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Accessibility
Particulate Matter Air Pollution Exposure, Distance to Road, and Incident Lung Cancer in the Nurses’ Health Study Cohort

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*These authors contributed equally to this manuscript.

Introduction

A number of general population studies around the world have demonstrated adverse associations of chronic exposures to ambient particulate matter (PM) and/or traffic-related pollutants with lung cancer (Beelen et al. 2008a, 2008b; Beeson et al. 1998; Cao and Gao 2012; Carey et al. 2013; Cesaroni et al. 2013; Hales et al. 2013; Hart et al. 2011; Heinrich et al. 2013; Hystad et al. 2013; Jerrett et al. 2013; Katanoda et al. 2011; Krewski et al. 2009; Lepeule et al. 2012; Lipsett et al. 2011; McDonnell et al. 2000; Naess et al. 2003; Nafstad et al. 2003; Nyberg et al. 2000; Raaschou-Nielsen et al. 2010, 2011) or using distance to major roadways or traffic volume surrounding a location (Beelen et al. 2008a, 2008b; Cao and Gao 2012; Lipsett et al. 2011), potential confounders have been assessed only once, even in prospective cohort studies. Despite these inconsistencies in the current body of literature, a link between lung cancer and ambient air pollution has been demonstrated.

The current study is based in the United States within the all-female Nurses’ Health Study (NHS) cohort. Our objective is to examine the association of lung cancer incidence with residential-level chronic exposure to PM2.5, PM between 2.5 and 10 μm in diameter (PM2.5–10), PM10, and residential distance to road. With a wealth of time-varying information on exposures and potential confounders, this cohort provides a unique opportunity to examine these associations.

Methods

Study population. The NHS is an ongoing prospective cohort of 121,700 female nurses who were enrolled in 1976 when they were age 30–55 years. All women were enrolled at least 1 year before May 1, 1976. There were 121,700 participants in the current study. Study participants were asked to complete a comprehensive baseline medical questionnaire and were followed for incident cases of lung cancer through 2010. The cohort has been previously described in detail (Hennekens et al. 1982; Colditz et al. 1989).

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Lung cancer and air pollution exposures in the NHS

between 30 and 55 years of age. Participants initially were recruited from 11 states, but as of the mid-1990s nurses now reside in each of the 50 states. A map of all residential addresses in the 48 contiguous states is presented in the Supplemental Material, Figure S1. Participants complete mailed biennial questionnaires to provide information on potential risk factors and to self-report new diagnoses of health outcomes. The response rates are > 90% for each follow-up cycle. Vital status is ascertained through next of kin and the National Death Index (http://www.cdc.gov/nchs/ndi.htm); both methods have identified an estimated 98% of deaths in the cohort. The analytical population for this study excluded all women who were dead or had a previous diagnosis of cancer (except for non-melanoma skin cancer) before follow-up or did not have information for the exposures of interest. The study was approved by the Internal Review Board of Brigham and Women’s Hospital; and informed consent was implied through return of the questionnaires. In addition, this study was approved by the Connecticut Department of Public Health (DPH) Human Investigations Committee. Certain data used in this publication were obtained from the DPH.

Case ascertainment. Lung cancers were self-reported by the participants or next of kin or were identified from death certificates; and first reports were subsequently confirmed with medical records by physicians blinded to exposure status. Medical records were obtained for 83% of reported cases; of those, 87% had primary lung cancer confirmed by pathology reports. However, because lung cancers were well reported in this cohort, we included any primary report reconfirmed by the participant where pathological reports were not available.

Exposure assessment. As part of the questionnaire mailing process, residential address information is updated every 2 years. All available addresses (1976, 1986–2010) have been geocoded to obtain the corresponding latitude and longitude. For women with a street segment–level geocode (i.e., highest quality, 80–90% of the available addresses in each follow-up cycle), we calculated distance to road at each address as a proxy for traffic-related exposures. Distance to the nearest road (meters) was determined using geographic information system (GIS) software (ArcGIS, version 9.3; ESRI, Redlands, CA) and the ESRI Streetmap Pro2007 data set. We calculated the shortest distances to the following road classes as defined by the U.S. Census Bureau (2001): A1 (primary roads, typically Interstate highways, with limited access, division between the opposing directions of traffic, and defined exits), A2 (primary major, non-Interstate highways and major roads without access restrictions), and A3 (smaller, secondary roads, usually with more than two lanes). Analyses were conducted using distance to the nearest of all three road types (A1–A3), distance to the two largest road types (A1, A2), and distance to the largest road type (A1). Given the distribution of distance to road in this cohort and previous exposure studies showing approximately exponential decay in exposures to traffic-related air pollutants with increasing distance from a road, we divided distance to road into the following categories: 0–50, 50–200, and ≥ 200 m (Adar and Kaufman 2007; Karner et al. 2010; Lipert and Wyra 2008; Lipert et al. 2006, 2008; Sahloind et al. 2007; Zhu et al. 2002). We also considered analyses of continuous distance to roads.

