HHS Public Access

Author manuscript

Environ Res. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

Environ Res. 2017 November ; 159: 257–263. doi:10.1016/j.envres.2017.08.015.

Residential Exposure to Vehicular Traffic-Related Air Pollution During Childhood and Breast Cancer Risk

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Abstract

Background—Some studies have supported an association between traffic-related air pollution exposure and breast cancer risk. However, few studies have considered exposures in early life, which may be a period of increased susceptibility.

Objectives—To examine the association of childhood residential exposure to traffic-related air pollution with breast cancer development.

Methods—The Sister Study is a prospective cohort of 50,884 initially breast cancer-free women, of whom 42,934 provided information at enrollment about roads and traffic near their primary childhood residence before age 14 as well as relevant covariates. Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for the association between traffic-related measures at childhood residence and adult incident breast cancer were estimated using Cox regression.

Results—During follow-up (mean=6.3 years), 2,028 breast cancers were diagnosed. Traffic-related characteristics were not consistently associated with breast cancer risk. However, incidence was elevated among women who reported a median/barrier dividing either their primary childhood residential road (aHR=1.2; 95% CI: 0.9–1.7) or the nearest cross-street (aHR=1.3; 95% CI: 0.9–1.8, if the cross-street was within 100 ft.), and among women whose nearest cross-street had the highest traffic, ≥3 lanes, and/or a median/barrier (aHR= 1.4; 95% CI: 1.0–1.9).

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Competing Financial Interests Declaration: The authors have no financial conflicts of interest to declare.

Institutional Review Board Approval: The Sister Study was approved by the Institutional Review Boards of the National Institute of Environmental Health Sciences and the Copernicus Group. Written informed consent was obtained from all participants.

Disclaimers: All authors have read and approved the paper. The paper has not been published previously nor is it being considered by any other peer-reviewed journal.

Color printing: Color printing is NOT required.

Conclusions—Measures of potential exposure to vehicular traffic were not consistently associated with breast cancer risk. However, living during childhood on or near a road with a median or other barrier, which may be a more easily remembered road characteristic than the others assessed, was associated with increased breast cancer risk.

Keywords

Epidemiology; Breast Cancer; Childhood exposure; Traffic-related Air Pollution

1. INTRODUCTION

Breast cancer has the highest incidence rate of all cancers affecting women in the US, and there has been a call for a better understanding of the role of environmental factors in breast cancer risk (Howlader et al., 2016; IOM, 2011). Air pollution levels are of substantial public health concern, particularly in urban areas and have been associated with a number of health outcomes, including lung cancer, cardiovascular disease, and childhood asthma (Brook et al., 2010; Khreis et al., 2016; Raaschou-Nielsen et al., 2013). The International Agency for Research on Cancer (IARC) has classified outdoor air pollution as a Group 1 carcinogen (Loomis et al., 2013), and traffic-related air pollution, specifically, contains many compounds with carcinogenic potential, including certain metals, carbonyls, volatile organic compounds, and polycyclic aromatic hydrocarbons (PAHs) (Chen and Bina, 2012; Crouse et al., 2010; Hamra et al., 2014; Hystad et al., 2015; Mordukhovich et al., 2016; Wei et al., 2012). PAHs, which are formed as a result of incomplete combustion of organic matter, are known to be lung carcinogens, and may be particularly relevant for breast cancer since they have the capacity to bind to DNA and form DNA adducts in breast tissue (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010). In addition, animal studies have shown that PAHs have the capacity to induce mammary tumors (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010).

