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Chronic disease prevalence in women and air pollution — A 30-year longitudinal cohort study

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ABSTRACT

Background: Air pollution, such as fine particulate matter ($PM_{2.5}$), can increase risk of adverse health events among people with heart disease, diabetes, asthma and chronic obstructive pulmonary disease (COPD) by aggravating these conditions. Identifying the influence of $PM_{2.5}$ on prevalence of these conditions may help target interventions to reduce disease morbidity among high-risk populations.
Objectives: The objective of this study is to measure the association of exposure of $PM_{2.5}$ with prevalence risk of various chronic diseases among a longitudinal cohort of women.
Methods: Women from Ontario who enrolled in the Canadian National Breast Screening Study (CNBSS) from 1980 to 1985 (n = 29,549) were linked to provincial health administrative data from April 1, 1992 to March 31, 2013 to determine the prevalence of major chronic disease and conditions (heart disease, diabetes, asthma, COPD, acute myocardial infarction, angina, stroke and cancers). Exposure to $PM_{2.5}$ was measured using satellite data collected from January 1, 1998 to December 31, 2006 and assigned to resident postal-code at time of entry into study. Poisson regression models were used to describe the relationship between exposure to ambient $PM_{2.5}$ and chronic disease prevalence. Prevalence rate ratios (PRs) were estimated while adjusting for potential confounders: baseline age, smoking, BMI, marital status, education and occupation. Separate models were run for each chronic disease and condition.
Results: Congestive heart failure (PR = 1.31, 95% CI: 1.13, 1.51), diabetes (PR = 1.28, 95% CI: 1.16, 1.41), ischemic heart disease (PR = 1.22, 95% CI: 1.14, 1.30), and stroke (PR = 1.21, 95% CI: 1.09, 1.35) showed over a 20% increase in PRs per 10 μg/m^3 increase in $PM_{2.5}$ after adjusting for risk factors. Risks were elevated in smokers and those with BMI greater than 30.
Conclusions: This study estimated significant elevated prevalent rate ratios per unit increase in $PM_{2.5}$ in nine of the ten chronic diseases studied.

1. Introduction

The adverse health effects associated with exposure to ambient air pollution, particularly traffic-related pollution, have been well established. In recent years, there has been extensive literature suggesting an increased risk in the incidence and mortality of several chronic diseases in association with long-term exposure to air pollutants. The biological plausibility is that air pollutants may promote inflammation, oxidative stress and endothelial dysfunction that may contribute to the development of chronic conditions such as cardiovascular disease, hypertension and diabetes (Brook et al., 2004; Coogan et al., 2012; Johnson and Parker, 2009; Kramer et al., 2010; Pearson et al., 2010; Puett et al., 2011; U.S. EPA, 2008, 2009, 2013). In addition, air pollution has also been linked to the worsening of diseases of the pulmonary system, including asthma and chronic obstructive pulmonary disease (COPD) (To et al., 2013a,b). Older adults living with a chronic condition such as hypertension, asthma and COPD may be at higher risk of having their conditions aggravated by exposure to air pollution.

A few population-based studies have quantified the association of air pollution exposure and incidence of chronic disease. For example, using

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data from Ontario, Canada, Chen et al. (2013, 2014) reported significantly elevated hazard ratios of incident hypertension and diabetes (HR = 1.13, 95% confidence interval: 1.05–1.22 and HR = 1.11; 95% CI: 1.02, 1.21, respectively) per 10-μg/m^3 increase of $PM_{2.5}$. Coogan et al. (2012) studied a cohort of 4204 women who lived in Los Angeles from 1995 to 2005 and reported elevated incidence rate ratios for hypertension and diabetes per unit (10 μg/m^3) increase in fine particulate matter ($PM_{2.5}$). Puett et al. (2011) used data from the final two years of a 23-year follow-up of the Nurses' Health Study and reported a statistically significant relative risk of type 2 diabetes per unit (4 μg/m^3) increase of $PM_{2.5}$. Johnson and Parker (2009) conducted cross-sectional analyses using the National Health Interview Survey data and reported statistically significant increased odds of self-reported prevalent hypertension associated with $PM_{2.5}$.

In this study, we used a large population-based cohort of women with over 30 years of follow-up data to quantify the prevalence risks of cardiovascular conditions, cancers, diabetes and respiratory diseases in association with $PM_{2.5}$ exposure. Since these conditions and diseases are chronic (i.e., with a relatively long duration), measures of disease prevalence would better characterize the burden of illness than incidence. A better understanding of the long-term risks of exposure to air pollution on these major chronic conditions will enable the development of new strategies to protect individuals at risk and reduce detrimental effects of air pollution on health as a whole.

