Spatial Association Between Ambient Fine Particulate Matter and Incident Hypertension

Hong Chen, PhD; Richard T. Burnett, PhD; Jeffrey C. Kwong, MD; Paul J. Villeneuve, PhD; Mark S. Goldberg, PhD; Robert D. Brook, MD; Aaron van Donkelaar, PhD; Michael Jerrett, PhD; Randall V. Martin, PhD; Alexander Kopp, MSc; Jeffrey R. Brook, PhD; Ray Copes, MD

Background—Laboratory studies suggest that exposure to fine particulate matter (≤2.5 μm in diameter) ($PM_{2.5}$) can trigger a combination of pathophysiological responses that may induce the development of hypertension. However, epidemiological evidence relating $PM_{2.5}$ and hypertension is sparse. We thus conducted a population-based cohort study to determine whether exposure to ambient $PM_{2.5}$ is associated with incident hypertension.

Methods and Results—We assembled a cohort of 35 303 nonhypertensive adults from Ontario, Canada, who responded to 1 of 4 population-based health surveys between 1996 and 2005 and were followed up until December 31, 2010. Incident diagnoses of hypertension were ascertained from the Ontario Hypertension Database, a validated registry of persons diagnosed with hypertension in Ontario (sensitivity=72%, specificity=95%). Estimates of long-term exposure to $PM_{2.5}$ at participants' postal-code residences were derived from satellite observations. We used Cox proportional hazards models, adjusting for various individual and contextual risk factors including body mass index, smoking, physical activity, and neighbourhood-level unemployment rates. We conducted various sensitivity analyses to assess the robustness of the effect estimate, such as investigating several time windows of exposure and controlling for potential changes in the risk of hypertension over time. Between 1996 and 2010, we identified 8649 incident cases of hypertension and 2296 deaths. For every 10-μg/m^3 increase of $PM_{2.5}$, the adjusted hazard ratio of incident hypertension was 1.13 (95% confidence interval, 1.05–1.22). Estimated associations were comparable among all sensitivity analyses.

Conclusions—This study supports an association between $PM_{2.5}$ and incident hypertension. **(*Circulation*. 2014;129:562-569.)**

Key Words: air pollution ■ cohort studies ■ epidemiology ■ hypertension

Long-term exposure to ambient air pollution increases cardiovascular mortality rates.[1,2] Air pollution has also been associated with the incidence of nonfatal myocardial infarction[3] and stroke,[4,5] indicating that exposure to air pollution may cause events at the later stages of vascular disease processes.[1] In contrast, far less is known about its possible effect at the earlier stages of developing cardiovascular disease.[1] Although air pollution has been linked to the progression of atherosclerosis,[6–8] whether air pollution may initiate or accelerate the development of other risk factors for cardiovascular disease is unclear.[1]

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Hypertension is one of the most important risk factors for cardiovascular disease.[9] Hypertension has been ranked as the leading cause for death and disability worldwide in 2010.[10] Recent studies have shown that individuals exposed to ambient fine particulate matter (particles with aerodynamic diameter ≤2.5 μm) ($PM_{2.5}$) exhibited elevations in arterial blood pressure within several hours to days after exposure.[11–15] Controlled exposure studies in humans[16,17] and animals[18,19] have shown similar associations. Increases in blood pressure have also been associated with long-term exposure to $PM_{2.5}$[20] and black carbon.[21] These observations implicate a potential link between air pollution and the development of new-onset hypertension.[22]

Until recently, only 2 studies have investigated the association between air pollution and incident hypertension,[23,24] with a positive relationship between incident hypertension and long-term exposure to $PM_{2.5}$ and nitrogen oxides reported in one study[23] but no association with nitrogen oxides in another.[24]

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From Public Health Ontario, Toronto, Ontario, Canada (H.C., J.C.K., R.C.); Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada (H.C., J.C.K., P.J.V., R.C.); Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada (H.C., J.C.K., A.K.); Population Studies Division, Health Canada, Ottawa, Ontario, Canada (R.T.B.); Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada (J.C.K.); Department of Health Sciences, Carleton University, Ottawa, Ontario, Canada (P.J.V.); Department of Medicine, McGill University, Montreal, Quebec, Canada (M.S.G.); Division of Clinical Epidemiology, McGill University Health Centre, Montreal, Quebec, Canada (M.S.G.); Division of Cardiovascular Medicine, University of Michigan Medical School, Ann Arbor (R.D.B.); Department of Physics and Atmospheric Science, Dalhousie University, Halifax, Nova Scotia, Canada (A.v.D., R.V.M.); Division of Environmental Health Sciences, School of Public Health, University of California, Berkeley (M.J.); Harvard-Smithsonian Center for Astrophysics, Cambridge, MA (R.V.M.); and Air Quality Research Division, Environment Canada, Toronto, Ontario, Canada (J.R.B.).

