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Hart, Jaime E
Bertrand, Kimberly A
DuPre, Natalie
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Long-Term Particulate Matter Exposures During Adulthood and Risk of Breast Cancer Incidence in the Nurses' Health Study II Prospective Cohort

Jaime E. Hart[1,2], **Kimberly A. Bertrand**[3], **Natalie DuPre**[4], **Peter James**[2,4], **Verónica M. Vieira**[5], **Rulla M. Tamimi**[1,4,*], and **Francine Laden**[1,2,4,*]

[1]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

[2]Exposure, Epidemiology, and Risk Program, Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA

[3]Slone Epidemiology Center at Boston University, Boston, MA, USA

[4]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA

[5]Program in Public Health, University of California, Irvine, CA, USA

Abstract

Background—There is increasing concern that environmental exposures, such as air pollution, may be related to increasing rates of breast cancer; however, results from cohort studies have been mixed. We examined the association between particulate matter and measures of distance to roadway with the risk of incident breast cancer in the prospective nationwide Nurses' Health Study II (NHSII) cohort.

Methods—Incident invasive breast cancer 1993-2011 (N=3,416) was assessed among 115,921 women in the NHSII cohort. Time-varying Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (95%CIs) for increases in ambient exposures to PM_{10}, $PM_{2.5\text{-}10}$, and $PM_{2.5}$ and residential roadway proximity categories.

Results—In multivariable adjusted models, there was little evidence of an increased risk of breast cancer (or any of the receptor-specific subtypes) overall or by menopausal status with PM exposure. There was, however, a suggestion of increased risks among women living <50m of the largest road type (HR of 1.60 (95%CI: 0.80-3.21)) or within <50m of the two largest road types (1.14 (95%CI: 0.84-1.54)) compared to women living farther (≥200m) away.

Conclusions—Among women in the NHSII, we found no statistically significant associations between particulate matter exposures and incidence of breast cancer overall, by menopausal status, or by hormone receptor subtype. There was, however, a suggestion that residential proximity to major roadways may be associated with increased risk.

Corresponding author: Jaime E Hart, ScD, 401 Park Drive, Landmark Center 3rd Floor West, Boston, MA 02215; phone: 1-617-525-2289; Jaime.hart@channing.harvard.edu.

*denotes shared senior authorship

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Impact—These results suggest no elevated breast cancer risk with increasing exposures to particulate matter air pollution, but that other traffic-related exposures may be important.

Keywords

air pollution; traffic exposure; roadway proximity; particulate matter; breast cancer risk

Introduction

The International Agency for Research on Cancer monograph on the carcinogenicity of ambient air pollution presented mixed evidence for air pollution and breast cancer risk.(1) However, some recent studies have suggested associations.(2-7) Studies with large numbers of breast cancer cases, information on specific breast cancer subtypes, and the ability to control for other breast cancer risk factors are needed. Therefore, we examined the association of particulate matter (PM) exposures and roadway proximity on risk of overall, hormone-receptor specific, and menopausal status-specific breast cancer risk among women in the nationwide, prospective Nurses' Health Study II (NHSII) cohort.

Materials and Methods

The NHSII is a cohort of 116,430 female nurses with no previous history of cancer (except non-melanoma skin cancer) enrolled in 1989 when they were aged 25-42 years. Mailed biennial follow-up questionnaires update information on risk factors and medical history. Self-reports of incident cancers are confirmed by medical record review.

Biennial residential addresses were geocoded, and roadway proximity was assigned as a proxy for traffic-related exposures. Specifically, we calculated the distance from each address to the nearest street segments in the ESRI StreetPro 2007 data layer listed as U.S. Census Feature class codes A1, A2, or A3. Based on case distributions and exposure studies, we categorized distance to road as 0-49m, 50-199m, and ≥200m, for all three road types together, for the two largest road types (A1, A2), and for the largest road type (A1). Forty-eight month moving average and cumulative average exposures to three size fractions of particulate matter, PM_{10}, $PM_{2.5-10}$, and $PM_{2.5}$, were assigned to each participant based on monthly spatio-temporal prediction models applied to the geocoded address history.(8) For participants who moved, we assumed they changed addresses at the beginning of the biennial cycle.

Time-varying Cox proportional hazards models on a biennial time scale were used to calculate hazard ratios (HR) and 95% confidence intervals (95%CI) for each roadway proximity category compared to the farthest, and for each 10μg/m^3 increase in each of the PM size fractions, after assessing linearity using splines. All models were adjusted for age, race, and calendar year; multivariable models were additionally adjusted for established breast cancer risk factors. Separate models assessed risk of overall breast cancer, and hormone-receptor specific subtypes (ER+/PR+ and ER-/PR-). We also stratified models by menopausal status.

