Published in final edited form as:

Environ Int. 2021 October ; 155: 106698. doi:10.1016/j.envint.2021.106698.

Commute patterns, residential traffic-related air pollution, and lung cancer risk in the prospective UK Biobank cohort study

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Abstract

Introduction: Commuting exposes millions of people to carcinogens from traffic-related air pollution (TRAP) but is seldomly considered in epidemiologic studies of lung cancer. In the

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Ethics approval and consent to participate

The UK Biobank study was approved by the National Information Governance Board for Health and Social Care and the NHS North West Multicenter Research Ethics Committee. Electronic informed consent was obtained from all volunteer participants. The study was performed in accordance with the Declaration of Helsinki.

Conflict of interest

The authors declare no conflict of interest.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Consent for publication

Not applicable.

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prospective United Kingdom (UK) Biobank cohort study, we investigated associations between commute patterns, residential nitrogen dioxide concentrations (NO₂; a surrogate for TRAP), and lung cancer risk.

Methods: We analyzed 234,124 employed participants at baseline (2006–2010). There were 493 incident lung cancer cases diagnosed over an average 7-year follow-up. Subjects were cross-classified into exclusive categories of commute mode (automobile, public transportation, walking, cycling, active mixture, and other mixture) and frequency (regular: 1–4, often: 5 work-bound trips/week). Annual average residential NO₂ concentrations in 2005–2007 were estimated with land use regression. Multivariable Cox regression was used to estimate associations between commute patterns, NO₂ quartiles, and incident lung cancer. We conducted analyses stratified by NO₂ (> median=28.3 µg/m³) and potential confounders such as sex and smoking.

Results: Compared to regular automobile use, commuting often by public transportation was associated with increased lung cancer risk (hazard ratio (HR)=1.58, 95% confidence intervals (CI):1.08–2.33). Additionally, we found a positive exposure-response relationship with residential NO₂ (HR_{Q2}=1.21, 95% CI:0.90–1.62; HR_{Q3}=1.48, 95% CI:1.10–1.99; HR_{Q4}=1.58, 95% CI:1.13–2.23; p-trend=3.1×10⁻³). The public transportation association was observed among those with higher NO₂ (p-interaction=0.02). Other commute categories were not associated with risk.

Conclusions: Commuters residing in high-NO₂ areas who often use public transportation could have elevated lung cancer risk compared to regular automobile users. These results warrant investigations into which component(s) of public transportation contribute to the observed association with increased lung cancer risk.

Introduction

Lung cancer is a substantial public health burden among western countries. In the United Kingdom (UK), an average of 47,235 new cases were diagnosed per year in 2014–2016 (UK 2019). Furthermore, lung cancer is a significant economic burden, with an estimated £10 billion spent annually on direct costs to the UK National Health Service (NHS) for treatment and care, along with £1 billion lost each year to missed workdays (Trueman 2017).

Understanding modifiable lung cancer risk factors is crucial for developing population-level interventions. Besides cigarette smoking, other factors also contribute to lung carcinogenesis. One notable risk factor is traffic-related air pollution (TRAP) (Hamra et al. 2014; Hamra et al. 2015), a complex mixture of carcinogenic components from motor vehicle emissions. TRAP is a significant contributor to outdoor air pollution and is composed of ultrafine, fine, and coarse particulate matter (PM), nitrogen oxides (NO_x), sulfur oxides (SO_x), metals, nitrated polycyclic aromatic hydrocarbons (nitro-PAHs) and other chemical compounds. Carcinogenic components of TRAP can infiltrate buildings and influence indoor air quality (Jones et al. 2000).

Outdoor air pollution, which encompasses TRAP, is an established risk factor for lung cancer incidence and mortality (Cui et al. 2015; Hamra et al. 2014; Yang et al. 2016). The nitrogen dioxide (NO₂) component of TRAP is a widely accepted surrogate marker for outdoor concentrations and has been consistently associated with elevated lung cancer risk (Hamra et al. 2015). However, the NO₂-lung cancer associations were nominally stronger

among the North American and Asian studies, and were marginally non-significant among European studies (Hamra et al. 2015). Additionally, a recent study of never-smokers from the Women's Health Initiative did not detect associations between NO₂, PM_{2.5}, and lung cancer risk (Gowda et al. 2019). As such, further investigations are warranted.

A recent systematic literature review of commuting exposure and health outcomes suggested that few epidemiologic studies of cancer have considered or accounted for work-related commuting (Dinu et al. 2019), an important source of TRAP exposure. To our knowledge, no prospective cohort study has reported associations between commute patterns and lung cancer risk. Commuters are especially impacted by TRAP due to their proximity and time spent near emission sources. Outdoor TRAP concentrations are correlated with roadway and population density in urban areas (Su et al. 2015) and vary by mode of transportation (Rivas et al. 2017), which commonly includes automobiles, public transportation (i.e., buses, subways, and light rail), bicycles, and walking. Interestingly, TRAP concentrations at residences were found to be unrelated to neighborhood socioeconomic status in the UK (Rivas et al. 2017), which makes it an encompassing environmental concern.