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Correspondence to Hong Chen, PhD, Public Health Ontario, 480 University Ave, Suite 300, Toronto, Ontario M5G 1V2, Canada. E-mail hong.chen@oahpp.ca

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Several cross-sectional studies have linked ambient air pollution to increased prevalence of hypertension.[25,26]

Given the ubiquitous nature of air pollution exposure, even a modest association between air pollution and hypertension would place a large number of people at increased risk for cardiovascular morbidity and mortality. We thus conducted a population-based cohort study in Ontario, Canada, to investigate whether hypertension incidence is associated with $PM_{2.5}$ exposure.

Methods

Study Design and Study Population

We conducted a cohort study that included Ontario respondents to the 1996/1997 cycle of National Population Health Survey[27] and the 2000/2001, 2003, and 2005 cycles of the Canadian Community Health Survey,[28] whom we followed until December 31, 2010 to determine the incidence of hypertension. Details of these surveys have been presented elsewhere.[29] Briefly, these population-based surveys were designed to estimate the prevalence rates of indices of health status, healthcare utilization, and determinants of health.[27,28] We included respondents who, at the time of the surveys: (1) resided in Ontario (response rates in Ontario=79–83%, depending on the year)[27,28]; (2) were aged ≥35 years; (3) were registered with Ontario's provincial health insurance plan; (4) agreed to share and link their responses to provincial health administrative data; and (5) were Canadian-born individuals. Hospital, laboratory, and physician services in Ontario are funded by the provincial government through a single-payer universal Medicare system that covers virtually all residents.[30]

We followed up the cohort using data linkage to provincial administrative databases developed from the Ontario Medicare system. Encrypted health card numbers were for data linkage across databases. We restricted the cohort to respondents who, according to Medicare data (since 1988), did not have physician-diagnosed hypertension at the time of the survey and had no prior history of hospital admissions for cardiovascular disease, including coronary heart disease, congestive heart failure, coronary revascularization, arrhythmia, and stroke. The Research Ethics Board of Sunnybrook Health Sciences Center, Toronto, approved the study.

Outcomes

We used the Ontario hypertension database, a validated registry of Ontario residents with diagnosed hypertension, to identify cohort members who developed hypertension during follow-up.[31,32] This database was created with the use of hospital discharge abstracts from the Canadian Institute for Health Information and physician service claims from the Ontario Health Insurance Plan database.[29,30] Any individual having at least 1 hospital admission with a diagnosis of hypertension (*International Classification of Diseases, Ninth Revision, Clinical Modification* diagnostic codes 401–405 or *International Classification of Diseases, Tenth Revision* codes I10 through I13 or I15 after 2002) or 2 physician claims for hypertension (codes 401–405) within a 2-year period was included in the hypertension database.[31] Cases of gestational hypertension were excluded.[31] The hypertension database has been validated by chart review and shown to identify individuals with hypertension with a sensitivity of 72% and specificity of 95% (positive and negative predictive values of 87% and 88%, respectively).[31] Once included in the database, individuals remain in it until death or termination of Ontario health coverage. People whose diagnosis date was at or before the time of survey were excluded from the analysis.

We also ascertained prior history of hospital admissions for coronary heart disease, stroke, arrhythmia, and coronary revascularization using hospital discharge abstracts (*International Classification of Diseases* codes are listed in the Appendix in the online-only Data Supplement). To identify cohort members with a previous diagnosis of heart failure, we linked the cohort to the Ontario Congestive Heart Failure Database, a validated database of all residents diagnosed with heart failure in Ontario.[33] People with a hospitalization for any of these cardiovascular outcomes occurring before cohort inception were excluded to minimize the possibility that these events might influence detection of incident hypertension.

Additionally, we ascertained 2 comorbidities at baseline, diabetes mellitus and chronic obstructive pulmonary disease (COPD), using their respective databases derived from hospital discharge abstracts and physician claim data (Appendix in the online-only Data Supplement).[34,35] Diabetes mellitus and COPD are often associated with increased risk for hypertension.[36,37]

We obtained vital status and eligibility for health insurance from the Registered Persons Database, a registry of all Ontario residents who have a health insurance number.[29] Follow-up ended when participants died, when participants were ineligible for provincial health insurance, or at the end of follow-up (December 31, 2010).

