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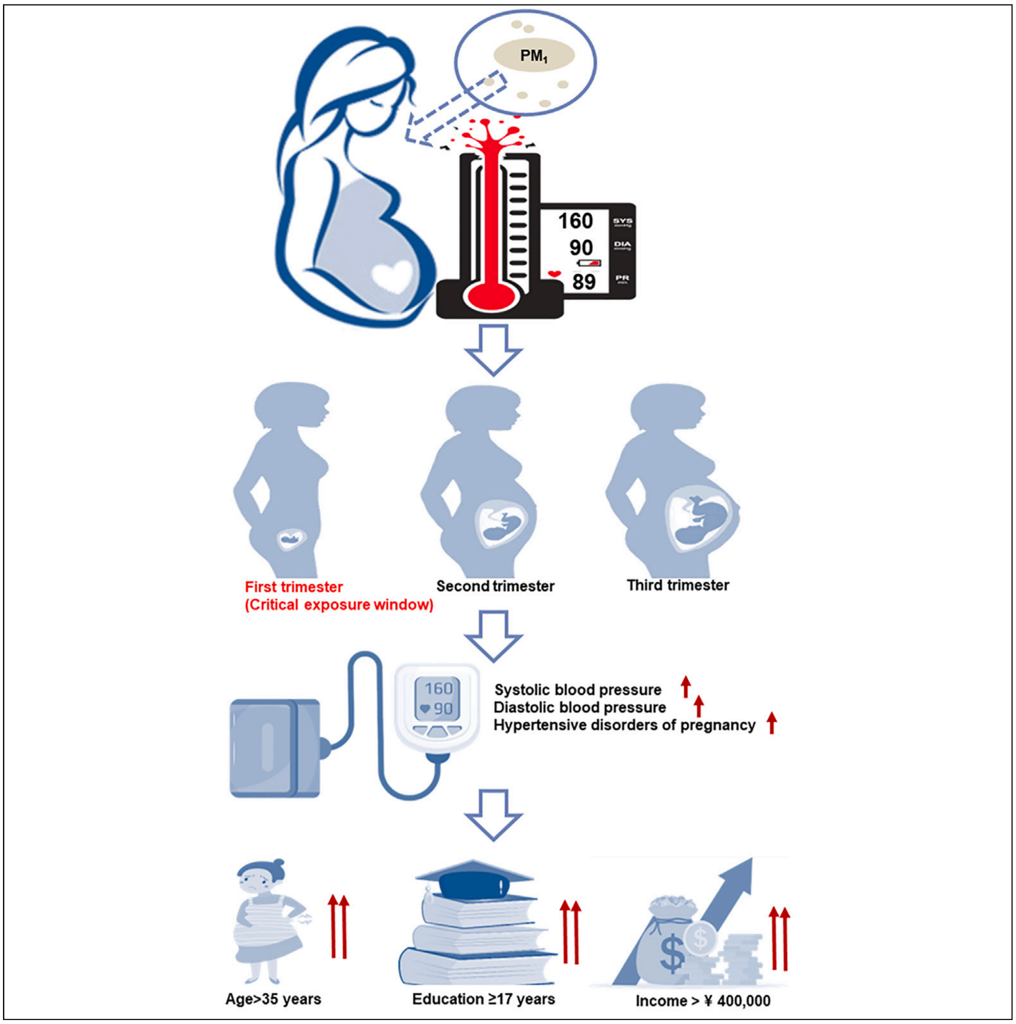

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Highlights

Our study provides novel evidence on PM1- BP/HDP associations among pregnant women

First trimester was the critical exposure window for PM_1-BP/HDP associations

Those > 35 years old, educated ≥ 17 years, income > 400,000 CNY were more susceptible

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Association of ambient PM_1 exposure with maternal blood pressure and hypertensive disorders of pregnancy in China

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SUMMARY

Evidence concerning PM_1 exposure, maternal blood pressure (BP), and hypertensive disorders of pregnancy (HDP) is sparse. We evaluated the associations using 105,063 participants from a nationwide cohort. PM_1 concentrations were evaluated using generalized additive model. BP was measured according to the American Heart Association recommendations. Generalized linear mixed models were used to assess the PM_1-BP/HDP associations. Each 10 $\mu g/m^3$ higher first-trimester PM_1 was significantly associated with 1.696 mmHg and 1.056 mmHg higher first-trimester SBP and DBP, and with 11.4% higher odds for HDP, respectively. The above associations were stronger among older participants (> 35 years) or those educated longer than 17 years or those with higher household annual income (> 400,000 CNY). To conclude, first-trimester PM_1 were positively associated with BP/HDP, which may be modified by maternal age, education level, and household annual income. Further research is warranted to provide more information for both health management of HDP and environmental policies enactment.

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) are one of the most common prenatal complications, with an incidence rate of 10–20% among all pregnancies.[1–4] The prevalence of HDP are rising as increased maternal age, obesity, diabetes mellitus, and greater mental stress have become more common in pregnant women.[5] HDP could increase the risk of maternal and offspring adverse outcomes,[6] potentially leading to placental abruption, preeclampsia, fetal growth restriction, preterm delivery, cesarean delivery, postpartum hemorrhage, low birth weight, and offspring neurodevelopmental disorders.[7–9] Furthermore, higher maternal blood pressure (BP), which even if is lower than the diagnostic threshold for HDP, has been identified with an association with adverse maternal and fetal outcomes.[10,11] It is of critical importance to identify dominant risk factors for HDP, as well as the increase in maternal BP.