Studies examining the association between adult air pollution exposure and breast cancer have not been consistent. Case-control studies of nitrogen dioxide (NO_2) (Crouse et al., 2010; Hystad et al., 2015) have reported positive associations, while prospective cohort studies (Andersen et al., 2016; Reding et al., 2015) have reported null or weak positive associations. For instance, a Canadian case-control study reported an odds ratio (OR) of 1.31 (95% confidence interval (CI): 1.00, 1.71) for every 5 ppb increase in NO_2 (Crouse et al., 2010), while a study examining the association between breast cancer risk and air pollution at the enrollment residence of Sister Study cohort participants did not find an overall increase in breast cancer risk, however, a modest positive association was observed between NO_2 exposure and estrogen/progesterone receptor positive breast cancer (risk ratio = 1.10, 95% CI: 1.02,1.19 for an interquartile range difference of 5.8 parts per billion) (Reding et al., 2015). Only one study, a US-based case-control study, evaluated the association between breast cancer and long-term vehicular traffic-related PAH exposure, reporting an OR of 1.44 (95% CI: 0.78, 2.68) for the top 5% level of exposure as compared to below the median (Mordukhovich et al., 2016). In contrast, prospective cohort studies have examined the association with particulate matter (PM) exposure (Andersen et al., 2016; Hart et al., 2016; Reding et al., 2015), and all have reported null results. Distance to nearest roadway

measures were found to be associated with a suggestively increased risk in a prospective cohort study (Hart et al., 2016) and to have no association in a case-control study (Hystad et al., 2015). Each of these proxy measures captures different components of traffic-related air pollution and there were differences in study design and duration of the adult exposure measures captured, which may help explain the mixed results.

Only two studies have examined the role of air pollution during early life (Bonner et al., 2005; Nie et al., 2007). Childhood and adolescence may be a time period that is particularly etiologically relevant to breast cancer development. Menarche is characterized by rapid breast cell proliferation and consequently less efficient DNA repair mechanisms, which is thought to make the breast tissue especially susceptible to carcinogenesis during the period between menarche and first childbirth (Hiatt et al., 2009; Okasha et al., 2003). This hypothesis is supported by substantial evidence of a relationship between other exposures and lifestyle factors during childhood/adolescence and later breast cancer risk (Potischman and Troisi, 1999). For instance, smoking initiation prior to menarche or after menarche but before first birth have each been associated with increased risk of breast cancer later in life (Gaudet et al., 2013) and environmental tobacco exposure during childhood has been associated with greater risk of breast cancer (White et al., 2017). Additionally, air pollution levels were likely higher during the childhood of US women who are at the highest risk of developing breast cancer today, as there has been a notable decline in emissions in the past two decades in the US (Wang et al., 2016). Therefore, it is of interest to determine whether air pollution exposure in early life is associated with future cancer risk. The objective of this study was to examine the association between potential childhood residential exposure to vehicular traffic-related air pollution and the development of adult incident breast cancer in the Sister Study cohort.

2. MATERIALS AND METHODS

2.1 Study Population

Study participants were from the Sister Study, a prospective cohort study of 50,884 women that was designed to assess environmental and genetic risk factors for breast cancer. Participants, aged 35–74, were recruited from the US and Puerto Rico during 2003–2009, and were eligible to participate if they had at least one sister who had been diagnosed with breast cancer but had not been diagnosed with breast cancer themselves at the time of enrollment. Women were recruited for the study using a multimedia campaign and a network of volunteers and advocates. The Sister Study was approved by the Institutional Review Boards of the National Institute of Environmental Health Sciences and the Copernicus Group. All participants provided written informed consent. The data presented in this study were obtained from Sister Study Data Release 4.1 (follow-up through July 1, 2014).

2.2 Exposure Assessment

At baseline, participants completed a Computer-Assisted Telephone Interview in which they reported information on characteristics of their longest lived residence before age 14, including information on nearby roads and exposure to traffic. Participants were asked about the number of lanes, presence of a median or barrier dividing the road (‘yes’/‘no’), and

traffic volume during rush hour (‘very light,’ ‘light,’ ‘moderate,’ ‘heavy,’ ‘very heavy,’ which were combined as ‘light,’ ‘moderate,’ and ‘heavy’ for most analyses) for their residential road. They were also asked about the distance to the nearest intersection/cross-street (‘within 100 feet,’ ‘more than 100 feet but less than a quarter mile,’ ‘between a quarter mile and one mile,’ and ‘more than one mile’). Participants who reported living within 100 feet of the nearest intersection were further asked about the number of lanes, presence of a median or barrier dividing the road (‘yes’/‘no’), and traffic volume during rush hour for that intersecting road (‘very light,’ ‘light,’ ‘moderate,’ ‘heavy,’ ‘very heavy,’ which were combined as ‘light,’ ‘moderate,’ and ‘heavy’ for most analyses). A combined measure suggestive of higher potential exposure to traffic-related pollutants (close proximity to nearest intersection, presence of median/barrier, multiple lanes, and heavy traffic) was also considered.