Assessment of Ambient Concentrations of $PM_{2.5}$

Estimates of ground-level $PM_{2.5}$ concentrations were derived from satellite observations of aerosol optical depth, a measure of light extinction as a result of scattering and absorption of light by aerosols in the atmosphere.[38] We used estimates from 2001 to 2006, thus obtaining a 6-year mean concentration of ground-level $PM_{2.5}$ produced at a spatial resolution of ≈10×10 km and covering North America below 70°N, which includes all of Ontario. These satellite-based concentrations of $PM_{2.5}$ closely agree with ground measurements at fixed-site stations across North America (Pearson correlation coefficient r=0.77; n=1057).[38] The satellite-based estimates have been applied previously to examine associations of $PM_{2.5}$ with mortality[39] and diabetes mellitus,[29] as well as global disease burden attributable to $PM_{2.5}$.[10]

Geographic location of residence for each participant was obtained from the Registered Persons Database for the period 1996 to 2010. Location was refined to the spatial scale provided by 6-character postal codes, which in urban areas represent a city block or a large apartment complex. We created annual estimates of exposure to $PM_{2.5}$ for each participant by interpolating the 6-year mean concentrations of $PM_{2.5}$ (2001–2006) to the centroid of their annual residential postal codes, thereby accounting for residential mobility. This approach assumes that the spatial pattern in $PM_{2.5}$ did not change appreciably during the follow-up period. This is a reasonable assumption because variability in $PM_{2.5}$ concentrations is primarily spatial rather than temporal, and areas in Ontario with higher concentrations of $PM_{2.5}$ have retained their spatial ranking between 1996 and 2010.[29]

Covariates

We obtained the following data from participants' responses to the surveys[27,28]: age; sex; marital status; race/ethnicity; education; smoking status (current/former/never); alcohol consumption (≥1 each month, <1 each month, former drinker, never drank); daily consumption of fruits and vegetables (<5 times/servings per day, ≥5 times/servings per day); physical activity (≥3.0, 1.5–2.9, <1.5 kcal/kg per day of energy expenditure for leisure activities); residency (urban/rural); and household income adequacy (lowest income, lower-middle income, middle income, upper-middle income, and upper income). These variables are either accepted risk factors for hypertension such as lifestyle[9] or may influence the risk of hypertension by mediating through lifestyle.[20] Household income adequacy is an index used by Statistics Canada that accounts for total household income and household size.[27,28] Because 98% of the cohort self-reported as white, we dichotomized race/ethnicity as white or nonwhite. In addition, we derived body mass index (kg/m^2) (BMI) using self-reported height and weight. Furthermore, we derived 3 neighborhood-level variables including (1) percentage of population aged ≥15 years with less than high school education; (2) unemployment rate; and (3) mean household income, using 1996, 2001, and 2006 Canadian Census Tract data (Appendix in the online-only Data Supplement).

To control for regional-scale spatial patterns in the incidence of hypertension that might be caused by factors other than pollution, we created an indicator variable classifying Ontario into southern and northern regions on the basis of the 14 Ontario Local Health Integrated Networks. The Local Health Integrated Networks are responsible for planning, integrating, and funding various local healthcare services in Ontario.

Statistical Analysis

We used a stratified Cox proportional hazards model with strata defined as single-year age groups, cycle of survey, and region (south/north). We included participants with nonmissing information on exposure and covariates. Because information on diet was not collected in the 1996/1997 National Population Health Survey (≈19% of the study population), we created a separate category of missing values for this variable to avoid losing substantial statistical power.

We measured follow-up time (in days) from the date of interview until the date of incident hypertension, death, ineligibility for provincial health insurance, or end of follow-up. We fitted a time-varying Cox model by modeling time-weighted exposure since cohort entry until the event, with weights for each individual defined by the time spent at each residence. We adjusted the Cox model for sex, marital status, education, household income adequacy, race, BMI (modeled as linear and quadratic), physical activity, smoking, drinking, diet, urban residency, preexisting diabetes mellitus or COPD, neighborhood-level unemployment, education, and mean household income. We hypothesized a priori that these factors could potentially confound the relationship between air pollution and hypertension. We tested for deviations from the proportional hazards assumption by adding the cross product of each variable with the natural logarithm of the time variable, but we did not find any violations of this assumption ($P>0.05$). We also verified the assumption of linearity for all continuous variables (except BMI) by using natural cubic spline functions with 2 and 3 degrees of freedom. We examined plots of concentration-response curves for $PM_{2.5}$ and evaluated the Akaike Information Criteria to determine whether the response function was nonlinear. Because there was no evidence of departure from linearity for the relation of $PM_{2.5}$ and hypertension (Figure I in the online-only Data Supplement), we report adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for each 10-μg/m^3 increase of $PM_{2.5}$ (referred to as HR_{10}).

Considering that certain characteristics, such as age, sex, and comorbidities, have been reported to enhance the susceptibility of populations to the effect of air pollution,[40] we investigated a priori potential effect modification by age, sex, BMI, education, race/ethnicity, household income adequacy, physical activity, smoking, and comorbidities by assessing whether the interaction term with $PM_{2.5}$ was statistically significant.

We performed a series of sensitivity analyses by considering mean annual exposures to $PM_{2.5}$ for other time windows, including 1, 2, and 5 years before an event; restricting the analysis to participants who had used any health services within 2 years before the baseline because of a concern that the frequency of healthcare utilization might influence the likelihood of detecting hypertension; restricting the analysis to participants who had lived at their baseline address for ≥5 years before enrollment; and restricting the analysis to southern Ontario, where 83% of the cohort lived.

