Long-Term Effects of Ambient Particulate Matter (With an Aerodynamic Diameter ≤2.5 μm) on Hypertension and Blood Pressure and Attributable Risk Among Reproductive-Age Adults in China

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***Background*—**Epidemiological evidence on the association between long-term exposure to ambient fine particulate matter (with an aerodynamic diameter ≤2.5 μm; $PM_{2.5}$) and hypertension is mixed. We investigated the long-term association between ambient fine particles and hypertension in reproductive-age adults.

***Methods and Results*—**This analysis included 39 348 119 reproductive-age (20–49 years) participants from the National Free Preconception Health Examination Project from April 22, 2010 to December 31, 2015 across China. The estimation of annual average ambient $PM_{2.5}$ concentrations for each community was realized through using satellite-based spatial statistical models. Linear mixed models and 2-level logistic regressions adjusted for potential confounders with natural cubic splines were used to investigate the shape of $PM_{2.5}$–blood pressure and $PM_{2.5}$-hypertension, respectively. The effect modification by sex, obesity, smoking status, age, diabetes mellitus, urbanity, race, and region was also taken into account. The concentration-response relationship between $PM_{2.5}$ and hypertension was nonlinear, with a threshold concentration of 47.9 μg/m^3. The odds ratio of hypertension related to a 10-μg/m^3 increase in $PM_{2.5}$ above threshold was 1.010 (95% confidence interval, 1.007–1.012). A 10-μg/m^3 increase in $PM_{2.5}$ above threshold corresponded to a 0.569 (95% confidence interval, 0.564–0.573) mm Hg elevation in systolic blood pressure and a 0.384 (95% confidence interval, 0.381–0.388) mm Hg elevation in diastolic blood pressure. There were 2.3% (95% confidence interval, 2.2%–2.4%) of the hypertension cases that could be attributed to $PM_{2.5}$ exposures in reproductive-age adult populations.

***Conclusions*—**Long-term exposures to $PM_{2.5}$ above certain levels might increase population risk for hypertension and might be responsible for China's avoidable hypertension burden in reproductive-age adults. **(*J Am Heart Assoc*. 2018;7:e008553. DOI: 10.1161/JAHA.118.008553.)**

Key Words: air pollution • blood pressure • China • hypertension

Ambient fine particulate matter ranked the sixth leading risk for mortality in 2016, and it contributed to 4.1 million deaths and 105.7 million disability-adjusted life-years, according to 7.5% of total global deaths and 4.4% of global disability-adjusted life-years.[1] China had the largest numbers of attributable deaths and disability-adjusted life-years: 26.3% and 21.0% of the respective global totals.[1]

High blood pressure (BP) ranked the first leading risk factor for cardiovascular morbidity and mortality.[1] In the past several years, a growing body of epidemiological studies has examined whether long-term exposures to ambient fine particulate matter (with an aerodynamic diameter ≤2.5 μm; $PM_{2.5}$) pollution increase the risk of hypertension, but the findings are inconsistent.[2–14] The inconsistent results may be attributable to the heterogeneity in particulate matter sizes or constituents between geographic regions. Furthermore, most research was conducted in European countries and the United States, where air pollutant concentrations were low compared with China.[4,7,9,14–16]

Some studies conducted in Chinese cities also reported that long-term exposure to ambient $PM_{2.5}$ had deleterious effects on hypertension and associated with elevated BP.[5,8,12,13]

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Clinical Perspective

What Is New?

- This is the largest epidemiological study that found that long-term exposure to ambient fine particulate matter (with an aerodynamic diameter ≤2.5 μm) was associated with higher hypertension prevalence and elevated blood pressure in Chinese reproductive-age (20–49 years) populations.
- The current findings show that the exposure-response relationship between particulate matter with an aerodynamic diameter ≤2.5 μm and hypertension was nonlinear and indicated a threshold effect.

What Are the Clinical Implications?

- Our findings contribute to improve the knowledge on the long-term effect of ambient particulate matter with an aerodynamic diameter ≤2.5 μm on hypertension and blood pressure for Chinese reproductive-age populations.
- Long-term exposures to particulate matter with an aerodynamic diameter ≤2.5 μm above certain levels might increase population risk for hypertension and might be responsible for China's avoidable hypertension burden in reproductive-age adults.

However, these studies were often conducted in one city or just a few cities, where air pollution was several times higher than in cities with less air pollution. As a result, previous study estimates may not be sufficient to contribute to policy making and standards setting at the national level.

The aim of the present study was to explore the association of long-term exposures to ambient $PM_{2.5}$ with hypertension and BP among reproductive-age adults in China, from April 22, 2010 through December 31, 2015, using large nationwide survey data.

Methods

Study Population

The National Free Preconception Health Examination Project is an ongoing program run by the Ministry of Finance and National Health and Family Planning Commission of China, initiating in 2010 across 2790 counties of 31 provinces in China. The aim is to provide free health examinations before conception, risk assessments, and counselling services for reproductive couples who intended to be pregnant for the next 6 months. Overall, 39 348 119 reproductive-age (20–49 years) participants participated in this program between 2010 and 2015 and were eligible for this study when excluding individuals with missing data that were used to estimate air pollution exposure or used in the concentration-response relationship analysis. Detailed project-related design, organization, and implementation have been previously described.[17–20] The research proposal was approved by the ethics committee of National Research Institute for Health and Family Planning. All participants provided written informed consent. Because of the data use agreement with the National Health and Family Planning Commission of China, the data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Outcome Assessment

Hypertension diagnosis was defined as systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, or self-reported antihypertensive medication use in the past 2 weeks before the health examinations. The study subjects' BP measurement was taken 3 times on the right arm of the seated participating adults by trained medical personnel using an electronic sphygmomanometers, and the mean value of the 3 measurements was applied as the BP for this study.