Recently, epidemiological studies have explored the associations of ambient particulates with BP among pregnant women. However, the results of these studies have been inconsistent. Evidence from the United States indicated that exposure to particulate with aerodynamic diameter $\leq$ 2.5 μm ($PM_{2.5}$) during pregnancy was positively associated with maternal BP.[12] In another study of the United States, no association of $PM_{2.5}$ exposure during pregnancy with elevated maternal BP was observed.[13] $PM_{2.5}$ was even inversely related to odds of hypertension of pregnant women in Australia.[14] Mechanistic studies indicated that PM could activate sympathetic nervous system, induce endothelial dysfunction and arterial stiffness, which could further lead to elevated BP and hypertension.[15] However, there are some disadvantages in existing studies: (a) sample sizes were small or conclusions remained inconsistent.[12–14] Most of these studies addressing the effects of PM on BP were performed in developed countries with lower PM concentrations, (b) these previous analyses mainly focused on $PM_{2.5}$ or larger particulates than particulate with diameter $\leq$ 1.0 μm (PM_1). PM_1 contributes to the majority of $PM_{2.5}$ in China, which has smaller diameter but greater surface area to mass ratio and carries larger number of toxic compounds than $PM_{2.5}$.[16] Thus, PM_1 tends to

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be more toxic than those larger particles as the small size allows them to easily reach the lung alveoli and enter the circulatory system, and eventually adversely affecting BP of pregnant women.[17] Due to cardiovascular changes during pregnancy, pregnant women might be more sensitive to the toxic effects of particulates,[18] especially in the first trimester.[19]

No research has been performed to investigate the association of PM_1 exposure during pregnancy with maternal BP and HDP to our knowledge. However, these are new critical epidemiological evidences for a comprehensive understanding of the health effects of PM_1. In the current study, we aimed to examine the associations of PM_1 exposure with maternal BP, as well as HDP prevalence based on a nationwide population-based study (the China birth cohort study, CBCS).

RESULTS

Descriptive statistics

As presented in Table 1, the average age of the participants was 29.59 years old, and 93.68% of them were of Han ethnicity. A total of 14,453 (13.76%) pregnant women were identified as HDP. Compared with the non-HDP, pregnant women with HDP were older, possessing higher pre-pregnancy body mass index (BMI), were more likely to be conceived in summer & autumn, were more likely to be multipara and to be exposed to secondhand smoke.

Table S3 summarizes the distributions of PM_1 concentrations during three trimesters in 38 hospitals from the CBCS and their pairwise correlations. The median (interquartile range) of PM_1 concentration was 28.80 $\mu g/m^3$ (13.00 $\mu g/m^3$), 28.50 $\mu g/m^3$ (12.50 $\mu g/m^3$), and 27.20 $\mu g/m^3$ (13.30 $\mu g/m^3$) for the first, second, and third trimester, respectively. PM_1 levels during three trimesters were positively correlated with each other ($r_{spearman} > 0$).

Associations of PM_1 during pregnancy with maternal BP and hypertensive disorders of pregnancy

Each 10 $\mu g/m^3$ higher first-trimester PM_1 exposure was positively associated with higher first-trimester systolic blood pressure (SBP) (β = 1.696, 95% CI: 1.537,1.855) and first-trimester diastolic blood pressure (DBP) (β = 1.056, 95% CI: 0.908,1.203). Similar effects of first-trimester PM_1 were observed on second-trimester SBP/DBP but not on the third-trimester SBP/DBP. The pro-hypertensive effect of second-trimester PM_1 was only observed on second- and third-trimester SBP. Furthermore, each 10 $\mu g/m^3$ elevation in the first-trimester PM_1 exposure was associated with 11.4% (OR = 1.114, 95% CI: 1.074,1.156) increase in the risk of HDP prevalence (Table 2). The impact of second-trimester PM_1 exposure on HDP were not statistically significant (Table 2).

Stratified analyses of first-trimester PM_1 with maternal BP and hypertensive disorders of pregnancy

Compared with pregnant women aged less than 35 years, older pregnant women (> 35 years) had greater effect estimates (β = 2.276 for first-trimester SBP, β = 1.237 for first-trimester DBP, β = 0.626 for second-trimester SBP, β = 0.283 for second-trimester DBP, β = 0.384 for third-trimester SBP, β = 0.043 for third-trimester DBP, *OR* = 1.103 for HDP with all $P_{interaction} < 0.05$) (Figures 1, 2, 3, and 4, and Tables S4–S7).

When the estimates were stratified by maternal education, we found that the association between first-trimester PM_1 and first-trimester SBP was greatest among pregnant women educated longer than 17 years (β = 2.677, 95% CI: 2.144, 3.211) followed by the estimate for participants educated 13 to 16 years (β = 2.017, 95% CI: 1.766, 2.269) and participants educated less than 12 years (β = 1.284, 95% CI: 1.066, 1.502), with overall disparity across maternal education groups being significant ($P_{interaction} < 0.001$) (Figure 1A). Similar trends were found for the first-trimester DBP, second-trimester SBP/DBP, third-trimester SBP/DBP, and HDP (all values for $P_{interaction} < 0.001$), although the direction of effect estimates was not consistent across income groups for second-trimester DBP and third-trimester SBP/DBP (Figures 1B, 2, 4, and Tables S4–S7).

We also found that pregnant women with a household annual income above 400,000 CNY had greater effect estimates (β = 2.680 for first-trimester SBP, β = 1.745 for first-trimester DBP, β = 0.536 for second-trimester SBP, β = 0.332 for third-trimester SBP, *OR* = 1.289 for HDP with all $P_{interaction} < 0.001$) than other income groups (Figures 1, 2, 3, 4, and Tables S4–S7). There were also significant modification effects found

Table 1. Main characteristics of the participants (n = 105,063)

