Dynamic Changes in Long-Term Exposure to Ambient Particulate Matter and Incidence of Hypertension in Adults

A Natural Experiment

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Abstract—Many countries dedicated in mitigation of air pollution in the past several decades. However, little is known about how air quality improvement affects health. Therefore, we conducted current study to investigate dynamic changes in long-term exposure to ambient particulate matter ($PM_{2.5}$) and incidence of hypertension in a large longitudinal cohort. We recruited 134 978 adults aged 18 years or above between 2001 and 2014. All the participants received a series of standard medical examinations, including measurements of blood pressure. The $PM_{2.5}$ concentration was estimated using a satellite-based spatiotemporal model at a high resolution (1×1 km^2). The change in long-term exposure to $PM_{2.5}$ ($\Delta PM_{2.5}$) was defined as the difference between the values measured during follow-up and during the immediately preceding visit, and a negative value indicated an improvement in $PM_{2.5}$ air quality. Time-varying Cox model was used to examine the associations between $\Delta PM_{2.5}$ and the development of hypertension. The results show that $PM_{2.5}$ concentrations increased in 2002, 2003, and 2004, but began to decrease in 2005. Every 5 μg/m^3 change in exposure to $PM_{2.5}$ (ie, a $\Delta PM_{2.5}$ of 5 μg/m^3) was associated with a 16% change in the incidence of hypertension (hazard ratio, 0.84; 95% CI, 0.82–0.86). Both stratified and sensitivity analyses generally yielded similar results. We found that an improvement in $PM_{2.5}$ exposure is associated with a decreased incidence of hypertension. Our findings demonstrate that air pollution mitigation is an effective strategy to reduce the risk of cardiovascular disease. (***Hypertension*. 2019;74:669-677. DOI: 10.1161/HYPERTENSIONAHA.119.13212.)** ● **Online Data Supplement**

Key Words: blood pressure ■ hypertension ■ particulate matter ■ quality improvement ■ risk

Ambient air pollution, which increases mortality and morbidity and shortens life expectancy, is the leading contributor to disease burden in the world. More than 90% of the global population resides in areas where the air quality does not reach the standards recommended by the World Health Organization.[1] It is estimated that fine particulate matter ($PM_{2.5}$) alone contributed to 105.7 million disability-adjusted life years and 4.1 million deaths worldwide in 2016.[2]

Many countries recognize air pollution as a critical risk factor affecting public health and thus have strived to reduce air pollution. Many cities and regions, especially those with advanced economies, have experienced dynamic increases and decreases in air pollution in the past several decades. In contrast to the abundant literature on the adverse effects of air pollution, only a few studies have directly examined the beneficial health effects of improvements in air quality, including decreased mortality,[3,4] a longer life expectancy,[5] and improvements in lung function growth[6] and respiratory symptoms.[7,8] However, the linkage between improvements in air quality and the associated beneficial effects is particularly interesting to the field of public health because it would inspire government agencies to adopt more aggressive strategies of air pollution mitigation if the benefits of decreased pollution could be demonstrated.

Hypertension, a leading risk factor for disability and death worldwide, accounted for >10.5 million deaths in 2016.[2] Findings from previous studies suggested that long-term exposure to $PM_{2.5}$ was associated with an increased risk of hypertension development.[9–13] The $PM_{2.5}$ concentration in Taiwan, which

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peaked in approximately 2004 and began to decrease thereafter, provides a good backdrop for a natural experiment to examine the beneficial effects of air quality improvement on hypertension. In this analysis, we investigated the relationship between dynamic changes in long-term exposure to ambient $PM_{2.5}$ ($\Delta PM_{2.5}$) during 2001 to 2014 and incident hypertension in a large longitudinal cohort consisting of 134 978 Taiwanese adults.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

Participants in the current study are from an ongoing longitudinal cohort since 1996. Details have been described in our previous publications.[9,14–16] In Brief, more than 0.5 million participants joined a standard medical screening program run by the MJ Health Management Institution between 1994 and 2014. The participants were encouraged to visit the firm periodically through a paid membership and underwent a series of medical examinations during each visit, including anthropometric measurements, physical examinations, and blood and urinary tests. Participants were also asked to complete a self-administered questionnaire to provide information on their lifestyle and medical history. The MJ Health Management Institution has started to computerize the data generated from the medical examinations since 1996. All participants were asked to sign an informed consent before they joined the medical screening program for authorizing the use of their data for research. Ethical approval for this study was obtained from the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee.