Ambient GIS-based spatiotemporal exposure model predictions of PM2.5 and PM10 were available for all months between January 1988 and December 2007 for the continental United States. These values were generated for each address from nationwide expansions of previously validated spatiotemporal models (Weuve et al. 2012; Yanosky et al. 2008, 2009, in press). The models used monthly average PM2.5 and/or PM10 data from the U.S. Environmental Protection Agency’s (EPA) Air Quality System (U.S. EPA 2009), the IMPROVE network (Visibility Information Exchange Web System 2009) and various other sources (Spengler et al. 1996; Suh et al. 1997). Generalized additive mixed models with monthly penalized spline smooth spatial terms, penalized spline smooth terms of geospatial predictors (listed below), and terms for time were used to create separate PM prediction surfaces for each month and each PM size fraction (Yanosky et al. 2009). The following geospatial predictors used by the models were generated using a GIS: distance to nearest A1–A4 roads, percent urban land use within 1 km, elevation, point sources of PM (PM2.5 emissions density within 7.5 km for PM2.5 models, and PM10 emissions density within 7.5 km for PM10 models), smoothed county population density, tract population density (only for PM10), and meteorological predictors: wind speed, total precipitation, temperature, and percent stagnant air days per month (Yanosky et al. 2009). Because monitoring data on PM2.5 are limited before 1999, PM2.5 in the period before 1999 was modeled using data on PM10 (Yanosky et al. 2008). By subtraction of the monthly PM10 and PM2.5 estimates, information was also obtained on PM10–5.0–10. Cross-validation results demonstrated that the models had high predictive accuracy (cross-validation R2 values of 0.59, 0.76, and 0.77 for PM10, pre-1999 PM2.5, and post-1999 PM2.5, respectively). Potential confounders and effect modifiers. We selected a priori a number of potential confounders or effect modifiers previously associated with lung cancer or exposure in this cohort. Information on the following time-varying variables was available every 2 or 4 years from the follow-up questionnaires: body mass index (BMI; kilograms per meter squared, continuous), physical activity in metabolic equivalent hours per week (MET hr/week; < 3, 3 to < 18, ≥ 18), overall diet quality (Alternative Health Eating Index, continuous) (Chiuye et al. 2012), alcohol consumption (dichotomized at 0 g/day), smoking status (current, former, never), months since quitting for former smokers (continuous), and pack-years (continuous). In 1982 a question was included on exposure to secondhand smoke at home and work and during childhood. We considered census-tract median household income and median house value as measures of area-level socioeconomic status (SES). To account for differences in exposure and other unmeasured regional factors, we also controlled for U.S. geographic region of residence (Northeast, South, Midwest, West). Statistical analysis. Time-varying Cox proportional hazards models were used to assess the relationship of incident lung cancer with residential distance to road and exposure to PM2.5, PM10, or PM2.5–10. Hazard ratios (HRs) and 95% CIs were calculated for each category of roadway proximity compared with the furthest category. We examined the linearity of the association with distance to road using cubic splines, and considered models examining the linear dose response with distances of 0–499 m, compared with values ≥ 500 m. For the metrics of PM we calculated HRs and 95% CIs for a 10-μg/m3 increase in each size fraction, after assessing linearity of the dose response. Because the appropriate averaging period is unknown, yet assumed to be more chronic than short-term, we considered 24-, 48-, 72-, 96-, and 120-month cumulative averages. We used Akaike’s information criterion (AIC) (Akaike 1974) to determine the best fit cumulative average for PM2.5 among individuals with at least 120 months of exposure, so that the AIC criteria were evaluated among a single population. In sensitivity analyses we considered the consistency of results for other possible averaging times. A p-value of 0.05 was used to determine statistical significance.