Characteristics	Overall (n = 105,063)	HDP (n = 14,453)	Non-HDP (n = 84,589)	p value
Maternal age, year, mean ± SD	29.59 ± 4.28	30.05 ± 4.59	29.50 ± 4.22	<0.001
Maternal pre-pregnancy BMI, kg/m^2, mean ± SD	21.84 ± 3.82	22.46 ± 4.43	21.74 ± 3.69	<0.001
Maternal ethnicity (%)				0.680
Han	98,425 (93.68%)	13,562 (93.84%)	79,291 (93.74%)	
Minority	6,638 (6.32%)	891 (6.16%)	5,298 (6.26%)	
Maternal education (%)				<0.001
≤ 12 years	51,043 (48.58%)	7,229 (50.02%)	40,905 (48.36%)	
13-16 years	42,792 (40.73%)	5,541 (38.34%)	34,919 (41.28%)	
≥ 17 years	11,228 (10.69%)	1,683 (11.64%)	8,765 (10.36%)	
Household annual income (%)				<0.001
< 100,000 CNY	36,124 (34.38%)	5,342 (36.96%)	28,883 (34.14%)	
100,000–400,000 CNY	56,493 (53.77%)	7,385 (51.10%)	45,886 (54.25%)	
> 400,000 CNY	12,446 (11.85%)	1,726 (11.94%)	9,820 (11.61%)	
Conception season (%)				<0.001
Spring	26,902 (25.61%)	2,967 (20.53%)	22,638 (26.76%)	
Summer	20,586 (19.59%)	3,098 (21.43%)	15,746 (18.62%)	
Autumn	28,554 (27.18%)	4,823 (33.37%)	22,137 (26.17%)	
Winter	29,021 (27.62%)	3,565 (24.67%)	24,068 (28.45%)	
Parity (%)				<0.001
Nullipara	50,778 (48.33%)	6,561 (45.40%)	41,310 (48.84%)	
Multipara	54,285 (51.67%)	7,892 (54.60%)	43,279 (51.16%)	
Maternal secondhand smoking (%)				0.006
No	92,490 (88.03%)	12,618 (87.30%)	74,533 (88.11%)	
Yes	12,573 (11.97%)	1,835 (12.70%)	10,056 (11.89%)	
Decoration (%)				0.602
No	98,234 (93.50%)	13,528 (93.60%)	79,071 (93.48%)	
Yes	6,829 (6.50%)	925 (6.40%)	5,518 (6.52%)	
Indoor chemical air pollution (%)				0.263
No	9,3608 (89.10%)	12,927 (89.44%)	75,377 (89.11%)	
Yes	11,455 (10.90%)	1,526 (10.56%)	9,212 (10.89%)	
First-trimester ambient temperature, °C; mean ± SD	16.84 ± 7.79	15.57 ± 8.31	16.93 ± 7.74	<0.001
Second-trimester ambient temperature, °C; mean ± SD	17.07 ± 7.32	15.93 ± 7.69	17.27 ± 7.25	<0.001
Third-trimester ambient temperature, °C; mean ± SD	17.03 ± 7.24	17.47 ± 7.25	16.95 ± 7.27	<0.001
First-trimester SBP, mmHg; mean ± SD	113.15 ± 12.92	121.92 ± 18.31	111.55 ± 10.93	<0.001
First-trimester DBP, mmHg; mean ± SD	71.49 ± 11.60	87.03 ± 13.79	68.64 ± 8.49	<0.001
Second-trimester SBP, mmHg; mean ± SD	113.57 ± 11.87	125.92 ± 14.46	111.43 ± 9.92	<0.001
Second-trimester DBP, mmHg; mean ± SD	69.27 ± 11.64	86.81 ± 13.47	66.24 ± 8.08	<0.001
Third-trimester SBP, mmHg; mean ± SD	114.33 ± 11.77	124.95 ± 15.56	112.50 ± 9.90	<0.001
Third-trimester DBP, mmHg; mean ± SD	69.59 ± 10.94	84.50 ± 13.38	67.03 ± 8.04	<0.001

HDP, hypertensive disorders of pregnancy; BMI, body mass index; CNY, China Yuan; SBP, systolic blood pressure; DBP, diastolic blood pressure; SD, standard deviation.

Table 2. Associations of each 10 $\mu g/m^3$ greater PM_1 concentrations during pregnancy with maternal blood pressure and hypertensive disorders of pregnancy

		SBP		DBP		HDP	
Exposure		aβ (95% CI)	p value	aβ (95% CI)	p value	aOR (95% CI)	p value
FT PM_1						1.313 (1.280, 1.347)[a]	< 0.001
						1.114 (1.074, 1.156)[b]	< 0.001
FT PM_1	FT	2.838 (2.727, 2.950)[a]	< 0.001	1.963 (1.861, 2.066)[a]	< 0.001		
	FT	1.696 (1.537, 1.855)[b]	< 0.001	1.056 (0.908, 1.203)[b]	< 0.001		
	ST	1.627 (1.529, 1.726)[a]	< 0.001	0.992 (0.896, 1.088)[a]	< 0.001		
	ST	0.456 (0.319, 0.592)[b]	< 0.001	0.102 (−0.032, 0.237)[b]	0.136		
	TT	0.750 (0.652, 0.848)[a]	< 0.001	0.486 (0.397, 0.576)[a]	< 0.001		
	TT	0.093 (−0.043, 0.229)[b]	0.179	−0.137 (−0.262, −0.012)[b]	0.031		
ST PM_1						0.997 (0.970, 1.023)[a]	0.813
						1.017 (0.981, 1.053)[b]	0.350
ST PM_1	ST	0.208 (0.107, 0.309)[a]	< 0.001	−0.127 (−0.226, −0.029)[a]	0.011		
	ST	0.051 (−0.079, 0.181)[b]	0.439	−0.103 (−0.231, 0.025)[b]	0.115		
	TT	1.045 (0.944, 1.145)[a]	< 0.001	0.359 (0.267, 0.451)[a]	< 0.001		
	TT	0.324 (0.195, 0.454)[b]	< 0.001	−0.037 (−0.156, 0.082)[b]	0.539		

FT, first-trimester; ST, second-trimester; TT, third-trimester; PM_1, particle with aerodynamic diameter ≤ 1.0 μm; aβ indicates adjusted estimate; CI, confidence interval; aOR, adjusted odds ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDP, hypertensive disorders of pregnancy.

[a]Crude model: adjusted for none.

[b]Adjusted model: adjusted for maternal age, pre-pregnancy body mass index, maternal ethnicity, maternal education, household annual income, conception season, and ambient temperature.

for second- and third-trimester DBP; however, the direction of effect estimates was not consistent across income groups (Figures 2 and 4), implying that further investigation is needed.

In addition, when the findings were stratified by maternal ethnicity, pre-pregnancy BMI, and conception season, interaction effects were not statistically significant for HDP (all $P_{interaction} > 0.05$).

