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Complex relationships between greenness, air pollution, and mortality in a population-based Canadian cohort[☆]

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ABSTRACT

Background: Epidemiological studies have consistently demonstrated that exposure to fine particulate matter ($PM_{2.5}$) is associated with increased risks of mortality. To a lesser extent, a series of studies suggest that living in greener areas is associated with reduced risks of mortality. Only a handful of studies have examined the interplay between $PM_{2.5}$, greenness, and mortality.

Methods: We investigated the role of residential greenness in modifying associations between long-term exposures to $PM_{2.5}$ and non-accidental and cardiovascular mortality in a national cohort of non-immigrant Canadian adults (i.e., the 2001 Canadian Census Health and Environment Cohort). Specifically, we examined associations between satellite-derived estimates of $PM_{2.5}$ exposure and mortality across quintiles of greenness measured within 500 m of individual's place of residence during 11 years of follow-up. We adjusted our survival models for many personal and contextual measures of socioeconomic position, and residential mobility data allowed us to characterize annual changes in exposures.

Results: Our cohort included approximately 2.4 million individuals at baseline, 194,270 of whom died from non-accidental causes during follow-up. Adjustment for greenness attenuated the association between $PM_{2.5}$ and mortality (e.g., hazard ratios (HRs) and 95% confidence intervals (CIs) per interquartile range increase in $PM_{2.5}$ in models for non-accidental mortality decreased from 1.065 (95% CI: 1.056–1.075) to 1.041 (95% CI: 1.031–1.050)). The strength of observed associations between $PM_{2.5}$ and mortality decreased as greenness increased. This pattern persisted in models restricted to urban residents, in models that considered the combined oxidant capacity of ozone and nitrogen dioxide, and within neighbourhoods characterised by high or low deprivation. We found no increased risk of mortality associated with $PM_{2.5}$ among those living in the greenest areas. For example, the HR for cardiovascular mortality among individuals in the least green areas was 1.17 (95% CI: 1.12–1.23) compared to 1.01 (95% CI: 0.97–1.06) among those in the greenest areas.

Conclusions: Studies that do not account for greenness may overstate the air pollution impacts on mortality. Residents in deprived neighbourhoods with high greenness benefitted by having more attenuated associations between $PM_{2.5}$ and mortality than those living in deprived areas with less greenness. The findings from this study extend our understanding of how living in greener areas may lead to improved health outcomes.

[☆] We declare that we have no competing financial interests.

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1. Introduction

A large international body of evidence has demonstrated nearly consistent associations between long-term exposures to fine particulate matter ($PM_{2.5}$) and increased risks of mortality from all-cause and cardiovascular disease (Beelen et al., 2014; Carey et al., 2013; Cesaroni et al., 2013; Crouse et al., 2012; Di et al., 2017; Krewski et al., 2009; Laden et al., 2006; Yang et al., 2018; Yin et al., 2017). This literature is informed in part by many large cohort studies, some of which are national in scope, and many of which consider both personal and contextual characteristics. In Canada, we have reported associations between cause-specific mortality and long-term exposures to $PM_{2.5}$ using national cohorts following ~2.5 million adults from 1991 through 2006 (Crouse et al., 2015), and from 2001 through 2011 (Pinault et al., 2017). A review and meta-analysis concluded that the random effects summary estimate for the percent excess risk per 10 $\mu g/m^3$ of $PM_{2.5}$ was 6.2% (95% confidence interval (CI): 4.1–8.4%) for all-cause mortality, and 10.6% (95% CI: 5.4–16.0%) for cardiovascular mortality (Hoek et al., 2013). In our most recent Canadian national cohort study (Pinault et al., 2017), we reported notably higher hazard ratios (HR) of 1.18 (95% CI: 1.15–1.21) and 1.25 (95% CI: 1.19–1.31) for these same causes of death, respectively.

A separate, much more limited, but growing body of literature is suggesting that living in greener areas (i.e., areas characterised by increased presence of trees, vegetation, and other green spaces) is associated with *reduced* risks of mortality (Crouse et al., 2017; James et al., 2016; Vienneau et al., 2017; Villeneuve et al., 2012; Wang et al., 2017). A recent review concluded that there was generally good evidence for a reduction of the risk of mortality from cardiovascular disease in areas with higher residential greenness, but evidence was more limited for associations with all-cause mortality (Gascon et al., 2016). Unlike the air pollution-mortality epidemiological literature, overall findings from the greenness-mortality literature are less generalizable, due in part to a smaller number of studies, but also because of heterogeneity in exposure assessment, study design, and geographic scales and contexts between studies. In our recent study of ~1.3 million adults living in urban areas across Canada, we reported reduced risks of non-accidental and cardiovascular mortality of approximately 9% per interquartile range increase in greenness within 250 m of individuals' residential postal code (Crouse et al., 2017).

One of the key potential pathways linking exposure to greenspace and health is that greener areas are associated with reductions in exposure to air pollution due to the absence of emissions sources (Markevych et al., 2017). Greener areas may also facilitate attention restoration and stress recovery and afford more opportunities for social interaction or physical activity (Markevych et al., 2017). Despite all of the above, the air pollution and greenness literatures have remained largely as 'two solitudes', with few studies examining how residential greenness may directly affect the association between exposure to air pollution and mortality.