Exposure Assessment

Hybrid geophysical-statistical method, with data from satellites, ground-based observations, and models, was used to predict annual average concentration of ambient $PM_{2.5}$ at $0.01^{\circ}\times0.01^{\circ}$ spatial resolution for each participant residing in China between 2007 and 2015. The methods for $PM_{2.5}$ exposure estimates have been validated in previous studies and are documented in detail elsewhere.[21–23] The community locations were geocoded using Gaode Map (http://www.amap.com). We then spatially matched the annual $PM_{2.5}$ concentration estimates to each participant in the corresponding communities. Average 3-year ambient $PM_{2.5}$ concentrations preceding the health examinations in the National Free Preconception Health Examination Project for each participant were used as the estimated surrogate of exposure.

Potential Confounders and Effect Modifiers

We collected variables of potential confounders and effect modification. Demographic, socioeconomic, and lifestyle characteristics were considered in the analyses, such as sex, age, race, smoking status, calendar year, body mass index (BMI), alcohol consumption, educational level, urbanity, region, and physician-diagnosed diabetes mellitus. We used the variable selection method, 10% variation in the main effect estimate criterion, to select potential confounding factors.[5,14] We evaluated effect modifiers through sex, obesity (BMI ≥24 kg/m^2), smoking status, age, diabetes mellitus, urbanity, race, and region through stratified analyses, and we assessed statistical significance as follows:

$$(\hat{Q}_1 - \hat{Q}_2) \pm \sqrt{(\hat{SE}_1)^2 + (\hat{SE}_2)^2}$$

where $\hat{Q}_1$ and $\hat{Q}_2$ were the effect estimates for each stratum, and $\hat{SE}_1$ and $\hat{SE}_2$ were the SEs.[12]

Statistical Analyses

Two-level logistic regression modeling approaches were applied to test the relationship between hypertension risk and the predicted 3-year average $PM_{2.5}$ exposure measures in reproductive-age (20–49 years) adults, where individuals were regarded as the first-level unit and the communities were regarded as the second-level unit.[8] Linear mixed models were used to study associations of 3-year exposures to $PM_{2.5}$ and BP. We modeled exposure in quintiles to assess for potential nonlinearity of exposure-response relationships.

Natural cubic splines were used for $PM_{2.5}$ to check whether the exposure-response relationships were linear or nonlinear. The *df* was selected by assessing the model fitting on the basis of the Akaike Information Criterion. If the relationship between $PM_{2.5}$ and hypertension was linear, the odds ratios (ORs) with corresponding 95% confidence intervals (CIs) of hypertension with a 10-μg/m^3 increment in $PM_{2.5}$ were calculated. On the contrary, if the relationship between $PM_{2.5}$ and hypertension was nonlinear, the ORs with corresponding 95% CIs of hypertension comparing the 75th and 95th percentiles of $PM_{2.5}$ versus the minimum hypertension concentration of $PM_{2.5}$ (threshold) were calculated. The ORs of hypertension associated with a 10-μg/m^3 increase in $PM_{2.5}$ above the thresholds were calculated as well. For BP, the absolute BP changes with corresponding 95% CIs were calculated to assess the effects of long-term ambient $PM_{2.5}$ exposure in reproductive-age adults across China.

To determine the threshold of the associations, we used the segment spline model to iteratively estimate the Akaike Information Criterion values of 2-level logistic regression models by 0.1-U increments in $PM_{2.5}$. The $PM_{2.5}$ concentration corresponding to the minimum Akaike Information Criterion value was selected as the threshold (minimum hypertension concentration of ambient $PM_{2.5}$).[24,25]

Estimating Attributable Hypertension Risk

Attributable cases and population-attributable fraction were used to estimate the burden of hypertension attributed to long-term exposure to ambient $PM_{2.5}$.[26] Hypertension attributable to $PM_{2.5}$ was calculated as follows:

$$AH = \sum p_0 \times (OR_i - 1) \times N_i$$

where i is $PM_{2.5}$ level category i; the range of every $PM_{2.5}$ category is 5 μg/m^3; AH is hypertension attributed to $PM_{2.5}$; p_0 is the hypertension prevalence among individuals exposed to $PM_{2.5}$ pollution level at threshold concentration; OR_i is the OR of hypertension associated with ambient $PM_{2.5}$ at the median concentration of category i against threshold; and N_i is population exposure to $PM_{2.5}$ category i.

Population-attributable fraction of hypertension because of $PM_{2.5}$ was calculated as follows:

$$Populationattributablefraction = \text{Attributable cases/Overall cases.}$$

Results

The descriptive statistics of the 39 348 119 participants are presented in Table 1. Our analysis population contained reproductive-age adults with a mean age of 27.7 years (SD, 5.0 years) and a balanced sex distribution (49.6% women versus 50.4% men). Among the analysis population, 23.7% had a BMI >24 kg/m^2. Of all 1 594 080 hypertensive participants, the self-reported physician-diagnosed hypertension accounted for 60 037 (0.2%), and 1 534 043 (3.9%) were hypertensive by this survey. Mean exposure concentration of ambient $PM_{2.5}$ pollutants in the past 36 months was 47.0 μg/m^3 (SD, 17.0 μg/m^3). Figure 1 shows the location of the 327 study cities and 36-month $PM_{2.5}$ exposure level for 39 348 119 participants.