2.3 Outcome Ascertainment

Incident breast cancer diagnoses were ascertained from annual health updates and biennial/triennial questionnaires that participants completed during follow-up. Women who reported a diagnosis during follow-up were asked for consent to review their medical records for confirmation and for diagnostic and treatment details. At the time of this analysis, medical records were available for 81% of cases. Due to the high concordance between self-report and medical records for first primary breast cancer diagnosis, self-reported diagnoses were included when medical record data were unavailable (D’Aloisio et al., 2017).

2.4 Statistical Analysis

Early enrollees in the Sister Study (n=2,297, “Vanguard women”) were not asked about their exposure to traffic at their childhood residential residence (see Fig. S1). Of the remaining participants, we excluded 2,851 who did not live at least 5 years in their longest childhood residence. We also excluded 1,592 participants whose current or longest lived adult residence was the same as their primary childhood residence since their responses to the traffic-related questions reflected their adult traffic levels rather than traffic levels during their childhood. Both exclusions were intended to maximize the quality of recall and minimize the potential for misclassification. Participants with missing residential characteristic information (n=616) were excluded. Thus, 43,528 women were eligible for inclusion in this analysis. We further excluded participants missing outcome, covariate, or follow-up time information (n=594), resulting in a total analysis population of 42,934, 98.6% of those eligible. Participants diagnosed with lobular carcinoma *in situ* (LCIS) were censored at the time of diagnosis since the mechanism by which this condition is related to increased breast cancer risk is unclear (King et al., 2015), while those diagnosed with ductal carcinoma *in situ* (DCIS) were included in the outcome of total breast cancer diagnosis.

Descriptive statistics were compared for incident breast cancer cases and non-cases by case status at the end of follow-up. Participants were followed from the time of the baseline interview until a breast cancer diagnosis (either invasive or DCIS), death, or loss to follow-up. Cox proportional hazards models were used to estimate hazard ratios (HRs) and corresponding 95% CIs for the association between characteristics of the primary childhood residence and incident breast cancer. In these models, age was the time-scale and person-

time was accrued from age at time of enrollment. The proportional hazards assumption was assessed by including interaction terms for the main exposure variables and time in the models.

Multivariable models were used to adjust for covariates that were identified *a priori* as potential confounders based on a directed acyclic graph (Glymour and Greenland, 2008). The potential confounders identified were age, race, and childhood socioeconomic status (SES) (see Fig S1). We adjusted for age, race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other), and highest level of education attained in the household at age 13 (High School or Less, Some College, Bachelor's degree, Graduate degree). These covariates were ascertained at baseline.

We stratified the results by neighborhood type (Urban/Suburban and Small Town/Rural) to determine if the association between the characteristics of the primary childhood residence and breast cancer differed by neighborhood type. To test for differences between the strata, we included an interaction term between the characteristics of the primary childhood residence and neighborhood type in the Cox model and tested its significance. We also evaluated the possibility of a potential birth cohort effect by treating year of birth as a continuous variable and testing the significance of the interactions between primary childhood residence characteristics and birth year.