The relationships between commute patterns, exposure to outdoor residential TRAP, and lung cancer risk remain unclear. Our primary study aim was to assess whether commute mode and frequency, with focus on comparing public transportation to automobile use, is associated with risk of incident lung cancer, adjusted for outdoor residential NO₂ levels and other confounders. Additionally, we explored whether this potential relationship differed by smoking status, sex, and outdoor residential NO₂ levels in separate stratified analyses. Our secondary study aim was to assess whether outdoor residential NO₂ levels are associated with risk of incident lung cancer, adjusted for commute mode and frequency and other confounders. Our secondary aim was to provide additional evidence for a potential NO₂-lung cancer relationship suggested in previous meta-analyses of European studies (Hamra et al. 2015). To address our primary and second study aims, we leveraged data from the UK Biobank, a prospective cohort study of nearly half a million adults.

Methods

Study Design

The study design and data access procedures of the UK Biobank have been described (<http://www.ukbiobank.ac.uk/>) (Fry et al. 2017; Sudlow et al. 2015). Briefly, the initial target population was adults aged 40–69 years who resided within 40 km of 22 assessment centers across the UK (Sudlow et al. 2015). Of the 9.2 million individuals registered in the UK's National Health Service (NHS) who were mailed study invitations, 503,317 individuals (5.5%) responded and visited the study assessment centers in 2006–2010 (Fry et al. 2017). Participants were administered touchscreen questionnaires, received physical examinations, and provided biological samples. Data from 502,616 participants were initially available and our analytic sample size was 234,124 after exclusions (Figure 1). This study sample was restricted to participants defined by the UK Office for National Statistics (ONS) using census data as those in England/Wales who lived in areas that were “urban/sparse”, “urban/less sparse”, “urban/town and fringe/less sparse; and those in Scotland who lived in “large or other urban areas”. Detailed information on the methods to derive population density is

found here: <https://biobank.ndph.ox.ac.uk/ukb/ukb/docs/UrbanRural.pdf>. Using ArcGIS Pro (Esri, Redlands, California, USA), we generated a density heat-map of the study population's residences in the United Kingdom based on their north and east grid coordinates (1 km² resolution) (Figure 2).

For each participant, follow-up time started at the date of visit to the assessment center and ended at the date of primary incident lung cancer diagnosis (outcome), death (censored), or administrative censoring (i.e., January 31, 2016 for England and Wales and November 30, 2015 for Scotland), whichever came first. The NHS Information Centre and the NHS Central Register Scotland provided vital status, as well as date and primary underlying cause of death for participants.

The UK Biobank study was approved by the National Information Governance Board for Health and Social Care and the NHS North West Multicenter Research Ethics Committee. Electronic informed consent was obtained from all volunteer participants (Fry et al. 2017; Sudlow et al. 2015).

Mode, Frequency, and Distance of Commute

Commute data were available for a subset of participants who answered employment-related questions at baseline. Among those who were currently working, the commute variables of interest included mode of travel (i.e., automobile only, public transportation only, cycle only, walk only, active mixture of cycling and walking, other mixture, missing/unknown), frequency (number of work-bound trips/week), and distance between home and work (km). We analyzed commute frequency dichotomized as regular: 1–4 and often: 5 work-bound trips/week. Distance between home and work was categorized as: <4.82, 4.82 to <8.05, 8.05 to <19.31, and 19.31 km. For the main analyses, we created a cross-classification variable between commute mode and frequency with regular automobile use as the reference category.

Outdoor Residential NO₂ Concentrations

Exposure assessment and modeling of outdoor NO₂ concentrations of baseline residential location were previously described (Vienneau et al. 2013). Briefly, air pollution estimates in 2005–2007 were derived from European Union (EU)-wide air pollution maps with 100 × 100 m resolution generated with land use regression (LUR) models. The grid coordinates of the residences of the UK Biobank participants were overlaid on these maps projected to the British National Grid and assigned their corresponding NO₂ concentrations. Annual average NO₂ concentrations were derived for each participant and were subsequently analyzed as quartiles (Q), dichotomized at the median, and continuous (per 10 µg/m³).

Lung Cancer Ascertainment

Incident and prevalent cancer diagnoses were provided to UK Biobank by the Health and Social Care Information Centre (HSCIC) and the NHS Central Register (NHSCR). Details of the lung cancer ascertainment can be found at the UK Association of Cancer Registries (<http://www.ukiacr.org/>). Lung cancer diagnosis was defined by International Classification of Diseases 10th revision (ICD-10 codes) C34.0–C34.9. ICD-O-3 code 8140 was used to

define adenocarcinoma, while 8052, 8084, 8073, and 8083 were used for squamous cell carcinoma (SCC).

Covariates

The baseline questionnaire collected information on various demographics, lifestyle factors, socioeconomic status, and anthropometric measurements. A detailed 25-level smoking variable was created as previously described (Loftfield et al. 2018). A cross-classification variable for sex and smoking was created for subsequent analyses (i.e., never-smoking women, never-smoking men, former-smoking women, former-smoking men, current-smoking women, current-smoking men, female cigar smokers, male cigar smokers, unknown/missing). We also created a variable for smoking duration (years) based on age started and stopped smoking and age at recruitment. A 6-level variable for alcohol intake was generated by combining data on drinking status and intensity (never, former, current infrequent (<3 times per month), current modest (<1 drink per day), current frequent (1 to 3 drinks per day), and current heavy (>3 drinks per day)). Body mass index (BMI) was categorized as <18.5, 18.5 to <25.0, 25.0 to <30.0, 30.0 to <35.0, and 35.0 kg/m². Self-reported race/ethnicity/ancestry was categorized as European, Asian (East and South), Black (African ancestry), mixed, other, and missing/unknown/no answer. Annual income was categorized as <£18,000, £18,000 to £30,999, £31,000 to £51,999, £52,000 to 100,000, > £100,000, and missing/no answer/unknown. We created an indicator variable for current employment in high-risk occupations/industries for lung cancer based on the Health and Safety Executive (HSE) 2012 report (Brown 2012) using 172 unique United Kingdom Standard Occupational Classification (SOC) 2000 occupation/industry codes that were derived via crosswalk with SOC 1990 codes.