The relationships between ambient $PM_{2.5}$ and hypertension were generally U shaped, as depicted in Figures 2 and 3, which indicated a threshold effect (namely, a minimum hypertension concentration of $PM_{2.5}$). Thus, we calculate the ORs with corresponding 95% CIs of hypertension comparing the 75th and 95th percentiles versus the threshold concentration of $PM_{2.5}$ in all following analyses.

The concentration-response relationships between ambient $PM_{2.5}$ and hypertension were nonlinear (Figures 2 and 3). The estimated $PM_{2.5}$ thresholds were 47.9 μg/m^3 for all hypertension, and 56.9, 45.4, 49.9, and 39.9 μg/m^3 for women, men, those aged 20 to 34 years, and those aged 35 to 49 years, respectively (Tables 2 and 3).

Increased concentrations of $PM_{2.5}$ above thresholds were connected to increased risks of hypertension. The OR of hypertension related to a 10-μg/m^3 increase in $PM_{2.5}$ above threshold was 1.010 (95% CI, 1.007–1.012). ORs for hypertension at the 75th and 95th percentiles of $PM_{2.5}$ against the thresholds were 1.031 (95% CI, 1.029–1.033) and 1.131 (95% CI, 1.125–1.137), respectively. Long-term exposure to ambient $PM_{2.5}$ above thresholds was also related to elevated systolic and diastolic BP. A 10-μg/m^3 increase in $PM_{2.5}$ above threshold corresponded to a 0.569 (95% CI, 0.564–0.573) mm Hg elevation in systolic BP and a 0.384 (95% CI, 0.381–0.388) mm Hg elevation in diastolic BP. The concentration of ambient $PM_{2.5}$ at the 75th percentile against the thresholds corresponded to an increment of 0.645 (95% CI, 0.642–

Table 1. Characteristics of 39 348 119 Participants Aged 20 to 49 Years in the National Free Preconception Health Examination Project From 2010 to 2015

Characteristics	Overall	Quintile Categorical 36-mo $PM_{2.5}$ Exposure, μg/m^3				
		<32.219	32.219–40.647	40.647–<51.063	51.063–<62.865	≥62.865
Age, y	27.71±4.97	28.33±5.33	27.94±5.17	27.60±5.01	27.44±4.81	27.21±4.41
36-mo Average $PM_{2.5}$, μg/m^3	46.95±17.01	24.17±5.59	36.63±2.32	45.17±3.03	57.14±3.40	71.68±6.74
Body mass index, kg/m^2	22.21±3.11	21.97±2.99	21.87±2.91	21.93±3.02	22.38±3.21	22.89±3.30
Systolic blood pressure, mm Hg	112.89±10.67	112.37±10.91	112.18±10.70	112.19±10.60	113.37±10.76	114.35±10.21
Diastolic blood pressure, mm Hg	73.68±7.81	73.52±8.05	73.32±7.87	73.25±7.75	73.84±7.76	74.49±7.52
Sex						
Male	19 834 788 (50.4)	3 986 802 (50.6)	3 970 052 (50.4)	3 950 240 (50.3)	3 967 320 (50.4)	3 960 374 (50.3)
Female	19 513 331 (49.6)	3 887 859 (49.4)	3 905 859 (49.6)	3 909 279 (49.7)	3 904 731 (49.6)	3 905 603 (49.7)
Education level						
Primary school or below	1 948 275 (5.0)	863 227 (11.0)	408 031 (5.2)	324 647 (4.1)	164 226 (2.1)	188 144 (2.4)
Junior high school	24 692 143 (62.8)	4 766 159 (60.5)	4 867 693 (61.8)	4 403 241 (56.0)	5 003 599 (63.6)	5 651 451 (71.8)
High school	7 066 215 (18.0)	1 243 970 (15.8)	1 426 126 (18.1)	1 737 155 (22.1)	1 520 283 (19.3)	1 138 681 (14.5)
College or above	5 641 486 (14.3)	1 001 305 (12.7)	1 174 061 (14.9)	1 394 476 (17.7)	1 183 943 (15)	887 701 (11.3)
Race						
Han nationality	33 147 461 (84.2)	6 142 065 (78.0)	6 378 733 (81.0)	7 349 515 (93.5)	7 686 224 (97.6)	7 308 832 (92.9)
Other nationality	6 200 658 (15.8)	1 732 596 (22.0)	1 497 178 (19.0)	510 004 (6.5)	185 827 (2.4)	557 145 (7.1)
Region						
East	3 515 192 (8.9)	736 066 (9.3)	271 102 (3.4)	200 444 (2.6)	319 449 (4.1)	1 988 131 (25.3)
North	1 508 385 (3.8)	459 591 (5.8)	391 579 (5)	602 848 (7.7)	54 367 (0.7)	0 (0)
Central	10 813 567 (27.5)	1 970 629 (25)	924 227 (11.7)	1 277 437 (16.3)	3 432 959 (43.6)	3 208 315 (40.8)
South	10 278 596 (26.1)	412 961 (5.2)	1 419 122 (18)	2 628 912 (33.4)	3 628 531 (46.1)	2 189 070 (27.8)
Southwest	4 929 859 (12.5)	1 439 572 (18.3)	2 463 544 (31.3)	1 024 759 (13)	1984 (0.025)	0 (0)
Northwest	4 998 899 (12.7)	2 067 569 (26.3)	1 572 597 (20.0)	1 218 895 (15.5)	139 655 (1.8)	183 (0.002)
Northeast	3 303 621 (8.4)	788 273 (10.0)	833 740 (10.6)	906 224 (11.5)	295 106 (3.7)	480 278 (6.1)
Household registration*						
Rural	36 153 077 (91.9)	7 212 915 (91.6)	7 101 389 (90.2)	7 069 988 (90.0)	7 324 850 (93)	7 443 935 (94.6)
Urban	3 195 042 (8.1)	661 746 (8.4)	774 522 (9.8)	789 531 (10.0)	547 201 (7.0)	422 042 (5.4)
Ever smoked	11 754 165 (29.9)	2 683 983 (34.1)	2 367 440 (30.1)	2 325 970 (29.6)	2 316 605 (29.4)	2 060 167 (26.2)
Drinking	11 705 363 (29.7)	2 520 923 (32)	2 371 802 (30.1)	2 300 627 (29.3)	2 225 482 (28.3)	2 286 529 (29.1)
Hypertension	1 594 080 (4.1)	337 971 (4.3)	305 280 (3.9)	290 166 (3.7)	342 139 (4.3)	318 524 (4.0)
Physician-diagnosed hypertension	1 534 043 (3.9)	324 187 (4.1)	293 197 (3.7)	278 920 (3.6)	330 245 (4.2)	307 494 (3.9)
Measured unknown hypertension	60 037 (0.2)	13 784 (0.2)	12 083 (0.2)	11 246 (0.1)	11 894 (0.2)	11 030 (0.1)
Diabetes mellitus	264 056 (0.7)	61 032 (0.8)	59 738 (0.8)	57 866 (0.7)	47 179 (0.6)	38 241 (0.5)