Building on extensive work we have conducted on associations between mortality and $PM_{2.5}$, and between mortality and greenness, our objective was to examine the role of residential greenness in modifying associations between long-term exposures to $PM_{2.5}$ and non-accidental and cardiovascular mortality in a national cohort of non-immigrant Canadian adults. Specifically, we present associations between estimates of long-term $PM_{2.5}$ exposures and mortality across quintiles of greenness measured within 500 m of individuals' annual residential postal codes during 11 years of follow-up (2001 – 2011). Previous studies have found that the oxidant capacity (O_x) of ozone (O_3) and nitrogen dioxide (NO_2) is more strongly associated with chronic health outcomes than either O_3 or NO_2 alone (Weichenthal et al., 2017; Williams et al., 2014). Oxidant capacity is an efficient way of studying the combined effects of NO_2 and O_3 with weighting upon their potential for oxidation. We therefore also consider here models that incorporate oxidant capacity (O_x). We hypothesized that individuals living in the areas characterised by higher amounts of greenness would experience attenuated risks of mortality associated with exposure to air pollution, due in part to lower concentrations of pollution, less noise, and increased opportunity for recovery and restoration from environmental and psychosocial stressors.

2. Material and methods

2.1. The study cohort

The 2001 Canadian Census Health and Environment Cohort (CanCHEC) has been described in detail elsewhere (Pinault et al., 2016, 2017). Briefly, the full cohort is a nationally-representative sample of approximately 3.5 million Canadian adults who responded to the mandatory 2001 Statistics Canada long-form census (1 in 5 households), and who were subsequently linked to the Canadian mortality database and to annual income tax filings through 2011 (Pinault et al., 2016). Individuals were eligible for the cohort if: they were ≥ 19 years of age; were a usual resident of Canada on the census day; were not a long-term resident of an institution; and, had filed a tax return during the follow-up period. The mortality database includes information on date of death and the underlying cause of death, extracted from death certificates coded nosologists according to the International Classification of Diseases, 10th Revision.

Linkage to the annual income tax files provided annual six-digit mailing address postal codes, which allowed us to consider individuals' annual residential mobility. In Canadian urban areas, the representative point (i.e., the corresponding geographic coordinates) for six-digit postal codes is determined probabilistically, and the location is weighted based on the population in the area captured by that postal code. The point location typically corresponds to one side of a street in a given block or the centre of an apartment building, and has positional accuracy within approximately 100–160 m. Positional uncertainty is greater in rural areas (i.e., typically accurate within about 1–5 km) (Healy and Gilliland, 2012; Khan et al., 2018). Missing postal codes were imputed using a method (Fines et al., 2017) that considered reported postal codes in years before and after a missing record, and which has been applied and validated elsewhere (Pinault et al., 2017). In total, 14.6% of all person-years were imputed; 64% of subjects had no missing data, and over 80% of subjects had three or fewer records imputed.

We excluded immigrants from this study given that they tend to have notably better health status and health behaviours than the Canadian-born population, with patterns persisting for approximately 20 years following immigration (Ng, 2011). Additionally, there are challenges in determining longer-term exposures for immigrants (i.e., pre-dating arrival in Canada) that would have implications for disease risk. We also restricted our study to individuals aged 25–89 at baseline due to lower rates of successful record-linkages to tax files among younger and older people.

2.2. Assignment of environmental exposures

First, we assigned satellite-derived annual estimates of $PM_{2.5}$ gridded at a spatial resolution of approximately 1 × 1 km to individuals' six-digit residential postal codes. These data have been described elsewhere (van Donkelaar et al., 2015), and have been used in several previous epidemiological analyses (e.g., Pinault et al., 2017, 2018; Weichenthal et al., 2017). These exposures were derived by relating total column aerosol optical depth retrievals from the Moderate Resolution Imaging Spectroradiometer (MODIS) to near-surface $PM_{2.5}$ concentrations based on the spatially and temporally varying relationship simulated by the GEOS-Chem chemical transport model. We then used geographically weighted regression to incorporate ground-based observations and adjust for residual bias. We excluded outliers > 20 $\mu g/m^3$ from the analysis because they likely represented inaccurate satellite retrievals.

Second, we calculated the combined oxidant capacity (O_x) of O_3 and NO_2 at each residential location as a weighted average with weights equivalent to their respective redox potentials (i.e. $Ox = [(1.07 \times NO_2) + (2.075 \times O_3)] / 3.145$) (Bratsch, 1989). The O_3, and NO_2 data used in this calculation came from existing datasets that have been described (i.e., O_3: Robichaud and Ménard, 2014; NO_2: Hystad et al., 2011), and used in previous epidemiological analyses (Crouse et al., 2015; Weichenthal et al., 2017). The O_3 data represent the eight-hour average daily maximum concentrations obtained from model-observation data fusion at a resolution of ~21 × 21 km in the warm seasons from 2002 to 2009. The NO_2 data were derived from a national 2006 land use regression model developed from observations from fixed-site stations and incorporating satellite-derived NO_2 estimates and land use predictors. That model incorporates spatial variability within 100 m. Both the O_3 and NO_2 datasets were year-adjusted using ground-based time series measurements using National Air Pollution Surveillance annual average measurements from 24 census divisions from 1981 to 2012. For each census division, we fit a cubic spline to model the association between year and concentration, and then used the ratios to adjust the original O_3 and NO_2 data (Weichenthal et al., 2017).