Statistical Analyses

Main Analyses—Multivariable Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) of incident lung cancer in relation to: 1) commute mode and frequency adjusted for residential NO₂ quartiles in 2005, and 2) residential NO₂ quartiles in 2005 adjusted for commute mode and frequency. These models were further adjusted for age at recruitment (continuous), a sex-smoking cross-classification variable (reference: never-smoking women), smoking duration (years), self-reported race/ethnicity/ancestry (reference: European), study assessment center, BMI (reference: 18.5 to <25.0 kg/m²), annual income (reference: £18,000 to £30,999), commute distance (reference: <4.82 km), and alcohol intake (reference: never-drinker). Follow-up time (days; “time-on-study”) was used as the underlying timescale (Wong et al. 2020).

We also considered physical activity (days/week with >10 mins of moderate-vigorous activity), secondhand smoke (SHS) exposure, self-reported respiratory disease at/before baseline, and current employment in a high-risk occupation/industry for lung cancer as covariates in the model. However, they did not change the estimates >10% and a more parsimonious model was chosen.

The analyses were further stratified by sex (male, female), age (≥ and < median of 53 years), smoking status (ever- and never-smoking), NO₂ in 2005 (≥ and < median of 28.33 µg/m³),

length of time living at current residence (and < 25 years chosen based on evidence of approximate exposure-disease latency (Turner et al. 2020); and < median of 13 years), commute distance (> and median of 8.0 km), annual income (> and £30,999), and main job duration (> and 10 years). Multiplicative effect modification was tested using interaction terms. When testing for effect modification in the Cox regression models, smoking was categorized as ever vs. never and sex was analyzed as male vs. female. We tested for effect modification of the indicator variables for commute mode/frequency by: 1) ever vs. never smoking, 2) male vs. female, 3) ordinal categories of outdoor residential NO₂, and 4) continuous age. Additionally, we tested for effect modification of outdoor residential NO₂ by: 1) ever vs. never smoking, 2) male vs. female, 3) continuous age, 4) length at current residence, 5) commute distance, 6) income, and 7) job duration. Missing categorical data were handled in the analyses by classifying subjects with missing data in a separate categorical indicator variable.

Sensitivity Analyses—We also conducted a sensitivity analysis restricted to European participants to assess the influence of race/ethnicity/ancestry. Additionally, we restricted to those who reported not being exposed to SHS (<1 hour/week) and those who reported never having a history of respiratory diseases in separate analyses. To investigate the influence of occupational diesel exhaust on our findings, we excluded 870 participants who reported being often exposed at work at baseline, as well as 286 participants who reported being often exposed in all past jobs. We also conducted additional analyses with confirmed lung cancer histological subtypes (i.e., adenocarcinoma and SCC) as outcomes. Smoking duration is arguably the most consistent measure of tobacco-use related to lung cancer risk; however, we did not have complete data on smoking behavior (multiple starts and cessations) throughout the lifecourse. We conducted a sensitivity analysis excluding ever-smokers who reported quitting >6 month any time before baseline to evaluate its potential influence on lung cancer and smoking duration. Additionally, we restricted analyses to current smokers and stratified by median smoking duration (and <36 years) and separately by smoking intensity (and <20 cigs/day).

SAS version 9.4 (SAS Institute Inc) and the computational resources of the National Institutes of Health's (NIH) High-Performance Computing Biowulf cluster were used to conduct the analyses. P-values <0.05 were considered significant. To conservatively account for multiple comparisons, we indicated highly significant p-values below a Bonferroni adjusted alpha-threshold of 0.0026 (0.05/19 total tests) in the tables showing the commute-lung cancer results.

Results

Descriptive characteristics of the study population

The baseline characteristics of the study population are described in Table 1. The participants were currently employed and were 56.25 +/- 8.10 SD years on average. Most of these participants only used automobiles to commute (56.5%), while 8.3% only used public transportation. An estimated 2.2% only cycled to work and 5.0% only walked. Most participants were of European ancestry (93.39%), had upper-normal BMIs (25 to <30 kg/m²:

42.13%), and earned an annual income of £31,000 to £51,999 (28.67%). Most participants were never-smokers (57.38%) and were not considerably exposed to SHS (79.44%).

In 2005, the median annual average residential NO₂ concentration was 28.33 µg/m³ (IQR: 23.08–34.66). Further, the concentrations in 2006 and 2007 were 27.84 µg/m³ (IQR: 22.79–33.27) and 28.85 µg/m³ (IQR: 23.61–34.90), respectively (Table 1). The annual average NO₂ concentrations in 2005–2007 were highly consistent with intraclass correlations (ICC) >0.98. Therefore, we used NO₂ concentrations in 2005 for the main analyses.