Figure S1 in the online-only Data Supplement shows participant's selection in this study. A total of 422 013 participants aged 18 years or older were recruited between 2001 and 2014, when $PM_{2.5}$ exposure assessments were available. Of this population, we excluded 234 765 participants because they had completed only one medical visit. We further excluded 35 203 participants with missing information on height or weight (n=215), lifestyle factors or educational level (n=19 418), systolic or diastolic blood pressure (n=8596), fasting glucose (n=166), or blood lipids (n=6808). Another 17 067 participants with hypertension at their first visit (ie, baseline) were further excluded. The remaining 134 978 participants were included in this analysis to investigate the association between $\Delta PM_{2.5}$ and incident hypertension. Compared with the excluded participants, the included participants were younger (mean: 37.92 versus 40.56 years), more educated (percentage of college/university or above: 68.72% versus 60.22%), less likely to be smokers (percentage of ever-smokers: 24.98% versus 26.82%) or drinkers (percentage of ever-drinkers: 13.38% versus 14.73%), and more physically active (percentage of participants engaged in moderate or high physical activity: 27.93% versus 27.82%). The included participants also had lower prevalence of dyslipidemia (20.86% versus 26.65%), diabetes mellitus (2.20% versus 5.04%), and self-reported cardiovascular disease or stroke (2.05% versus 3.29%).

Participants were followed-up for a mean of 4.8 years (range: 1–14 years; interquartile range: 2–7 years). During this time, they participated in a mean of 3.5 medical visits (range: 2–19; interquartile range: 2–4). The visits were spaced at a mean interval of 23.5 months (range: 3–167 months; interquartile range: 12–26 months).

Air Pollution Exposure Assessment

The detailed method used to estimate $PM_{2.5}$ exposure has been described in our previous studies.[14,15,17,18] In brief, we used a satellite-based spatiotemporal model with a high resolution of 1 km^2 to estimate the $PM_{2.5}$ exposure at each participant's address. The spatiotemporal model was developed based on aerosol optical depth data derived from the spectral data from the 2 Moderate Resolution Imaging Spectroradiometer instruments aboard the US National Aeronautics and Space Administration Terra and Aqua satellites. The model combined the satellite aerosol optical depth data and meteorologic data (ie, visibility and relative humidity) to estimate ground-level $PM_{2.5}$ concentrations. The model was then applied to estimate long-term $PM_{2.5}$ concentrations over the period of 2000 to 2014. We validated the model using ground-measured $PM_{2.5}$ data from more than 70 monitoring stations in Taiwan and obtained correlation coefficients of 0.72 to 0.83 between the monitored and modeled annual average $PM_{2.5}$ values.

We collected each participant's mailing address during each medical visit to enable postal delivery of the medical reports. Thus, the changes of addresses for each participant in this study were recorded and were taken into account in the exposure assessment and data analysis. Of the participants, 36 315 (26.9%) changed their addresses during the study. The addresses were geocoded to yield latitude and longitude data that were used to estimate address-specific annual average $PM_{2.5}$ concentrations.[19] We used the 2-year average concentration as an indicator of long-term exposure to $PM_{2.5}$ and calculated this value based on the concentrations during the year of the medical examination and the preceding year. The $\Delta PM_{2.5}$ was defined as the value at a follow-up visit minus the corresponding value at the immediately preceding visit. A negative value from this calculation represented an improvement in the $PM_{2.5}$ air quality.

Outcome Ascertainment

Incident hypertension was the health outcome for the current study. For each participant, the seated systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the morning using a computerized auto-mercury sphygmomanometer (CH-5000, Citizen, Tokyo, Japan) which were made in the right arm after a 10-minute rest. If the SBP or DBP was ≥140 or ≥90 mm Hg, respectively, a second measurement was conducted after another 10 minutes' rest and used for the data analysis. Incident hypertension was defined as an SBP ≥140 mm Hg or a DBP ≥90 mm Hg. The end point was the first occurrence of hypertension or the last visit if hypertension did not occur.

Covariates

Information on a wide range of potential confounders/modifiers was also collected. Details of the health examination and quality control were described previously and in Technical Reports by the MJ Health Research Foundation.[19–21] A standard paper-based self-administered questionnaire was used to collect information on the participants' demographic characteristics, lifestyle factors, and medical history. All questionnaire questions were close-end. Information was then captured and stored in computers via optical scanning. Data cleansing was conducted by train statisticians to detect, diagnose, and edit faulty data before release for research. The body heights and weights were measured using an auto-anthropometer (Nakamura KN-5000A, Tokyo, Japan) while the participants wore light indoor clothing and no shoes. The body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m^2). Blood samples were collected in the morning after an overnight fast, and the plasma glucose and lipid profiles were measured using an automated chemical analyzer.