Sensitivity analyses

The associations were not substantially changed in sensitivity analyses when we excluded participants who lived in urban areas, when we excluded participants who lived in south China, when we excluded participants exposed to indoor decoration, when we excluded participants exposed to indoor chemical air pollution, when we excluded participants with indoor coal combustion emissions at home, when we excluded participants who kept animals during pregnancy, or when we excluded participants who were multipara (Table S8). The results were also similar to the main analyses when we repeated the analyses by adjusting additional confounding factors including ozone and $PM_{1\text{-}2.5}$ (calculated by subtracting PM_1 from $PM_{2.5}$) (Table S9).

DISCUSSION

Main findings

In this nationwide study of PM_1-BP/HDP associations, we found positive associations of greater first-trimester PM_1 exposure with first- and second-trimester BP, as well as odds of HDP. Pregnant women who were older or those with higher education level or higher household annual income may be more vulnerable to the pro-hypertensive effects of PM_1 exposure. The results remained robust after a series of sensitivity analyses.

Comparison with previous studies

To date, previous studies have examined the PM_1-BP association in adults and children. Wang et al.[20] conducted a study involving 1.2 million couples (aged 18–45 years old) who were planning for pregnancy and reported that a 10 $\mu g/m^3$ greater PM_1 was associated with a 0.26 mmHg higher SBP and 0.22 mmHg higher DBP in females, as well as a 0.29 mmHg higher SBP and 0.17 mmHg higher DBP in males. Wu et al.[21] found that each

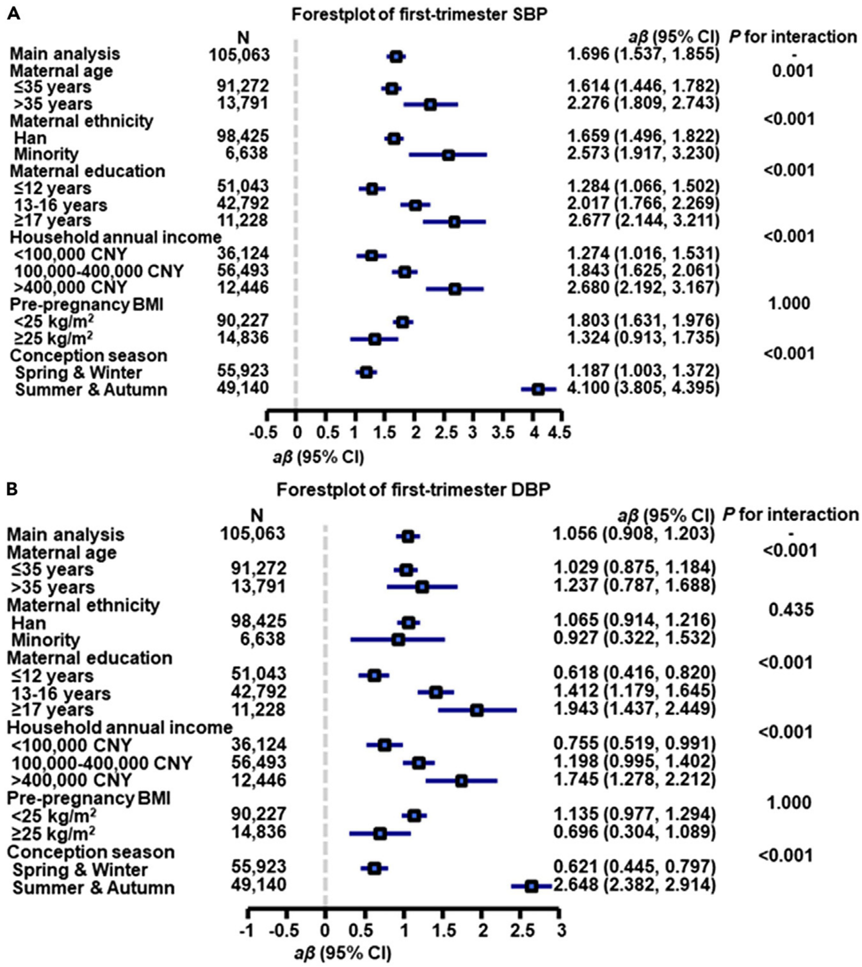

Figure 1. Associations of each 10 μg/m³ greater first-trimester PM_1 concentration with first-trimester SBP (A) and DBP (B) by potential effect modifiers*

aβ, adjusted regression coefficient, CI, confidence interval, CNY, China yuan. SBP, systolic blood pressure, DBP, diastolic blood pressure.

*Adjusted for maternal age, pre-pregnancy body mass index, maternal ethnicity, maternal education, household annual income, conception season, and ambient temperature.

10 μg/m³ greater PM_1 was associated with 2.56 mmHg elevated SBP and 61% higher odds for hypertension among children. Nevertheless, no previous study has examined the associations of PM_1 during pregnancy with maternal BP and HDP, and so further investigation is warranted to confirm the associations.

Although evidence on PM_1 exposure and maternal BP, as well as HDP is limited, several previous studies have investigated the association between $PM_{2.5}$ exposure and BP during pregnancy, among which $PM_{2.5}$ levels were evaluated in different trimesters. In the current study, first-trimester PM_1 was positively associated with first- and second-trimester BP, as well as odds of HDP, which are in line with some previous studies on PM. Exposure to $PM_{2.5}$ during pregnancy has been found to be associated with maternal elevated BP during pregnancy in the United States,[12,22] Korea,[23] Poland,[24] and China.[8,25–27] However, the results of some other studies have been inconsistent. Savitz et al.[28] did not find a significant association of $PM_{2.5}$ exposure in the first and second trimesters with hypertension during pregnancy based on a study of 268,601 pregnant women in New York City. In another study from the United States, there was also no association between $PM_{2.5}$ and HDP.[13] Interestingly, in a study of Australia involving 285,594 singleton pregnancies, $PM_{2.5}$ was inversely related to odds of hypertension (RR = 0.95, 95% CI: 0.93, 0.97).[14] The inconsistent conclusions may result from a number of factors, including difference in exposure level, exposure estimates methods, the study populations as well as the research methods.[29]