In secondary sensitivity analyses, we first explored whether the results differed for pre- and post-menopausal breast cancer by carrying out a stratified analysis. For the pre-menopausal analysis, all participants were pre-menopausal at baseline and were followed from baseline age until the first of reported age at menopause, end of follow-up, or breast cancer diagnosis. For the post-menopausal analysis, participants were either post-menopausal at baseline or became menopausal over follow-up, and were followed from either baseline age or age at menopause (whichever was greatest) until the end of follow-up or breast cancer diagnosis. Second, we examined whether the results differed by molecular tumor subtype (estrogen receptor (ER) positive or negative) among participants with invasive disease, since molecular tumor testing was not as consistently done for individuals diagnosed with *in situ* disease. For these stratified analyses, the outcome of interest was either ER+ or ER- invasive breast cancer, and all other breast cancer types and disease-free individuals were censored at last known follow-up age. We also evaluated the influence of exposure during puberty by excluding participants who did not live at the reported primary childhood residence prior to menarche or whose age at menarche was missing (n= 730). We further examined if the results varied by family history by stratifying results by the number of first degree relatives known to have been diagnosed with breast cancer. Lastly, we considered whether cigarette smoking exposure before menarche (both active smoking and environmental tobacco smoke (ETS)) could act as proxy measures and account for potential residual confounding by childhood SES. All statistical analyses were conducted using SAS software, version 9.3 (SAS Institute, Cary, NC).

3. RESULTS

During follow-up (mean=6.3 years), 2,028 incident breast cancer diagnoses were observed. At baseline, the mean age of the participants was 55.6 years, and the majority (84.7%) of participants identified as Non-Hispanic White. 54.0% of participants reported that the highest level of education of any household member at age 13 was high school or less (Table 1). While characteristics of cases and non-cases were generally similar, cases tended to be slightly older at baseline than non-cases.

The age-adjusted and fully-adjusted results for the association between childhood residential characteristics and overall breast cancer risk are shown in Table 2. The characteristics of the main childhood residential road, including number of lanes, presence of a median/barrier, and traffic during rush hour, were not consistently associated with increased breast cancer risk, although participants who reported that their residential road was divided by a median or barrier of any type were at an elevated risk relative to those who reported no median/barrier (aHR: 1.2; 95% CI: 0.9–1.7). Characteristics of the cross-street or intersecting road nearest to their childhood residential road were also not consistently associated with increased risk of breast cancer. However, women whose nearest cross-street or intersecting road was within 100 feet and had three or more lanes (aHR: 1.1; 95% CI: 0.9–1.4) or had a median or barrier dividing it (aHR: 1.3; 95% CI: 0.9–1.8) had a higher risk of breast cancer. Furthermore, women who reported that the nearest intersecting road to their childhood home was within 100 ft., had heavy traffic during rush hour as well as three or more lanes and/or a median or barrier dividing it were also at a suggestively increased risk (aHR: 1.4; 95% CI: 1.0–1.9).

Results were largely similar by menopausal status at diagnosis, although the association for women whose nearest cross-street or intersecting road had heavy traffic, three or more lanes and/or a median/barrier was more pronounced in women with post-menopausal breast cancer (aHR= 1.5; 95% CI: 1.1–2.0) (Table 3). We considered whether the associations varied by ER status of the tumor among participants with invasive disease. Results were largely similar for ER+ and ER- tumors, with the exception of finding an increased risk associated with having a median or barrier dividing the residential road for ER- (aHR: 2.4; 95% CI: 1.2–4.8) but not for ER+ (aHR: 1.1; 95% CI: 0.7–1.8) breast cancer. However, this difference is likely influenced by the small number of exposed ER- cases (n=8) (see Table S1).

When we restricted the analysis to women who reported living at their primary childhood home prior to menarche, we found that the results were qualitatively the same as those for all participants, with women who reported living where the nearest cross-street or intersecting road was divided by a median or barrier were at increased risk of breast cancer (results not shown). Results were qualitatively different in strata defined by family history (1 first-degree relative vs. 2+ first-degree relatives with breast cancer), with associations between presence of a median/barrier on the residential road (aHR= 1.3; 95% CI: 0.9–1.9) and nearest cross-street (aHR=1.5; 95% CI: 1.0–2.3) apparent only among those with a single first degree relative with breast cancer, although results for the combined measure of distance, median/barrier, and traffic were similar by strata of family history (see Table S2).

Associations were also stronger for participants from small town/rural areas than from urban/suburban areas although a test for effect measure modification on the multiplicative scale was not significant (see Table S3). When we assessed a potential birth cohort effect by testing an interaction between characteristics of the primary childhood residence and birth year (treated as a continuous variable), we did not see any multiplicative effect measure modification of the effect estimates (p-values > 0.05) (data not shown). Results were qualitatively similar after adjustment for cigarette smoking exposure prior to menarche.