Data are represented as mean±SD or number (percentage). $PM_{2.5}$ indicates particulate matter with an aerodynamic diameter ≤2.5 μm.
*Household registration data were derived from the Hukou system of households in China.

0.649) mm Hg systolic BP and an increment of 0.364 (95% CI, 0.361–0.366) mm Hg diastolic BP. Ambient $PM_{2.5}$ concentration at the 95th percentile against the thresholds corresponded to a 1.735 (95% CI, 1.726–1.745) mm Hg higher systolic BP and a 1.039 (95% CI, 1.032–1.046) mm Hg higher diastolic BP (Table 2).

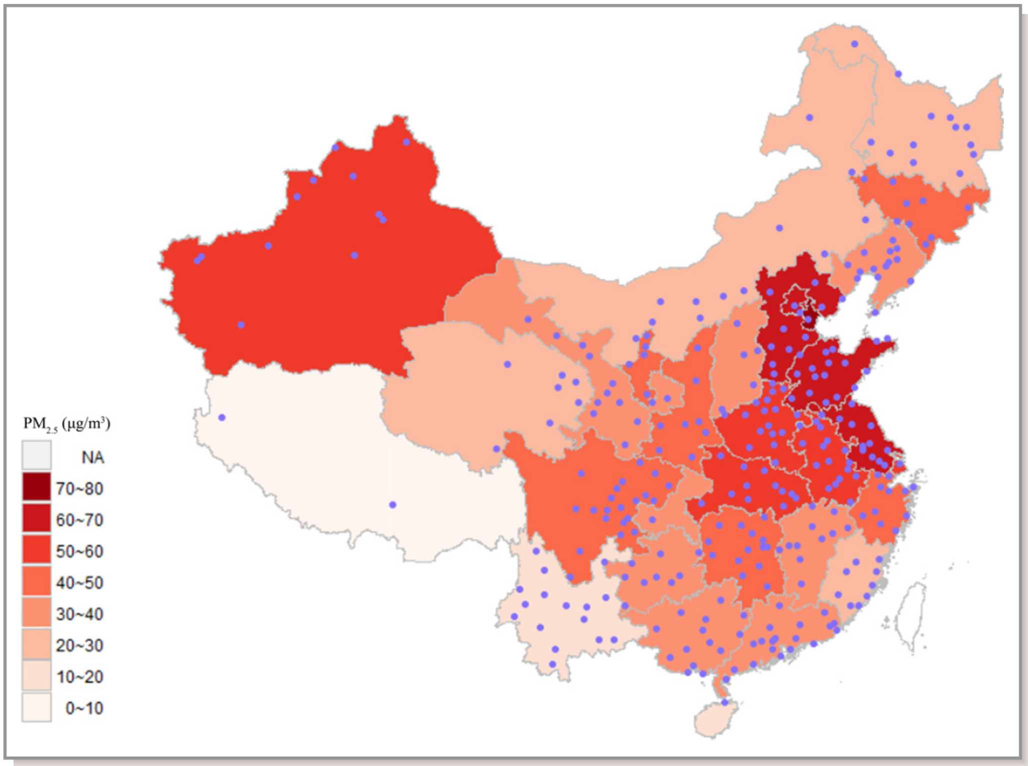

Figure 1. Location of the 327 study cities and 36-month particulate matter with an aerodynamic diameter ≤2.5 μm exposure level for 39 348 119 participants aged 20 to 49 years in China, from 2010 to 2015. NA indicates not applicable.

The OR for hypertension at the 95th percentile of $PM_{2.5}$ against the thresholds for women was 1.029 (95% CI, 1.022–1.036); for men, it was 1.196 (95% CI, 1.189–1.204); for obese subjects (BMI ≥24 kg/m^2), it was 1.099 (95% CI, 1.091–1.106); for those with a BMI <24 kg/m^2, it was 1.144 (95% CI, 1.136–1.152); for ever-smokers, it was 1.041 (95% CI, 1.038–1.045); for never-smokers, it was 1.028 (95% CI, 1.026–1.030); for those aged 20 to 34 years, it was 1.140 (95% CI, 1.134–1.146); for those aged 35 to 49 years, it was 1.119 (95% CI, 1.105–1.133); for subjects with diabetes mellitus, it was 1.314 (95% CI, 1.249–1.382); for subjects without diabetes mellitus, it was 1.129 (95% CI, 1.123–1.135); for rural subjects, it was 1.114 (95% CI, 1.108–1.119); for urban subjects, it was 1.659 (95% CI, 1.612–1.707); for Han nationality subjects, it was 1.064 (95% CI, 1.053–1.076); for other nationality subjects, it was 1.394 (95% CI, 1.362–1.427); for east China subjects, it was 1.182 (95% CI, 1.170–1.194); for north China subjects, it was 1.224 (95% CI, 1.131–1.325); for central China subjects, it was 1.770 (95% CI, 1.744–1.797); for south China subjects, it was 1.471 (95% CI, 1.444–1.497);