Third, we assigned estimates of exposure to greenness to the representative point of each individual's six-digit residential postal code during each year of follow-up. Estimates of greenness were based on the remotely-sensed Normalized Difference Vegetation Index (NDVI). The NDVI is a widely used indicator of the intensity of green vegetation on the ground (Rouse Jr. et al., 1974) and has been used as a marker for exposure to greenness and green spaces in many previous epidemiological studies (e.g., Crouse et al., 2017; Hystad et al., 2014; James et al., 2016; Villeneuve et al., 2012). The index has a range of −1 to 1, with negative values representing water, values around zero representing bare soil, and higher positive values representing dense green vegetation. Here, large water bodies (e.g., lakes and ocean coastline) were masked (i.e., excluded) from the NDVI calculations for the purpose of disentangling the potential effects of greenness from those of blue spaces. Some smaller rivers and water bodies could not masked, but their contribution to local NDVI values would be relatively minor for most locations. Specifically, we used estimated annual maximum greenness values from 30 m resolution images taken by the United States Geological Survey's Landsat 5 (United States Geological Survey (USGS), n.d.-a) and Landsat 8 (United States Geological Survey (USGS), n.d.-b) satellites during the growing season (defined as May 1st through August 31st). We thus excluded observations from winter months when much of the ground would be covered by snow, and which would have provided incomplete or inaccurate information on the presence of vegetation. In this way, our estimates of greenness describe the levels and spatial variability of vegetation when plants are fully developed and in peak bloom, rather than the average level of vegetation throughout the year. We then aggregated these data to circular buffers of 500 m around the centroid of each individual's postal code. We used buffers of this size given the potential positional inaccuracies in geocoding postal code centroids (as noted above). That is, there would be greater risk of exposure misclassification had we used smaller buffers. Furthermore, we and because we found strong, protective associations between risk of mortality and area of greenness within buffers of this size previously (Crouse et al., 2017). Finally, we assigned individuals into quintiles of greenness values (lowest to highest) for each year.

All environmental exposures were assigned using 3-year moving averages with a 1-year lag time (and updated annually for residential mobility). First, exposures were calculated annually based on residential location in the previous year. For example, at baseline in 2001, individuals would be assigned the mean of values from exposures assigned to each of their annual postal codes over the period 1998 to 2000. We apply this methodology for several reasons. First, the lagged exposures ensure that exposures predate the events. Second, using multi-year means for these satellite-derived exposures ensures more comprehensive and reliable exposure estimates (e.g., due to potential cloud cover or missing data in any single year period).

2.3. Contextual characteristics

We also considered several other contextual characteristics of individuals' home communities that may contribute to the association between environmental exposures and the risk of mortality. First, individuals' residential postal codes allowed us to identify the size of their home community, according to the most recent census data (i.e., 2001, 2006, or 2011). Specifically, we grouped communities into six categories, from rural to large cities according to the following population ranges: < 10,000; 10,000–29,999; 30,000–99,999; 100,000–499,999; 500,000–1,499,999; and 1.5 million +.

Next, we assigned indicators of community level marginalization from the Canadian Marginalization Index (CAN-Marg), which describes community-level material deprivation, residential instability, dependency, and ethnic concentration (Matheson et al., 2012). Here, we defined the variables based on census tracts (i.e., neighbourhoods) within cities, and on census subdivisions outside of larger metropolitan areas. Census tracts correspond roughly to the size of one to several neighbourhoods, whereas census divisions correspond roughly to the size of a town or community. These indicators were assigned as quintiles (from low to high marginalization).

Lastly, we included a variable indicating the airshed within which individuals resided. Canada is subdivided into six airsheds (western, prairie, west central, southern Atlantic, east central, and northern) based on large-scale differences in air masses and meteorology (Crouse et al., 2016). Airsheds allows us to adjust for broad regional differences in mortality rates and in the composition of $PM_{2.5}$ across Canada that are not captured by other variables in our models..

2.4. Main statistical analyses

We used Cox proportional hazards models to estimate hazard ratios and their 95% confidence intervals for the associations between $PM_{2.5}$ and mortality from all non-accidental causes (ICD-10: A to R); cardiometabolic (i.e., circulatory plus diabetes; ICD-10: I10 to I69, E10 to E14); and cardiovascular diseases (ICD-10: I10 to I69). We considered only the primary underlying cause of death as mentioned on the death certificate.

The survival models were stratified by sex and by five-year age groups. We adjusted our models for the following individual-level risk factors for mortality: Aboriginal identity, visible minority status, marital status, highest level of education, employment status, and household income adequacy quintiles. Visible minorities are persons (other than Aboriginal persons) who self-identify as non-Caucasian in race or non-white in colour. Income adequacy quintiles are calculated from the ratio between the pre-tax income of economic families to the Statistics Canada low-income cut-off for family and community size, adjusted for regional economic differences. The CanCHEC cohort creation involves linking the Census respondents to income tax files, and the rate of successful linkage varies somewhat among people in different income quintiles (with a slightly lower linkage rate among those in the lower income quintiles; (Pinault et al., 2016)). As such, the cohort is composed of a greater proportion of people in the higher income quintiles. We do not re-base the quintiles for CanCHEC, as they still correspond to cut points in the broader Canadian population. We also controlled for the time-varying contextual variables described above.

First, we ran fully-adjusted models for $PM_{2.5}$, followed by models adjusted additionally for residential greenness within 500 m. The purpose of these second models was to identify to what extent inclusion of greenness in the models impacted the associations. Next, we split the cohort into quintiles of greenness within 500 m and ran models for $PM_{2.5}$ among individuals in each quintile separately.

2.5. Sensitivity analyses

For our first set of sensitivity analyses, we ran models similar to our main models, but adjusted additionally for O_x. Next, we repeated the main models, but restricted the cohort to residents of urban areas (i.e., those living in cities with populations > 100,000 people; here, due to sample size limitations, we grouped subjects into tertiles of greenness instead of into quintiles).

In an effort to disentangle the effects of greenness from those of neighbourhood socioeconomic position, we identified individuals living in each of the following four possible situations: 1) living in one of the two lowest quintiles of community-level material deprivation *and* in one of the two lowest quintiles of greenness (i.e., low deprivation and low greenness); 2) those living in one of the two highest quintiles of community-level deprivation *and* in one of the two highest quintiles of greenness (i.e., high deprivation and high greenness); 3) those living in low deprivation and high greenness; and, 4) those living high deprivation and low greenness.