2. Methods

2.1. Data source

2.1.1. Study population

The Canadian National Breast Screening Study (CNBSS) included 89,835 women between the ages of 40 and 59 recruited between 1980 and 1985 (Miller et al., 1992, 1996). The CNBSS was a randomized controlled trial of screening for breast cancer with the original objective of determining whether screening contributed to lower breast cancer mortality, as well as answering questions about what ages to screen and frequency of screening. Detailed risk factor data were collected using questionnaires administered at baseline (1980–1985) and included questions about smoking, anthropometry (including body mass index), physical activity levels, and diet. Height and weight were measured at baseline. Smoking history was collected using 3 questions. First, women were asked if they have ever smoked (Y/N). Those who responded YES were then asked a) how many cigarettes per day they did/do smoke and b) how long they did/have smoke(d). Those who were no longer smoking were asked to indicate when they stopped. Number of pack-years was calculated as packs smoked per day × years as a smoker. The number of pack-years was included as a covariate in all regression models.

Among CNBSS participants, 31,972 women resided in Ontario (hereafter referred to as the ONBSS cohort) and provided consent to use their health card number for data linkage. Of these women, 29,981 (93.8%) were successfully linked to provincial administrative data maintained by the Institute for Clinical Evaluative Sciences (ICES) in Toronto. These administrative data included hospital discharges, emergency visits and Ontario Health Insurance Claims (i.e., physician outpatient claims) — detailed in Outcomes section. A total of 188 women (0.6%) who died before April 1, 1992 were excluded as their chronic disease prevalence could not be determined. In addition, 182 (0.6%) with missing $PM_{2.5}$ data and 52 (0.2%) with incomplete data on covariates were excluded, yielding 29,549 women (92.4%) in the study population.

2.1.2. Exposure data

Long-term exposure to $PM_{2.5}$ was measured using satellite-based estimates of surface concentrations of $PM_{2.5}$ (Chen et al., 2013; van Donkelaar et al., 2010). The satellite-based concentrations were derived from aerosol optical depth data from the Moderate Resolution Imaging Spectroradiometer (MODIS) and Multiangle Imaging Spectroradiometer (MISR) instruments onboard the National Aeronautics and Space Administration (NASA)'s Terra satellite (Chen et al., 2013; van Donkelaar et al., 2010). Using satellite data collected from January 1, 1998 to December 31, 2006, long-term average concentrations of $PM_{2.5}$ were derived at a resolution of approximately 10 × 10 km. These satellite-based long-term average concentrations of $PM_{2.5}$ have been shown to correlate well with ground measurements at fixed-site stations across North America (Pearson correlation coefficient r = 0.77, n = 1057) (Brook et al., 2013; Crouse et al., 2012; van Donkelaar et al., 2010). Exposure surface concentrations of $PM_{2.5}$ were then assigned to residences of ONBSS women using the centroids of six-character postal codes at baseline.

2.1.3. Outcomes — disease prevalence

Three health administrative databases with 12 years of data available from April 1, 1992 to March 31, 2013 were used to determine the prevalence of major chronic diseases in the study population. A total of 188 women who died before April 1, 1992 were excluded as their chronic disease prevalence could not be determined. For the remaining cohort, the prevalence of chronic disease was assembled from 1992 to 2013. The health administrative data used include: 1) the Ontario Health Insurance Plan Database — contains information on fee-for-service billings for physician services rendered; 2) the National Ambulatory Care Reporting System — contains data for emergency department (ED) visits; and 3) the Canadian Institute for Health Information Discharge Abstract Database — records primary and secondary diagnoses for all hospitalizations. International Classification of Disease codes (ICD-9 and ICD-10) and algorithms were used to define diseases and conditions (details outlined in Appendix 1). The ONBSS women who had ever been diagnosed with any of the following 10 major chronic diseases and conditions were identified: ischemic heart disease, congestive heart failure, hypertension, diabetes, asthma, chronic obstructive pulmonary disease (COPD), angina, acute myocardial infarction (AMI), stroke, and cancers (breast, lung and others). The prevalence of chronic disease in ONBSS women was compared to that of the population of women living in Ontario. The comparison population included Ontario women who were born between 1921 and 1945 (equivalent birth years of the ONBSS women) were identified from the Ontario Registered Persons Database housed at ICES.

2.1.4. Potential confounders

Demographic data of the ONBSS women were collected by self-administered questionnaires at time of enrollment in the CNBSS. These data include age at enrollment, marital status (never married, divorced, separated, widowed), education (less than high school, completed high school, trade or vocational school, college or business training), occupation (unemployed, homemaker, arts, clerical, management or administration, medicine and health, retired, sales, service, social sciences, teaching or other), smoking status and body mass index (BMI calculated based on height and weight measured at baseline). We also included four contextual variables derived from census area measures and they were mean income, proportion with high school education, percentage of low-income households, and unemployment rate.