Statistical Analysis

Descriptive data are presented as means (standard deviations) for continuous variables and numbers (percentages) for categorical variables.

Because $\Delta PM_{2.5}$ and all other covariates (except for sex) changed over the study period, we adopted the time-varying Cox regression model, which included time-invariant and variant variables, to examine the relationship between $\Delta PM_{2.5}$ and development of hypertension:

$$h\left(t, X\left(t\right)\right) = h_0\left(t\right)\exp\left[\sum_{i=1}^{p_1}\beta_i X_i + \sum_{i=1}^{p_2}\delta_j X_j\left(t\right)\right]$$

Where $h_0\left(t\right)$ represents the baseline hazard function, X_i represents the time-invariant variables, and X_j represents the time-variant variables.

Time-in-study (ie, follow-up time) was used as the timescale in the model. In addition to treating $\Delta PM_{2.5}$ as a continuous variable, we categorized this variable into tertiles and used the second tertile (ie, smallest change) as the reference value for comparisons of the effects of air quality deterioration and improvement.

Four models were developed. Model 1 did not include any adjusted variables. Model 2 was adjusted for age (years, continuous variable), sex (male or female), educational level (lower than high school, <10; high school, 10–12; college or university, 13–16; or postgraduate, >16 years), smoking habit (never, former, or current), alcohol use (seldom, <1 time/wk; occasional, 1–3 times/wk; or regular, >3 times/wk), physical activity (defined as the product of the metabolic equivalent value [MET=1 kcal/h per kg body weight] and duration of exercise [hours][22] as inactive, <3.75; low, 3.75–7.49; medium, 7.50–16.49; high, 16.50–25.49; or very high, ≥25.50 MET-h), fruit intake (seldom, <1; moderate, 1–2; or frequent, >2 servings/d), vegetable intake (seldom, <1; moderate, 1–2; or frequent, >2 servings/d), occupational exposure to dust or organic solvents in the workplace (yes or no), and season (calendar season, categorical variable). Model 3 was further adjusted for BMI (kg/m^2; continuous variable), diabetes mellitus (defined as a fasting blood glucose level ≥126 mg/dL or self-reported physician-diagnosed diabetes mellitus; yes or no), dyslipidemia (defined as a total cholesterol level ≥240 mg/dL, triglyceride level ≥200 mg/dL, or high-density lipoprotein cholesterol level <40 mg/dL; yes or no), self-reported physician-diagnosed cardiovascular disease (yes or no), and self-reported physician-diagnosed cancer (yes or no). Model 4 was further adjusted for the $PM_{2.5}$ concentration at baseline (continuous variable) for comparison. We set Model 3 as our main model to address concerns that including the baseline $PM_{2.5}$ concentration might lead to an overadjustment. The restricted cubic spline function was used to evaluate the shape of the concentration-response relationship between the $\Delta PM_{2.5}$ and incident hypertension.

Subgroup analyses were conducted to investigate whether the relationship between the $\Delta PM_{2.5}$ and incident hypertension was modified by age (<65 or ≥65 years), sex (male or female), BMI (<25 or ≥25 kg/m^2), educational level (<13 or ≥13 years), smoking status (never or ever), alcohol drinking (seldom or occasional/regular), and diabetes mellitus (yes or no). Each potential modifier was examined in a separate model by adding a multiplicative interaction term (ie, potential modifier×$\Delta PM_{2.5}$ tertile category).

To test the stability of the relationship, 5 sensitivity analyses were conducted: (1) excluding participants who used their workplace rather than their home address to eliminate the potential misclassification of exposure due to different types of addresses; (2) excluding individuals with diabetes mellitus, self-reported physician-diagnosed cardiovascular disease, or cancer at baseline to eliminate the potential effects of comorbidity such as medications affecting blood pressure; (3) using the threshold of 130/80 mmHg according to New AHA/ACC definition of hypertension[22]; (4) further adjusting for calendar year to eliminate the potential effects of temporal trend as suggested by Adar SD et al[23] study; and (5) using annual average $PM_{2.5}$ concentration as an indicator for long-term exposure to $PM_{2.5}$.

All statistical analyses were conducted using R software, version 3.3.2 (R Core Team, Vienna, Austria). A 2-sided *P* value <0.05 was considered statistically significant.