4. DISCUSSION

In this large prospective cohort study, we examined the association between exposure to vehicular traffic-related air pollution during childhood and incident adult-onset breast cancer. We found that while individual characteristics of the main childhood residential road and nearest cross-street were not consistently associated with increased breast cancer risk, women who reported that either their primary childhood residential road or the cross-street nearest their primary childhood residence was divided by a median/barrier had a modest increase in risk of breast cancer. A combined measure suggestive of higher potential exposure to traffic-related pollutants (close proximity, presence of median/barrier, multiple lanes, and heavy traffic) was significantly associated with increased risk for overall breast cancer, post-menopausal breast cancer, and invasive ER- breast cancer.

It is notable that, in this study, the reported presence of a median/barrier dividing either the childhood residential road or nearest cross-street was associated with a slight increase in breast cancer risk, while the other potential indicators of traffic density were not individually positively associated with risk. Traffic at rush hour may be variable over time and as it was self-reported in this study, it is likely prone to subjectivity. Number of lanes is a more objective measure; however, it too may be subject to some degree of misclassification since the distinction between a one- and two-lane road may be unclear as wide and potentially bidirectional roads are not always demarcated. We grouped participants who reported one- or two-lane roads to address this issue. Nonetheless, number of lanes may not be a consistent indicator of traffic density since traffic patterns vary on a daily and seasonal basis and the actual traffic may not correspond with a road’s theoretical capacity. Only in the mid-1950s, once the need for road organization became apparent, was the scientific study of traffic flow undertaken (Lighthill and Whitham, 1955). A median/barrier is a safety feature, often used to prevent cross-median crashes on high speed and volume roads, for which implementation criteria that incorporate daily traffic estimates and median width have been available since the 1970s (Donnell and Mason, 2006). Medians/barriers may better represent actual traffic patterns than do number of lanes, since older roads may have had more/fewer lanes than were needed, and median/barriers were developed after there was a better understanding of traffic patterns. Furthermore, they are likely more memorable features and hence less subject to recall bias than the other traffic characteristics assessed.

Nonetheless, it is likely that the individual characteristics of the residential road and nearest cross-street do not fully account for the contribution of vehicular traffic-related air pollution exposure from the surrounding environment. To address this concern, we included a combined measure of distance to road, presence of a median/barrier, and traffic volume.

Proximity of residence to major roadways, rather than traffic characteristics of the residential road, is a validated and frequently used proxy measure for traffic-related pollution (Danysh et al., 2016; Finkelstein et al., 2004; Hoek et al., 2002; van Roosbroeck et al., 2006). Additionally, a previous study on traffic-related PAH modeling reported that intersections accounted for 40–80% of total emissions and average exposures, which corroborates the importance of accounting for the contribution of intersections in classifying an individual's exposure (Beyea et al., 2006).

Previous epidemiological studies examining the role of early life exposure to markers of traffic-related air pollution on breast cancer development have also reported some positive associations. A population-based case-control study, (analysis population total n=3,271; cases n=1,166) measured total suspended particles (TSP), as a proxy for PAHs, and reported an adjusted OR of 2.42 (95% CI: 0.97–6.09), comparing exposure at birth to high concentrations of TSP relative to low concentrations, among post-menopausal women (Bonner et al., 2005). In the same study, Nie et al. reported an OR of 2.05 (95% CI: 0.92–4.54) for the association between high exposure to traffic emissions at menarche and premenopausal breast cancer (Nie et al., 2007). In contrast to these studies, our stratified results generally did not suggest differences by menopausal status. Nie et al. also stratified by estrogen and progesterone receptor status, but reported no differences. In our study, we had insufficient power to examine this, and did not find a clear pattern. Variability in the results across these studies may be due, at least in part, to differences in study design, exposure assessment, geographic region, and timing of the exposure.