2.2. Statistical analysis

The risk of chronic disease prevalence and exposure to $PM_{2.5}$ were measured using Poisson regression models. Poisson regression is an appropriate approach for binomial outcomes. To avoid overestimating the error of the estimated risk (Zocchetti et al., 1995), a robust error variance procedure (sandwich estimation) (Royall, 1986) was used leading to the modified Poisson regression defined by Zou (2004). The modified Poisson regression made it possible to directly estimate prevalence rate ratio from cross-sectional data, with adjustment for

confounders as oppose to an odds ratio from a logistic regression which tends to overestimate the relative risk when the rare disease assumption is not met. Potential confounders were included in the regression model as covariates, which include age at enrolment, marital status, education, occupation, smoking status, BMI and the four census variables outlined above. The prevalence rate ratios for breast cancer were also adjusted for reproductive history (number of live births, number of pregnancies and number of pregnancies lasted less than four months). Results were presented as prevalence rate ratios (PRs) with 95% confidence intervals (CIs) per unit (10 μg/m^3) increase in $PM_{2.5}$. Missing data were excluded in the regression models. All analyses were carried out using SAS version 9.3 (SAS Institute Inc., Cary, NC).

3. Results

Table 1 shows the demographic characteristics of the ONBSS population. The study population consisted of 29,549 women with valid health card number for data linkage, which represented 92.4% of the total ONBSS cohort. Approximately 79% of these women were still alive at the end of the study (March 31, 2013) with a mean age of 77.3 years (±6.3). The majority of the women were Canadian born (72.6%), married (81.1%), had at least completed high school education (81.4%) and were in the workforce (66.3%) at baseline. The overwhelming majority (81.1%) of the ONBSS had not moved from their residence since entry to the study. Using the World Health Organization (WHO) definition of overweight and obesity, the majority (60.7%) of the ONBSS women had normal weight at baseline, while 26.3% were overweight (with BMI ≥ 25.0 and <30.0) and 11.2% were obese (with BMI ≥ 30.0). Approximately half (52.0%) of the ONBSS women had ever smoked with an average of 15.4 (±13.7) packed years.

Table 2 shows the prevalence of chronic diseases in the ONBSS compared to the overall Ontario female population. The ONBSS women were similar to the overall Ontario female population with the top five highest prevalent chronic conditions being: hypertension (70.6%), ischemic heart disease (41.2%), angina (25.2%), diabetes (21.8%) and COPD (21.6%). Compared to the Ontario female population, the ONBSS cohort has a higher prevalence of breast cancer, which may be attributable to the breast cancer screening they received while participating in the CNBSS. This could have contributed to over diagnosis as suggested by other screening programs in Europe (Heinävaara et al., 2014; Njor et al., 2013). Table 3 stratified the distributions of chronic diseases in the ONBSS women by the two most common modifiable lifestyle risk factors, smoking and BMI. As expected, the prevalence of COPD doubled in those who were ever smokers (28.2% versus 14.4%, $p < 0.0001$) while the prevalence of most chronic diseases were higher in those who were obese, particularly in hypertension (87.0% versus 64.3%, $p < 0.0001$) and diabetes (48.9% versus 13.8%, $p < 0.0001$).

Table 4 and Fig. 1 show the results of the Poisson regressions that estimated the prevalence rate ratios (PRs) of chronic disease prevalence with each unit increase in $PM_{2.5}$ (10 μg/m^3). Since smoking and BMI are known lifestyle risk factors for various chronic diseases, their respective PRs are also presented in Table 4. Most of the 10 chronic diseases and conditions examined showed a statistically significant elevated PR with each unit increase in $PM_{2.5}$, with the exception of lung cancer, breast cancer and AMI. The highest PRs were seen in congestive heart failure, ischemic heart disease, diabetes, stroke and COPD with each showing a greater than 20% increase in disease risk with each unit increase in exposure to $PM_{2.5}$. Details of mean exposure to $PM_{2.5}$ among those with or without chronic disease can be found in Appendix 2. Details of chronic disease PRs per $PM_{2.5}$ exposure in subgroups (those who did not move, those who were still alive, and those who never smoked) can be found in Appendix 3. As a comparison, we considered chronic diseases identified after 1996 (i.e., "free" of these conditions prior to 1997) as incidence and calculated incidence rate ratios (IRs), which are also shown in Table 4. In most cases, the PRs and IRs were similar, however the IRs had wider confidence intervals due to reduced sample sizes.