Results

The general characteristics of the study participants are presented in Table 1. A total of 134 978 participants (49.33% men) without hypertension (mean age, 37.92±11.19 years at baseline) were included in the analysis to investigate the association between $\Delta PM_{2.5}$ and incident hypertension. During the follow-up period, 14 356 incident hypertension cases were identified. A majority of the participants did not use alcohol, had never been smokers, and had a relatively high level of education. Table S1 further presents the information of the participants by enrolled year.

Table 1. Characteristics of the Participants

Variable	All Observations* (n=469 819)	Baseline of Nonhypertension† (n=134 978)
Age, y	40.95 (11.13)	37.92 (11.19)
Male	233 140 (49.62%)	66 578 (49.33%)
Education		
High school or lower	138 318 (29.44%)	42 210 (31.27%)
College or university	265 975 (56.61%)	75 810 (56.16%)
Postgraduate	65 526 (13.95%)	16 958 (12.56%)
Smoking status		
Never	358 212 (76.24%)	101 260 (75.02%)
Former	26 480 (5.64%)	7060 (5.23%)
Current	85 127 (18.12%)	26 658 (19.75%)
Alcohol drinking		
<1 time/wk	404 005 (85.99%)	116 915 (86.62%)
1–3 times/wk	45 688 (9.72%)	12 597 (9.33%)
>3 times/wk	20 126 (4.28%)	5466 (4.05%)
Physical activity intensity		
Inactive	216 280 (46.03%)	68 153 (50.49%)
Low	97 197 (20.69%)	29 118 (21.57%)
Moderate	86 818 (18.48%)	21 991 (16.29%)
High	69 524 (14.8%)	15 716 (11.64%)
Occupational exposure, solvent/dust	36 943 (7.86%)	11 238 (8.33%)
Body mass index, kg/m^2	22.81 (3.32)	22.61 (3.38)
Systolic blood pressure, mm Hg	113.09 (13.50)	113.36 (12.73)
Diastolic blood pressure, mm Hg	68.60 (9.50)	68.05 (8.95)
Diabetes mellitus‡	12 156 (2.59%)	2968 (2.20%)
Self-reported cardiovascular disease or stroke	10 749 (2.29%)	2765 (2.05%)
Dyslipidemia§	98 251 (20.91%)	28 157 (20.86%)
2-year average $PM_{2.5}$, μg/m^3	26.63 (7.69)	26.77 (7.99)

The statistical data are shown as means (standardized deviations) for continuous variables and counts (percentages) for categorical variables.

Data are complete for all variables.

*Characteristics of the 469 819 observations from the 134 978 participants.

†Characteristics of the 134 978 nonhypertensive participants at baseline.

‡Diabetes mellitus: fasting blood glucose ≥126 mg/dL or self-reported physician-diagnosed diabetes mellitus.

§Dyslipidemia: total cholesterol ≥240 mg/dL, triglyceride ≥200 mg/dL, or high-density lipoprotein cholesterol <40 mg/dL.

The spatial distribution of study participants/observations by year is presented in Figure 1. As demonstrated, the participants generally lived in the Western part of the island of Taiwan. The $PM_{2.5}$ concentrations increased in 2002, 2003, and 2004 and began to decrease in 2005. The values of 2-year average concentrations of $PM_{2.5}$ in Taiwan from 2001 to 2014 are shown in Table S2.

The effects of $\Delta PM_{2.5}$ on hypertension development are presented in Table 2 and Figure 2. Compared with participants whose exposure corresponded to the second tertile of $\Delta PM_{2.5}$,

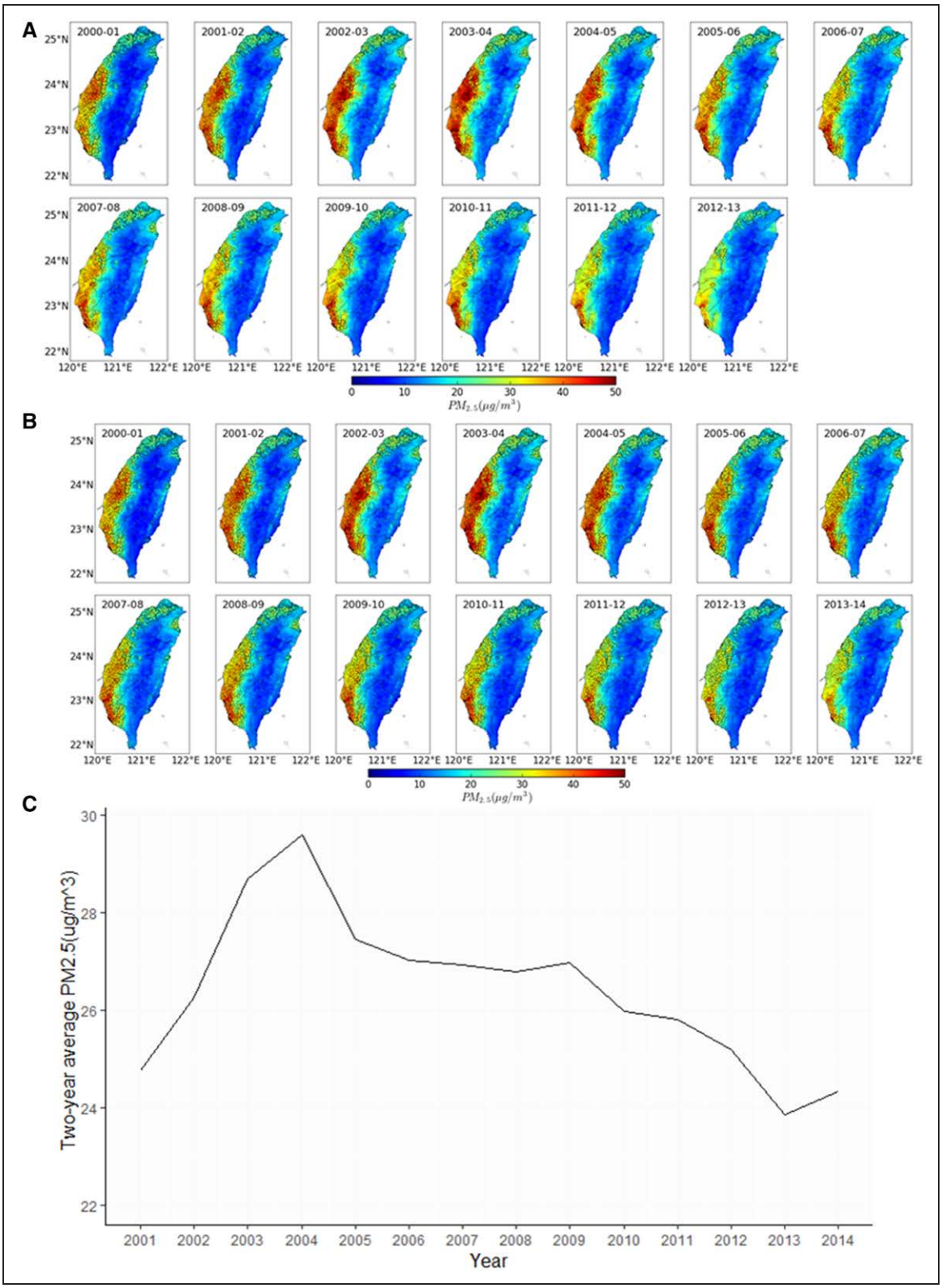

Figure 1. Maps of the participants' location and the trends in the 2-year average concentrations of particulate matter ($PM_{2.5}$) in Taiwan from 2001 to 2014. **A**, is the map of the address locations (circles) of the 134 978 participants at baseline by year. **B**, is the map of the address locations (circles) of the 469 819 observations from the 134 978 participants by year. **C**, shows the trends in the 2-year average concentrations of $PM_{2.5}$ in the 469 819 observations in Taiwan between 2001 and 2014.

(the smallest change in $PM_{2.5}$), those in the first tertile (ie, improved $PM_{2.5}$ air quality) exhibited a decreased risk of developing hypertension (hazard ratio, 0.81; 95% CI, 0.78–0.85] while those in the third tertile (deteriorated $PM_{2.5}$ air quality) faced in an increased risk of developing hypertension (hazard ratio, 1.16; 95%CI, 1.11–1.21). A liner concentration-response

Table 2. The Associations of $\Delta PM_{2.5}$ With Hypertension Development

			Model 2		Model 3		Model 4	
$PM_{2.5}$ Exposure	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
First tertile (<−0.92)	0.80 (0.78–0.83)	<0.001	0.82 (0.78–0.85)	<0.001	0.81 (0.78–0.85)	<0.001	0.78 (0.75–0.82)	<0.001
Second tertile (−0.92 to 0.33)	Ref		Ref		Ref		Ref	
Third tertile (>0.33)	1.16 (1.11–1.21)	<0.001	1.14 (1.10–1.19)	<0.001	1.16 (1.11–1.21)	<0.001	1.16 (1.11–1.21)	<0.001
Trend test		<0.001		<0.001		<0.001		<0.001
Every 5 μg/m^3 decrease	0.84 (0.82–0.86)	<0.001	0.85 (0.83–0.87)	<0.001	0.84 (0.82–0.86)	<0.001	0.81(0.80–0.83)	<0.001

Data are completed for all variables.