We also performed additional sensitivity analyses by further adjusting for a linear term for time to account for potential changes in the diagnosis and risk of hypertension over time; adjusting for a categorical variable indicating the population size of participants' home community (rural; <30 000; 30 000–99 999; 100 000–499 999; ≥500 000); and including all participants with missing information on covariates that we imputed using multiple imputation (n=41 170) (Appendix in the online-only Data Supplement).

We also investigated whether the HRs might be influenced by any spatial dependence among study participants. In doing this, we fitted the Cox model with a frailty term (random effect) for Ontario Local Health Integration Networks to allow for the possibility that the effect estimates for hypertension vary from network to network in the estimation of the main effect and its variance. A gamma distribution for the frailties was assumed, with an exchangeable correlation structure within networks. We compared the models with and without a frailty term using Akaike Information Criteria. We repeated this analysis by using a frailty term for grids from $PM_{2.5}$ exposure surface (10×10 km) as a random effect.

Finally, we examined whether the effects of $PM_{2.5}$ on hypertension changed over time by testing for an interaction between 3 time periods (1996–2000, 2001–2005, and 2006–2010) and $PM_{2.5}$. These 3 periods were defined according to long-term trends of $PM_{2.5}$ in Ontario (Appendix in the online-only Data Supplement).

Results

Among the 79 942 potentially eligible respondents to the health surveys, the following exclusions were made: 25 042 (31%) because of a diagnosis of hypertension before cohort inception; 8309 (10%) because they were not Canadian-born individuals; 5521 (7%) because they had a prior history of hospitalization for cardiovascular disease; and 5867 (7%) because they had missing covariates (except diet). This left a total of 35 303 respondents in our analytical cohort.

At time of entry, the mean age was 50.3 years, 47% were men, 30% were current smokers, 43% were former smokers, 53% were either overweight or obese (BMI ≥25 kg/m^3), and 67% were regular drinkers (Table 1). In addition, 4% of the cohort had diabetes mellitus, and 7% had COPD. Average unemployment among the census tracts was 7%, and the mean household income was approximately Can $63 000.

Of the cohort, 19%, 29%, 27%, and 25% of the participants were enrolled from the surveys in 1996/1997, 2000/2001, 2003, and 2005, respectively (Table I in the online-only Data Supplement). The cohort contributed 259 110 person-years of observation, with a mean follow-up of 7.3 years. During the follow-up period, ≈42% of participants changed their addresses, and 24% moved out of the city that they lived in when surveyed. Residential mobility decreased with increasing age (Table II in the online-only Data Supplement). The average concentration of $PM_{2.5}$ according to participants' residences at baseline was 10.7 μg/m^3 (range, 2.9–19.2), with the highest average concentrations in southern Ontario (Figure). Between 1996 and 2010, we identified 8649 incident cases of hypertension and 2296 deaths.

We found a positive association between $PM_{2.5}$ and hypertension, with a HR of 1.11 (95% CI, 1.03–1.19) for each 10-μg/m^3 increase in $PM_{2.5}$, after adjusting only for age and sex (Table 2). Controlling for education, smoking, BMI, diet, and several other individual-level factors strengthened the association (HR_{10}=1.15; 95% CI, 1.07–1.24). In a model adjusted for all individual- and neighborhood-level covariates and comorbidities, the HR_{10} was 1.13 (95% CI, 1.05–1.22).

An analysis of selected subgroups did not provide compelling evidence supporting effect modification of $PM_{2.5}$ by individual risk factors, although there seemed to be a trend toward a stronger association found in individuals with diabetes mellitus (HR_{10}=1.52; 95% CI, 1.09–2.41) compared with those without diabetes mellitus (HR_{10}=1.11; 95% CI, 1.03–1.21) ($P_{interaction}$=0.07) (Table 3).

The HR_{10} estimates during 3 other time windows were similar to those with the use of the time-weighted exposure since cohort entry, with a tendency for a slightly stronger association with $PM_{2.5}$ averaged over longer time periods (Table 4). In addition, the estimated HRs for $PM_{2.5}$ were not altered appreciably after restricting the analysis to participants who lived at their baseline addresses for ≥5 years, adding a frailty term to allow for potential spatial clustering, or other sensitivity analyses that we performed (Figure II and Tables III through VII in the online-only Data Supplement). Furthermore, we found no evidence of interaction between time periods and $PM_{2.5}$ ($P_{interaction}$=0.54 for 1996–2000 and $P_{interaction}$=0.58 for 2006–2010).

