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Neighbourhood deprivation and lung cancer risk: a nested case–control study in the USA

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ABSTRACT

Objectives To examine the association between neighbourhood deprivation and lung cancer risk.

Design Nested case–control study.

Setting Southern Community Cohort Study of persons residing in 12 states in the southeastern USA.

Participants 1334 cases of lung cancer and 5315 controls.

Primary outcome measure Risk of lung cancer.

Results After adjustment for smoking status and other confounders, and additional adjustment for individual-level measures of socioeconomic status (SES), there was no monotonic increase in risk with worsening deprivation score overall or within sex and race groups. There was an increase among current and shorter term former smokers (p=0.04) but not among never and longer term former smokers. There was evidence of statistically significant interaction by sex among whites, but not blacks, in which the effect of worsening deprivation on lung cancer existed in males but not in females.

Conclusions Area-level measures of SES were associated with lung cancer risk in current and shorter term former smokers only in this population.

INTRODUCTION

Cigarette smoking is the predominant cause of lung cancer, but additional environmental factors may contribute to risk and be amenable to detection via examination of geographic patterns of cancer in relation to neighbourhood economic indices. Although lung cancer rates have decreased over time in the USA, from 2010 to 2014, the age-adjusted incidence rate was 55.8 per 100 000, and the comparable death rate was 44.7 per 100 000.[1] Our prior work identified lung cancer mortality hot spot maps within US counties from the 1980s to 2009.[2 3] The greatest concentration occurred across southeastern states and varied by sex and race. These distinct geographic patterns of lung cancer mortality may be indicating different exposures and/or causal pathways. Analyses of county-level data showed positive associations between lung cancer mortality and smoking,

Strengths and limitations of this study

► Large size and diversity of cohort under observation enhancing our ability to detect trends.
► Adjustment for individual-level smoking status using several dimensions of smoking exposure history.
► Use of the Nam-Powers-Boyd occupational status score as a measure of individual-level socioeconomic status.
► Neighbourhood deprivation index was developed at the census tract level rather than the block group level, but smaller block groups should be more homogenous and span a wider range of values.
► Inability to completely rule out residual confounding by smoking suggesting caution in interpretation of the study findings.

poverty, coronary heart disease mortality and National Air Toxics Assessment excess cancer deaths.[4]

The present analysis focuses on poverty that may be present at the individual level and/or at the area level. Krieger *et al*[5] postulated that area-level socioeconomic status (SES) may be a more comprehensive measure of SES than individual-level SES, because it captures social characteristics of communities that are not typically measured. A meta-analysis of 64 studies of individual-level measures of socioeconomic position (SEP) and lung cancer incidence reported significantly increased risk for lowest versus highest educational SEP (relative risk (RR) 1.61, 95% CI 1.40 to 1.85), occupational SEP (RR 1.48, 95% CI 1.34 to 1.65) and income-based SEP (RR 1.37, 95% CI 1.06 to 1.77).[6] Few studies have examined lung cancer incidence associated with area-level measures of SES alone[7 8] or in combination with individual-level measures of SES,[9–11] and only one of these studies has been conducted in the USA.[12]

We performed a multilevel nested case–control study of lung cancer incidence within the prospective Southern Community Cohort Study (SCCS) to examine the association

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between area-level neighbourhood deprivation together with smoking and other individual-level risk factors. We hypothesised that area-level socioeconomic deprivation would be positively associated with lung cancer, independently of smoking, and other individual-level risk factors. In addition, we hypothesised this positive association would persist after control for individual-level measures of SES. