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Exposure to traffic-related air pollution and the risk of developing breast cancer among women in eight Canadian provinces: A case–control study

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ABSTRACT

A few recent studies have reported positive associations between long-term exposure to traffic-related air pollution and the incidence of breast cancer. We capitalized on an existing Canadian multi-site population-based case–control study to further investigate this association.

We used the National Enhanced Cancer Surveillance System, a population-based case–control study conducted in eight of 10 Canadian provinces from 1994 to 1997. A total of 1569 breast cancer cases and 1872 population controls who reported at least 90% complete self-reported addresses over the 1975–1994 exposure period were examined. Mean exposure levels to nitrogen dioxide (NO_2) (an indicator of traffic-related air pollution) were estimated for this period using three different measures: (1) satellite-derived observations; (2) satellite-derived observations scaled with historical fixed-site measurements of NO_2; and (3) a national land-use regression (LUR) model. Proximity to major roads was also examined. Using unconditional logistic regression, stratified by menopausal status, we estimated odds ratios (ORs) adjusted for many individual-level and contextual breast cancer risk factors.

We observed positive associations between incident breast cancer and all three measures of NO_2 exposure from 1975 to 1994. In fully adjusted models for premenopausal breast cancer, a 10 ppb increase in NO_2 exposure estimated from the satellite-derived observations, the scaled satellite-derived observations, and the national LUR model produced ORs of 1.26 (95% confidence intervals (CIs): 0.92–1.74), 1.32 (95% CI: 1.05–1.67) and 1.28 (95% CI: 0.92–1.79). For postmenopausal breast cancer, we found corresponding ORs of 1.10 (95% CI: 0.88–1.36), 1.10 (95% CI: 0.94–1.28) and 1.07 (95% CI: 0.86–1.32). Substantial heterogeneity in the ORs was observed across the eight Canadian provinces and reduced ORs were observed when models were restricted to women who had received routine mammography examinations. No associations were found for road proximity measures.

This study provides some support for the hypothesis that traffic-related air pollution may be associated with the development of breast cancer, especially in premenopausal women. With the few studies available, further research is clearly needed.

1. Introduction

Exposure to traffic-related air pollution is ubiquitous and has been linked to a wide range of chronic diseases, including asthma, decreased lung function, cardiovascular disease, diabetes, and lung cancer (Brook et al., 2010; Chen et al., 2008; HEI, 2010). In urban areas, vehicular emissions are one of the largest sources of air pollution. In Canada, it is estimated that 10 million individuals (32% of the population) live within 100 m of a major urban road or 500 m of a highway, and are thus potentially exposed to high levels of traffic-related air pollution (Brauer et al., 2013). Vehicular emissions contain a number of accepted human

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carcinogens, such as benzene, 1,3-butadiene and certain polycyclic aromatic hydrocarbons (PAHs) (Health Effects Institute, 2010). The International Agency for Research on Cancer (IARC) also recently classified outdoor air pollution as carcinogenic to humans (Loomis et al., 2013).

Lung cancer has been the focus of studies on cancer and traffic-related air pollution (Fajersztajn et al., 2013), due to the direct contact of inhaled air pollutants with the lung and the strong impacts from tobacco smoke. However, in recent studies, results for breast cancer have been reported (Bonner et al., 2005; Crouse et al., 2010; Lewis-Michl et al., 1996; Nie et al., 2007; Ole Raaschou-Nielsen and Zorana, Andersen, 2011). For example, in a case–control study of 383 breast cancer cases and 416 cancer controls in Montreal, Canada, an odds ratio (OR) of 1.31 (95% confidence interval (CI): 1.00–1.71) was observed for a 5 ppb increase in exposure to NO_2 (Crouse et al., 2010). A weaker not statistically significant association was observed in a Danish cohort that included 987 breast cancer cases, where a rate ratio of 1.16 (95% CI: 0.89–1.51) was observed for a 100 $\mu g/m^3$ increase in NO_x (Ole Raaschou-Nielsen and Zorana, Andersen, 2011). In addition, Han et al. (2013) found clustering of women's place of birth among premenopausal breast cancer cases with positive estrogen and progesterone receptors and negative HER2 status; suggesting that early life environmental exposures may influence breast cancer risk decades later. Although there is insufficient evidence to make any conclusions regarding the role that traffic-related pollution has in the etiology of breast cancer, there are a number of proposed mechanisms by which air pollution may increase the risk of developing breast cancer. The majority of mechanisms are related to xenoestrogens (compounds that mimic estrogen) (Brody and Rudel, 2003; Davis et al., 1993) and carcinogens such as benzene and polycyclic aromatic hydrocarbons. For example, within the Long Island breast cancer population-based case–control study, a 50% increase in the odds of breast cancer was observed for women with the highest quintile of PAH adduct levels compared to the lowest (Gammon et al., 2002). Chen et al. (2013) examined the effects of urban, suburban, and rural particulate matter on human MCF-7 and T47D-KBluc breast cancer cells and found further evidence of DNA damaging activity and estrogenicity associated with urban air pollution exposure.