Table 1. Baseline Characteristics of Study Population

Baseline Characteristics	Cohort (n=35 303)
Individual risk factors	
Age, y	50.3±12.0
Men	47
Marital status	
Married	65
Single	12
Separated, widowed, or divorced	23
Race/ethnicity	
White	98
Nonwhite	2
Body mass index, kg/m^2	26.0±4.7
<18.5	2
18.5–24.9	45
25.0–29.9	37
≥30	16
Education	
Less than high school	17
High school	19
More than high school	64
Annual household income adequacy*	
Lowest income quintile	3
Lower-middle income quintile	6
Middle income quintile	17
Upper-middle income quintile	36
Upper income quintile	38
Smoking status	
Never smoker	27
Current smoker	30
Former smoker	43
Type of drinker†	
Regular drinker	67
Occasional and former drinker	30
Never drinker	3
Total daily consumption of fruits and vegetables	
<5 times/servings per day	50
≥5 times/servings per day	31
Missing	19
Energy expenditure, kcal/kg per day‡	
≥3.0 (active)	23
1.5–2.9 (moderate)	26
<1.5 (inactive)	51
Preexisting comorbidity	
Diabetes mellitus	4
COPD	7
Lived in an urban area§	65
Lived in southern Ontario	83
Area-level risk factors‖	
Percentage of population aged ≥15 y, with less than high school education	28
Percentage of population aged ≥15 y, without employment	7
Mean household income (in Can$ 1000)	63.0±17.8

Values are percentage or mean±SD. COPD indicates chronic obstructive pulmonary disease.

*Household income adequacy is an index used by Statistics Canada that accounts for total household income and household size.

†Regular drinker: ≥1 time each month; occasional drinker: <1 time each month; former drinker: ever had a drink.

‡Average daily energy expenditure of participants in their leisure activities. For each physical activity, energy expenditure was estimated with the use of frequency and time per session as well as metabolic energy cost expressed as a multiple of resting metabolic rate.

§Urban areas are defined by Statistics Canada as continuously built-up areas having a population ≥1000 and a population density ≥400/km^2. All other areas were considered rural.

‖At the Canadian Census Tract level.

Discussion

We found that exposure to ambient $PM_{2.5}$ was associated with an increased incidence of hypertension, with HRs varying between 1.11 (95% CI, 1.03–1.20) and 1.13 (95% CI, 1.05–1.22) for each 10-μg/m^3 increase of $PM_{2.5}$. The association was robust to various sensitivity analyses and appeared to be stronger for people with diabetes mellitus.

To date, only 2 epidemiological studies have examined the effect of air pollution on the incidence of hypertension, and the results were mixed.[23,24] In an incidence study of 3236 black women in Los Angeles, CA, with follow-up from 1995 to 2005, Coogan et al[23] reported an adjusted HR_{10} for $PM_{2.5}$ of 1.48 (95% CI, 0.95–2.31) and a HR of 1.11 (95% CI, 1.03–1.20) per an increase of 10 parts per billion of nitrogen oxides. Because black women are at markedly high risk for hypertension,[41] and in the United States they experience higher levels of air pollution than whites,[42] the cohort likely represented a susceptible subpopulation.

A second study of 33 275 residents of Copenhagen and Aarhus, Denmark, with follow-up from 1993 to 2005, reported a rate ratio of 1.06 (95% CI, 0.92–1.23) for incident hypertension among individuals who were exposed to nitrogen oxides in the highest quartile (>26.6 parts per billion) compared with those in the lowest quartile (<16.1 parts per billion).[24]

The last study also assessed the association between nitrogen oxides and blood pressure and found a decrease of 0.62 mm Hg (95% CI, −1.35 to 0.11) in systolic blood pressure.[24] In contrast, another cohort study of 853 male veterans in Boston, MA, showed an increase of 2.64 mm Hg of systolic blood pressure (95% CI, 1.47–3.80) and 2.41 mm Hg of diastolic blood pressure (95% CI, 1.77–3.05) per increase of 0.32 μg/m^3 of black carbon (a marker for traffic-related pollution).[21] Similarly, 4 cross-sectional studies reported positive associations between air pollution levels and blood pressure[14,20,25,43]: three reported increases in systolic blood pressure from 3 to 15 mm Hg per 10-μg/m^3 increase of $PM_{2.5}$,[14,20,43] and 1 reported associations between systolic and diastolic blood pressure and PM_{10}, ozone, and sulfur dioxide.[25]