Table 1
Demographic characteristics of the ONBSS study population, N = 29,549.

Characteristic	Number	%
Age at entry (years)		
40–44	8022	27.1
45–49	7743	26.2
50–54	7810	26.4
55–59	5974	20.2
Current mean age	77.33 ± 6.25	
Average years of follow-up ± SD	28.64 ± 4.27	
Deaths	6280	21.3
Birth place		
Canada	21,467	72.6
United Kingdom	3941	13.3
European (excluding UK)	2521	8.5
USA	786	2.7
Other	834	2.8
Marital status		
Never married	1648	5.6
Married	23,957	81.1
Divorced/separated/widowed	3944	13.3
Education		
Less than high school	5521	18.7
Completed high school/trade or vocational school	6280	21.3
College or business training	10,630	36.0
University	7118	24.1
Occupation		
Homemaker or unemployed	9973	33.8
Employed	18,672	63.2
Unknown	904	3.1
Ever moved residence since baseline	5592	18.9
Body mass index (kg/m^2)[a]		
<25	17,938	60.7
≥25 to <30	7776	26.3
≥30	3302	11.2
Unknown	533	1.8
Skinfold thickness		
Lowest quartile	6705	22.7
Lower–middle quartile	6786	23.0
Middle–upper quartile	6636	22.5
Highest quartile	6845	23.2
Unknown	2577	8.7
Cigarette smoker		
Never	14,076	47.6
Ever	15,364	52.0
<5 pack years	4040	13.7
5–<15 pack years	3891	13.2
15–<25 pack years	3335	11.3
25+ pack years	3027	10.2
Unknown pack years	1071	3.6
Mean pack years ± SD	15.35 ± 13.71	
Missing	109	0.4
Mean level of $PM_{2.5}$ ± SD		
Overall	12.47 ± 2.40	
Smoking status:		
Smokers	12.55 ± 2.45	
Non-smokers	12.38 ± 2.35	
BMI:		
BMI < 30	12.47 ± 2.41	
Obese (BMI ≥ 30)	12.43 ± 2.46	

SD = standard deviation.
[a] Based on the World Health Organization BMI classifications.

4. Discussion

To date, this is one of the largest longitudinal cohort studies examining the impact of air quality on the prevalence of major cardiovascular conditions, cancer, diabetes and respiratory diseases in women. This study estimated significant elevated prevalence per unit increase in $PM_{2.5}$ for nine out of the ten chronic diseases studied.

Table 2
Prevalence of chronic disease in ONBSS cohort compared to general Ontario female population.

Chronic disease	Total ONBSS cohort (N = 29,549)		Ontario female population[a] (N = 1,409,664)	
	Number	Percent	Number	Percent
Acute myocardial infarction	1233	4.17	72,173	5.12
Angina	7440	25.18	336,025	23.84
Asthma	4813	16.29	198,651	14.09
Cancer				
Breast cancer	2789	9.44	98,166	6.96
Lung cancer	781	2.64	47,215	3.35
All other cancers	4383	14.83	184,268	13.07
Congestive heart failure	3590	12.15	206,080	14.62
COPD	6387	21.61	329,653	23.39
Diabetes	6447	21.82	377,378	26.77
Hypertension	20,866	70.61	958,532	68.00
Ischemic heart disease	12,169	41.18	535,694	38.00
Stroke	5993	20.28	255,199	18.10

[a] The comparison cohort consisted Ontario women who were born between 1921 and 1945 comparable to the ONBSS women who were aged between 40 and 59 years in 1980. Data were obtained from the Ontario Registered Persons Database housed at the Institute for Clinical Evaluative Sciences.

The ONBSS study population consisted of nearly 30,000 women who were recruited for the CNBSS in the 1980s when they were between 40 and 59 years of age. The majority of them were still alive at the end of the study period with an average age of 77 years. The distribution of chronic disease prevalence was similar between the ONBSS cohort and the Ontario female population suggesting good generalizability of our study findings to the female population. The 5% lower prevalence of diabetes in the ONBSS group may be due to the difference in ethnic distribution between the two groups. Compared to the Ontario female population, the ONBSS has a relatively smaller percentage of South Asian and Chinese individuals — ethic groups known to have higher prevalence of diabetes. Of the major chronic diseases and conditions examined, congestive heart failure, diabetes, ischemic heart disease and stroke showed over 20% increased rate ratio in prevalence per unit increase in $PM_{2.5}$ after adjusting for demographic and common lifestyle risk factors of smoking and obesity. Exposure to $PM_{2.5}$ also increased the prevalence risk of COPD and asthma.