Lastly, to describe some of the differences in environmental characteristics between the greenest and least green areas, we conducted a subsample analysis using 170,303 postal codes locations across Vancouver, Toronto, and Montreal (Canada's three largest cities). Among these point locations, we identified those in each of the highest (n = 18,688) and lowest quintiles (n = 151,942) of greenness (based on the categories used in the main analysis). Then, in each of those two groups of points separately, we calculated correlations between greenness, $PM_{2.5}$, NO_2, and, using geospatial data from DMTI Spatial Inc., distance to the nearest expressway or highway, area of parks within 2 km, and area of residential land use within 2 km.

Hazard ratios for all models were calculated per interquartile ranges in $PM_{2.5}$.

3. Results

Our full cohort consisted of 2,400,825 individuals at baseline (Table 1). Counts presented here have been rounded randomly to the nearest five to conform to institutional confidentiality requirements.

Table 1 provides ranges of greenness, $PM_{2.5}$, and O_x among all individuals at baseline, and among those in each quintile of greenness. Overall, the mean (± SD) of $PM_{2.5}$ exposure was 8.4 (2.7) μg/m^3. Among those living in the least and most green areas at baseline, the mean (± SD) of $PM_{2.5}$ exposures were 9.1 (2.9) and 6.6 (2.4) μg/m^3, respectively. In terms of greenness, the overall mean (± SD) was 0.48 (0.10) units of NDVI. The mean greenness value among those in the greenest quintile was almost double that among those in the least green quintile, namely: 0.64 (0.04) vs. 0.35 (0.05). Values for O_x were generally similar to each other across the four lowest quintiles of greenness, but were lower in the greenest quintile. Across the full cohort, greenness was negatively correlated with $PM_{2.5}$ ($r = -0.37$).

Table 2 provides characteristics of individuals overall, and within each quintile of greenness. Generally, the distributions of individuals by age, sex, and other characteristics were similar across quintiles of greenness. Overall, 15% of individuals were in the lowest income quintile, and 23% were in the highest. Among those living in the least green areas, however, there was a relatively greater proportion in the lowest income quintile (i.e., 20%) and fewer in the highest (i.e., 18%). As might be expected, the least green quintiles were characterised by greater proportions of individuals based in larger cities and smaller proportions in rural areas, whereas the greenest quintile reflected the opposite pattern.

In the case of all four contextual indicators of marginalization, the least green areas tended to be characterised by larger proportions of people living in marginalized neighbourhoods, and the greenest areas tended to be characterised by lower proportions of the same. For example, across the full cohort at baseline, 13% of individuals were living in neighbourhoods with high residential instability (e.g., neighbourhoods with higher proportions of people living alone, in crowded dwellings, and with higher population turnover). In the least green areas, however, this proportion was 31%, and in the greenest, it was only 5%.

In total, 194,270 people died of non-accidental causes during the 10.6 years of follow-up; 61,410 died of cardiometabolic causes, and 54,990 died of cardiovascular causes. In our main models, we report HRs and 95% CIs (per IQR, (i.e., 3.5 μg/m^3) increase of $PM_{2.5}$) for deaths from non-accidental, cardiometabolic, and cardiovascular disease of: 1.065 (1.056, 1.075), 1.087 (1.071–1.104), and 1.083 (1.065–1.100), respectively. HRs from models that included the linear term for residential greenness within 500 m were all attenuated compared to the main models, namely: 1.041 (1.031–1.050), 1.068 (1.051–1.086), and 1.064 (1.046–1.082), respectively.

We examined associations between $PM_{2.5}$ and mortality across quintiles of residential greenness (Fig. 1). Here, increased risks were limited to strata reflecting the least green areas (i.e., quintiles 1–3; which also tended to have the lowest concentrations of $PM_{2.5}$, as noted above) with no evidence of a positive association observed in the greenest areas (i.e., quintiles 4–5). There were noticeably graded associations decreasing in magnitude of effect from the largest, among those living in the least green areas, to the weakest, among those living in the greenest areas.

The models adjusted for O_x were attenuated compared to the main models, but not as much as those that adjusted additionally for greenness, as noted above. For example, here we found HRs (per IQR, (i.e., 3.5 μg/m^3) for deaths from non-accidental, cardiometabolic, and cardiovascular disease of 1.047 (1.037–1.058), 1.028 (1.010–1.046), and 1.031 (1.012–1.050), respectively. The models adjusted for O_x across quintiles of greenness reflected the same patterns as those noted above, namely positive associations with mortality in the least green areas, and no increased risks of mortality (and sometimes inverse associations) in the greenest areas (Appendix A1).

Similar to the models that were adjusted for O_x, the models

Table 1

Distributions of greenness (i.e., NDVI) within 500 m, $PM_{2.5}$, and O_x as assigned to individuals at baseline (2001) in the full cohort (n = 2,400,825) and across quintiles of greenness within 500 m.