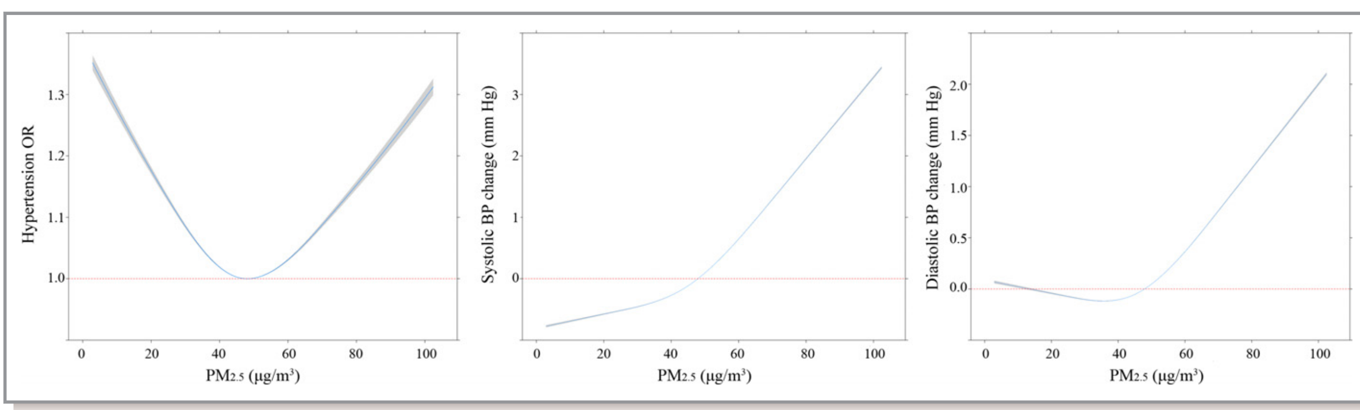

Figure 2. The concentration-response curves for the long-term effects of ambient particulate matter with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) on hypertension, systolic blood pressure (BP), and diastolic BP. OR indicates odds ratio.