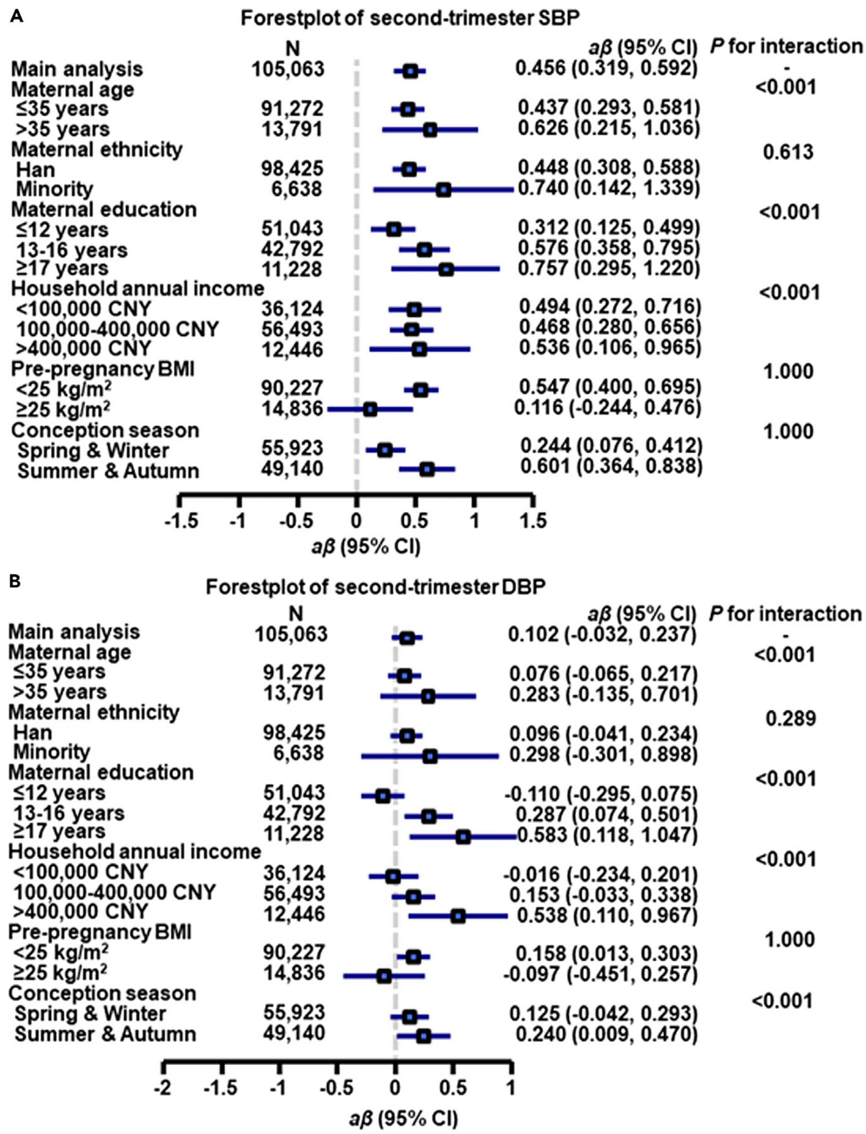

Figure 2. Associations of each 10 μg/m^3 greater first-trimester PM_1 concentration with second-trimester SBP (A) and DBP (B) by potential effect modifiers*

aβ, adjusted regression coefficient, CI, confidence interval, CNY, China yuan. SBP, systolic blood pressure, DBP, diastolic blood pressure.

*Adjusted for maternal age, pre-pregnancy body mass index, maternal ethnicity, maternal education, household annual income, conception season, and ambient temperature.

Environmental factors, such as air pollution, ambient temperature, noise, and greenness may contribute to the development of hypertension,[30] so the further investigations of environmental factors based on a nationwide sample are highly warranted. In our previous study, we found that exposure to cold ambient temperature in the second and third trimesters were associated with elevated BP, as well as increased HDP prevalence among most Chinese pregnant women.[31] There are few reports of the health effects of PM_1 worldwide due to the unavailability of PM_1 data. Although no prior study has examined the effect of PM_1 exposure on BP of pregnant women, the current study offers a new perspective on the association of maternal PM_1 exposure with BP and risk of HDP. This finding may be used to provide information for public health interventions and environmental policies enactment.

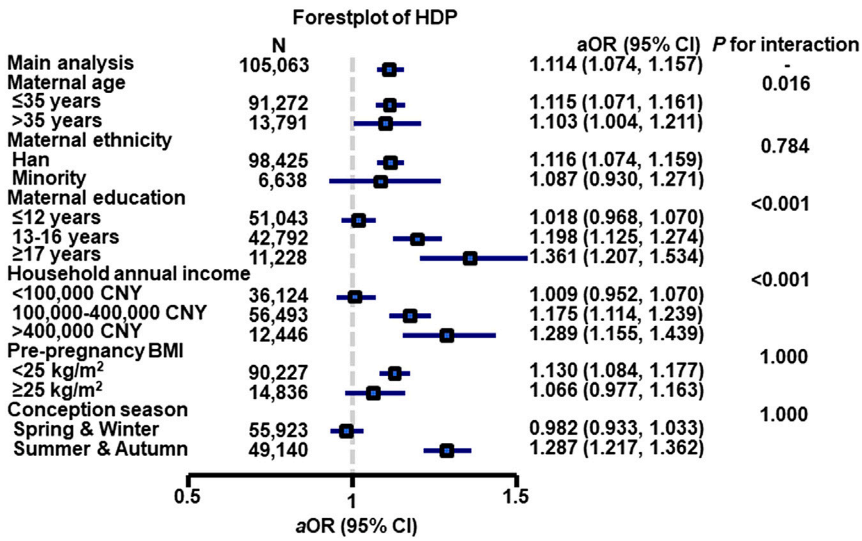

Figure 3. Associations between first-trimester PM_1 and hypertensive disorders of pregnancy by potential effect modifiers*

aOR, adjusted odds ratio, CI, confidence intervals, CNY, China yuan.

*Adjusted for maternal age, pre-pregnancy body mass index, maternal ethnicity, maternal education, household annual income, conception season, and ambient temperature.