In the Cox models, person-months were calculated from the start of disease follow-up until June 2010, the end of follow-up, censoring at event, death from another cause, or loss to follow-up, whichever occurred first. We determined the start of disease follow-up based on the selected cumulative average. All models were based on a biennial time scale, were stratified by age in months and time period, and were adjusted for geographic region. Separate models were run for the
distance to road types and for each size fraction of PM. Potential confounders (or sets of confounders) were entered separately into the basic model to determine their influence on the association with lung cancer. We included variables in the final models that changed the effect estimate for PM$_{2.5}$ and lung cancer at least 10%. For comparability, we used the same confounders across the different size fractions and distance to road models.

To examine effect modification by smoking status, we performed stratified models and created multiplicative interaction terms. Because of small numbers of cases among never-smokers, we also considered effect modification combining never-smokers with former smokers who had quit at least 10 years previously (“long-term former smokers”). Sensitivity analyses were performed restricted to nonmovers, defined as women who remained at the same address between 1976 and the start of follow-up, and the start of follow-up, SAS version 9.2 (SAS Institute Inc., Cary, NC) was used for all analyses.

### Results

Based on the assessment of averaging times described in the methods, the 72-month average was identified as the optimal cumulative average, and therefore we began disease follow-up for all analyses in 1994. A total of 103,650 participants were available for analysis of PM exposures (4,548 died before 1994, 10,710 had a previous diagnosis of cancer, and an additional 2,753 had no information on air pollution).

Age-adjusted characteristics during follow-up are presented overall and by smoking status in Table 1. The mean (± SD) age was 67.0 ± 8.3 years, the age-adjusted mean BMI was 25.6 ± 7.5 and about 39% reported between 3 and 18 MET hr/week of physical activity. About half of the women lived in the Northeast, and 52% of participants reported secondhand smoke exposure at work and from their parents and about 35% at home. More never-smokers were nondrinkers and were less exposed to secondhand smoke, whereas more current smokers reported < 3 MET hr/week of physical activity. Distributions of the three size fractions of PM overall and by region and correlations between the three size fractions within and across cumulative averages are presented in Supplemental Material, Tables S1 and S2, respectively.

All of our a priori potential confounders met our definition of confounding and were included in the final multivariable adjusted models. Physical activity, diet, and census-tract median income and median home value (U.S. Census Bureau 2001) attenuated the effect estimate when added to the basic models.

### Table 1. Age-adjusted descriptive characteristics averaged over follow-up (1994–2010) among 103,650 participants in the Nurses’ Health Study overall and stratified by smoking status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All participants</th>
<th>Never-smokers</th>
<th>Former smokers</th>
<th>Current smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years (%)</td>
<td>1,510,027 (100)</td>
<td>668,581 (44)</td>
<td>663,062 (44)</td>
<td>175,563 (12)</td>
</tr>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>67.0 ± 8.3</td>
<td>67.1 ± 8.5</td>
<td>67.4 ± 8.2</td>
<td>64.8 ± 7.9</td>
</tr>
<tr>
<td>BMI (kg/m$^2$) (mean ± SD)</td>
<td>25.6 ± 7.5</td>
<td>25.8 ± 7.4</td>
<td>26.4 ± 6.8</td>
<td>22.1 ± 9.4</td>
</tr>
<tr>
<td>Pack-years of smoking (mean ± SD)</td>
<td>13.4 ± 20.0</td>
<td>0.0 ± 0.0</td>
<td>19.3 ± 18.5</td>
<td>43.0 ± 23.0</td>
</tr>
<tr>
<td>Months since quit smoking (mean ± SD)</td>
<td>123.9 ± 178.8</td>
<td>0.0 ± 0.0</td>
<td>279.2 ± 167.4</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Alternative healthy eating index (mean ± SD)</td>
<td>180.4 ± 108.5</td>
<td>182.8 ± 108.0</td>
<td>190.6 ± 106.5</td>
<td>129.4 ± 102.1</td>
</tr>
<tr>
<td>Census-tract median household income (mean ± SD)</td>
<td>63,518 ± 24,491</td>
<td>62,648 ± 23,194</td>
<td>64,849 ± 24,978</td>
<td>61,954 ± 23,644</td>
</tr>
<tr>
<td>Census-tract median home value (mean ± SD)</td>
<td>170,126 ± 125,261</td>
<td>166,431 ± 123,720</td>
<td>176,055 ± 128,456</td>
<td>161,998 ± 118,139</td>
</tr>
</tbody>
</table>