The annual average residential NO₂ concentrations were highest among those who often only used public transportation (38.21 µg/m³ ±12.54 SD) and lowest among those who commuted regularly only by automobile (28.55 µg/m³ ±7.69 SD; Kruskal-Wallis test $p<0.0001$) (Supplementary Table 1). Most participants were considered residentially stable with a median length of time at the current residential address of 13.0 years (IQR: 7.0–22.0) and mean of 15.0 years ±11.7 SD. As such, we assumed that the residential NO₂ concentrations measured in 2005 reflected past levels in etiologic windows relevant to lung cancer development.

Associations between commute patterns and risk of lung cancer

There were 493 incident lung cancer cases diagnosed among 1.63 million person-years over an average 7-year follow-up (10-year maximum). Among the cases, the median time interval from baseline to lung cancer diagnosis was 3.5 years (IQR: 2.1–4.9).

Compared to regular automobile use, commuting often only by public transportation was associated with elevated lung cancer risk (HR=1.58, 95% CI: 1.08–2.33, $p=0.02$), adjusted for residential NO₂ and other potential confounders (Table 2). In the stratified analyses, the association was observed among ever-smokers (Table 3), men (Table 4), and participants living in high-NO₂ areas (Table 5).

The public transportation-lung cancer associations were modestly stronger among those who lived at their current residence for ≥13 years (HR=1.70, 95% CI: 1.04, 2.76, $p=0.03$); among those who lived at their current residence for <25 years (HR=1.62, 95% CI: 1.02, 2.56, $p=0.04$); and among those who earned £30,999 per year (HR=1.88, 95% CI: 1.12, 3.16, $p=0.02$) (full data not shown). Conversely, the main findings were similar, but not significant, among participants ≥53 years of age (Supplementary Table 2) and those with a commute ≥8.0 km (HR=1.67, 95% CI: 0.97, 2.87, $p=0.06$) (full data not shown).

There was evidence of multiplicative interactions between commuting often by public transportation and residential NO₂ (p -interaction=0.02) and sex (p -interaction= 4.0×10^{-3} with only 12 female cases who often used public transportation), but not smoking status (p -interaction=0.15) and age (p -interaction=0.70). Other categories of commuting were not associated with lung cancer risk (Table 2).

While the direction of the association with often using only public transportation was the same for overall lung cancer and lung adenocarcinoma, no associations were found with the histological subtypes. However, the case numbers for subtype analyses were limited (Supplementary Table 3). When the analyses were stratified by main job duration, the

magnitude of the estimates were generally consistent with the overall analyses (Supplementary Table 4), but similarly imprecise.

Excluding ever-smokers who reported ever quitting for >6 months before baseline did not considerably change the estimates (Supplementary Table 5). Among current smokers, the estimates for those who smoked <36 years and ≥36 years, and <20 cigs/day and ≥20 cigs/day were similar to estimates from the overall analyses; however, the case numbers in the strata were limited (Supplementary Table 6). Lastly, excluding those who reported often being exposed to occupational diesel engine exhaust did not affect the results (data not shown).

Associations between residential outdoor NO₂ and risk of lung cancer

We found a positive exposure-response relationship between residential NO₂ and lung cancer risk (p-trend=3.1×10⁻³) (Table 6). The association was driven by the highest quartiles of NO₂-exposure (HR_{Q2}=1.21, 95% CI:0.90–1.62; HR_{Q3}=1.48, 95% CI:1.10–1.99; HR_{Q4}=1.58, 95% CI:1.13–2.23) while mutually adjusted for commute patterns and other potential confounders. When analyzed as a continuous variable, each 10 µg/m³ increase in NO₂ was associated with a 1.02 (95% CI: 1.00–1.03, p=0.01) times increase in risk (Table 6).

The exposure-response relationship was apparent among participants who lived in their current residence <25 years (p-trend=5.2×10⁻³), but not ≥25 years (p-trend=0.26, p-interaction=0.12); which was similar when stratified by a median of 13 years (full data not shown). Further, the trend was apparent among those who commuted ≥8.0 km (p-trend=0.02), but not <8.0 km (p-trend=0.37, p-interaction=0.27) (full data not shown). We found some evidence for a positive interaction between NO₂ and ever-smoking (p=0.05).

Restricting the analyses to those of European ancestry, those who were not exposed to SHS, and those who reported not having respiratory diseases at/before baseline had little or no impact on the risk estimates for both commute patterns and NO₂ (data not shown).

Discussion

In our primary analyses, we found that commuting often and exclusively by public transportation was associated with increased lung cancer risk compared to regularly commuting only by automobile, among those residing in high-NO₂ areas and men. In our secondary analyses, we found a positive exposure-response relationship between residential NO₂ concentrations and lung cancer risk that was in agreement with previous meta-analyses of European studies (Hamra et al. 2015). There was some evidence that ever smoking strengthened the NO₂-lung cancer association, which was consistent with findings from a study of air pollution, smoking, and lung cancer mortality in the U.S. Cancer Prevention Study (CPS II) cohort (Turner et al. 2014). However, another study of particulate matter and lung cancer risk found stronger associations among never-smokers (Hamra et al. 2014). Taken together, our findings suggest that the elevated lung cancer risk found among those who often use public transportation could be enhanced by residing in areas with high NO₂ levels, which is a surrogate for levels of TRAP.