Given the suggestive findings from the few studies that have been conducted, and that traffic-related carcinogens in the ambient environment are wide-spread, further studies are warranted. We therefore capitalized on a large existing Canadian population-based case–control study to determine associations between the incidence of breast cancer and several measures of past exposure to traffic-related air pollution.

2. Methods

2.1. The case–control study

We used the National Enhanced Cancer Surveillance System (NECSS), a collaborative population-based case–control study of 19 sites of cancer that was conducted in eight of Canada's 10 provinces (all but Quebec and New Brunswick). Previous studies have used the female breast cancer component of the study to investigate passive and active smoking (Johnson et al., 2000), obesity (Pan et al., 2004), diet (Hu et al., 2008; Pan et al., 2004, 2011b) and proximity to industrial facilities (Pan et al., 2011a).

Johnson et al. (1998) provided a detailed description of the overall study design and rationale. Briefly, each provincial cancer agency randomly sampled one in four eligible breast cancer cases over approximately one year in the mid-1990s, until a population-based quota was met (some provinces continued to enroll breast cancer cases after they reached their quota). Premenopausal women with breast cancer were over-sampled to optimize the statistical power needed to adequately characterize the relationships between several different risk factors and breast cancer in younger women. A total of 3310 histologically-confirmed, invasive, primary breast cancer cases among women age 25 to 74 at the time of diagnosis were identified and consent from physicians to contact their patients was obtained for 3023 women (92.7%). Completed questionnaires were received from 2340 cases, 77.4% of those women contacted, and 71.8% of the cases for which physician consent was sought. For this analysis, premenopausal women were defined as those women less than 55 years of age who also reported that they were still menstruating one year before interview.

Population controls were identified by each participating provincial cancer registry and were frequency-matched to the overall age and sex distribution across all 19 types of cancer included in the entire case–control study. Five provinces (Prince Edward Island, Nova Scotia, Manitoba, Saskatchewan, British Columbia) used universal, provincial health insurance plans to obtain a random sample of the population. More than 95% of residents were covered by these public plans, and individuals were excluded only if covered through other federal plans (i.e., first nations, military and prisoners). In one province (Ontario), the database of the Ministry of Finance Property Assessment, which included all residents of the province updated monthly, was used to obtain a random sample. In two provinces (Newfoundland and Alberta) random-digit dialing was used. Questionnaires were mailed to 3980 women selected as potential controls. For 430 of these women (10.8%), the mailed questionnaire was returned to the registry indicating an incorrect address. In total, 2531 women completed and returned the questionnaire, which represent 71.3% of controls who were contacted and 63.6% of those ascertained. For many established risk factors (e.g. smoking and obesity), risk estimates obtained from the NECSS data (e.g. Mao et al., 2001 and Pan et al., 2004) are very consistent with the literature, suggesting minimal potential biases introduced from participation rates.

Subjects completed a questionnaire that included a broad set of questions on accepted and possible risk factors. These are summarized in Table 1. Questions collected current information at the time of breast cancer diagnosis or study entry (e.g. BMI), two years prior to breast cancer diagnosis or study entry (i.e. diet, physical activity, alcohol consumption), or lifetime exposures (e.g. smoking and occupational histories). Detailed information on the NECSS survey questionnaire can be found in Johnson et al. (1998). Residential histories were also collected for all participants and formed the basis of the spatial exposure assessments conducted herein. Residential histories were converted to Canadian six-character postal codes used in 1996 and then geocoded. In cities, a six-character postal code typically represents one side of a block face between two intersecting streets or a large apartment building, but in rural areas can cover much larger geographic areas (e.g. >100 km^2 in remote locations, although few study participants reside in these areas). The centroid of each postal code was mapped to assign residential exposures.

The 10 participating provincial cancer registries obtained ethics approval for the NECSS study protocol through their respective ethics review boards. All participants in this population based case–control study provided informed consent.

2.2. Assessment of exposure to ambient concentrations of NO_2

We assigned mean exposure levels to traffic-related air pollution from participants' residential histories derived for each year of the 20-year period (1975–1994). Only individuals with at least 18 exposure-years were included in the main analyses (we conducted sensitivity analyses to examine how this cut-point affected results). This restriction reduced our sample size to 1759 cases and 1872 controls. The 20-year exposure period was selected to correspond to expected latency periods associated with certain environmental exposures for breast cancer (Directions and Medicine, 2012) and because of constraints on the availability of self-reported residential histories,