Our findings are consistent with those reported in recent literature. For example, the Israel Study of First Acute Myocardial Infarction study followed 1626 patients aged 65 years or less for 10 to 13 years after their incident AMI and reported an increased risk of recurrence of cardiovascular events (i.e., AMI, heart failure and stroke) per 10 μg/m^3 increase in $PM_{2.5}$ exposure (Koton et al., 2013). Similarly, the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults study of 6392 adults between 29 and 73 years of age reported a 1.4-fold increased odds of diabetes prevalence per 10 μg/m^3 increase in PM_{10} (Eze et al., 2014). As for prevalence risk of respiratory diseases, the European Studies on Chronic Air Pollution Effects cohort study of 3692 adults recruited from 1985 to 1999 and followed up with between 2001 and 2011 reported significantly increased odds of COPD prevalence and traffic-related pollution in females (Schikowski et al., 2014). Further, a previous study of ours, using data from the Ontario Asthma Surveillance Information System, showed an elevated rate ratio for prevalence of asthma events (i.e., ED visits) per 10 μg/m^3 increase in $PM_{2.5}$ exposure (To et al., 2013b). While our study focused on prevalence rate ratios, previous studies have also found an increase in incidence and mortality risks in association with increased exposure to air pollution (Coogan et al., 2012; Johnson and Parker, 2009; Kramer et al., 2010). When included and considered chronic diseases identified only after 1996 as incidence, the results were similar.

This study has several strengths, including the use of a large population-based dataset and linkage to provincial health administrative data to ascertain the prevalence of multiple major chronic diseases and conditions over 30 years. To date, very few published studies are of comparable magnitude. The use of large sample sizes allowed us to estimate disease-specific prevalence rate ratios using the modified Poisson regression models while fully adjusting for multiple potential confounders, including demographic characteristics of the study population and important lifestyle factors such as smoking and BMI. Furthermore, exposures were measured using satellite-based estimates of surface concentrations of $PM_{2.5}$ collected from 1998 to 2006 providing a cumulative estimate of exposure to $PM_{2.5}$ with wider coverage that correlate well with ground measurements at fixed-site stations (Brook et al., 2013; Crouse et al., 2012; van Donkelaar et al., 2010).

Despite these strengths, a few limitations should be noted. Firstly, since we do not have historical medical records of the study population, we were not able to determine the incidence of the chronic diseases studied and we were limited to focusing on prevalence risks. Furthermore, since the information of chronic disease comorbidity was not collected by the CNBSS, we were unable to exclude baseline prevalence chronic diseases. Secondly, without incidence date of the chronic diseases, we were not able to determine the prevalence of multiple comorbidity of more than one chronic disease at any given time. Some women may have more than one chronic disease and therefore they

Table 3
Prevalence of chronic diseases by lifestyle risk factors.

Chronic disease	ONBSS by smoking status		ONBSS by weight categories	
	Non-smokers	Smokers	Normal	Obese
	Percent	Percent	Percent	Percent
Acute myocardial infarction	3.91	4.43*	3.34	7.12**
Angina	24.84	25.47 NS	21.85	34.74**
Asthma	14.47	17.95**	14.53	22.80**
Cancer				
Breast cancer	9.07	9.82*	9.33	9.84 NS
Lung cancer	0.74	4.39**	2.78	1.88*
All other cancers	14.44	15.16 NS	13.53	19.05**
Congestive heart failure	11.18	13.04**	9.14	23.41**
COPD	14.42	28.23**	20.30	26.56**
Diabetes	22.30	21.30*	13.80	48.91**
Hypertension	71.92	69.41**	64.31	86.98**
Ischemic heart disease	40.42	41.87*	37.57	50.88**
Stroke	19.87	20.64 NS	18.97	24.02**

Obese = BMI ≥ 30.
NS = Not statistically significant or p-value ≥ 0.05.
* p-Value < 0.05.
** p-Value < 0.0001.

Table 4
Adjusted prevalence (PRs) and incidence (IRs) rate ratios of chronic diseases per unit (10 μg/m^3) increase in $PM_{2.5}$.[a]