Potential mechanisms

PM_1 could be created by burning of fossil fuel, coal, and biomass.[32] The mechanisms through which PM could elevate BP have not been fully clarified. One plausible pathway is that PM could stimulate receptors and nerve endings in the airways, and thereby activate sympathetic nervous system, which could further lead to elevated BP.[33] The second hypothesized pathway is that PM could elicit inflammation and oxidative stress, resulting in endothelial dysfunction and further elevated BP.[15,34–36] The third possible pathway is that sustained endocrine gland-derived vascular endothelial growth factor after the first trimester could lead to higher BP.[37] Other mechanisms may via arterial stiffness and DNA hypomethylation induced by PM.[15,38] The aerodynamic diameter of PM is an important factor that determining the health effects.[39,40] PM_1 showed smaller diameter but greater surface area to mass ratio than $PM_{2.5}$, and thus has greater ability to reach the lung alveoli and enter the circulatory system, thus exerting adverse effects such as inflammatory responses on the BP.[17,41,42] Additionally, PM_1 absorbed more toxic substances such as organic compounds, which could induce localized oxidative and inflammatory response.[43] Considering that PM_1 contributes to the majority of $PM_{2.5}$ in China, it is reasonable to speculate that PM_1 may play an important role in the pro-hypertensive effect of $PM_{2.5}$.

Susceptible population

In stratified analyses, we found pregnant women who were older or those with higher education level or higher household annual income may be more vulnerable to the pro-hypertensive effects of ambient PM_1 exposure. The reason for this finding may be that advanced age-related endothelial dysfunction may amplify the endothelial dysfunction effect, which could also be caused by PM, leading to vascular damage and further development of hypertension.[44] People with higher household annual income or higher education level tended to intake more total energy, meat, animal fat, protein, sugar, and sweetener, leading to an increased prevalence of overweight/obesity and dyslipidaemia, which may further increase arterial stiffness caused by PM,[45,46] and these people often engaged in less physical activities, which is imperative for the maintenance of normal BP.[47,48] In the current study, more participants who was educated longer than 17 years (88.28%, 9,912 of 11,228) or possessing a household annual income more than 400,000 CNY (86.06%, 10,711 of 12,446) lived in urban areas than rural areas. Urban areas were high in air pollution, noise, and heavy in traffic compared with rural areas, which could synergistically cooperate with PM to activate sympathetic nervous system, and further lead to elevated BP.[49] Further study is warranted to investigate the associations of maternal age, education level, and household annual income with BP.

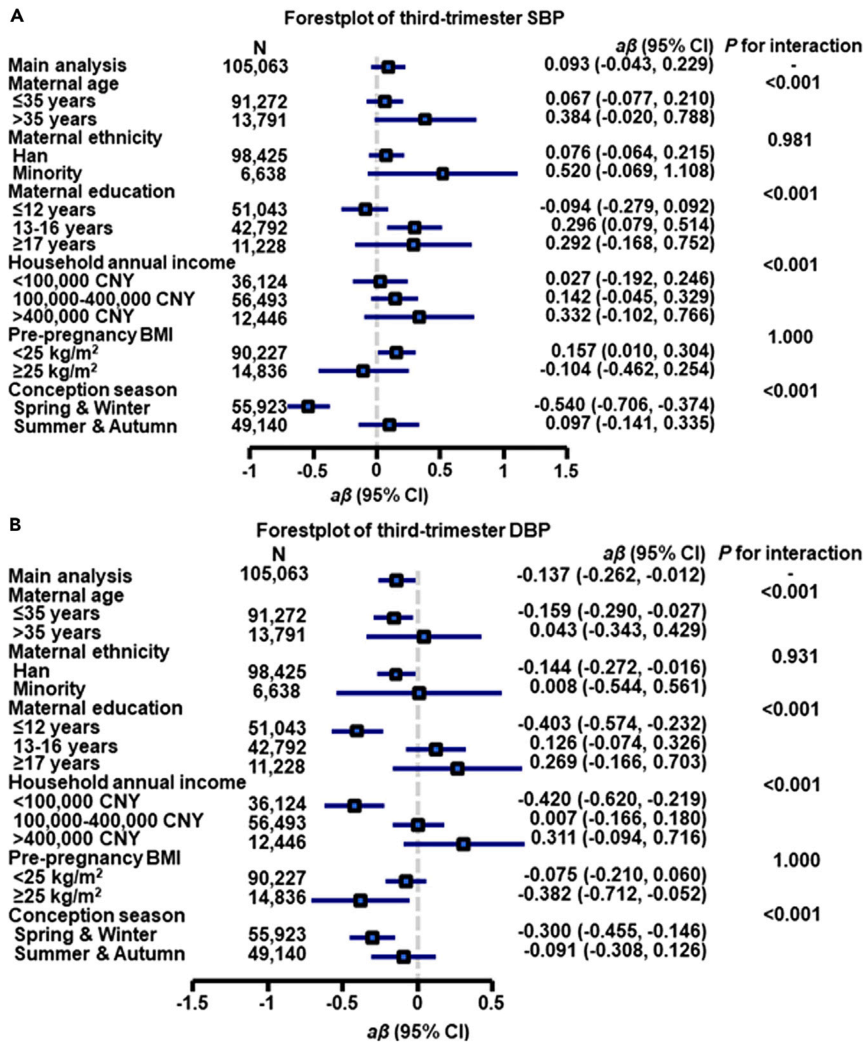

Figure 4. Associations of each 10 $\mu g/m^3$ greater first-trimester PM_1 concentration with third-trimester SBP (A) and DBP (B) by potential effect modifiers*

$a\beta$, adjusted regression coefficient, CI, confidence interval, CNY, China yuan. SBP, systolic blood pressure, DBP, diastolic blood pressure.

*Adjusted for maternal age, pre-pregnancy body mass index, maternal ethnicity, maternal education, household annual income, conception season, and ambient temperature.

Conclusion

Exposure to first-trimester PM_1 might be positively associated with elevated first- and second-trimester BP, as well as HDP prevalence, particularly among pregnant women who were older or those with higher education level or higher household annual income. Further studies are warranted to investigate the mechanisms of increased vulnerability to PM_1 and validate our findings. Corresponding work should also be conducted for government to protect pregnant women from adverse effects associated with PM_1 exposure.