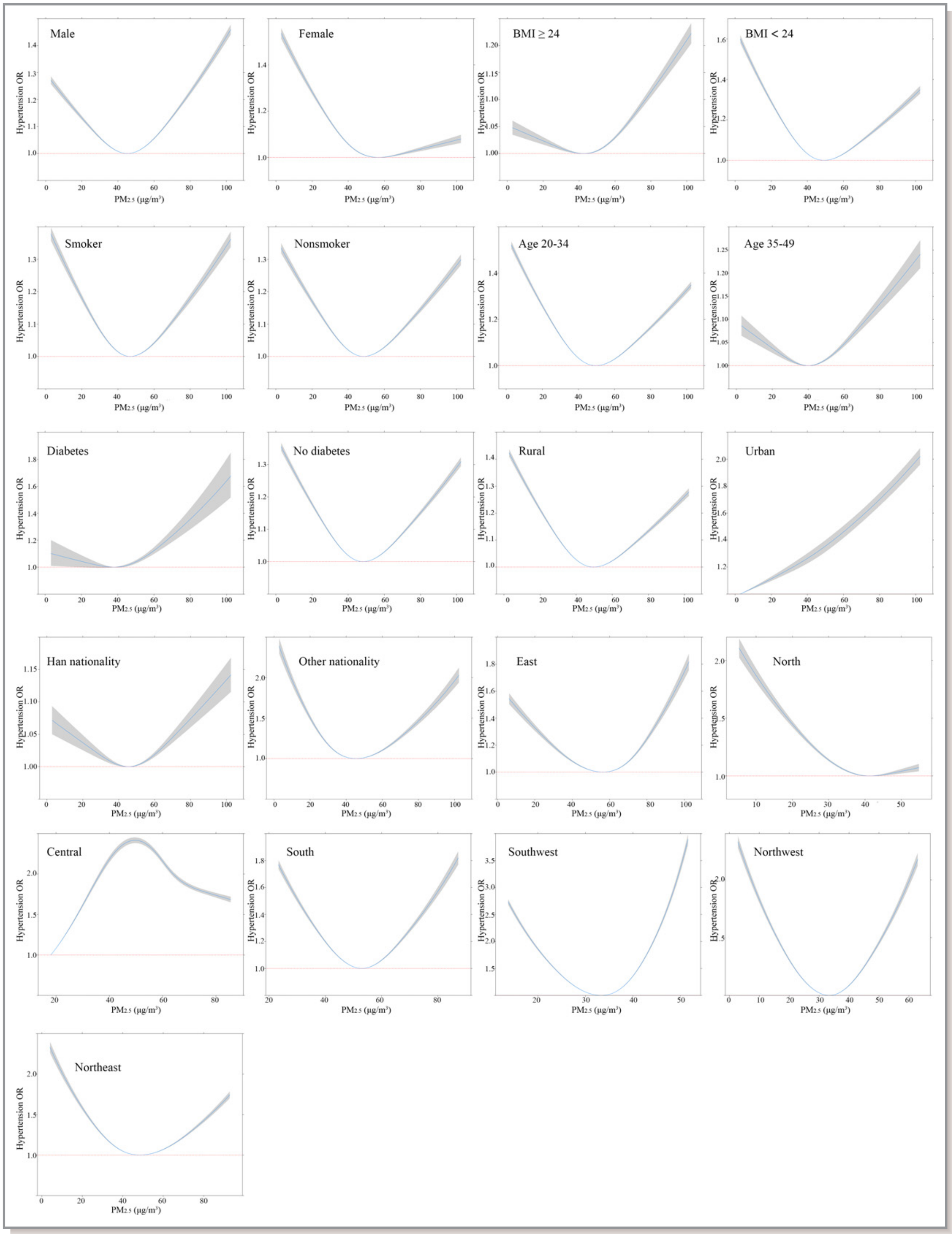

Figure 3. The concentration-response curves for the long-term effects of ambient particulate matter with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) on hypertension, systolic blood pressure (BP), and diastolic BP by level of demographic factors. BMI indicates body mass index; and OR, odds ratio.

Table 2. Estimated Effects of Hypertension and BP Associated With Ambient $PM_{2.5}$*

$PM_{2.5}$, μg/m^3	Effect Size (95% CI)		
	Hypertension†	SBP, mm Hg‡	DBP, mm Hg‡
Continuous variable			
Per 10-μg/m^3 increase above threshold	1.010 (1.007 to 1.012)	0.569 (0.564 to 0.573)	0.384 (0.381 to 0.388)
75th Percentile vs threshold	1.031 (1.029 to 1.033)	0.645 (0.642 to 0.649)	0.364 (0.361 to 0.366)
95th Percentile vs threshold	1.131 (1.125 to 1.137)	1.735 (1.726 to 1.745)	1.039 (1.032 to 1.046)
Quintile categories			
<32.219	1.170 (1.164 to 1.176)	−0.073 (−0.083 to −0.063)	0.173 (0.166 to 0.181)
32.219–40.647	1.079 (1.073 to 1.085)	−0.129 (−0.139 to −0.119)	0.027 (0.020 to 0.035)
40.647–<51.063	1.0 (Reference)	0 (Reference)	0 (Reference)
51.063–<62.865	1.194 (1.187 to 1.200)	1.138 (1.129 to 1.149)	0.619 (0.612 to 0.627)
≥62.865	1.091 (1.085 to 1.096)	2.146 (2.136 to 2.156)	1.301 (1.294 to 1.309)

BP indicates blood pressure; CI, confidence interval; DBP, diastolic BP; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; and SBP, systolic BP.
*The threshold, 75th percentile, and 95th percentile of $PM_{2.5}$ concentrations were 47.9, 60.0, and 76.7 μg/m^3, respectively. Data are adjusted for sex, age, race, smoking status, body mass index, alcohol consumption, education, diabetes mellitus, urbanity, regions, and calendar year.
†The effect for hypertension was odds ratio.
‡The effect for BP was absolute change in mm Hg.

for southwest China subjects, it was 38.411 (95% CI, 35.940–41.051); for northwest China subjects, it was 3.337 (95% CI, 3.209–3.471); and for northeast China subjects, it was 1.355 (95% CI, 1.337–1.374). For hypertension prevalence, the ORs were significantly larger among those who were men, had a BMI <24 kg/m^2, smoked, were aged 20 to 34 years old, had diabetes mellitus, resided in urban areas, were other nationality, or lived in central, south, southwest, northwest, or northeast China. Similar results of stratified analyses were observed for the association of $PM_{2.5}$ at the 75th percentile against the thresholds (Table 3 and Figure 3).

Table 4 showed the hypertension burden attributed to long-term ambient $PM_{2.5}$ exposure. Among all the study participants, the population-attributable risk because of $PM_{2.5}$ higher than threshold (47.9 μg/m^3) was 2.3% (95% CI, 2.2%–2.4%), corresponding to 36 817 (95% CI, 35 121–38 520) hypertension cases. Compared with 0.5% (95% CI, 0.3%–0.6%) in women, 3.6% (95% CI, 3.4%–3.7%) of hypertension in men could be explained by $PM_{2.5}$. The attributed hypertension cases were 2649 (1931–3370) among women and 36 868 (35 426–38 317) among men. And similarly, 2.3% (95% CI, 2.2%–2.4%) and 1.7% (95% CI, 1.5%–2.0%) of hypertension in those aged 20 to 34 and 35 to 49 years, respectively, were attributed to $PM_{2.5}$.

The associations of hypertension to long-term ambient $PM_{2.5}$ exposure did not substantially alter in the sensitivity analyses by using 1- to 5-year average $PM_{2.5}$ concentrations (Table 5).

Discussion

Our study results showed that long-term exposure to ambient $PM_{2.5}$ above thresholds (concentration of the $PM_{2.5}$ pollutant corresponding to minimum hypertension) was linked to higher hypertension risk and elevated BP among reproductive-age (21–49 years) adults by using large-scale research population and location information to improve estimates of 3-year average $PM_{2.5}$ exposure. Comparing with the threshold, we demonstrated that ≈2.3% of the hypertension cases were attributed to exceeding ambient $PM_{2.5}$ exposures in the research population.