	Full cohort			Quintile 1 (lowest)			Quintile 2			Quintile 3			Quintile 4			Quintile 5 (highest)		
	NDVI	$PM_{2.5}$	O_x	NDVI	$PM_{2.5}$	O_x	NDVI	$PM_{2.5}$	O_x	NDVI	$PM_{2.5}$	O_x	NDVI	$PM_{2.5}$	O_x	NDVI	$PM_{2.5}$	O_x
Mean	0.48	8.4	30.3	0.35	9.11	30.7	0.44	8.9	30.9	0.48	8.8	30.8	0.55	8.1	30.2	0.64	6.6	28.3
Standard deviation	0.10	2.7	5.1	0.05	2.9	5.5	0.02	2.9	5.5	0.02	2.1	4.3	0.02	2.7	5.4	0.04	2.4	4.8
95th %	0.65	13.3	39.0	0.41	14.1	39.3	0.46	13.8	39.5	0.51	12.8	38.7	0.58	12.9	39.1	0.72	11.0	37.7
75th %	0.54	10.0	33.5	0.39	11.3	34.3	0.45	11.0	36.3	0.49	9.1	31.4	0.56	10.0	35.2	0.67	8.0	30.6
Median	0.46	8.7	30.7	0.37	8.9	30.7	0.44	8.7	30.3	0.47	8.7	30.7	0.54	7.9	29.5	0.63	6.3	27.2
25th %	0.43	6.6	26.7	0.33	7.0	27.1	0.42	6.8	26.8	0.46	8.0	29.1	0.53	6.2	26.0	0.60	4.8	25.0
5th %	0.33	4.1	22.8	0.24	4.5	22.8	0.41	4.4	22.9	0.47	5.0	23.9	0.52	4.0	22.4	0.59	3.3	22.1
Interquartile range	0.11	3.5	6.8	0.06	4.4	7.2	0.03	4.2	9.6	0.02	1.2	2.3	0.03	3.8	9.2	0.06	3.3	5.6

Table 2
Characteristics of individuals at baseline (2001) in the full cohort (n = 2,400,825) and across quintiles of greenness (i.e., NDVI) within 500 m.

	Full cohort	Greenness quintile				
		1 (lowest)	2	3	4	5 (highest)
	%	%	%	%	%	%
Age						
25–64	83.9	82.1	83.4	84.4	84.4	85.4
65+	16.1	17.9	16.6	15.6	15.6	14.6
Sex						
Men	48.3	47.0	47.3	48.8	48.4	50.1
Women	51.7	53.0	52.7	51.2	51.6	49.9
Visible minority						
No	98.6	97.5	98.0	98.9	99.1	99.5
Yes	1.4	2.5	2.0	1.1	0.9	0.5
Aboriginal ancestry						
No	95.0	96.7	96.9	89.6	98.3	97.8
Yes	5.0	3.3	3.2	10.4	1.7	2.2
Marital status						
Common-law or married	72.8	61.2	69.5	76.4	77.3	80.1
Separated, divorced, widowed	14.0	18.3	15.7	12.3	12.6	11.1
Single/never married	13.2	20.5	14.9	11.2	10.2	8.8
Highest level of education						
Did not complete high school	28.2	28.8	25.5	31.1	24.0	29.3
High school diploma	36.3	35.1	36.0	36.4	36.5	37.8
Any post-secondary without university degree	19.5	19.1	20.5	18.7	20.8	19.0
University degree or higher	16.0	17.0	18.1	13.8	18.7	14.0
Income adequacy quintiles						
1 (lowest)	15.3	20.3	15.6	15.0	12.3	12.2
2	19.0	20.9	19.4	18.9	17.6	17.5
3 (middle)	20.8	20.7	21.4	20.7	20.9	20.5
4	22.0	20.2	22.2	21.8	23.2	22.9
5 (highest)	23.0	17.9	21.4	23.6	26.1	26.9
Labour force status						
Employed	64.8	63.0	65.6	64.4	66.5	65.1
Unemployed-looking for work	4.1	3.9	3.6	4.8	3.3	4.3
Not in the labour force	31.1	33.1	30.8	30.8	30.2	30.6
Community size						
1.5 million+	24.7	39.6	34.3	17.2	21.7	11.8
500,000–1,499,999	18.1	27.0	23.5	12.4	17.4	12.1
100,000–499,999	19.0	14.6	19.6	16.2	25.4	22.5
30,000–99,999	8.0	6.7	7.0	7.4	9.1	10.9
10,000–29,999	5.1	5.1	4.8	3.8	6.9	5.7
Rural (fewer than 10,000)	25.3	7.0	10.8	43.1	19.6	37.0
Airshed						
Western	10.9	9.9	11.2	11.6	11.9	9.1
Prairie	13.8	26.4	16.3	16.5	2.2	1.3
West central	6.2	6.0	7.9	9.7	2.6	1.2
Southern Atlantic	10.6	2.3	5.3	11.9	11.9	23.9
East central	57.0	53.2	58.5	47.3	71.1	64.3
Northern	1.6	2.2	0.8	3.0	0.3	0.4
CAN-Marg: Neighbourhood instability						
1 (lowest)	23.5	11.6	17.4	28.5	24.3	35.8
2	25.5	13.7	19.9	28.9	30.5	35.0
3 (middle)	20.6	19.8	23.0	21.0	22.3	15.8
4	17.6	24.3	24.1	14.7	15.9	8.4
5 (highest)	12.9	30.6	15.7	6.9	7.0	5.0
CAN-Marg: Neighbourhood deprivation						
1 (lowest)	15.8	11.6	15.8	14.2	22.4	17.0
2	20.8	14.0	20.2	21.9	25.0	23.2
3 (middle)	19.5	18.3	22.7	19.6	19.9	16.4
4	18.8	22.7	22.0	18.0	15.1	15.2
5 (highest)	25.2	33.3	19.3	26.3	17.6	28.1
CAN-Marg: Neighbourhood dependence						
1 (lowest)	15.9	24.0	17.4	15.2	12.1	8.6
2	17.0	15.3	17.9	17.8	17.1	16.3
3 (middle)	16.4	15.8	17.0	14.9	18.6	17.0
4	21.6	20.1	20.7	20.8	22.5	25.4
5 (highest)	29.2	24.8	27.2	31.3	29.6	32.7
CAN-Marg: Neighbourhood ethnic concentration						
1 (lowest)	35.7	13.5	24.7	42.2	39.7	60.7
2	26.2	20.8	26.8	26.5	31.8	25.8
3 (middle)	17.9	24.7	22.1	15.9	16.5	9.5
4	12.5	24.7	14.9	10.3	7.9	2.9
5 (highest)	7.7	16.3	11.6	5.1	4.2	1.0