Several studies have found the highest concentrations of certain air pollutants (e.g., PM and black carbon) were in public transportation microenvironments (e.g., urban buses and subways), followed by automobiles, urban cycling and walking, and suburban walking (Karanasiou et al. 2014; Kaur et al. 2007; Moreno et al. 2015; Rivas et al. 2017). In particular, the higher particulate levels in public buses compared to automobiles in London, UK (Adams et al. 2001) and Dublin, Ireland (McNabola et al. 2008) are thought to be attributed to lower infiltration of particulates into automobile cabins or perhaps differences in fuel types. In contrast, some studies have found higher air pollutant concentrations in automobiles, followed by buses and other active commute modes (Cepeda et al. 2017). There is a high degree of variance between modes of travel and these trends can depend on many factors including the time of daily commute, season, city and country, route density, meteorological conditions, type of vehicle and the availability of air conditioning.

In a previous UK Biobank analysis, Celis-Morales et al. found that compared to non-active commuting, walking was associated with a lower risk of CVD incidence and mortality, while cycling was associated with the lowest risk of CVD incidence and mortality along with all-cause mortality and cancer (Celis-Morales et al. 2017). Similarly, the ONS Longitudinal Study of England and Wales (ONS-LS) found that compared to private motorized vehicles, bicycle commuting was associated with decreased all-cause, CVD, and overall cancer mortality (Patterson et al. 2020). Further, rail commuters had decreased all-cause mortality, CVD mortality, and risk of overall cancer in the ONS-LS. Our study differs in its study question and expands upon the previous work in distinct ways. First, we focused on incident lung cancer diagnosis rather than overall cancer because cancer is a collection of vastly different diseases, each with unique etiologies and risk factors. Second, we primarily focused on associations between commute mode and frequency and lung cancer risk, adjusted for residential NO₂. Third, the previous study combined automobile and public transportation into a single “non-active” commute reference group, whereas we separated them because air pollutant concentrations have been found to differ across commuting microenvironments (Karanasiou et al. 2014; Kaur et al. 2007; Lovett et al. 2018; Moreno et al. 2015; Rivas et al. 2017). Importantly, we were specifically interested in evaluating the main effects of public transportation use and other modes relative to automobile use.

A comprehensive meta-analysis of 20 cohort and case-control studies estimated a 4% increased risk of lung cancer associated with each incremental 10-μg/m³ increase in NO₂ overall (Hamra et al. 2015). The meta-effect was more prominent among North American (RR=1.07 (95% CI:1.01–1.14)) and Asian (RR=1.11 (95% CI:1.03–1.20)) studies, and marginally non-significant among European studies (RR=1.02 (95% CI:0.99, 1.06)). We found a exposure-response relationship between increasing NO₂ concentration and lung cancer risk of nearly the same magnitude observed among the previous study of Europeans (Hamra et al. 2015). NO₂ and other NO_x are not considered carcinogenic agents (Valavanidis et al. 2008). Rather, numerous investigations have considered these gases as surrogate markers for other carcinogenic pollutants that compose TRAP (Agency 1999; Brook et al. 2007; Curren et al. 2006; Ito et al. 2007).

Our study has numerous strengths. Most notably, this was one of the few epidemiologic studies of lung cancer to incorporate information on commute mode, frequency, and

distance, which are important factors that influence TRAP-exposure. The nationally representative ONS-LS has detailed commute data and long 25-year follow-up but focused on overall cancer incidence and mortality (Patterson et al. 2020). Additionally, the Shanghai Women's Health Study has rich lung cancer data and some commute data (Jurj et al. 2007), while the China Kadoorie Biobank has elements of these data but has yet to report lung cancer analyses (Fan et al. 2019). Second, the prospective study design supports temporality between the main exposures and lung cancer. Third, the sample size was large, which allows for deeper investigation with the stratified analyses. Lastly, we had extensive information on population density, measures of socioeconomic status, and smoking, which helps control for confounding.

Our study has limitations. First, we did not have more specific information on the types of public transportation. However, this exposure misclassification would result in conservative risk estimates. Second, the influence of air pollution on lung cancer development is often complicated by long induction periods between exposure and disease onset. We assumed that the participants' commute patterns and NO₂ levels around baseline were reflective of those in the past during the relevant etiologic window for lung cancer. Third, we had outdoor NO₂ concentrations at residential locations, but not along commute routes or workplaces. Therefore, TRAP exposures experienced while commuting are not explicitly addressed in our study. Fourth, we had limited information on other residential TRAP components. PM_{2.5} measurements started in 2010, a few years into the prospective follow-up in which many of the incident lung cancer cases had already occurred. Lastly, we did not have information on time spent commuting, a likely determinant of TRAP exposure. However, we accounted for commute distance, which is correlated with commute time within modes of travel.