The effect of $PM_{2.5}$ to hypertension estimated in our study was lower than the effects estimated in some other studies. We estimated an OR of 1.010 (95% CI, 1.007–1.012) per 10-μg/m^3 $PM_{2.5}$ increment above threshold. In the ESCAPE (European Study of Cohorts for Air Pollution Effects) of 41 072 nonhypertensive participants, a 10-μg/m^3 increase of $PM_{2.5}$ was related to a hazard ratio (HR) of 1.13 (95% CI, 1.02–1.24).[9] A Canadian cohort study reported an HR of 1.13 (95% CI, 1.05–1.22) per 10-μg/m^3 increase in ambient $PM_{2.5}$ concentration.[27] Likewise, another cohort of 44 255 postmenopausal women of the Women's Health Initiative clinical trials observed an HR of 1.13 (95% CI, 1.08–1.17) for each interquartile range increase (3.98 μg/m^3) in ambient $PM_{2.5}$ concentration.[11] Furthermore, a cross-sectional study of 12 665 participants, aged ≥50 years and residing in China, observed that each 10-μg/m^3 increment of ambient $PM_{2.5}$ concentration was linked to an OR of 1.14 (95% CI, 1.07–1.22).[12] Another cross-sectional study in China including 13 975 participants estimated an OR of 1.11 (95% CI, 1.05–1.15) for an interquartile range increase (41.7 μg/m^3) in ambient $PM_{2.5}$ concentration.[13] A prospective cohort of 74 880 residents of the NHS (Nurses' Health Study) from 11 states of America estimated an HR of 1.04 (95% CI, 1.00–

Table 3. Risks of Hypertension at 75th and 95th Percentiles of $PM_{2.5}$ Against the Minimum Hypertension Concentration of $PM_{2.5}$ (Threshold) by Level of Demographic Factors*

Variables	Threshold, μg/m^3	75th Percentile vs Threshold		95th Percentile vs Threshold	
		OR (95% CI)	*P* Value for Difference	OR (95% CI)	*P* Value for Difference
Sex					
Female	56.9	1.001 (1.000–1.002)	<0.001	1.029 (1.022–1.036)	<0.001
Male	45.4	1.056 (1.054–1.058)		1.196 (1.189–1.204)	
Obesity					
Yes	42.4	1.030 (1.027–1.032)	0.202	1.099 (1.091–1.106)	<0.001
No	48.9	1.032 (1.030–1.034)		1.144 (1.136–1.152)	
Smoking					
Yes	46.9	1.041 (1.038–1.045)	<0.001	1.155 (1.145–1.165)	<0.001
No	48.4	1.028 (1.026–1.030)		1.124 (1.117–1.131)	
Age, y					
20–34	49.9	1.028 (1.027–1.030)	<0.001	1.140 (1.134–1.146)	0.008
35–49	39.9	1.047 (1.041–1.053)		1.119 (1.105–1.133)	
Diabetes mellitus					
Yes	38.0	1.123 (1.098–1.148)	<0.001	1.314 (1.249–1.382)	<0.001
No	48.4	1.030 (1.028–1.031)		1.129 (1.123–1.135)	
Household registration†					
Rural	49.9	1.023 (1.021–1.025)	<0.001	1.114 (1.108–1.119)	<0.001
Urban	2.9	1.460 (1.416–1.506)		1.659 (1.612–1.707)	
Race					
Han nationality	45.4	1.019 (1.015–1.022)	<0.001	1.064 (1.053–1.076)	<0.001
Other nationality	45.4	1.103 (1.093–1.113)		1.394 (1.362–1.427)	
Region					
East	56.5	1.005 (1.004–1.006)	Reference	1.182 (1.170–1.194)	Reference
North	41.2	1.106 (1.061–1.152)	<0.001	1.224 (1.131–1.325)	0.386
Central	18.1	2.159 (2.130–2.187)	<0.001	1.770 (1.744–1.797)	<0.001
South	52.9	1.062 (1.058–1.066)	<0.001	1.471 (1.444–1.497)	<0.001
Southwest	33.3	8.370 (8.049–8.704)	<0.001	38.411 (35.940–41.051)	<0.001
Northwest	33.4	1.986 (1.941–2.032)	<0.001	3.337 (3.209–3.471)	<0.001
Northeast	48.2	1.070 (1.065–1.075)	<0.001	1.355 (1.337–1.374)	<0.001

CI indicates confidence interval; OR, odds ratio; and $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm.
*The 75th and 95th percentiles of $PM_{2.5}$ concentrations were 60.0 and 76.7 μg/m^3, respectively. Data are adjusted for sex, age, race, smoking status, body mass index, alcohol consumption, education, diabetes mellitus, urbanity, regions, and calendar year.
†Household registration data were derived from the Hukou system of households in China.

1.07) per 10-μg/m^3 increase of $PM_{2.5}$, which was of comparable magnitude with our study.[14] However, nonsignificant associations were reported in several studies. A study of 33 771 black women of the BWHS (Black Women's Health Study) observed a nonsignificant association, with an HR of 0.99 (95% CI, 0.93–1.06).[7] Nonsignificant effects were also observed in studies from Germany[2] and Taipei.[5] The smaller effects of $PM_{2.5}$ in our study than in Europe and North America might be attributable to the distinct characteristics of China. First, as shown in our exposure-response curves, there were threshold effects of long-term ambient $PM_{2.5}$ exposure to hypertension. Second, our study population has a younger age structure, making it less sensitive to long-term exposure to ambient $PM_{2.5}$. Third, the composition of particulate matter in China has high content of crustal materials because of transported dust caused by desert and arid loess-land and locally induced dust because of the lower vegetation coverage and intensive urban construction.[28] Crustal components or

Table 4. Estimated Hypertension Burden Attributable to Ambient $PM_{2.5}$

Variable	No. of Subjects With Hypertension	Population-Attributable Fraction, % (95% CI)	Attributed Hypertension Cases (95% CI)
Overall	1 594 080	2.3 (2.2–2.4)	36 817 (35 121–38 520)
Sex			
Female	556 105	0.5 (0.3–0.6)	2649 (1931–3370)
Male	1 037 975	3.6 (3.4–3.7)	36 868 (35 426–38 317)
Age, y			
20–34	1 285 135	2.3 (2.2–2.4)	29 994 (28 607–31 387)
35–49	308 945	1.7 (1.5–2.0)	5363 (4678–6054)