Chronic disease	Prevalence rate ratios						Incidence rate ratios					
	$PM_{2.5}$		Smoking		BMI ≥ 30		$PM_{2.5}$		Smoking		BMI ≥ 30	
	PR	95% CI	PR	95% CI	PR	95% CI	IR	95% CI	IR	95% CI	IR	95% CI
Acute myocardial infarction	1.06	[0.81, 1.37]	1.51	[1.28, 1.77]	1.80	[1.55, 2.09]	1.04	[0.78, 1.40]	1.38	[1.15, 1.66]	1.65	[1.39, 1.95]
Angina	1.20	[1.09, 1.31]	1.21	[1.13, 1.28]	1.43	[1.35, 1.51]	1.10	[0.97, 1.24]	1.10	[1.01, 1.20]	1.36	[1.26, 1.47]
Asthma	1.14	[1.01, 1.29]	1.58	[1.46, 1.70]	1.56	[1.45, 1.68]	1.03	[0.84, 1.25]	1.66	[1.47, 1.88]	1.27	[1.12, 1.44]
Cancer												
All other cancers	1.17	[1.03, 1.33]	1.20	[1.10, 1.31]	1.38	[1.27, 1.49]	1.23	[1.05, 1.45]	1.14	[1.02, 1.27]	1.35	[1.22, 1.50]
Breast cancer	1.11	[0.93, 1.31]	1.11	[0.99, 1.26]	1.10	[0.98, 1.22]	1.24	[0.99, 1.55]	1.05	[0.89, 1.24]	1.12	[0.97, 1.30]
Lung cancer	1.04	[0.75, 1.42]	14.61	[11.73, 18.19]	0.63	[0.49, 0.82]	1.03	[0.72, 1.45]	13.60	[10.75, 17.20]	0.63	[0.47, 0.84]
Congestive heart failure	1.31	[1.13, 1.51]	1.65	[1.51, 1.79]	2.22	[2.05, 2.40]	1.30	[1.11, 1.52]	1.58	[1.44, 1.74]	2.12	[1.94, 2.31]
COPD	1.12	[1.01, 1.23]	3.15	[2.98, 3.33]	1.22	[1.14, 1.30]	1.17	[1.02, 1.33]	2.76	[2.55, 2.98]	1.21	[1.11, 1.31]
Diabetes	1.28	[1.16, 1.41]	1.06	[0.99, 1.13]	3.30	[3.13, 3.48]	1.28	[1.13, 1.45]	0.97	[0.88, 1.06]	2.17	[2.02, 2.34]
Hypertension	1.11	[1.07, 1.14]	1.00	[0.98, 1.03]	1.30	[1.27, 1.32]	1.04	[0.97, 1.11]	0.96	[0.91, 1.01]	0.80	[0.76, 0.85]
Ischemic heart disease	1.22	[1.14, 1.30]	1.14	[1.10, 1.19]	1.28	[1.23, 1.33]	1.18	[1.08, 1.29]	1.03	[0.97, 1.10]	1.23	[1.16, 1.30]
Stroke	1.21	[1.09, 1.35]	1.21	[1.13, 1.29]	1.17	[1.09, 1.25]	1.26	[1.11, 1.43]	1.12	[1.03, 1.22]	1.11	[1.03, 1.21]

[a] All prevalence and incidence rate ratios in the table were adjusted for age at baseline, education, occupation, marital status, smoking, BMI and four contextual variables derived from census area measures (mean income, proportion with high school education, percentage of low income households, and unemployment rate). The prevalence and incidence rate ratios for breast cancer were also adjusted for reproductive history (number of live births, number of pregnancies and number of pregnancies lasted less than four months). Prevalence and incidence rate ratios of modifiable lifestyle covariates (smoking [adjusted for pack years] and obesity) are also listed in the table.

may be included more than once in the prevalence analyses. Thirdly, cumulative exposure measures were based on data from 1998 to 2006 and extrapolated to other years. This extrapolation may under- or over-estimate exposures. $PM_{2.5}$ was higher in earlier years, but lower in more recent years. Thus, $PM_{2.5}$ levels may be underestimated from 1992 to 1997 and overestimated from 2007 to 2013. Lastly, as demographic and lifestyle covariates were only collected at baseline, we were not able to model potential time-dependent effects. For example, lack of BMI data over time limits our ability to truly understand the effects of changing BMI on disease prevalence. A study in Canada by Hopman et al. (2007) found that although men under the age of 45 and women under the age of 55 gained approximately 0.45 kg (1 lb) per year, which leveled off with increased age and reversed in the oldest age groups, most remained in the same BMI category. This suggests that the BMI categories in our ONBSS cohort likely remained relatively stable over time. The potential for reverse causality between obesity and disease prevalence should also be noted and caution should be taken when interpreting the BMI results.

In conclusion, this large cohort study adds evidence of associations between exposure to $PM_{2.5}$ and prevalence risks of multiple major chronic cardiovascular conditions, cancer, diabetes and respiratory diseases. The effect of $PM_{2.5}$ exposure and disease prevalence was significantly and substantially larger among smokers and obese individuals.

