of urban greenery planning in preventing GDM especially for vulnerable populations with low SES and in regions with high levels of air pollution.

Abbreviations

ADE	Average direct effect
AOD	Aerosol optical depth
aOR	Adjusted odds ratio
BMI	Body mass index
CI	Confidence interval
CS	Cesarean section
CV	Cross-validation
E-R	Exposure-response
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IQR	Interquartile range
MICE	Multivariate imputation with chained equations
MODIS	Moderate-resolution Imaging Spectroradiometer
NASA	National Aeronautics and Space Administration
NDVI	Normalized difference vegetation index
OGTT	Oral glucose tolerance test
RCS	Restricted cubic spline
RMSE	Root-mean-square error
SD	Standard deviations
SES	Socioeconomic status
U.S.	United States

Supplementary Information

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Supplementary Material 1

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Not applicable.

Author contributions

QLZ and WPY contributed to the conceptualization of the study; TZ and WJ conducted the data analysis and drafted the manuscript; CPW, YH, WQ and JC contributed to the exposure data; QLZ, JZ and RH supervised the project; JZ and WPY acquired funding. All authors substantially revised the manuscript and have approved the submitted version.

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Data availability
The dataset generated and/or analyzed in the current study are not publicly available but can be obtained from the corresponding author on a reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the principles outlined in the Declaration of Helsinki and received ethical approval from the Institutional Review Boards of the Xinhua Hospital Center affiliated to Shanghai Jiao Tong University School of Medicine (XHEC-C-2016-095). Written informed consent was obtained from the participants in this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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