Model 1: no adjustment; Model 2: adjusted for age, sex, education, smoking, alcohol drinking, leisure-time physical activity, fruit intake, vegetable intake, occupational exposure to dust and organic solvent and season; Model 3: further adjusted for body mass index, diabetes mellitus (yes or no), dyslipidemia (yes or no), self-reported physician-diagnosed cardiovascular disease (yes or no), and self-reported physician-diagnosed cancer (yes or no). Model 4: further adjusted for the baseline $PM_{2.5}$ concentration.

curve was observed. Every 5 μg/m^3 change in the $PM_{2.5}$ was associated with a 16% change in the incidence of hypertension. In other words, a 5 μg/m^3 improvement in $PM_{2.5}$ air quality was associated with a 16% decrease in the risk of developing hypertension (hazard ratio, 0.84; 95%CI, 0.82–0.86; Figure 2).

The subgroup analyses generally yielded results consistent with the above findings (Table 3). Statistically significant interactions were observed in the following analyses: age/BMI and first tertile $\Delta PM_{2.5}$, BMI, and third tertile $\Delta PM_{2.5}$. The sensitivity analyses also generally yielded similar results (Table S3).

Discussion

To the best of our knowledge, this is the first large longitudinal study to investigate the relationship between dynamic changes in long-term exposure to $PM_{2.5}$ (including air quality improvement and deterioration) and incident hypertension. We found that deteriorations in the ambient $PM_{2.5}$ air quality are associated with a higher risk of hypertension development, whereas improvements in long-term exposure to $PM_{2.5}$ are associated with a lower risk of hypertension development. The concentration-response relationship is generally linear.

Limited information is available regarding the relationship between dynamic changes in exposure to air pollution, particularly long-term exposure and hypertension development. There is a few trials that investigated the short-term effects on blood pressure: one clinical trial in the United States suggested that short-term use of portable air filtration systems might lower systolic BP among older adults living in a typical US urban location[24]; another 3 trials reported that air purification decreased both SBP[25–27] and DBP.[25,27] One cohort study in China investigated the health effects of drastic air quality changes surrounding the 2008 Beijing Olympics and found significantly lower SBP measurements during the Olympics (ie, a period of low air pollution) than during the post-Olympics period (ie, high air pollution). However, the authors did not observe higher SBP measurements during the pre-Olympics period (ie, high air pollution), compared with the Olympics period.[28,29] In contrast, another panel study by Mu et al[30] observed an increase in DBP but not SBP during the Olympics.

It might be difficult to compare our results directly with those of the above studies, which evaluated relatively short exposure periods and used blood pressure as continuous outcomes. The effects of short-term exposure on blood pressure might be reversed quickly when the exposure is removed. We used 2-year average $PM_{2.5}$ or annual $PM_{2.5}$ (in the sensitivity analysis) as an indicator of long-term exposure in this study. It was possible that short-term (days or weeks) fluctuations in $PM_{2.5}$ may sway blood pressure. We thus used hypertension as the outcome to assess the long-term effect because it takes a while for a normal person to develop hypertension. Besides, many other factors can easily fluctuate blood pressure and might lead to unstable results. A dichotomous outcome (hypertension) based on a well-defined cutoff value is more certain and stable unless the fluctuation in blood pressure is big and across the cutoff value.

We observed an association between decreased exposure to $PM_{2.5}$ and decreased risk of hypertension development, consistent with previous studies that have shown the benefits of air quality improvements on mortality, life expectancy, lung function, and respiratory systems.[3,5–8] A few studies also used modeling methods to estimate the benefits of air quality improvements, although most addressed mortality.[31–34] These modeling studies were generally based on

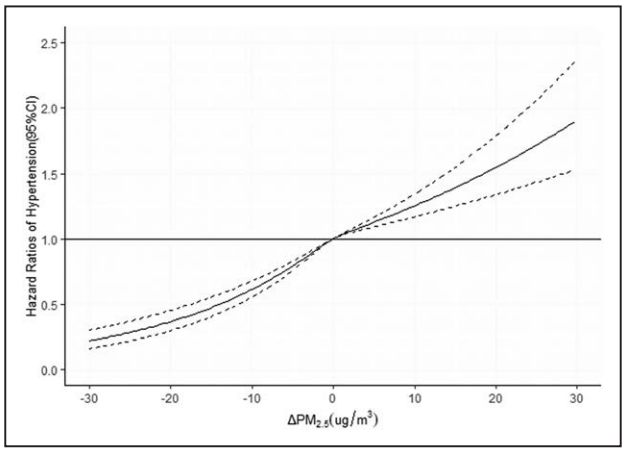

Figure 2. Shape of the concentration-response relationship between the change in particulate matter ($PM_{2.5}$; $\Delta PM_{2.5}$) and incident hypertension.