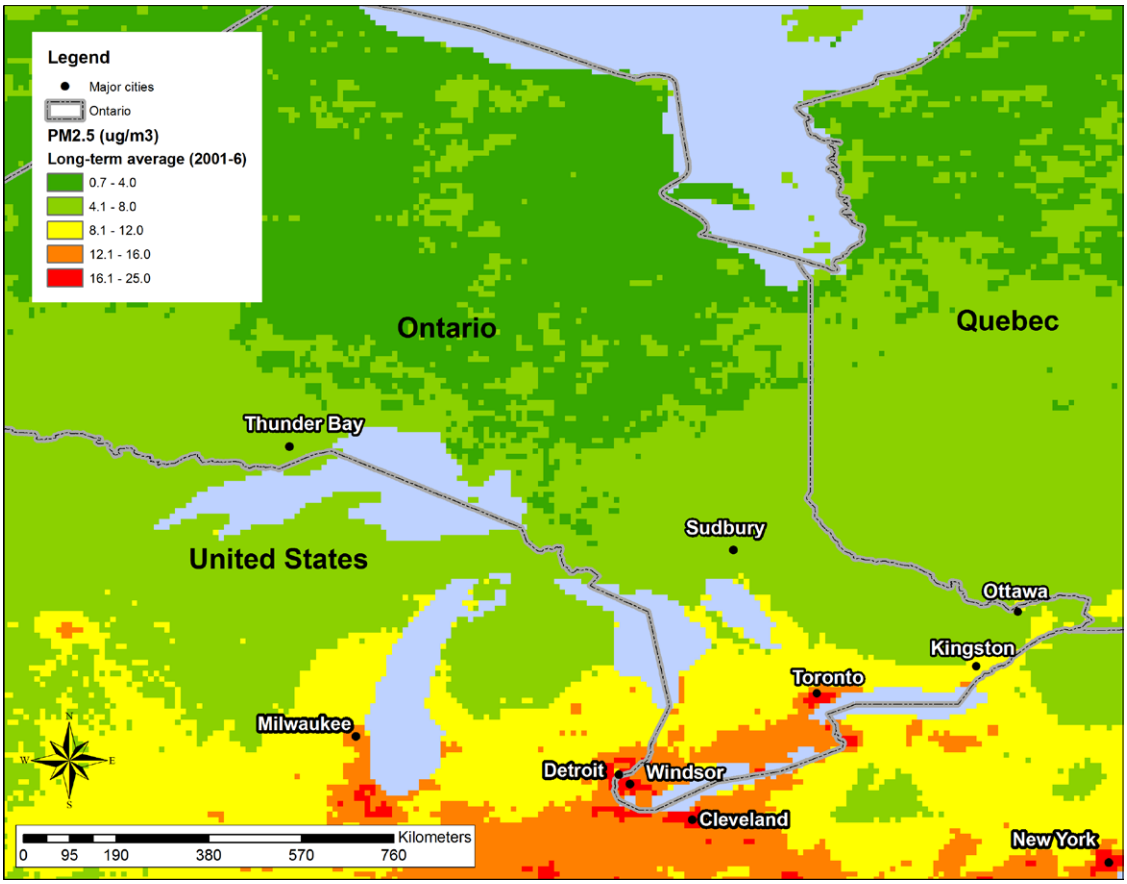

Figure. Mean satellite-derived estimates of particulate matter with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) across Ontario, Canada, 2001 to 2006.

Our analysis of the characteristics of the cohort suggested that individuals with diabetes mellitus may be at increased risk, but we could not rule out the possibility of chance finding. This observation is consistent with the findings from previous studies showing that diabetics were more susceptible to the adverse health effects of air pollution, such as mortality[44] and hospitalizations for cardiovascular disease.[45] Because hypertension is an important risk factor for diabetes mellitus,[9] our exclusion of hypertensives at baseline reduced the number of individuals with diabetes mellitus, resulting in reduced statistical power. Further replicating and understanding the potential interaction between diabetes mellitus and $PM_{2.5}$ in the risk of hypertension are merited.

To our knowledge, this is the largest study of incident hypertension in a population-based cohort to date. We obtained extensive individual-level information, which allowed for better control for known risk factors. Aspects of our analytical approach also reduce the concerns about confounding, such as our examination of the influence of potential clustering by participants. It is possible that residents living in neighboring communities are likely more similar than those living farther apart, but we found little evidence that our study would be affected significantly by potential spatial clustering. In addition, our study benefited from identification of cases with the use of a province-wide registry and an algorithm with high sensitivity and specificity.[31,32] Furthermore, the use of satellite-based long-term average estimates of $PM_{2.5}$ ensures virtually complete spatial coverage of $PM_{2.5}$ among all cohort members. It is worth noting that ambient concentrations of $PM_{2.5}$ in Ontario (annual mean in 2000: 11.2 $\mu g/m^3$) were much lower than those observed in many cities in the United States and in Europe (eg, annual mean $PM_{2.5}$ in Los Angeles, CA[23] was 20.7 $\mu g/m^3$ in 2000 and in Rome, Italy[46] was 19.9 $\mu g/m^3$ in 2010).

This study is subject to several limitations. First, we could not identify undiagnosed cases of hypertension. However, the estimates were unchanged when we restricted the analysis to participants who had used healthcare services within the 2 years before baseline as a proxy of healthcare utilization, which may be related to the diagnosis of hypertension. Because of universal healthcare in Ontario, incomplete diagnosis may lead to an underestimatation of the true effect because this measurement error was likely independent of the exposure.