In conclusion, our findings suggest that commuters who frequently used public transit could be at greater risk for lung cancer compared to commuters who regularly used automobiles. This increased risk could be further enhanced by residing in areas with high levels of NO₂, which is a surrogate measure of overall outdoor TRAP levels. However, caution is recommended when interpreting these results. We emphasize that NO₂ and TRAP levels experienced while commuting are not addressed in our study and can be largely different from NO₂ and TRAP levels at the place of residence, with some overlapping constituents. There are numerous global and public health benefits of public transit (Patterson et al. 2020). The overall health benefits of active travel may outweigh the risks related to air pollution exposure (Tainio et al. 2016). Our findings require replication and refinement to determine which, if any, component of public transportation use might be associated with lung cancer risk. It is important to explore further in a larger sample of never-smokers as well as smokers. Future studies would also benefit from assessing commute duration and personal TRAP exposure along travel routes and within transit microenvironments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank Michael Stagner at Information Management Services (IMS) for technical and programming support. We extend our appreciation to Erikka Loftfield and Neal Freedman (NCI) for their scientific input on smoking and lifestyle factors. Additionally, we thank Lesley Rushton (Imperial College London) and Sarah Locke (NCI) for their guidance on standardized occupational classification coding. We thank Abigail Flory (Westat) for ArcGIS cartography support. The computational resources of the National Institutes of Health's (NIH) High-Performance Computing Biowulf cluster were utilized.

Funding

This work was supported by the Intramural Research Program of the Division of Cancer Epidemiology and Genetics, National Cancer Institute. This research was conducted using resources from the UK Biobank (Application 28072). The UK Biobank was established by the Wellcome Trust, the Medical Research Council, the UK Department of Health, and the Scottish Government. The UK Biobank has also received funding from the Welsh Assembly Government, the British Heart Foundation, and Diabetes United Kingdom.

None of the authors were paid to write this article by a pharmaceutical company or other agency. All authors had full access to the full data in the study and accept responsibility to submit for publication.

Data availability

Data are publicly available at: <https://www.ukbiobank.ac.uk/register-apply/>

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Highlights

- Traffic-related air pollution (TRAP) is a complex mixture of carcinogenic components from motor vehicle emissions and is a lung cancer risk factor.
- Commuting to work is a major source of TRAP exposure for millions of people worldwide.
- In the UK Biobank prospective cohort study, we are the first to report that commuters residing in high-NO₂ areas who often use public transportation (i.e., buses, subways, light rail) have elevated lung cancer risk compared to automobile users.
- Our findings have the potential to inform policies pertaining to urban planning and development.

Figure 1:
UK Biobank study sample and exclusion criteria

Figure 2:
Density heat-map of the study populations' residences in the United Kingdom based on north and east grid coordinates (1 km² resolution), generated using ArcGIS

Table 1:**Baseline Study Population Characteristics in the UK Biobank (n=234,124)**

Commute type and frequency (regular: 1–4, often: 5 work-bound trips/week), n, %		
Automobile only, regular	39,140	(16.72)
Automobile only, often	93,204	(39.81)
Walk only, regular	3,677	(1.57)
Walk only, often	7,964	(3.40)
Public transportation only, regular	5,935	(2.53)
Public transportation only, often	13,598	(5.81)
Cycle only, regular and often	5,114	(2.18)
Active mixture of walking and cycling, regular and often	8,405	(3.59)
Other mixture, regular and often	16,969	(7.25)
Unknown, missing, no answer	40,118	(17.13)
Commute distance (km), median, IQR	9.65	(9.65–19.31)
Outdoor residential NO ₂ concentration, annual average (µg/m ³), median, IQR		
2005	28.33	(23.08, 34.66)
2006	27.84	(22.79, 33.27)
2007	28.85	(23.61, 34.90)
ONS-defined urban density of residential location, n, %		
England/Wales - Urban - sparse	2	(0.0009)
England/Wales - Urban - less sparse	202,004	(86.28)
England/Wales - Town and Fringe - less sparse	15,858	(6.77)
Scotland - Large Urban Area	13,672	(5.83)
Scotland - Other Urban Area	2,588	(1.10)
Study Assessment Center, n, %		
Stockport	278	(0.12)
Manchester	7,429	(3.17)
Oxford	6,432	(2.75)
Cardiff	8,992	(3.84)
Glasgow	8,909	(3.80)
Edinburgh	7,350	(3.14)
Stoke	84,450	(3.61)
Reading	14,202	(6.07)
Bury	13,153	(5.62)
Newcastle	16,984	(7.25)
Leeds	21,082	(9.00)
Bristol	20,381	(8.70)
Barts	7,041	(3.01)
Nottingham	14,976	(6.40)
Sheffield	13,317	(5.69)
Liverpool	14,594	(6.23)
Middlesbrough	8,568	(3.66)