A key strength is that this is one of the first studies to examine the association between exposure to vehicular traffic-related air pollution during childhood and breast cancer development. We had a large sample size and participants were enrolled across the US and Puerto Rico. Since exposure information was ascertained prior to breast cancer diagnosis, recall bias of the exposure is expected to be non-differential by case status. Furthermore, we examined exposure duration, by restricting the analysis to individuals who lived at least five years at their childhood residence and considered their place of residence relative to puberty onset, since participants reported the time lived at their primary childhood residence.

One major limitation is that the exposure assessment relied on self-report of childhood residential characteristics rather than direct measurement of specific air pollutants or roadway traffic density. Our exposure measure is only a proxy for actual vehicular traffic-related air pollution exposure during childhood and is subject to exposure misclassification. It does not account for meteorological dispersion and the geophysical features, each of which can affect air pollutant concentrations (Korek et al., 2016). However, modeled estimates may also be subject to misclassification and be limited by the availability and quality of historical monitored estimates. Furthermore, participants in our study were born as early as 1928 and asked about exposures during childhood/adolescence, and systematic air pollution data on a national scale was not available in the US prior to the 1970s (Schwartz and Hayward, 2007). Another limitation is that, given the lag between the time of exposure and the exposure ascertainment, there is the potential for recall bias. We tried to reduce potential recall bias by limiting the analysis to participants who reported residing in their primary childhood residence for a minimum of five years, and therefore, presumably,

had stronger recall of their place of residence. We also could not account for changes in exposure during childhood due to relocation since the participants were only asked about their primary childhood residence.

5. CONCLUSIONS

We observed modest and suggestive associations between breast cancer and certain characteristics of childhood neighborhood roads that may be indicative of increased vehicular traffic-related air pollution exposure. Studies examining the association between childhood exposure to vehicular traffic-related air pollution and incident breast cancer that utilize pollutant measurements or measured residential proximity to major roadways are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This study was supported by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences [Z01-ES044005]; and the NIEHS grant [T32ES007018] (A Herring, PI).

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Highlights

- Evaluated the association of residential childhood air pollution with breast cancer
- Traffic-related characteristics were not consistently associated with breast cancer
- Living on/near a road divided by a barrier during childhood was associated increased risk

Table 1

Study Participant Descriptive Characteristics by Breast Cancer Status at the End of Follow-up

CHARACTERISTIC	Cases (N= 2,028)	Non-Cases (N= 40,906)	Total (N= 42,934)
Age at Baseline (yrs), n (%)			
<50	464 (23)	11,499 (28)	11,963 (28)
50 – <55	359 (18)	8,028 (20)	8,387 (20)
55 – <60	402 (20)	8,196 (20)	8,598 (20)
60 – <65	377 (19)	6,217 (15)	6,594 (15)
65+	426 (21)	6,966 (17)	7,392 (17)
Race/Ethnicity, n (%)			
Non-Hispanic, White	1,760 (87)	34,623 (85)	36,383 (85)
Non-Hispanic, Black	143 (7)	3,413 (8)	3,556 (8)
Hispanic	67 (3)	1,866 (5)	1,933 (5)
Other	58 (3)	1,004 (2)	1,062 (2)
Highest Level of Education in the Household at Age 13, n (%)			
High School or Less	1,076 (53)	22,088 (54)	23,164 (54)
Some College	409 (20)	7,726 (19)	8,135 (19)
Bachelor's Degree	336 (17)	6,752 (17)	7,088 (17)
Graduate Degree	207 (10)	4,340 (11)	4,547 (11)
Characteristics of the Main Road at Childhood Residence			
Number of Lanes, n (%)			
1–2 Lanes	1,975 (97)	39,644 (97)	41,619 (97)
3+ Lanes	53 (3)	1,262 (3)	1,315 (3)
Presence of Median/Barrier, n (%)			
Without Median or Barrier of Any Kind	1,989 (98)	40,236 (98)	42,225 (98)
With Median or Barrier of Any Kind	39 (2)	670 (2)	709 (2)
Traffic during rush hour, n (%)			
Light Traffic	1,662 (82)	33,180 (81)	34,842 (81)
Moderate Traffic	266 (13)	5,438 (13)	5,704 (13)
Heavy Traffic	100 (5)	2,288 (6)	2,388 (6)
Characteristics of the Nearest Cross-Street or Intersecting Road			
Distance of Residence to Nearest Road and…			
Number of Lanes on Intersecting Road, n (%)			
100 ft.+	1,378 (68)	26,823 (66)	28,201 (66)
Within 100 ft. 1–2 lanes	581 (29)	12,856 (31)	13,437 (31)
Within 100 ft. 3+ lanes	69 (3)	1,227 (3)	1,296 (3)
Median/Barrier on Intersecting Road, n (%)			
100 ft.+	1,378 (68)	26,823 (66)	28,201 (66)
Within 100 ft., Without Median or Barrier of Any Kind	622 (31)	13,610 (33)	14,232 (33)
Within 100 ft., With Median or Barrier of Any Kind	28 (1)	473 (1)	501 (1)
Traffic During Rush Hour on Intersecting Road, n (%)			
100 ft.+	1,378 (68)	26,823 (66)	28,201 (66)