- **Moved between 1976 and 1994 (%)**
  - No: 65.4
  - Yes: 34.6

- **Region (%)**
  - Northeast: 51.1
  - Midwest: 17.3
  - West: 13.7
  - South: 18.0

- **Alcohol category (%)**
  - Nondrinker (0 g/day): 15.0
  - Drinker: 71.4
  - Missing: 13.6

- **Physical activity (%)**
  - < 3 MET hr/week: 21.5
  - ≥ 18 MET hr/week: 38.8
  - 3 to < 18 MET hr/week: 39.7

- **Secondhand smoke during childhood (%)**
  - None: 25.1
  - From mother: 3.8
  - From father: 33.9
  - From both parents: 14.7

- **Home secondhand smoke (%)**
  - None: 33.2
  - Occasional: 18.6
  - Regular: 17.1
  - Missing: 31.2

- **Occupational secondhand smoke (%)**
  - None: 15.0
  - Occasional: 29.3
  - Regular: 22.6

Women can be in multiple smoking status categories throughout follow-up. *Not age-adjusted.
Among all lung cancer cases, 44% were adenocarcinoma, 14% were squamous, 14% were small cell, 16% were other histologies (large cell and non-small cell carcinoma, carcinoid, or papillary, mixed sarcoma), and 12% were unknown histology. There were sufficient numbers only of adenocarcinomas to perform subtype-specific analyses. In general, HRs for associations with adenocarcinomas were stronger than corresponding HRs for all lung cancer subtypes combined (Table 2).

In sensitivity analyses, the HRs for PM$_{2.5}$ and all lung cancers, the HRs for associations with adenocarcinomas specifically, and the HRs based on models restricted to never- or long-term former smokers were slightly stronger when analyses were restricted to 66,051 women who did not move residence between 1976 and 1994 (896,370 person-years, 1,441 total cases) (see Supplemental Material, Table S3). Furthermore, our conclusions were unchanged when we used the 24-, 48-, 96-, or 120-month cumulative averages for PM (data not shown).

There were a total of 1,291,229 person-years of follow-up and 1,841 lung cancer cases (1,654 definite) among the 88,596 women moving between 1976 and 1994, results were observed in most of the previous equivalent studies (Beelen et al. 2008a, 2008b; Beeson et al. 1998; Cao and Gao 2012; Carey et al. 2013; Cesaroni et al. 2013; Jerrett et al. 2013; Katanoda et al. 2013; Krewski et al. 2009; Lepeule et al. 2012; Turner et al. 2011). Within 50 m of an A1 road (vent > 200 m from an A1 road) was positively associated with lung cancer risk, but numbers of exposed participants were small and there was no evidence of an association with distance from a road modeled as a continuous variable.

Our estimated HRs for a 10-μg/m$^3$ increase in PM$_{2.5}$ and PM$_{10}$ in the full cohort are at the lower end of the distribution of associations observed in most of the previous equivalent studies (Beelen et al. 2008a, 2008b; Beeson et al. 1998; Cao and Gao 2012; Carey et al. 2013; Cesaroni et al. 2013; Jerrett et al. 2013; Katanoda et al. 2013; Krewski et al. 2009; Lepeule et al. 2012; Turner et al. 2011). These studies have reported associations in ranges of 0.95–1.40 for PM$_{2.5}$ and 0.93–2.40 for PM$_{10}$ when estimated for increments of 10 μg/m$^3$. To our knowledge, to date, only one other study has presented assessment of PM$_{2.5}$ (Raschou-Nielsen et al. 2013).

Table 2. HRs (95% CIs) of the association of incident lung cancer 1994–2010 per 10-μg/m$^3$ increase in 72-month cumulative average PM exposures among 103,650 members of the Nurses’ Health Study.