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Results

Eligible participants (N=115,921) were 47 years old on average during follow-up, with an average BMI of 26 kg/m^2. Sixteen percent were nulliparous, 10% were current users of postmenopausal hormone therapy, and 64% were never smokers. There was no association between exposures to 48 month PM with breast cancer overall or for specific hormone receptor subtypes, or by menopausal status (Tables 1 and 2); estimates were similar for cumulative average exposures (not shown). Although case numbers were small, there was a suggestion of increasing risk with residential proximity to the two largest road types, with a multivariable adjusted HR of 1.60 (95%CI: 0.80-3.21) for women living <50m of the largest road type, and 1.14 (95%CI: 0.84-1.54) for women closest to the two largest road types compared to those living ≥200m away. These risks were consistent across the various breast cancer subtypes

Discussion

We did not observe an association between PM exposures and breast cancer incidence in this prospective cohort study. This is in contrast to an earlier case-control study in Western New York, where total suspended particulate exposures were associated with increased odds of postmenopausal breast cancer, but not premenopausal breast cancer (detailed in (1)). Our results are similar to a recent analysis in the Sister Study, where no elevations in overall or hormone-receptor specific breast cancer risk were observed with increasing PM_{10} or $PM_{2.5}$ exposures.(2)

Our suggestive findings of an elevated risk with roadway proximity, although not statistically significant and based on small numbers of exposed cases, are in contrast to several studies that have found no association (1, 3); but does agree with some studies using other measures of traffic exposure (traffic density, motor vehicle density).(1, 7) Our findings also agree with numerous studies that have observed positive associations between exposures to nitrogen oxides or other traffic-related pollutants and breast cancer. (1-3, 5-7)}

Our analyses in a large, nationwide, prospective cohort has many strengths, including fine control for potential confounders, high spatial and temporal resolution estimates of PM exposure, and large numbers of cases in many subcategories of interest (e.g. premenopausal, ER-/PR-). However, we only had information on adult exposures, which may not be an important etiological period. The findings in this cohort may not be generalizable to populations with more racial/ethnic diversity or a broader range of socioeconomic status. Future studies should examine the association of traffic-related exposures in these groups.

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Table 1

Risk of overall and hormone-receptor subtype invasive breast cancer with exposures to particulate matter and roadway proximity among 115,921 women in the Nurses' Health Study II followed 1993-2011.

	Invasive breast cancer			ER+/PR+ invasive breast cancer			ER−/PR− invasive breast cancer		
Exposure	**Cases**	**Basic[1] HR (95%CI)**	**Multivariable[2] HR (95%CI)**	**Cases**	**Basic[1] HR (95%CI)**	**Multivariable[2] HR (95%CI)**	**Cases**	**Basic[1] HR (95%CI)**	**Multivariable[2] HR (95%CI)**
48-month average									
PM_{10} (per 10μg/m^3)	3,416	0.98 (0.92-1.04)	1.00 (0.93-1.07)	1,853	1.02 (0.94-1.11)	1.05 (0.95-1.15)	492	0.94 (0.79-1.11)	0.97 (0.80-1.18)
$PM_{2.5-10}$ (per 10μg/m^3)	3,416	1.01 (0.93-1.09)	1.06 (0.96-1.17)	1,853	1.07 (0.96-1.19)	1.13 (0.99-1.29)	492	0.91 (0.73-1.13)	0.96 (0.73-1.26)
$PM_{2.5}$ (per 10μg/m^3)	3,416	0.89 (0.78-1.01)	0.90 (0.79-1.03)	1,853	0.92 (0.77-1.10)	0.95 (0.79-1.14)	492	0.99 (0.70-1.39)	0.97 (0.68-1.40
Proximity to A1-A3 roads (m)									
0-49	341	0.92 (0.82-1.03)	0.95 (0.85-1.07)	194	0.98 (0.84-1.14)	1.01 (0.86-1.18)	52	0.95 (0.71-1.28)	1.02 (0.75-1.37)
50-199	777	1.00 (0.92-1.09)	1.00 (0.92-1.09)	431	1.05 (0.93-1.17)	1.04 (0.93-1.16)	100	0.87 (0.69-1.09)	0.91 (0.72-1.14)
≥200	1,954	Reference	Reference	1,050	Reference	Reference	289	Reference	Reference
Proximity to A1-A2 roads (m)									
0-49	43	1.06 (0.78-1.43)	1.14 (0.84-1.54)	19	0.87 (0.55-1.36)	0.93 (0.59-1.47)	8	1.36 (0.67-2.73)	1.44 (0.71-2.92)
50-199	177	1.14 (0.97-1.32)	1.16 (1.00-1.35)	102	1.21 (0.99-1.48)	1.23 (1.00-1.50)	25	1.12 (0.75-1.69)	1.18 (0.79-1.78)
≥200	2,852	Reference	Reference	1,554	Reference	Reference	408	Reference	Reference
Proximity to A1 roads (m)									
0-49	8	1.52 (0.76-3.05)	1.60 (0.80-3.21)	4	1.40 (0.52-3.75)	1.48 (0.55-3.97)	14	1.41 (0.83-2.41)[3]	1.52 (0.89-2.60)[3]
50-199	76	1.10 (0.87-1.38)	1.11 (0.89-1.40)	40	1.07 (0.78-1.47)	1.08 (0.79-1.48)			
≥200	2,988	Reference	Reference	1,631	Reference	Reference	427	Reference	Reference