Limitations of the study

The current study has several limitations. First, the temporal association between first-trimester PM_1 exposure and BP of pregnant women could not be confirmed due to the cross-sectional nature of the current study. Second, PM_1 concentrations during pregnancy were predicted based on ground monitoring data, satellite remote sensing, meteorologic data, and land use information. Although the satellite-based prediction of PM_1 has been widely used by many epidemiological studies, predictive error of PM_1 still exists.

The accuracy and spatial resolution of estimated PM_1 could be improved in future by including more detailed environmental data with novel models. More advanced devices and technologies are needed to measure exposure level more accurately in future research. Third, maternal BP could be affected by humidity, diet, exercise, and the technical proficiency of the tester. However, maternal BP was measured by trained nurses with same digital BP monitors according to the American Heart association recommendations for BP measurements. Forth, although we adjusted for the important potential confounders in this study, like most previous studies, we cannot rule out the possibility of the bias related to residual confounders, such as maternal stress, family history of hypertension, heart, and kidney disease, diabetes, other metabolic disorders, pregnancy via *in vitro* fertilization, physical activity, traffic noise exposure, and other pollutants, which might affect the BP but were not included in this study.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2023.106863.

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AUTHOR CONTRIBUTIONS

Conceptualization, M.Z., Y.Q.S., W.T.Y., C.H.Y., G.H.D., and W.J.Z., methodology, M.Z., B.Y.Y., Y.Q.S., Y.Q.Z., G.B.C., and W.J.Z., formal analysis, M.Z., B.Y.Y., Y.Q.Z., and Y.Q.S., investigation, R.X.L., Y.Z., S.F.S., E.J.Z., X.T.Z., Q.Z.W., L.X.H., Y.T.Z., L.B.W., Y.N.L., X.X.L., J.X.L., S.H.W., and X.M., resources, C.H.Y., W.T.Y., R.X.L., Y.Z., S.F.S., E.J.Z., and X.T.Z., data curation, R.X.L., Y.Z., S.F.S., E.J.Z., X.T.Z., Q.Z.W., L.X.H., Y.T.Z., L.B.W., Y.N.L., X.X.L., J.X.L., S.H.W., and X.M., writing—original draft, M.Z. and Y.Q.S., writing—review & editing, B.Y.Y., W.T.Y., C.H.Y., G.H.D., and W.J.Z., visualization, M.Z., Y.Q.S., and Y.Q.Z., funding acquisition, W.T.Y., C.H.Y., Y.Q.S., and M.Z., supervision, W.T.Y., C.H.Y., G.H.D., and W.J.Z.

DECLARATION OF INTERESTS

The authors declare no competing interests.

INCLUSION AND DIVERSITY

We support inclusive, diverse, and equitable conduct of research.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
R Version 4.1.1	R Foundation	https://www.r-project.org/

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources and reagents should be directed to and will be fulfilled by the lead contact, Wentao Yue (yuewt@ccmu.edu.cn).

Materials availability

This study did not generate new unique reagents.

Data and code availability

- Data reported in this study cannot be deposited in a public repository due to confidentiality reasons, which are mandatory according to the Ethical Committee. However, they might be available upon request to the lead contact. To request access, contact Wentao Yue (yuewt@ccmu.edu.cn).
- This paper does not report original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

METHOD DETAILS

Study population

Data was collected from the CBCS, a nationwide cohort study, that investigating the risk factors underlying maternal-fetal health. Details of the CBCS have been presented elsewhere.[50] Briefly, the CBCS covering 38 research centers in 17 provinces in China from November 2017 through December 2021 (Table S1 and Figure S1). In CBCS, pregnant women were enrolled in the first trimester (6-12 weeks' gestation). At this time, each participant was asked to complete a self-filled questionnaire, including social and demographic characteristics, previous medical status, health lifestyle behaviors, residential environments as well as housing information. The first and second follow-up visits were conducted in the second (20-24 weeks' gestation) and third trimesters (28-34 weeks' gestation), respectively. Medical examination records during pregnancy were collected by trained researchers, doctors, or nurses. If a participant experienced a pregnancy loss, all clinical information would also be recorded. The third follow-up visit was conducted after delivery to collect the birth records of newborns for further analysis.

In the current study, pregnant women (n = 106,087) were initially included, their information (i.e., maternal age, ethnicity, pre-pregnancy weight, height, education, household annual income, secondhand smoke exposure, alcohol consumption, conception season, parity, blood pressure, residential addresses, etc.) was collected using the unique identification numbers. Exclusion criteria was that participants who failed to complete the survey (n = 957), participants with outliers or missing data for maternal age (n = 13) or pre-pregnancy BMI (n = 54). Thus, 105,063 pregnancies were eligible for final analyses (Figure S2).

The current study was approved by the Ethics Committee of Beijing Obstetrics and Gynecology Hospital, Capital Medical University (number: 2018-KY-003-01). Written informed consents were signed by each participant before data collection.

BP measurement and HDP definition

Maternal BP was measured by trained nurses at 6-12 weeks, 20-24 weeks, and 28-34 weeks of gestation with digital blood pressure monitors (A&D Medical Life Source TM-2655) according to the American Heart

Association recommendations for BP measurements. Before the measurement, pregnant women should stop smoking, eating, drinking alcohol/caffeinated drinks, or physical exercising for more than 30 minutes and have a break for more than five minutes in a comfortable room.[21,51] SBP and DBP on the upper right arm were measured with pregnant women in a sitting position, and the elbow was at the same level with heart when measuring. The measurements were repeated in three successive pairs after an interval of at least two minutes, and mean values of the three measurements were recorded in the electronic data capturing system.