| Case definition/cohort | Person-years | PM$_{10}$ | PM$_{2.5}$ | PM$_{2.5}$-to-10 |
|------------------------|--------------|-----------|-----------|----------------|----------------|
| All cases              | 2,155        | 1,510,027 | 1.00 (0.98, 1.18) | 1.04 (0.95, 1.14) | 1.05 (0.90, 1.23) | 1.06 (0.91, 1.25) | 1.12 (0.98, 1.27) | 1.05 (0.92, 1.20) |
| Never-smokers          | 176          | 668,581   | 1.12 (0.85, 1.46) | 1.11 (0.85, 1.46) | 1.24 (0.74, 2.05) | 1.25 (0.75, 2.07) | 1.13 (0.75, 1.70) | 1.11 (0.74, 1.88) |
| Never or quit smoking 10 years | 828 | 1,203,946 | 1.11 (0.97, 1.28) | 1.10 (1.00, 1.32) | 1.22 (0.95, 1.57) | 1.37 (1.06, 1.77) | 1.11 (0.91, 1.37) | 1.11 (0.90, 1.37) |
| Current or smoked in the last 10 years | 1,327 | 306,081 | 0.96 (0.86, 1.08) | 0.99 (0.88, 1.12) | 0.88 (0.72, 1.08) | 0.94 (0.76, 1.15) | 1.01 (0.85, 1.21) | 1.03 (0.86, 1.24) |

Adenocarcinomas

| Case definition/cohort | Person-years | PM$_{10}$ | PM$_{2.5}$ | PM$_{2.5}$-to-10 |
|------------------------|--------------|-----------|-----------|----------------|----------------|
| Full cohort            | 847          | 1,510,027 | 1.15 (0.95, 1.39) | 1.18 (0.97, 1.45) | 1.28 (0.89, 1.63) | 1.33 (0.92, 1.93) | 1.18 (0.87, 1.59) | 1.23 (0.89, 1.70) |
| Never or quit smoking 10 years | 425 | 1,203,946 | 1.18 (0.82, 1.67) | 1.41 (0.95, 2.08) | 1.41 (0.73, 2.72) | 1.66 (0.88, 3.14) | 1.14 (0.63, 2.06) | 1.49 (0.65, 2.83) |

*Models were adjusted for age, time period, and geographic region. *Additionally adjusted for BMI, alcohol consumption, physical activity, overall diet quality, smoking status (when not stratified by status) and pack-years, months since quitting smoking, secondhand smoke exposure at home, work, and during childhood, and census-tract median home value and median income.
and the HR was 1.19 (95% CI: 0.77, 1.82) if expressed as a 10-μg/m³ increase.

In its recent assessment of the carcinogenicity of outdoor air pollution in general and particulate matter in particular, IARC determined that the evidence was remarkably consistent in epidemiological studies from Europe, North America, and Asia, in studies of experimental animals, and across a wide range of mechanisms related to cancer (Loe¨mis et al. 2013). IARC determined that for lung cancer the most informative epidemiologic studies were the European Study of Cohorts for Air Pollution Effects (ESCAPE) and the American Cancer Society Study (ACS). ESCAPE combined data from 17 cohort studies based in nine European countries, including 312,944 individuals and 2,095 incident lung cancer cases over 12.8 years of follow-up (Raaschou-Nielsen et al. 2013). Using land-use regression models incorporating data from 2008–2011, they predicted PM exposures at the participants’ baseline address (in the 1990s for most cohorts). They observed associations of lung cancer with PM₁₀ (HR = 1.22; 95% CI: 1.03, 1.45 per 10 μg/m³), PM₂.₅ (HR = 1.18; 95% CI: 0.96, 1.46 per 5 μg/m³), and PM₂.₅₁₀ (HR = 1.09; 95% CI: 0.88, 1.33 per 5 μg/m³) after adjusting for sex, smoking variables, secondhand smoke, occupational variables, fruit intake, and area-level SES (Raaschou-Nielsen et al. 2013). The most recent updates of the full ACS Cancer Prevention Study II (CPS-II) study included about 500,000 individuals residing in metropolitan statistical areas (MSAs) throughout the United States with information on air pollution (Krewski et al. 2009; Pope et al. 2002). The investigators estimated MSA-level average baseline exposures to PM₂.₅ from 1979–1983 and toward the end of the follow-up in 1999–2000. HRs were adjusted for sex, age, race, and baseline information on smoking, educational status, BMI, alcohol consumption, occupational exposure, and diet. With follow-up from 1982–1998, the adjusted HRs for a 10-μg/m³ increase in PM₂.₅ using the baseline average, the 1999–2000 average, or the average of the two time periods were 1.08 (95% CI: 1.01, 1.16), 1.13 (95% CI: 1.04, 1.12), and 1.14 (95% CI: 1.04, 1.23), respectively (Pope et al. 2002). The adjusted HR per 28.8 μg/m³ for exposure to PM₁₀ averaged from 1987–1996 was not elevated (HR = 0.94; 95% CI: 0.86, 1.02) (Krewski et al. 2009). An additional 2 years of follow-up and extensive consideration of additional individual-level and ecological-level covariates, as well as assessment of autocorrelation, did not materially change these results (Krewski et al. 2009).