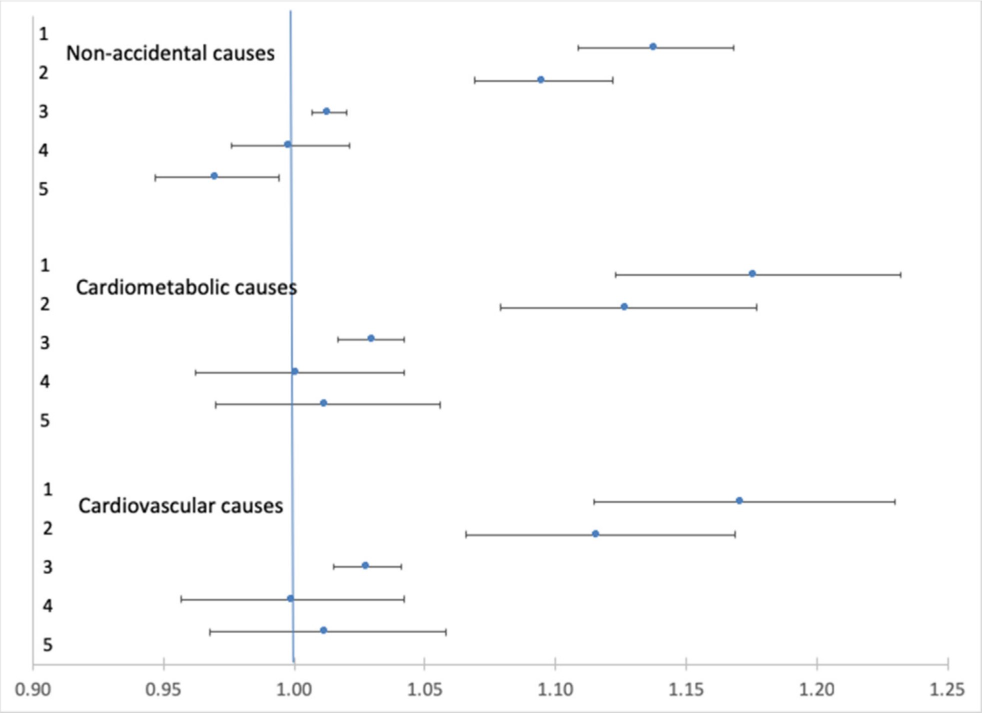

Fig. 1. Associations between $PM_{2.5}$ and mortality across quintiles of greenness within 500 m (1 = least green quintile; 5 = greenest). HRs calculated per IQR (see Table 1). Models are stratified by sex and by 5-year age groups; adjusted for visible minority status, Aboriginal status, marital status, education, income quintile, employment status; plus adjusted for four indices of neighbourhood deprivation, community size, and airshed.

restricted to urban residents produced HRs that were attenuated compared to the main models (Appendix A2). Here we again observed the pattern of positive associations with mortality among those in the least green areas (e.g., HR for non-accidental mortality: 1.042 (1.019–1.065)), and no increased risks among those in the greenest areas.

We present in Fig. 2, results of models stratified by high and low community deprivation and greenness. Similar to our other results, we again found the strongest associations between $PM_{2.5}$ and mortality among residents in the least green areas; both where community-level deprivation was high (series 1 in Fig. 2) and where it was low (series 2 in Fig. 2).

We also found no positive associations between $PM_{2.5}$ and mortality among subjects in the greenest areas (series 3 and 4), and in fact an inverse association between $PM_{2.5}$ and non-accidental mortality in the areas with high greenness and high community-level deprivation. Somewhat unexpectedly, we found larger effects of $PM_{2.5}$ among those living in the low deprivation areas than among those in the high deprivation areas.

Finally, we present in Table 3 correlations between selected environmental variables across the sub-sample of postal code locations in the highest and lowest greenness quintiles in Canada's three largest cities. Greenness and $PM_{2.5}$ were equally negatively correlated among postal codes in the lowest quintile (i.e., $r = -0.31$) and within the highest (i.e., $r = -0.35$). We found a moderately positive correlation between $PM_{2.5}$ and area of residential land use within 2 km (i.e., $r = 0.37$) among those in the greenest areas, and a small, negative correlation (i.e., $r = -0.07$) among those in the least green areas. We also found a small negative correlation (i.e., $r = -0.08$) between $PM_{2.5}$ and distance to nearest highway among those in the greenest areas, and a small positive correlation (i.e., $r = 0.05$) between those in the least green areas.