[1] Adjusted for current age, race, and calendar period;

[2] Additionally adjusted for history of BBD, family history, age at menarche, parity, age at first birth, height, BMI at age 18, current BMI, alcohol consumption at ages 15-17 and 18-22, overall diet quality (AHEI-2010), oral contraceptive use, menopausal status and hormone use, smoking status, physical activity, individual level socioeconomic status (marital status, living arrangements, household income) and area level socioeconomic status (Census tract level median income and median home value), and region of residence;

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[3] The two closest proximity categories were consolidated due to small case numbers.

Note: Distance to road measures were only calculated for women with a street level geocode or better (N=111,545).

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Table 2

Risk of invasive breast cancer by menopausal status with exposures to particulate matter and roadway proximity among women in the Nurses' Health Study II

	Pre-menopausal			Post-menopausal		
Exposure	**Cases**	**Basic[1] HR (95%CI)**	**Multivariable[2] HR (95%CI)**	**Cases**	**Basic[1] HR (95%CI)**	**Multivariable[2] HR (95%CI)**
48-month average						
PM_{10} (per 10μg/m^3)	1,966	0.98 (0.90-1.07)	1.03 (0.93-1.13)	1,296	0.99 (0.89-1.10)	0.97 (0.86-1.09)
$PM_{2.5-10}$ (per 10μg/m^3)	1,966	0.98 (0.87-1.09)	1.07 (0.93-1.22)	1,296	1.08 (0.96-1.22)	1.07 (0.92-1.25)
$PM_{2.5}$ (per 10μg/m^3)	1,966	0.98 (0.83-1.16)	0.99 (0.83-1.18)	1,296	0.75 (0.60-0.93)	0.76 (0.61-0.95)
Proximity to A1-A3 roads (m)						
0-49	194	0.98 (0.84-1.14)	1.01 (0.86-1.17)	130	0.83 (0.69-1.00)	0.87 (0.72-1.05)
50-199	471	1.09 (0.98-1.22)	1.08 (0.97-1.21)	273	0.88 (0.76-1.01)	0.88 (0.77-1.01)
≥200	1,082	Reference	Reference	782	Reference	Reference
Proximity to A1-A2 roads (m)						
0-49	25	1.18 (0.79-1.75)	1.23 (0.83-1.83)	17	1.03 (0.64-1.67)	1.14 (0.70-1.84)
50-199	106	1.20 (0.99-1.47)	1.20 (0.98-1.46)	62	1.01 (0.78-1.30)	1.06 (0.82-1.38)
≥200	1,616	Reference	Reference	1,106	Reference	Reference
Proximity to A1 roads (m)						
0-49	5	1.80 (0.74-4.35)	1.74 (0.72-4.21)	3	1.34 (0.43-4.17)	1.48 (0.47-4.62)
50-199	49	1.27 (0.95-1.69)	1.26 (0.94-1.67)	25	0.93 (0.62-1.38)	0.97 (0.65-1.45)
≥200	1,693	Reference	Reference	1,157	Reference	Reference

[1] Adjusted for current age, race, and calendar period;

[2] Additionally adjusted for history of BBD, family history, age at menarche, parity, age at first birth, height, BMI at age 18, current BMI, alcohol consumption at ages 15-17 and 18-22, overall diet quality (AHEI-2010), oral contraceptive use, menopausal status and hormone use, smoking status, physical activity, individual level socioeconomic status (marital status, living arrangements, household income) and area level socioeconomic status (Census tract level median income and median home value), and region of residence.

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Note: Distance to road measures were only calculated for the 115,921 women with a street level geocode or better (N=111,545) and women can contribute person-time to both pre- and post-menopausal models.