Table 3. Stratified Analyses of the Associations of $\Delta PM_{2.5}$ With Incident Hypertension by Covariates at Baseline

Covariate	Case/ Participants	First Tertile		Second Tertile	Third Tertile	
		HR (95% CI)	*P* Value	HR (95% CI)	HR (95% CI)	*P* Value
Sex						
Male	9334/66 578	0.82 (0.78–0.86)	<0.001	Ref	1.14 (1.08–1.20)	<0.001
Female	5022/68 400	0.81 (0.75–0.86)	<0.001	Ref	1.21 (1.13–1.31)	<0.001
$P_{interaction}$		0.105			0.203	
Age, y						
<65	13 136/131 530	0.81 (0.78–0.85)	<0.001	Ref	1.14 (1.09–1.19)	<0.001
≥ 65	1220/3448	0.72 (0.63–0.83)	<0.001	Ref	1.25 (1.09–1.44)	<0.001
$P_{interaction}$		0.006			0.855	
BMI, kg/m^2						
<25	8224/105 315	0.88 (0.83–0.93)	<0.001	Ref	1.21 (1.15–1.29)	<0.001
≥ 25	6132/29 663	0.73 (0.69–0.78)	<0.001	Ref	1.09 (1.03–1.16)	0.004
$P_{interaction}$		<0.001			<0.001	
Education						
<13 y	6449/42 210	0.81 (0.76–0.86)	<0.001	Ref	1.22 (1.15–1.30)	<0.001
≥13 y	7907/92 768	0.81 (0.77–0.86)	<0.001	Ref	1.12 (1.06–1.18)	<0.001
$P_{interaction}$		0.987			0.077	
Smoking status						
Never	10 061/101 260	0.81 (0.77–0.85)	<0.001	Ref	1.16 (1.11–1.22)	<0.001
Ever	4295/33 718	0.83 (0.78–0.90)	<0.001	Ref	1.14 (1.06–1.23)	<0.001
$P_{interaction}$		0.507			0.317	
Alcohol drinking						
Seldom	11 563/116 915	0.81 (0.77–0.85)	<0.001	Ref	1.17 (1.12–1.23)	<0.001
Occasional or regular	2793/18 063	0.83 (0.76–0.91)	<0.001	Ref	1.13 (1.03–1.25)	0.010
$P_{interaction}$		0.574			0.541	
Diabetes mellitus						
No	13 573/132 010	0.81 (0.78–0.85)	<0.001	Ref	1.15 (1.10–1.20)	<0.001
Yes	783/2968	0.77 (0.65–0.92)	0.003	Ref	1.27 (1.07–1.52)	0.007
$P_{interaction}$		0.884			0.142	

Data are completed for all variables.

Adjusted for age, sex (except in the sex-stratified analysis), education (except in the education-stratified analysis), smoking (except in the smoking-stratified analysis), alcohol consumption (except in the alcohol-stratified analysis), leisure-time physical activity, fruit intake, vegetable intake, occupational exposure to dust and organic solvents, season, body mass index, diabetes mellitus (except in the diabetes mellitus-stratified analysis), dyslipidemia (yes or no), self-reported physician-diagnosed cardiovascular disease (yes or no), and self-reported physician-diagnosed cancer (yes or no).

the literature-derived risk of air pollution and assumed no changes in exposure, which is not the reality. The effect magnitude and the concentration-response relationship for exposure change may be quite different. Our previous study, which was based on the same cohort and assumed no changes in $PM_{2.5}$ exposure during the study period, shows that each 10 μg/m^3 increment in $PM_{2.5}$ was associated with an increased risk of 3% in hypertension development.[9] On the contrary, the present study shows a linear relationship with an hazard ratio of 0.84 for every 5 μg/m^3 change in $PM_{2.5}$ (ie, every 5 μg/m^3 decrease in $PM_{2.5}$ was associated with a decreased risk of 16% in hypertension development). More studies are needed to directly assess the beneficial effects of air improvement on various health outcomes and facilitate better policy development.