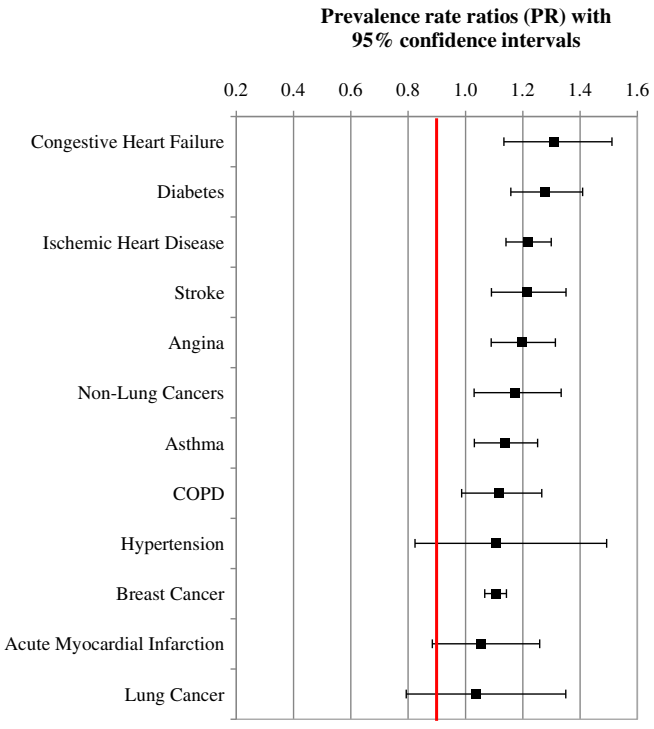

Fig. 1. Adjusted prevalence rate ratios (PRs) of chronic diseases per unit (10 μg/m^3) increase in $PM_{2.5}$.

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Contributors

TT and PV initiated and designed the study, interpreted findings and drafted the manuscript. JZ conducted all statistical analysis. JS, LF, CG and DW conducted a search of the literature, summarized relevant study findings and reviewed the manuscript. JS, HC, PV, SW, CW and ABM interpreted findings, reviewed and commented on drafts. All authors have seen and approved the final version.

Conflicts of interest

We declare that we have no conflicts of interest.

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Appendix 1. International classification of disease (ICD-9 and ICD-10) codes of chronic diseases

Conditions	ICD-9	ICD-10	Algorithm
Acute myocardial infarction (AMI)	410	I21	Women with a most responsible diagnosis of AMI ICD-9 code 410 or ICD-10 code I21 in the CIHI-DAD, CIHI-SDS database.
Angina	413	I20	Women with a most responsible diagnosis of any of the listed ICD-9 or ICD-10 codes in the CIHI-DAD, CIHI-SDS database, NACRS and OHIP claims.
Asthma	493	J45, J46	Women with ≥1 hospital admission with an asthma diagnosis or ≥2 OHIP claims with asthma diagnosis within two years.
Cancer			The Ontario Cancer Registry (OCR) is a computerized database of information on all adult Ontario residents who have been newly diagnosed with cancer (incidence) or who have died of cancer (mortality). All new cases of cancer are registered, except non-melanoma skin cancer.
Breast cancer	174	C50	Women in the OCR database who had any of these listed ICD-9 and ICD-10 codes indicated as primary cancer will be considered as having "breast cancer".
Lung cancer	162, 163	C34.0–C34.9, C38.4, C45.0	Women in the OCR database who had any of the listed ICD-9 or ICD-10 indicated as primary cancer will be considered as having "lung cancer".
All other cancers			Women in the OCR database who had any of these listed ICD-9 and ICD-10 codes (except for lung and breast cancers specified above) indicated as primary cancer will be considered as having "all other cancers".
Congestive heart failure (CHF)	428	I500, I501, I509	Women with ≥1 hospital admission with a CHF diagnosis or ≥1 OHIP claim/NACRS ED record with a CHF diagnosis followed within one year by a second record with a CHF diagnosis from any source.
Chronic obstructive pulmonary disease (COPD)	491, 492, 496	J41, J42, J43, J44	Women with ≥1 COPD diagnosis in OHIP or CIHI-SDS or CIHI-DAD databases.
Diabetes	250	E10, E11, E13, E14	Women in the Ontario Diabetes Database (ODD) with ≥2 OHIP claims with the listed ICD-9 or ICD-10 diagnostic codes or ≥1 OHIP claim with fee code Q040, K029 or K030 or ≥1 CIHI admission within 2 years.
Hypertension	401, 402, 403, 404, 405	I10, I11, I12, I13, I15	Women with ≥1 hospital admission with a hypertension diagnosis, or ≥1 OHIP claim with a hypertension diagnosis followed within two years by either ≥1 OHIP claim or ≥1 hospital admission with a hypertension diagnosis will be included as those with hypertension.
Ischemic heart disease (IHD)	411, 414	I24, I251, I258, I259	Women with a most responsible diagnosis of any of the listed IHD ICD-9 or ICD-10 codes in the CIHI-DAD, CIHI-SDS database, NACRS and OHIP claims will be included as individuals with IHD.
Stroke	433, 434, 435, 436	G45, G46, I63, I64	Women with a most responsible diagnosis of any of the listed stroke ICD-9 or ICD-10 codes in the CIHI-DAD, CIHI-SDS database, NACRS and OHIP claims will be included as individuals with stroke.