	Hounslow	14,865 (6.35)
	Croydon	13,959 (5.96)
	Birmingham	12,074 (5.16)
	Swansea	834 (0.36)
	Wrexham	254 (0.11)
Age at recruitment, years, mean, SD		50.2 (8.1)
Genetic Sex, n, %		
	Female	118,489 (50.01)
	Male	115,035 (49.39)
Self-Reported Race/Ethnicity/Ancestry, n, %		
	European	218,053 (93.39)
	Black, African	4,599 (1.90)
	Asian, East and South	0,170 (2.04)
	Mixed	1,008 (0.71)
	Other	2,317 (0.99)
	Unknown, missing, no answer	711 (0.30)
Body Mass Index, BMI, kg/m ² , n, %		
	<18.5	900 (0.41)
	18.5 - <25	70,377 (32.02)
	25 - <30	98,044 (42.13)
	30 - 35	39,948 (17.00)
	35	15,129 (0.40)
	Missing	3,000 (1.31)
Currently employed in high-risk occupation/industry for lung cancer, n, %		114,080 (48.98)
Annual Income, n, %		
	<£18000	22,800 (9.74)
	£18000 to £30999	47,050 (20.10)
	£31000 to £51999	07,121 (28.07)
	£52000 to £100000	59,022 (25.47)
	>£100000	14,929 (0.38)
	Missing/no answer/do not know	22,590 (9.05)
Sex-smoking status cross-classification, n, %		
	Female, never-smoker	72189 (30.83)
	Female, former-smoker	34,808 (14.89)
	Female, current-smoker	11,013 (4.70)
	Female, cigar-smoker	85 (0.04)
	Male, never-smoker	02,143 (20.54)
	Male, former-smoker	37,359 (15.90)
	Male, current-smoker	13,152 (5.02)
	Male, cigar-smoker	2,054 (1.13)
	Unknown/missing	001 (0.28)
Secondhand smoke exposure at home or outside, n, %		
	Unexposed (<1 hour/week)	185,993 (79.44)

	Exposed (1 hour/week)	48,131 (20.50)
History of respiratory disease, n, %	No	200,018 (88.00)
	Yes	28,100 (12.00)
Alcohol Consumption, n, %	Never	8,273 (3.53)
	Former	0,427 (2.74)
	Current, <3 drinks/month	51,709 (22.09)
	Current, <1 drink/day	59,087 (25.24)
	Current, 1–3 drinks/day	87,967 (37.57)
	Current, >3 drinks/day	20,394 (8.71)
	Missing	267 (0.11)
Time to diagnosis of incident lung cancer, years, median, IQR		3.5 (2.1–4.9)

Table 2:

Commute patterns and risk of incident lung cancer in the UK Biobank

	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value
Automobile only, regular (Reference)	78	39140	272768	1.00	-	-	-
Automobile only, often	202	93204	655529	1.26	0.96	1.64	0.10
Public transportation only, regular	10	5935	39999	0.71	0.37	1.39	0.32
Public transportation only, often	44	13598	92144	1.58	1.08	2.33	0.02 *
Walk only, regular	14	3677	25427	1.58	0.87	2.88	0.13
Walk only, often	19	7964	55933	1.14	0.67	1.95	0.63
Cycle only, regular and often	5	5114	36244	0.78	0.31	1.95	0.59
Active mixture, regular and often	14	8405	58790	1.10	0.61	1.99	0.74
Other mixture, regular and often	28	16969	117377	1.05	0.68	1.62	0.83
Unknown, missing, no answer	79	40118	277823	1.04	0.72	1.49	0.84

* P-values <0.05.

** P-values below a Bonferroni adjusted alpha-threshold of 0.0026. Analyses were restricted to currently working participants. Travel frequency: regular: 1–4, often: 5 work-bound trips/week. II) Cox regression model was adjusted for average annual residential NO₂, age, sex-smoking status, smoking duration, study site, race/ethnicity, body mass index, alcohol, income, and commute distance. Abbreviations: Hazard Ratio (HR), Confidence Intervals (CI). There were 17,111 employed participants, including 33 lung cancer cases, who reported commuting zero times a week and did not report commute mode. These participants were assigned to the missing/unknown/no answer indicator category.

Table 3:

Commute patterns and risk of incident lung cancer among ever- and never-smokers of the UK Biobank

	I) Ever-Smokers					II) Never-Smokers				
	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years
Automobile only, regular (Reference)	58	16342	113781	1.00	-	-	-	20	22798	158987
Automobile only, often	176	40557	284718	1.41	1.04	1.92	0.03	* 26	52647	370811
Public transportation only, regular	8	2535	17034	0.73	0.35	1.55	0.42	2	3400	22965
Public transportation only, often	39	5851	39634	1.76	1.15	2.69	0.01	* 5	7747	52510
Walk only, regular	11	1517	10505	1.52	0.77	2.99	0.22	3	2160	14922
Walk only, often	17	3332	23396	1.20	0.68	2.14	0.53	2	4632	32538
Cycle only, regular and often	2	2150	15190	0.41	0.10	1.71	0.22	3	2964	21054
Active mixture, regular and often	13	3214	22473	1.36	0.73	2.54	0.33	1	5191	36317
Other mixture, regular and often	22	6792	46769	1.13	0.69	1.85	0.64	6	10177	70608
Unknown, missing, no answer	59	17502	121129	0.93	0.61	1.40	0.72	20	22616	156694

* P-values <0.05.

** P-values below a Bonferroni adjusted alpha-threshold of 0.0026. Analyses were restricted to currently working participants living. There were 405 lung cancer cases among 99,792 ever-smokers and 88 cases among 134,332 never-smokers. Travel frequency: regular: 1–4, often: 5 work-bound trips/week. Cox regression model was adjusted for average annual residential NO₂, age, sex, study site, race/ethnicity, body mass index, alcohol, income, and commute distance. Ever-smokers were further adjusted for smoking duration. Abbreviations: Hazard Ratio (HR), Confidence Intervals (CI).