The biological mechanism underlying the relationship of $PM_{2.5}$ exposure with blood pressure and hypertension is not fully understood. Hypothetically, $PM_{2.5}$ might affect blood pressure by impairing endothelial function via oxidative stress and systemic inflammation.[35,36] Our previous studies[15,20] and other studies[37–39] suggested that PM could elicit systemic inflammation, as indicated by pollution-related increases in C-reactive protein, and IL (interleukin)-6 levels and white blood cell and platelet counts. The downregulation of nitric oxide synthase may also contribute to this mechanism. PM exposure can inhibit the

production of endogenous nitric oxide,[40] and the reduced bioavailability of nitric oxide may contribute to the elevation of blood pressure.[41,42] Besides, PM exposure might impair renal D1 receptor-mediated sodium excretion,[43] activate hypothalamus-pituitary-adrenal axis,[44] and cause imbalance in vascular homeostatic responses due to vascular endothelial dysfunction.[45] However, different mechanisms may overlap and contribute to blood pressure elevations at different time points.

This study has several important strengths. First, the longitudinal study design allowed us to examine the relationship between air pollution and incident hypertension in a dynamic and prospective manner. We assessed the effects of both air quality improvement and deterioration and thus demonstrated the beneficial effects of the former. In contrast to reality, most previous cohort studies assumed no changes in exposure to air pollution and covariates throughout the study period, even if a long period was explored. Second, our large sample size and relatively long follow-up period enabled us to detect small effect sizes and provide more precise estimates. Finally, we used a spatiotemporal model based on high resolution (1 km^2) satellite data to estimate the $PM_{2.5}$ exposure at each participant's address. This technology permitted us to overcome the spatial coverage limitation that typically occurs when using data obtained only from monitoring stations. It also enabled us to determine individual-level exposure and to track the $PM_{2.5}$ air pollution levels over time.

Despite these strengths, the study also had several limitations. First, we lacked information about indoor pollutants. Although some studies have indicated a strong correlation between the indoor and outdoor PM concentrations, we could not exclude some potential influences on indoor PM concentrations, such as the characteristics of home ventilation and type of cooking fuel. However, we have included the effect of smoking, an important source of household air pollution. Second, information about other gaseous pollutants, such as NOx and ozone, was not available. Therefore, it was impossible for us to determine whether the observed effects were specifically attributable to $PM_{2.5}$ or to the combined effects of the pollutants. Third, participants' blood pressure was measured only once if the first blood pressure reading was not hypertensive. This is not strictly in accordance with the clinical guidelines which require multiple measurements. However, a second measurement was conducted if the first measurement was hypertensive. The second measurement could greatly minimize white coat effects. Fourth, we could not eliminate clustering effects of geographic areas. The study participants were residents across Taiwan. Some geographic factors, such as socioeconomic status and lifestyle patterns, might differ in different cities/areas and had potential effects on the association. Finally, the 134 978 participants included in this study were nonhypertensive. Thus, compared with the excluded participants, they were slightly younger, healthier, and more educated, and had slightly healthier behaviors. This selection should not affect the conclusion, as we investigated the association rather than prevalence estimate in this study. Moreover, a series of subgroup analyses and sensitivity analyses, which took into account these variables, yielded similar results, demonstrating the robustness of the association.

Perspectives

The current study provided the first evidence that improvement in $PM_{2.5}$ exposure is associated with a lower risk of incident hypertension, whereas deterioration in ambient $PM_{2.5}$ is associated with a higher risk of incident hypertension. The findings help advance our understanding of the health effects of $PM_{2.5}$ on hypertension. Our study, therefore, demonstrates the beneficial effects of air quality improvement on hypertension and reinforces that mitigation of air pollution is an effective strategy to improve cardiovascular health.

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Disclosures

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Novelty and Significance

What Is New?

- This is the first study to evaluate the association between air quality improvement in particulate matter ($PM_{2.5}$) and incident hypertension.

What Is Relevant?

- More than 90% of the global population resides in areas where the air quality does not reach the standards recommended by the World Health Organization.
- Many countries dedicated in mitigation of air pollution in the past several decades.
- Long-term exposure to $PM_{2.5}$ is associated with an increased risk of hypertension development.

Summary

- $PM_{2.5}$ concentrations increased in 2002, 2003, and 2004, but began to decrease in 2005 in Taiwan.
- Every 5 $\mu g/m^3$ decrease in long-term exposure to $PM_{2.5}$ (ie, a $\Delta PM_{2.5}$ of -5 $\mu g/m^3$) is associated with a decrease of 16% in the risk of hypertension development (hazard ratio, 0.84; 95% CI, 0.82–0.86).