CHARACTERISTIC	Cases (N= 2,028)	Non-Cases (N= 40,906)	Total (N= 42,934)
Within 100 ft., Light Traffic	440 (22)	9,653 (24)	10,093 (24)
Within 100 ft., Moderate Traffic	136 (7)	2,778 (7)	2,914 (7)
Within 100 ft., Heavy Traffic	74 (4)	1,652 (4)	1,726 (4)
Multiple lanes, Median/Barrier, and Traffic During Rush Hour on Intersecting Road, n (%)			
100 ft.+ and/or (Neither 3+ Lanes nor Median/Barrier)	1,948 (96)	39,484 (97)	41,432 (97)
Within 100 ft., 3+ Lanes and/or Median/Barrier and…			
Light Traffic	14 (1)	224 (1)	238 (1)
Moderate Traffic	19 (1)	479 (1)	498 (1)
Heavy Traffic	47 (2)	719 (2)	766 (2)

Table 2

Cox regression hazard ratios (HRs) and 95% Confidence Intervals (CIs) for the Association Between Reported Childhood Residence Characteristics and Incident Breast Cancer Diagnosis

CHARACTERISTIC	Total Breast Cancer			
	Person- Years	Cases	Age-Adjusted HR (95% CI)	Fully- Adjusted HR (95% CI)[a]
Characteristics of the Main Road at Childhood Residence				
Number of Lanes				
1–2 Lanes	264,261	1,975	(REF)	(REF)
3+ Lanes	8,249	53	0.8 (0.6, 1.1)	0.8 (0.6, 1.1)
Presence of Median/Barrier				
Without Median or Barrier of Any Kind	268,173	1,989	(REF)	(REF)
With Median or Barrier of Any Kind	4,337	39	1.2 (0.9, 1.7)	1.2 (0.9, 1.7)
Traffic During Rush Hour				
Light Traffic	222,017	1,662	(REF)	(REF)
Moderate Traffic	35,654	266	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)
Heavy Traffic	14,839	100	0.9 (0.7, 1.1)	0.9 (0.7, 1.1)
Characteristics of the Nearest Cross-street or Intersecting Road				
Distance of Residence to Nearest Road and…				
Number of Lanes on Intersecting Road				
100 ft.+	179,299	1,378	(REF)	(REF)
Within 100 ft. 1–2 Lanes	85,166	581	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)
Within 100 ft. 3+ Lanes	8,044	69	1.1 (0.9, 1.4)	1.1 (0.9, 1.4)
Median/Barrier on Intersecting Road				
100 ft.+	179,299	1,378	(REF)	(REF)
Within 100 ft., Without Median or Barrier of Any Kind	90,230	622	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)
Within 100 ft., With Median or Barrier of Any Kind	2,981	28	1.3 (0.9, 1.8)	1.3 (0.9, 1.8)
Traffic During Rush Hour on Intersecting Road				
100 ft.+	179,299	1,378	(REF)	(REF)
Within 100 ft., Light Traffic	64,838	440	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)
Within 100 ft., Moderate Traffic	17,876	136	1.0 (0.8, 1.2)	1.0 (0.8, 1.2)
Within 100 ft., Heavy Traffic	10,497	74	0.9 (0.7, 1.2)	0.9 (0.7, 1.2)
Multiple Lanes, Median/Barrier, and Traffic During Rush Hour on Intersecting Road				
100 ft.+ and/or (Neither 3+ Lanes Nor Median/Barrier)	263,248	1,948	(REF)	(REF)
Within 100 ft., 3+ Lanes and/or Median/Barrier and…				
Light Traffic	1,549	14	1.2 (0.7, 2.0)	1.2 (0.7, 2.0)
Moderate Traffic	3,083	19	0.8 (0.5, 1.3)	0.8 (0.5, 1.3)
Heavy Traffic	4,631	47	1.4 (1.0, 1.9)	1.4 (1.0, 1.9)