Table 4:
Commute patterns and risk of incident lung cancer among men and women of the UK Biobank

	I) Men							II) Women						
	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value
Automobile only, regular (Reference)	31	13734	95550	1.00	-	-	-	47	25406	177218	1.00	-	-	-
Automobile only, often	135	54195	380743	1.48	0.99	2.20	0.06	67	39009	274786	1.07	0.73	1.57	0.72
Public transportation only, regular	3	1947	12958	0.71	0.22	2.35	0.57	7	3988	^27041	0.69	0.31	1.55	0.37
Public transportation only, often	32	6159	41466	2.51	1.49	4.22	5.4x10 ⁻⁴	** 12	7439	50678	0.78	0.40	1.49	0.44
Walk only, regular	4	662	4586	2.48	0.84	7.35	0.10	10	3015	20841	1.30	0.62	2.70	0.48
Walk only, often	8	2989	20997	1.42	0.62	3.26	0.40	11	4975	34936	0.96	0.47	1.94	0.90
Cycle only, regular and often	2	3411	24046	0.51	0.12	2.15	0.36	3	1703	12198	1.36	0.41	4.50	0.62
Active mixture, regular and often	4	2538	17838	1.06	0.37	3.09	0.91	10	5867	40953	1.06	0.52	2.16	0.88
Other mixture, regular and often	9	7815	53916	0.78	0.37	1.65	0.52	19	9154	63461	1.24	0.72	2.12	0.44
Unknown, missing, no answer	44	22185	153644	1.07	0.64	1.81	0.79	35	17933	124179	1.06	0.63	1.76	0.84

* P-values <0.05.

** P-values below a Bonferroni adjusted alpha-threshold of 0.0026. Analyses were restricted to currently working participants. Travel frequency: regular:1-4, often: 5 work-bound trips/week. Cox regression model was adjusted for average annual residential NO₂, age, smoking status and duration, study site, race/ethnicity, body mass index, alcohol, income, and commute distance. Abbreviations: Hazard Ratio (HR), Confidence Intervals (CI).

Commute patterns and risk of incident lung cancer among residences with high and low outdoor NO₂ concentrations in the UK Biobank

Table 5:

	D) High NO ₂ residences (>28.33 µg/m ³)						II) Low NO ₂ residences (<28.33 µg/m ³)							
	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value
Automobile only, regular (Reference)	35	17758	122459	1.00	-	-	-	43	21382	150309	1.00	-	-	-
Automobile only, often	114	45708	318514	1.44	0.98	2.12	0.07	88	47496	337016	1.12	0.77	1.64	0.55
Public transportation only, regular	6	4246	27976	0.70	0.29	1.68	0.43	4	1689	12023	0.88	0.31	2.47	0.81
Public transportation only, often	40	10389	68982	2.23	1.40	3.57	8.2x10 ⁻⁴	** 4	3209	23162	0.53	0.19	1.50	0.23
Walk only, regular	9	2292	15739	1.79	0.83	3.85	0.14	5	1385	9688	1.46	0.54	3.91	0.45
Walk only, often	13	5412	37749	1.22	0.62	2.40	0.56	6	2552	18184	1.24	0.50	3.09	0.65
Cycle only, regular and often	3	3397	23357	0.78	0.24	2.59	0.69	2	1717	12887	0.90	0.21	3.87	0.89
Active mixture, regular and often	7	4816	33498	1.05	0.46	2.42	0.91	7	3589	25292	1.28	0.55	2.95	0.57
Other mixture, regular and often	17	9825	66499	1.20	0.67	2.15	0.54	11	7144	50878	0.94	0.48	1.83	0.86
Unknown, missing, no answer	57	24346	165313	1.36	0.85	2.19	0.20	22	15772	112510	0.73	0.40	1.34	0.31

* P-values <0.05.

** P-values below a Bonferroni adjusted alpha-threshold of 0.0026. Analyses were restricted to currently working participants. Travel frequency: regular: 1-4, often: 5 work-bound trips/week. Cox regression model was adjusted for continuous age, sex-smoking status, smoking duration, study site, race/ethnicity, body mass index, alcohol, income, and commute distance. Abbreviations: Hazard Ratio (HR), Confidence Intervals (CI).

Table 6:

Traffic-related air pollution as reflected by annual average residential NO₂ concentrations and risk of incident lung cancer in the UK Biobank

Annual average residential NO ₂ concentration in 2005, $\mu\text{g}/\text{m}^3$	No. incident lung cancer cases	Total No. of Subjects	Cumulative person-years	HR	95%CI Lower	95%CI Upper	p-value
Q1, <23.08	70	44622	315803	1.00			
Q2, >23.08 to 28.33	122	61313	436147	1.21	0.90	1.62	0.21
Q3, >28.33 to 34.66	153	62967	444468	1.48	1.10	1.99	9.2×10^{-3} *
Q4, >34.66	148	65222	435618	1.58	1.13	2.23	8.3×10^{-3} *
Continuous, per 10 $\mu\text{g}/\text{m}^3$ increase	493	234124	1632035	1.02	1.00	p-trend 1.03	3.1×10^{-3} *
							0.01 *

* P-values <0.05. Analyses were restricted to currently working participants. Cox regression model was adjusted for commute mode, frequency, and distance, along with age, sex-smoking status, smoking duration, study site, race/ethnicity, body mass index, alcohol, and income. Abbreviations: Hazard Ratio (HR), Confidence Intervals (CI), Quartile (Q).