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The association between the incidence of postmenopausal breast cancer and concentrations at street-level of nitrogen dioxide and ultrafine particles

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ABSTRACT

Background: There is scant information as to whether traffic-related air pollution is associated with the incidence of breast cancer. Nitrogen dioxide (NO_2) and ultrafine particles (UFPs, < 0.1 μm), are two pollutants that capture intra-urban variations in traffic-related air pollution and may also be associated with incidence.

Methods: We conducted a population-based, case-control study of street-level concentrations of NO_2 and UFPs and incident postmenopausal breast cancer in Montreal, Canada. Incident cases were identified between 2008 and 2011 from all but one hospital that treated breast cancer in the Montreal area. Population controls were identified from provincial electoral lists of Montreal residents and frequency-matched to cases using 5-year age groups. Concentrations of NO_2 and UFPs were estimated using two separate land-use regression models. Exposures were assigned to residential locations at the time of recruitment, and we identified residential histories of women who had lived in these residences for 10 years or more. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression models adjusting for individual-level and ecological covariates. We assessed the functional form of NO_2 and UFP exposures using natural cubic splines.

Results: We found that the functional form of the response functions between incident postmenopausal breast cancer and concentrations of NO_2 and UFPs were consistent with linearity. For NO_2, we found increasing risks of breast cancer for all subjects combined and stronger associations when analyses were restricted to those women who had lived at their current address for 10 years or more. Specifically, the OR, adjusted for personal covariates, per increase in the interquartile range (IQR = 3.75 ppb) of NO_2 was 1.08 (95%CI: 0.92–1.27). For women living in their homes for 10 years or more, the adjusted OR was 1.17 (95%CI: 0.93–1.46; IQR = 3.84 ppb); for those not living at that home 10 years before the study, it was 0.93 (95%CI: 0.64, 1.36; IQR = 3.65 ppb). For UFPs, the ORs were lower than for NO_2, with little evidence of association in any of the models or sub-analyses and little variability in the ORs (about 1.02 for an IQR of ~3500 cm^{-3}). On the other hand, we found higher ORs amongst cases with positive oestrogen and progesterone receptor status; namely for NO_2, the OR was 1.13 (95%CI: 0.94–1.35) and for UFPs it was 1.05 (95%CI: 0.96–1.14).

Conclusions: Our findings suggest that exposure to ambient NO_2 and UFPs may increase the risk of incident postmenopausal breast cancer especially amongst cases with positive oestrogen and progesterone receptor status.

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1. Introduction

Breast cancer has the highest incidence in women worldwide: in 2012 an estimated 1.67 million new cases were diagnosed (25% of all incident cancer cases), with age-adjusted rates in Canada at about 100 per 100,000 women (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2015). It is the fifth most common cause of death from cancer worldwide, with about 522,000 deaths attributed to it (International Agency for Research on Cancer, 2017). A myriad number of risk factors have been identified, but they account for about 25–33% of all cancer cases (Coyle, 2004; Jemal et al., 2011).

We have reported previously the results of a case-control study conducted in the mid-1990s in Montreal, Quebec, in which we found a number of occupational risk factors for postmenopausal breast cancer (Labreche et al., 2010), including combustion-related exposures, especially amongst women with positive oestrogen receptor and positive progesterone receptor status. We found in the same study (Crouse et al., 2009a, 2010) an association with ambient nitrogen dioxide (NO_2) measured at street-level, which is an accepted marker for traffic-related air pollution (Beckerman et al., 2008; HEI Panel on the Health Effects of Traffic-Related Air Pollution, 2010). More recently, in a case-control study conducted in eight Canadian provinces, we found associations between both postmenopausal and premenopausal breast cancer and street-level concentrations of NO_2 (Hystad et al., 2015).

There have been only a handful of other reports of excess risks for breast cancer in association with ambient air pollution or markers of traffic-related pollution. In a case-control study based in New York State, an association was found with increased volumes of vehicular traffic (Lewis-Michl et al., 1996) and higher concentrations of total suspended particulates were associated positively with exposures to benzo[a]pyrene (Bonner et al., 2005; Nie et al., 2007). In the Nurses' Health Study II (Hart et al., 2016), no associations were found for incident breast cancer and fine particulates but increased rates were found among premenopausal and postmenopausal women living within 50 m of major roads. In the Sister Cohort (Reding et al., 2015) measurements made at fixed-site monitors were developed into a national Kriged surface (Sampson et al., 2013) and concentrations were evaluated at subjects' addresses at time of enrolment. The adjusted hazards ratios for incident breast cancer for increases in the interquartile ranges of concentrations of fine particulates (3.6 $\mu g/m^3$) and NO_2 (5.8 parts per billion (ppb)) were 1.03 (95% confidence interval (CI): 0.96–1.11) and 1.02 (95%CI: 0.97–1.02), respectively. Increased risks for NO_2 were also found among cases with positive oestrogen receptor and positive progesterone receptor status (hazard ratio of 1.10; 95%CI: 1.02–1.19).