[a]Fully-adjusted models are adjusted for age, race/ethnicity, and highest level of education attained in the household at age 13.

Table 3

Cox regression hazard ratios (HRs) and 95% Confidence Intervals (CIs) for the Association Between Reported Childhood Residence Characteristics and Incident Pre- and Post-Menopausal Breast Cancer

	Pre-Menopausal Cancer		Post- Menopausal Cancer	
CHARACTERISTIC	**Cases**	**Fully- Adjusted HR (95% CI) [a]**	**Cases**	**Fully- Adjusted HR (95% CI) [a]**
Characteristics of the Residential Road at Childhood Residence				
Number of Lanes				
1–2 Lanes	425	(REF)	1,533	(REF)
3+ Lanes	14	1.3 (0.8, 2.2)	39	0.8 (0.6, 1.0)
Presence of Median/Barrier				
Without Median or Barrier of Any Kind	429	(REF)	1,543	(REF)
With Median or Barrier of Any Kind	10	1.5 (0.8, 2.7)	29	1.1 (0.8, 1.7)
Traffic During Rush Hour				
Light Traffic	360	(REF)	1,287	(REF)
Moderate Traffic	57	1.0 (0.8, 1.3)	208	1.0 (0.9, 1.2)
Heavy Traffic	22	1.0 (0.7, 1.6)	77	0.9 (0.7, 1.1)
Characteristics of the Nearest Cross-street or Intersecting Road				
Distance of Residence to Nearest Road and…				
Number of Lanes on Intersecting Road				
100 ft.+	289	(REF)	1,079	(REF)
Within 100 ft., 1–2 Lanes	135	1.0 (0.8, 1.2)	440	0.9 (0.8, 1.0)
Within 100 ft., 3+ Lanes	15	1.1 (0.7, 1.9)	53	1.1 (0.8, 1.4)
Median/Barrier on Intersecting Road				
100 ft.+	289	(REF)	1,079	(REF)
Within 100 ft., Without Median or Barrier of Any Kind	144	1.0 (0.8, 1.2)	472	0.9 (0.8, 1.0)
Within 100 ft., With Median or Barrier of Any Kind	6	1.3 (0.6, 2.9)	21	1.3 (0.8, 2.0)
Traffic During Rush Hour on Intersecting Road				
100 ft.+	289	(REF)	1,079	(REF)
Within 100 ft., Light Traffic	110	1.0 (0.8, 1.3)	327	0.9 (0.8, 1.0)
Within 100 ft., Moderate Traffic	25	0.9 (0.6, 1.3)	108	1.0 (0.8, 1.2)
Within 100 ft., Heavy Traffic	15	0.9 (0.5, 1.5)	58	0.9 (0.7, 1.2)
Multiple Lanes, Median/Barrier, and Traffic During Rush Hour on Intersecting Road				
100 ft.+ and/or (Neither 3+ Lanes nor Median/ Barrier)	422	(REF)	1,510	(REF)
Within 100 ft., 3+ Lanes and/or Median/Barrier and…				
Light/Moderate Traffic	8	1.2 (0.6, 2.5)	25	0.9 (0.6, 1.3)
Heavy Traffic	9	1.1 (0.6, 2.2)	37	1.5 (1.1, 2.0)

[a] Fully-adjusted models are adjusted for age, race/ethnicity, and highest level of education attained in the household at age 13.