There is no clear evidence in the literature of sex differences in the relation of PM with lung cancer. To date, only two other studies have focused specifically on women. In the California Teachers Study, a prospective cohort of 133,479 female public school professionals (20–80 years of age at baseline) residential-level cumulative exposures to PM₂.₅ and PM₁₀ were quantified. From 1997 through 2005, 234 and 275 participants with PM₂.₅ and PM₁₀ exposure information, respectively, died from lung cancer. Adjusted analyses showed no association with a 10-μg/m³ change in PM₂.₅ (HR = 0.95; 95% CI: 0.70–1.28) or PM₁₀ (HR = 0.93; 95% CI: 0.81–1.07) (Lipsett et al. 2011). In a German cohort study of 4,800 women, air pollution exposure was assessed for up to 18 years using air monitoring–station data to calculate yearly averages of PM₁₀. Adjusted analysis showed an increase of 7 μg/m³ PM₁₀ was associated with an increased HR for lung cancer mortality (HR = 1.84; 95% CI: 1.23, 2.74) (Heinrich et al. 2013). In other studies that presented results stratified by sex, no clear patterns of effect modification emerged (Abbey et al. 1999; Cesaroni et al. 2013; Katanoda et al. 2011; Naess et al. 2007; Pope et al. 2002).

Our findings of stronger associations when we restricted to never-smokers and participants who had quit at least 10 years before death raise important considerations that will be explored in our future analyses. Due to the association of smoking with lung cancer, there is a concern that exposure estimates from the different time periods may have been measured differently. Additionally, smoking behaviors change as there are more smoking restrictions in public places. Furthermore, sociodemographic changes may have influenced participants’ exposure to PM. We therefore restricted our analysis to women who had quit smoking at least 10 years before death. We compared the HRs for current and never-smokers as well as never-smokers that had quit smoking for at least 10 years.

A total of 1,237 cases were included. The average duration of follow-up was 19.6 years. Our findings of stronger associations from PM exposure are consistent with those from other studies. However, we observed stronger associations for never-smokers that had quit smoking for at least 10 years compared to current smokers or smoked in the last 10 years. We did not observe any association for never-smokers who had quit smoking ≥ 10 years (HR = 1.00; 95% CI: 0.95, 1.05). The HRs for PM exposure were further calculated for various exposure categories and are presented in Table 3.

Table 3. HRs (95% CIs) for incident lung cancer 1994–2010 in association with residential proximity to roads in 1994 among 88,596 members of the Nurses’ Health Study.