CIHI-DAD = Canadian Institute for Health Information Discharge Abstract Database; CIHI-SDS = Canadian Institute for Health Information Same Day Surgery Database; NACRS = National Ambulatory Care Reporting System; OHIP = Ontario Health Insurance Plan.

Appendix 2. Exposure to $PM_{2.5}$ among those with or without various chronic diseases

Chronic disease	Exposure to $PM_{2.5}$					
	Those with the disease			Those without the disease		
	Mean	±SD	IQR	Mean	±SD	IQR
Acute myocardial infarction	12.56	2.45	11.20–14.60	12.47	2.40	10.70–14.60
Angina	12.59	2.35	11.30–14.60	12.44	2.42	10.50–14.60
Asthma	12.57	2.43	10.50–14.60	12.45	2.40	10.80–14.60
Cancer						
Breast cancer	12.54	2.37	11.10–14.60	12.47	2.41	10.70–14.60
Lung cancer	12.70	2.39	11.20–14.60	12.47	2.40	10.70–14.60
All other cancers	12.59	2.34	11.10–14.60	12.45	2.41	10.60–14.60
Congestive heart failure	12.70	2.36	11.40–14.60	12.44	2.4	10.60–14.60
COPD	12.62	2.43	11.10–14.60	12.43	2.39	10.70–14.60
Diabetes	12.59	2.35	11.10–14.60	12.44	2.42	10.60–14.60
Hypertension	12.51	2.35	11.10–14.60	12.39	2.51	10.00–14.60
Ischemic heart disease	12.61	2.38	11.10–14.60	12.38	2.42	10.40–14.60
Stroke	12.62	2.361	1.20–14.60	12.44	2.41	10.60–14.60

SD = standard deviation; IQR = interquartile range.

Appendix 3. Sub-group analysis, adjusted prevalence rate ratios[a] (PRs) of chronic diseases per unit (10 μg/m^3) increase in $PM_{2.5}$

Chronic disease	Sub-group analysis					
	Only those not moved		Only those still alive		Only those never smoked	
	PR	95% CI	PR	95% CI	PR	95% CI
Acute myocardial infarction	1.07	[0.81, 1.42]	0.99	[0.70, 1.40]	1.06	[0.72, 1.55]
Angina	1.21	[1.09, 1.35]	1.27	[1.14, 1.41]	1.20	[1.05, 1.38]
Asthma	1.25	[1.08, 1.44]	1.05	[0.92, 1.21]	1.16	[0.96, 1.41]
Cancer						
Breast cancer	1.06	[0.87, 1.28]	1.17	[0.96, 1.43]	0.99	[0.77, 1.27]
Lung cancer	1.12	[0.78, 1.60]	1.00	[1.00, 1.00]	1.16	[0.46, 2.95]
All other cancers	1.10	[0.96, 1.28]	1.36	[1.13, 1.63]	1.27	[1.05, 1.55]
Congestive heart failure	1.30	[1.11, 1.53]	1.24	[1.01, 1.52]	1.36	[1.09, 1.69]
COPD	1.08	[0.96, 1.20]	1.06	[0.94, 1.19]	0.99	[0.82, 1.20]
Diabetes	1.23	[1.10, 1.37]	1.31	[1.17, 1.47]	1.30	[1.13, 1.51]
Hypertension	1.06	[1.02, 1.10]	1.11	[1.07, 1.16]	1.11	[1.06, 1.17]
Ischemic heart disease	1.22	[1.14, 1.32]	1.21	[1.12, 1.30]	1.20	[1.09, 1.32]
Stroke	1.19	[1.06, 1.34]	1.17	[1.03, 1.34]	1.18	[1.00, 1.38]

[a] All prevalence rate ratios in the table were adjusted for age at baseline, education, occupation, marital status, smoking, BMI and four contextual variables derived from census area measures (mean income, proportion with high school education, percentage of low income households, and unemployment rate). The prevalence rate ratios for breast cancer were also adjusted for reproductive history (number of live births, number of pregnancies and number of pregnancies lasted less than four months).

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