Second, the spatial pattern of $PM_{2.5}$ was derived for the period 2001 to 2006 only. However, we have shown previously that the spatial gradients of ambient $PM_{2.5}$ in Ontario were stable over time and that variability in $PM_{2.5}$ concentrations is primarily spatial rather than temporal.[29] Because 76% of cohort members never moved or moved only within the city of residence, the spatial contrasts in $PM_{2.5}$ over 2001 to 2006 are expected to be a reasonable representation of longer-term spatial exposures to $PM_{2.5}$ in Ontario.[29] Although we attempted to identify critical time windows of exposure, we were unable to observe clear patterns because the HRs of $PM_{2.5}$ were similar between time windows. The time window of exposure biologically required to

Table 2. Associations of Incident Hypertension With an Increase of 10 μg/m³ of $PM_{2.5}$

Model	Incidence of Hypertension	
	Hazard Ratio	95% CI
$PM_{2.5}$ adjusted for sex and stratifying age, survey year, and region	1.11	1.03–1.19
+Marital status*	1.12	1.04–1.20
+Education	1.13	1.05–1.21
+Household income adequacy	1.13	1.05–1.22
+Body mass index	1.15	1.07–1.24
+Physical activity	1.15	1.07–1.24
+Smoking	1.15	1.07–1.24
+Alcohol consumption	1.15	1.07–1.24
+Consumption of fruits and vegetables	1.16	1.07–1.24
+Race/ethnicity	1.15	1.07–1.24
+Urban residency†	1.13	1.05–1.22
+Neighborhood-level covariates‡	1.13	1.05–1.22
+Comorbidities§	1.13	1.05–1.22

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

*Each variable was added to the model, including base model and all previous variables labeled with "+".

†Model stratified by age, survey year, and region and adjusted for sex, marital status, education, household income adequacy, body mass index, physical activity, smoking, alcohol consumption, diet, race/ethnicity, and urban residency.

‡Also adjusted for unemployment rate, education, and mean household income.

§Also adjusted for diabetes mellitus and chronic obstructive pulmonary disease.

Table 3. Associations of Incident Hypertension With Every 10-μg/m³ Increase of $PM_{2.5}$ by Selected Characteristics*

Covariates	No. of Cases	Incidence of Hypertension		*P* Value for Interaction With $PM_{2.5}$
		Hazard Ratio	95% CI	
Age				
<60 y	5400	1.09	0.99 –1.20	
60–69 y	1877	1.19	1.01–1.40	
≥70 y	1372	1.20	0.99–1.45	0.51
Sex				
Men	3990	1.11	0.99–1.24	
Women	4659	1.15	1.03–1.27	0.68
Body mass index, kg/m²				
<25.0	3067	1.17	1.04–1.33	
25.0–29.9	3539	1.11	0.99–1.26	
≥30.0	2043	1.07	0.91–1.26	0.65
Education				
Less than or equal to high school	3873	1.14	1.01–1.28	
More than high school	4776	1.15	1.04–1.27	0.88
Smoking				
Never smoker	2429	1.13	0.98–1.31	
Former smoker	2320	1.23	1.06–1.43	
Current smoker	3900	1.05	0.93–1.17	0.24
Preexisting diabetes mellitus				
Yes	592	1.52	1.09–2.14	
No	8057	1.11	1.03–1.21	0.07
Preexisting COPD				
Yes	768	1.13	0.86–1.50	
No	7881	1.14	1.06–1.24	0.96

CI indicates confidence interval; COPD, chronic obstructive pulmonary disease; and $PM_{2.5}$, particulate matter with particles with aerodynamic diameter ≤2.5 μm.

*Model stratified by age, survey year, and region and adjusted for sex, marital status, education, household income, body mass index, physical activity, smoking, alcohol consumption, diet, race/ethnicity, urban residency, neighborhood-level unemployment rate, education, and household income.

potentiate the development of overt hypertension (ie, change the natural history of the rate of hypertension onset in a population) remains uncertain. We have previously reviewed the complexity of the temporal associations between exposure estimations and acute cardiovascular events.[47] However, in this case regarding the development of a chronic disease state, we expect that it would take the cumulative effect of at least years of exposure to $PM_{2.5}$ to elevate risks. Given the strong temporal correlation in exposure, it remains unclear if only exposure over a single year or several years is the true physiological culprit. Regardless, we have shown that exposure over relatively brief periods (1–5 years) is capable of potentiating hypertension onset.

Third, because the spatial resolution of $PM_{2.5}$ exposure surface is 10×10 km, we were unable to examine effects at finer spatial scales. In addition, we did not have information on daily activity. Given the inherent imprecision of the spatially derived exposure, our assessment of exposure was likely subject to nondifferential misclassification that may have attenuated the estimates.