Between 2008 and 2011, we conducted another population-based case-control study of incident breast cancer among postmenopausal women living in Montreal, Quebec, to investigate associations with occupational and environmental exposures. Using data from this case-control study, the objectives of the present paper were to determine whether ambient concentrations of NO_2 and ultrafine particles (UFPs, < 0.1 μm in diameter) measured at street level were associated with the incidence of postmenopausal breast cancer.

2. Methods

We identified incident cases diagnosed between 2008 and 2011 using pathology records at all 18 hospitals in Montreal that treated breast cancer, except one (Sacré-Coeur Hospital) that refused to participate. Women were eligible if they fulfilled criteria for being menopausal (i.e., the WHO criteria for menopausal status, accounting for hormone replacement therapy, hysterectomy, and bilateral oophorectomy)(WHO, 1981; WHO scientific group on research on the menopause in the, 1990, 1996), had never had a previous occurrence of any type of cancer, were between 50 and 70 years of age, lived on the Island of Montreal, were registered with the universal Provincial Electoral List, and were alive at time of interview. Eligibility status was determined through a "screening" interview. Control subjects who met the same eligibility criteria as the cases and did not have a previous breast cancer were selected randomly from the Provincial Electoral List and were frequency-matched to cases by 5-year age bins. We excluded women with a previous or concurrent malignant neoplasm.

The refusal of Sacré-Coeur Hospital to participate raised concerns about possible selection biases should we include population controls from their referral area. The hospital discharge data showed that patients treated at this hospital lived in a circumscribed area near the institution. We thus excluded potential control subjects who lived in this area according to the proportion of hospitalizations for breast cancer in the target age range.

We conducted face-to-face or telephone interviews with women who agreed to participate. The interview comprised a questionnaire to ascertain demographic data and information about most accepted and suspected risk factors, potential household exposures, and an occupational history.

Participants provided detailed information on their date of birth, previous breast disease, family history of breast cancer, educational attainment, ethnicity and language, age at menarche, reproductive history, breastfeeding, oral contraceptive use and hormonal replacement therapy, body mass index, active and involuntary smoking exposures, alcohol consumption, marital status, and home address (as well as duration of residence at that address) at time of interview. Neighbourhood measures of recent immigrants, unemployment rate, education, and median household income were obtained by linking participant's addresses to the 2006 Canadian Census at the census tract level. (A census tract on the Island of Montreal varied between 0.5 km^2 to more than 20 km^2, and the population of the 501 census tracts used here ranged from 293 to 9288 individuals).

2.1. Exposure assessment

2.1.1. Nitrogen dioxide

We have described previously our dense sampling of ambient NO_2, which was conducted in 2005 and 2006 (Crouse et al., 2009a, 2010). The locations for the samplers were selected using a location-allocation model that placed samplers in areas likely to have high spatial variability in traffic-related pollution and high population densities (Kanaroglou et al., 2003). Samplers were deployed at 133 locations across the Island of Montreal on three occasions (spring, summer, winter) for two-week periods each time. We used Ogawa passive diffusion samplers that make use of triethanolamine-impregnated filters as an absorbent. Valid observations at 129 locations were obtained from all three sampling periods.

We used these observations to develop a land use regression model to predict concentrations of mean annual NO_2 for 2005–2006, at a resolution of 5 m across the Island. The main predictors were land use (industrial space, residential space), population density, lengths of nearby roads and highways, density of buildings, and traffic counts. We modelled the natural logarithm of NO_2 on land use and traffic-related variables to generate an exposure surface. The model explained 80% of the variability in concentrations of NO_2 (Crouse et al., 2009a).

2.1.2. Ultrafine particles

We also developed a land use regression model (Weichenthal et al., 2016) to estimate ambient concentrations of UFPs across the island of Montreal. Briefly, this model was derived from data collected during a mobile monitoring campaign conducted between 2011 and 2012 (Weichenthal et al., 2016). Data from 414 road segments, including major and minor roads, were used for model development. Model parameters included variables for park space (200-meter buffer), open space (100-meter buffer), local roads (100-meter buffer), length of rail (100-meter buffer), and annual NOx emissions (100-meter buffer). The R^2 from the land-use regression model was 0.62 and the cross-validation R^2 was 0.60.