CI indicates confidence interval; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm.

dust may have relatively weaker toxicity than that mainly originated from fossil combustion.[29]

Long-term exposure to ambient $PM_{2.5}$ was positively associated with higher systolic and diastolic BP in this study. The results of previous studies have been mixed. A study in Chinese adults, aged ≥50 years, reported that ambient $PM_{2.5}$ was linked to an increment of both systolic and diastolic BP.[12] Two other epidemiological studies have also observed significant associations between ambient $PM_{2.5}$ exposure and BP.[6,10] A cross-sectional study of residents >65 years in Taiwan reported an increased diastolic BP was related to 1-year exposures to $PM_{2.5}$, whereas they did not find a significant increase for systolic BP.[5] However, a cross-sectional study conducted in China of residents aged ≥35 years indicated a significant association between $PM_{2.5}$ and systolic BP, but there was a null association with diastolic BP.[13] Similar results have been reported in the Sister Study.[4] These mixed results may be related to the variation in sources or composition of particulate matter and to the different study populations (ethnicity, age structure, and lifestyle).[3]

Most previous studies assumed a linear association between air pollutant concentrations and hypertension that was limited in revealing the real exposure-response relationship. This assumption may be because of the much lower concentrations of $PM_{2.5}$ pollutants in European countries and the United States than in China. Therefore, the nonlinear association at high concentrations of $PM_{2.5}$ was not observed in most prior studies.[4,7,9,14–16] However, our study demonstrated the threshold effects ($PM_{2.5}$ concentration corresponding to minimum hypertension) of $PM_{2.5}$ on hypertension. Accordingly, any previous study estimated the hypertension burden that assuming a linear association may result in an excessively high hypertension burden estimate attributed to ambient $PM_{2.5}$, which had certain public health significance.

The hypertension burden attributable to $PM_{2.5}$ was assessed in these analyses. Most of prior articles have mainly quantified the relation between $PM_{2.5}$ and hypertension using relative risks or ORs, which provided information in the cause of the associations. Compared with the metrics of the association, the attributable cases and population-attributable fraction might provide additional information in developing air pollution standards and planning potential interventions.[12] A recent study of 12 665 Chinese adults >50 years of age of the SAGE-China (Study on Global Ageing and Adult Health—China) conducted in China reported that 11.75% (95% CI, 5.82%–18.53%) of the hypertension cases could be attributable to ambient $PM_{2.5}$.[12] Our estimated hypertension burden attributable to $PM_{2.5}$ pollutant was lower than those in the SAGE-China study,[12] partly because our study populations were younger.

To our best knowledge, this is the largest epidemiological study to date to investigate the relation between long-term $PM_{2.5}$ pollutant exposure and hypertension prevalence, with ≈1.6 million hypertension cases in the study population of 39 million individuals. Another strength of our study is that we evaluated the concentration-response curve between

Table 5. Estimated Effects of Hypertension at 75th and 95th Percentiles of $PM_{2.5}$ Against the Minimum Concentration of $PM_{2.5}$ (Threshold) in Sensitivity Analyses

Models	Threshold, μg/m³	75th Percentile, μg/m³	95th Percentile, μg/m³	OR (95% CI)	
				75th Percentile vs Threshold	95th Percentile vs Threshold
With 1 y $PM_{2.5}$	48.8	59.90	77.41	1.019 (1.017–1.020)	1.090 (1.085–1.095)
With 2 y $PM_{2.5}$	48.95	60.00	77.39	1.022 (1.021–1.024)	1.104 (1.099–1.110)
With 3 y $PM_{2.5}$	47.9	60.0	76.7	1.031 (1.029–1.033)	1.131 (1.125–1.137)
With 4 y $PM_{2.5}$	48.26	60.32	76.91	1.036 (1.034–1.038)	1.146 (1.140–1.151)
With 5 y $PM_{2.5}$	48.42	60.71	76.92	1.038 (1.037–1.040)	1.151 (1.145–1.157)

CI indicates confidence interval; OR, odds ratio; and $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm.

$PM_{2.5}$ and hypertension; no studies have previously evaluated the concentration-response relationship for hypertension.

This study has several limitations. First, similar to previous cross-sectional studies, we could not establish a causal relationship between $PM_{2.5}$ and hypertension. Second, as in most previous studies, exposure measurement errors were inevitable because we applied a 3-year mean satellite-based estimate of ambient $PM_{2.5}$ levels as the alternative for true population exposures. Measurement error in exposure might lead to random errors that could dilute real associations between $PM_{2.5}$ and hypertension, because this kind of nondifferential error may attenuate the association between $PM_{2.5}$ and hypertension.[30]

In conclusion, we found average 3-year exposures to ambient $PM_{2.5}$ were associated with hypertension and increased BP among residents aged 20 to 49 years in the National Free Preconception Health Examination Project living throughout 2790 counties of 31 provinces across China, with threshold effects. Our study added to the existing epidemiological evidence with regard to the long-term effects of $PM_{2.5}$ on hypertension that the improvement in air quality has the potential to lower the burden of hypertension in China. These suggestive findings might be of benefit to the public and to policymakers in planning public health interventions and attaining environmental standards and guidelines. Hypertension is the leading preventable risk factor for cardiovascular disease, with a high prevalence, so even a small change should be a key public health priority.

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Disclosures

None.

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