HDP were divided into four categories as follows: (a) gestational hypertension, (b) preeclampsia or eclampsia, (c) chronic hypertension, and (d) superimposed preeclampsia.[52] Gestational hypertension was defined as new-onset hypertension (mean SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg) after 20 weeks of gestation.[53] Preeclampsia was defined as hypertension (SBP/DBP $\geq$140/90 mmHg) and proteinuria of 1+ or more on a dipstick test or the protein level in the urine $\geq$ 300 mg/24-hour after 20 weeks of gestation, or hypertension plus the involvement of one organ or system in women with previously normal blood pressure.[54] Eclampsia was defined as new-onset grand mal seizures in women with pre-eclampsia.[55] Chronic hypertension refers to hypertension ($\geq$140/90 mmHg) predating the pregnancy or before 20 weeks of gestation.[56] Superimposed preeclampsia refers to chronic hypertension associated with preeclampsia.[55]

PM_1 exposure assessment

Daily PM_1 concentrations in 17 provinces of CBCS were predicted at a spatial resolution of 0.1° × 0.1° from 2017 to 2021, based on a combination of ground monitoring data, satellite remote sensing, meteorologic data, and land use information, which were previously reported.[32,57] Briefly, we combined two Moderate Resolution Imaging Spectroradiometer (MODIS) aerosol optical depth (AOD) product, Dark Target and Deep Blue data, using an inverse variance weighting method, after filling their gaps. Daily meteorological data (*i.e.*, temperature, barometric pressure, relative humidity, and wind speed) were obtained from the China meteorological data sharing service system (http://data.cma.cn/). We obtained annual land cover data (*i.e.*, urban cover, forest cover, and water cover) at a spatial resolution of 500 m from Global Mosaics of the standard MODIS land cover type data Collection 5.1 product of Global Land Cover Facility (http://glcf.umd.edu/). We downloaded monthly average Normalized Difference Vegetation Index data (MODIS Level 3) from the NASA Earth Observatory (http://neo.sci.gsfc.nasa.gov). Aqua and Terra active fires during the study period were downloaded from NASA Fire Information for Resource Management System (https://earthdata.nasa.gov/data/near-real-time-data/firms). In addition, elevation (http://srtm.csi.cgiar.org/) were also collected.

We developed a generalized additive model (GAM) to link the ground monitored PM_1 concentrations with information of AOD, meteorology, land cover, vegetation, active fires, and other spatial predictors.[16] During the process of developing GAM, AOD was included firstly, and then other predictors were included sequentially to achieve an optimal model that maximized the explained variability in air pollutant concentrations. In addition, we have considered the variability of PM_1 level in different areas and over time by using a range of spatial and temporal predictors, including region (province), month, and day of the week.[16] Results of 10-fold cross-validation method showed the adjusted coefficient of determination (R^2) and root mean squared error (RMSE) were 59% and 22.5 $\mu g/m^3$ for daily predicted PM_1, respectively.

Collected residential addresses of participants were geocoded into longitude and latitude using the Application Programming Interface (API) provided by Auto Navi Map (https://www.autonavi.com). We then assigned trimester (*i.e.*, first, second, and third trimesters) average PM_1 concentrations to each study participant based on their coordinates.

Confounders

According to the suggestion of Textor et al.,[58] potential confounders were identified based on three primary criteria as follows: (a) it could lead to elevated BP or hypertension, (b) it should be a "cause" of air pollution, and (c) it should not be the "effect" of exposure (air pollution), nor be an intermediate factor in the causal chain of outcome (hypertension). A directed acyclic graph (DAG, Figure S3) presenting the published studies (Table S2) was constructed with DAGitty v3.0 software (http://www.dagitty.net/development/dags.html) to identify a minimally sufficient set of potential confounders,[59] leaving maternal age, pre-pregnancy BMI, maternal ethnicity, maternal education, household annual income, conception season, and ambient temperature as confounders in the adjusted models.

We obtained the individual information of pregnant women using self-filled questionnaires: maternal age (years), maternal ethnicity (Han versus Minority), maternal pre-pregnancy BMI (kg/m^2), maternal education ($\leq$12 years versus 13-16 years versus $\geq$17 years), household annual income(<100,000 CNY versus 100,000-400,000 CNY versus >400,000 CNY), maternal secondhand smoke exposure (yes versus no), maternal alcohol consumption (yes versus no), conception season (spring versus summer versus autumn versus winter), parity (nullipara versus multipara). Pre-pregnancy BMI was obtained as the weight in kilograms divided by the square of the height in meters before conception. Secondhand smoke exposure was identified as non-smokers being exposed to cigarette smoke for more than 15 minutes daily for more than one day per week.[60] Maternal alcohol consumption was defined as pregnant women who drinking once a week for more than six months.[61] Ambient temperature from 2017 to 2021 (period of data collection) were collected from the ERA5-land reanalysis dataset of the European Centre for Medium-Range Weather Forecasts (ECMWF) (https://www.ecmwf.int/).

QUANTIFICATION AND STATISTICAL ANALYSIS

Descriptive statistics

Continuous and categorical variables were presented as mean $\pm$ standard deviation (SD) or as frequency with percentage, respectively.

Main analyses

Generalized linear mixed models with a random intercept for hospital were used to evaluate the associations of PM_1 with SBP/DBP levels of three trimesters or HDP prevalence, respectively. The effect estimates were presented as regression coefficient (β for continuous outcomes) and odds ratio (OR for dichotomous outcomes), respectively per 10 $\mu g/m^3$ higher PM_1. The unadjusted models and adjusted models were developed. The variance inflation factors (VIFs) of all the variables in the models were calculated to ensure the absence of collinearity for the adjusted models (all VIFs < 5).

Stratified analyses

Furthermore, the PM_1-BP/HDP associations may be different among subgroups of participants. To explore potential effect modification, we performed stratified analyses by maternal age of the participants ($\leq$ 35 years versus > 35 years), maternal ethnicity (Han versus Minority), maternal education ($\leq$12 years versus 13-16 years versus $\geq$ 17 years), household annual income (<100,000 CNY versus 100,000-400,000 CNY versus >400,000 CNY), pre-pregnancy BMI (<25 kg/m^2 versus $\geq$ 25 kg/m^2), and conception season (spring & winter versus summer & autumn).

Sensitivity analyses

To assess the robustness of our findings, several sensitivity analyses were performed. The PM_1-BP/HDP associations were estimated by individually excluding participants who lived in urban areas, participants who lived in south China, participants exposed to indoor decoration, participants exposed to indoor chemical air pollution, participants with indoor coal combustion emissions at home, participants who kept animals during pregnancy, or multipara. In addition, we reran our models by adjusting additional confounding factors including ozone and $PM_{1\text{-}2.5}$.

Statistical analyses were performed using R 4.1.1. Statistical significance of main effects and interactions were assumed at P < 0.05 for a 2-tailed test.