4. Discussion and conclusions

In this large, national cohort, we present for the first-time associations between long-term exposure to $PM_{2.5}$ and risk of cardiovascular mortality among individuals living in areas characterised by relatively high and low levels of residential greenness. We present a pattern of decreasing risks of mortality associated with exposure to $PM_{2.5}$ among individuals in each successive quintile of increased greenness. Moreover, we found no risk of mortality associated with $PM_{2.5}$ among those living in the two greenest quintiles. We note here that even though $PM_{2.5}$ and greenness were negatively correlated with each other, the distribution of $PM_{2.5}$ was still fairly similar across greenness quintiles (e.g., ranging from about 4 to 13 $\mu g/m^3$ in the lowest quintile and from about 3 to 11 $\mu g/m^3$ in the highest). Altogether, these results suggest that greenness (or unmeasured factors associated with greenness) may be an effect modifier (rather than a confounder) in the relationship between exposure to $PM_{2.5}$ and mortality. Given that greenness appears to have a protective affect against mortality, the HRs for $PM_{2.5}$ in our main models in fact reflect a mixture of the effect of high $PM_{2.5}$ and low greenness. Therefore, the results of the models that adjust for greenness provide more accurate estimates of the true effect of $PM_{2.5}$ on mortality.

The different patterns between high and low greenness areas are likely due to a combination of differences in characteristics of the populations, pollution, and other environmental factors between places. We controlled for many personal and contextual characteristics in our analyses, and we found largely similar distributions of people according to demographic characteristics and to several indicators of socio-economic position (e.g., education, marital status, labour force participation) across quintiles of greenness. We also ran models stratified by community-level material deprivation. It remains possible, however, that there were important differences in health behaviours and susceptibilities to the effects of exposure among people living in different strata of greenness. For example, people living in greener areas may be more active, less obese, and generally lead more healthy lifestyles, and/or may have had different smoking or drinking patterns. In addition to the possibility of residual confounding due to missing information on health behaviours, there may also be important differences in other environmental exposures between more- and less-green areas. There may also be differences in sources, composition, or oxidative potential of $PM_{2.5}$ across strata of greenness. For example, the pollution in areas with denser concentrations of trees may originate from more distal, regional sources, than from local sources, such as vehicular exhaust

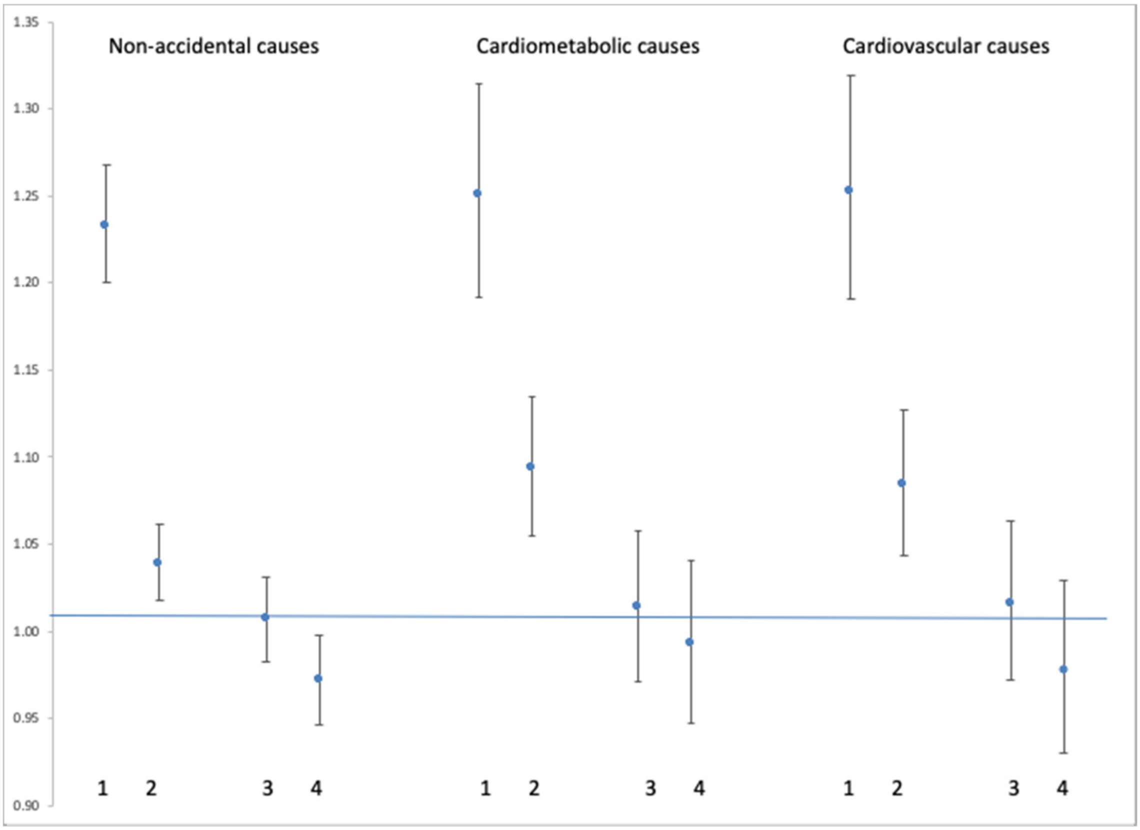

Fig. 2. Associations between $PM_{2.5}$ and mortality across areas of relatively high/low community-level material deprivation and greenness (1 = low greenness & low deprivation; 2 = low greenness & high deprivation; 3 = high greenness & low deprivation; 4 = high greenness & high deprivation). HRs calculated per IQR (i.e., 3.5 μg/m^3). Models are stratified by sex and by 5-year age groups; adjusted for visible minority status, Aboriginal status, marital status, education, income quintile, employment status; plus adjusted for four indices of neighbourhood deprivation, community size, and airshed.

(Nowak et al., 2018). Additionally, greener areas may tend to be cooler, have less noise, or may allow for less-stressful living in general. In our sensitivity analysis, we showed that there were moderate differences in associations between concentrations of $PM_{2.5}$ and area of residential space and distances to highways between the upper and lower quintiles of greenness, respectively. In addition to those noted above, there are likely other differences in the environmental characteristics between these areas that we were not able to consider here.