Fourth, community noise, especially from traffic sources, has been implicated as a risk factor for hypertension.[20] However, previous studies from the United States[48] and Canada[49] have shown that noise levels are weakly associated with $PM_{2.5}$. Thus, traffic noise would unlikely substantially bias our risk estimates.

Fifth, information on family history of hypertension as well as dietary behaviors such as sodium intake was unavailable, although it is unclear whether these factors would be associated with $PM_{2.5}$. Finally, information on potential confounding variables was obtained at baseline only. However, it is unlikely that these characteristics would change considerably over the study period because of the relatively short follow-up (mean=7.3 years).

A potential mechanism relating exposure to $PM_{2.5}$ to hypertension may be its indirect effects mediated through systemic proinflammatory and oxidative responses, which may lead to increased sympathetic tone and potentially cause arterial remodeling.[22] Oxidative stress may also increase the circulation of activated immune cells and inflammatory cytokines, which may subsequently induce endothelial dysfunction, leading to an imbalance in vascular homeostatic responses.[22] If this happens repeatedly, it could result in an increased total peripheral resistance and a fixation of elevated blood pressure.[20] Other mechanisms by which $PM_{2.5}$ may elevate blood pressure include autonomic nervous system imbalance and direct vasoconstriction.[23] Finally, PM exposure can reduce daytime sodium excretion and blunt the normal nocturnal reduction in blood pressure.[50] Over time, impaired renal handling of excess sodium may be partly responsible for elevated blood pressure.[50]

Table 4. Sensitivity Analyses for Associations of Incident Hypertension With Every 10-μg/m³ Increase of $PM_{2.5}$*

Sensitivity Analysis	No. of Cases	Incidence of Hypertension	
		Hazard Ratio	95% CI
Modeled 3 different time windows of exposure			
1 y before event	8649	1.11	1.03–1.20
2 y before event	8649	1.12	1.04–1.21
5 y before event	8649	1.13	1.05–1.22
Restricted to participants who had ≥1 healthcare contact† within			
Last year	7849	1.13	1.05–1.22
Last 2 y	8329	1.13	1.04–1.22
Restricted to participants who lived at their baseline addresses for ≥5 y before cohort entry	6592	1.17	1.07–1.27
Restricted to participants in southern Ontario	7137	1.15	1.06–1.24
Included all participants regardless of missing covariates‡	10 330	1.14	1.07–1.22
Added a frailty term (random effect) to investigate spatial dependence as a source of bias			
+Frailty term for Ontario Local Health Integration Networks§	8649	1.12	1.04–1.22
+Frailty term for grids from exposure surface of $PM_{2.5}$ (10×10 km)	8649	1.13	1.05–1.23

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

*Model stratified by age, survey year, and region and adjusted for sex, marital status, education, household income, body mass index, physical activity, smoking, alcohol consumption, diet, race/ethnicity, urban residency, as well as neighborhood-level unemployment rate, education, and household income, diabetes mellitus, and chronic obstructive pulmonary disease.

†A healthcare contact is defined as having any record of physician claim, drug benefit claim, hospitalization, same-day surgery, ambulatory care, chronic care service, home care service, inpatient rehabilitation, or inpatient mental healthcare.

‡Missing values were imputed with the use of multiple imputation (Appendix in the online-only Data Supplement).

§Fourteen Local Health Integration Networks in Ontario.

In summary, we investigated the effects of long-term exposure to $PM_{2.5}$ on the rates of developing hypertension in Ontario, Canada. Results from this study support an association between $PM_{2.5}$ and the incidence of hypertension.

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Disclosures

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CLINICAL PERSPECTIVE

Mounting evidence now links millions of cardiovascular deaths worldwide to ambient air pollutants, especially from fine particulate matter (particles with an aerodynamic diameter ≤2.5 μm) ($PM_{2.5}$). There is also growing evidence associating long-term exposure to $PM_{2.5}$ with the incidence of myocardial infarction, stroke, and other clinical events that typically occur at the later stages of the vascular disease processes. However, far less is known about the possible effect of air pollution at the earlier stages of the disease. This study extends the detrimental actions of air pollution to include an augmented risk for the development of hypertension, one of the most important risk factors for cardiovascular disease and the leading cause of global mortality. By following 35 303 adults who lived across Ontario, Canada, between 1996 and 2010, this study found that long-term exposures to low levels of $PM_{2.5}$ were associated with increased incidences of hypertension, especially among individuals with diabetes mellitus. Given that billions of people worldwide are exposed to higher concentrations of $PM_{2.5}$, these findings may have serious global public health implications. For healthcare providers, these results emphasize that patients with or at high risk for cardiovascular diseases should be educated about the potential harmful health effects posed by air pollution. From the pubic health perspective, these observations add further support to the continuing public efforts to improve overall air quality, even considering present-day low levels of $PM_{2.5}$ in locations such as Ontario.