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>Cases</th>
<th>Basic</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoker or smoked in the last 10 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance to A1 (m)</td>
<td>≥ 200</td>
<td>1,212</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>50–199</td>
<td>19</td>
<td>0.79 (0.48, 1.31)</td>
<td>0.86 (0.52, 1.42)</td>
</tr>
<tr>
<td>0–49</td>
<td>6</td>
<td>2.74 (1.19, 6.32)</td>
<td>2.48 (1.04, 5.90)</td>
</tr>
<tr>
<td>Continuous (per 100 m)</td>
<td>1,237</td>
<td>1.00 (0.91, 1.09)</td>
<td>0.98 (0.89, 1.07)</td>
</tr>
<tr>
<td>Distance to A1–A2 (m)</td>
<td>≥ 200</td>
<td>1,142</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>50–199</td>
<td>69</td>
<td>0.96 (0.73, 1.28)</td>
<td>0.98 (0.75, 1.33)</td>
</tr>
<tr>
<td>0–49</td>
<td>26</td>
<td>1.01 (0.62, 1.62)</td>
<td>0.95 (0.58, 1.56)</td>
</tr>
<tr>
<td>Continuous (per 100 m)</td>
<td>1,237</td>
<td>1.02 (0.96, 1.08)</td>
<td>1.02 (0.96, 1.08)</td>
</tr>
<tr>
<td>Distance to A1–A3 (m)</td>
<td>≥ 200</td>
<td>647</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>50–199</td>
<td>370</td>
<td>1.10 (0.94, 1.28)</td>
<td>1.10 (0.94, 1.29)</td>
</tr>
<tr>
<td>0–49</td>
<td>220</td>
<td>1.10 (0.91, 1.33)</td>
<td>1.10 (0.92, 1.34)</td>
</tr>
<tr>
<td>Continuous (per 100 m)</td>
<td>1,237</td>
<td>0.98 (0.94, 1.02)</td>
<td>0.97 (0.93, 1.01)</td>
</tr>
<tr>
<td>Nevar-smoker or quit smoking ≥ 10 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance to A1 (m)</td>
<td>≥ 200</td>
<td>587</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>50–199</td>
<td>13</td>
<td>0.86 (0.49, 1.49)</td>
<td>0.90 (0.52, 1.57)</td>
</tr>
<tr>
<td>0–49</td>
<td>4</td>
<td>3.15 (1.16, 8.50)</td>
<td>3.26 (1.17, 9.11)</td>
</tr>
<tr>
<td>Continuous (per 100 m)</td>
<td>604</td>
<td>0.98 (0.88, 1.09)</td>
<td>0.98 (0.88, 1.09)</td>
</tr>
<tr>
<td>Distance to A1–A2 (m)</td>
<td>≥ 200</td>
<td>557</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>50–199</td>
<td>36</td>
<td>0.99 (0.71, 1.39)</td>
<td>1.03 (0.73, 1.45)</td>
</tr>
<tr>
<td>0–49</td>
<td>11</td>
<td>1.05 (0.56, 1.91)</td>
<td>1.07 (0.59, 1.96)</td>
</tr>
<tr>
<td>Continuous (per 100 m)</td>
<td>604</td>
<td>0.98 (0.91, 1.04)</td>
<td>0.97 (0.90, 1.03)</td>
</tr>
<tr>
<td>Distance to A1–A3 (m)</td>
<td>≥ 200</td>
<td>324</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>50–199</td>
<td>188</td>
<td>1.10 (0.91, 1.31)</td>
<td>1.09 (0.91, 1.31)</td>
</tr>
<tr>
<td>0–49</td>
<td>92</td>
<td>1.00 (0.79, 1.26)</td>
<td>1.03 (0.81, 1.30)</td>
</tr>
<tr>
<td>Continuous (per 100 m)</td>
<td>604</td>
<td>1.00 (0.95, 1.04)</td>
<td>0.99 (0.95, 1.04)</td>
</tr>
</tbody>
</table>

*Models were adjusted for age, time period, and geographic region. **Additionally adjusted for BMI, alcohol consumption, physical activity, overall diet quality, smoking status (when not stratified by status) and pack-years, months since quitting smoking, secondhand smoke exposure at home, work, and during childhood, and census-tract median home value and median income.
levels, residents in urban areas showed significantly increased risks for adenocarcinoma (OR = 1.92; 95% CI: 1.09, 3.38) compared with those in rural areas (López-Cima et al. 2011). Adenocarcinomas are the lung cancer subtype most commonly observed among nonsmokers (Schuller 2002), and time-trend and geographic studies have also suggested associations of this subtype with ambient air pollution (Chen et al. 2007, 2009).

Conclusions from studies specifically assessing the association of lung cancer with traffic exposures have been inconclusive. Six previous studies in Europe and Canada have looked at measures of distance to roadway or traffic intensity (Beelen et al. 2008a, 2008b; Cesaroni et al. 2013; Hystad et al. 2013; Raaschou-Nielsen et al. 2011, 2013; Vineis et al. 2006). Similar to our findings, the results have suggested a modest association, though the different metrics are difficult to compare and no results are statistically significant. Four studies, all in Europe, have modeled NO\(_2\) or NO\(_x\) specifically from traffic sources (Naftيد et al. 2003; Nyberg et al. 2000; Raaschou-Nielsen et al. 2010, 2011). Overall, these studies indicate a possible contribution from traffic, but again they are difficult to compare due to differences in exposure assessment.

Our study has a number of limitations. We used a spatiotemporal model to assign monthly residential-level PM exposures for each participant. However, we do not account for differences in time–activity patterns, time spent outdoors, or time spent at the residence. Additionally, because of a paucity of monitoring for PM\(_{2.5}\) before 1999, our models for PM\(_{2.5}\) have lower precision than our models in the later years. Even though our study was conducted within the same region, our models are less precise than our models in the later years. We were unable to assess exposures throughout the previous 72 months. Associations were stronger when analyses were restricted to never-smokers. This study provides additional support of an association of air pollution exposure and lung cancer, particularly among nonsmokers.

**References**