In our models stratified by neighbourhood deprivation, we found that regardless of deprivation status, those in greener areas had more attenuated associations between $PM_{2.5}$ and mortality than those in the least green areas. For example, we observed attenuated effects of $PM_{2.5}$ on mortality among those living in areas that were deprived but green, compared to those living in areas that were deprived but less green.

Consistent with previous Canadian cohort studies (Crouse et al., 2012; Pinault et al., 2017; Weichenthal et al., 2017), we found, in all of our models, that risks for mortality associated with exposures to $PM_{2.5}$ were slightly higher for cardiovascular causes than for non-accidental causes. We observed generally similar patterns of association across quintiles of greenness, and according to neighbourhood deprivation, among all three causes of death. Results from models for cardiovascular and cardiometabolic causes were nearly identical.

In the only other study that directly examined effect modification by greenness on the association between long-term exposure to $PM_{2.5}$ and mortality, Kioumourtzoglou et al. (2016) reported that living in greener areas was associated with increased effects of $PM_{2.5}$ in their large

Table 3
Correlations between selected environmental variables across a subsample of postal codes in the highest quintiles of greenness (n = 18,688; shaded top half of table) and in the lowest quintiles of greenness (n = 151,942; bottom half of table).

	$PM_{2.5}$ (1999–2001 median)	NO_2 (2006 annual mean)	Greenness within 500m	Distance to nearest highway	Area of parks within 2 km	Area of residential land use within 2 km
$PM_{2.5}$ (1999–2001 median)	1	0.34	−0.35	−0.08	0.28	0.37
NO_2 (2006 annual mean)	0.27	1	−0.16	−0.20	0.06	0.13
Greenness within 500m	−0.31	−0.36	1	0.15	−0.20	−0.41
Distance to nearest highway	0.05	−0.37	0.27	1	0.19	−0.28
Area of parks within 2 km	0.25	0.07	0.09	0.09	1	−0.01
Area of residential land use within 2 km	−0.07	−0.23	0.24	0.10	−0.06	1

analysis of > 35 million Medicare enrolees in 207 U.S. cities. Those authors hypothesized that that unexpected finding could have be due in part to the fact that greenness was also positively correlated with smoking rates and the proportion of black and elderly residents in a city. Furthermore, the levels of $PM_{2.5}$ observed in those US cities were likely much higher than those in Canada.

In some of our previous analyses with this cohort we have also examined other causes of death (e.g., stroke, dementia, respiratory diseases). Unfortunately, the number of deaths for several of these outcomes was very low in the individual greenness quintile groups, such that we lacked the statistical power to assess the associations between $PM_{2.5}$ and these outcomes adequately. Our estimates of exposure to greenness were assigned using 500 m buffers around individuals' residential postal codes. As described above, in rural areas, errors in positional accuracy of postal code locations may exceed 1 km, such that we could expect some exposure misclassification among such individuals. Patterns of greenness across rural areas, however, are fairly homogenous, such that we do not expect that this exposure error would impact our results substantially. A limitation of working with satellite-derived NDVI as a marker for the presence of vegetation is that, although the data are of similar quality across space, they do not allow us to differentiate between different kinds of vegetation (e.g., trees vs grass, or deciduous vs coniferous trees) across space. That is, NDVI is an effective measure of greenness, but it does not allow us to consider how different kinds of natural or green areas are patterned and/or how they may benefit health differently. A somewhat related limitation of our study is the fact that the process of imputing missing postal codes likely introduced some exposure misclassification bias (i.e., in cases where our imputed residential location differed substantially from the individuals' true residential location in that year).

A key strength of our study is the large, broadly representative nature of the cohort. An additional strength of our study is the fact that our satellite-derived estimates of $PM_{2.5}$ and of greenness (i.e., NDVI) were available in consistent quality across Canada, thereby allowing us to include individuals living in all regions of the county. Further, we investigated how the root-mean-square deviation (RMSD) error of the satellite-derived $PM_{2.5}$ estimates varied as a function of NDVI and did not find any evidence to suggest that greener regions were subject to greater uncertainties.

Overall, our results contribute to the growing body of literature demonstrating benefits to health associated with living in greener, more natural areas. Specifically, these results suggest that living in greener areas may be protective against the adverse effects of exposure to $PM_{2.5}$. An implication of our findings is that air pollution studies that do not account for greenness may overstating the air pollution effect. It is worth noting here, however, that Canada has generally lower concentrations of $PM_{2.5}$ than many other places in the world, so it may be difficult to generalize these findings to areas with higher exposures.

As noted above, it has been hypothesized that greenspace (defined broadly) may lead to improved health outcomes through three main pathways, namely: mitigation (e.g., reduced exposures to air pollution); restoration (e.g., stress recovery); and building capacities (e.g., encouraging physical activity) (Markevych et al., 2017). Our data show that individuals living in greener areas did tend to have somewhat lower exposures to $PM_{2.5}$, but with these data we are unable to identify whether they also had lower levels of stress or greater levels of physical activity than those living elsewhere. There remains great interest, therefore, in teasing out the mechanisms through which exposures to greenness and contact with nature influence health status, and future studies should seek to differentiate between the effects of the various proposed mechanisms for different outcomes.

The findings from this study extend our understanding of how living in greener areas may lead to improved health outcomes. Additionally, our findings suggest that residents in deprived neighbourhoods with high amounts of trees and green spaces may benefit by having more attenuated effects of $PM_{2.5}$ on risk of mortality than those living in deprived areas with lower amounts of greenness.

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The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by any of the named supporters is intended or should be inferred.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.04.047.

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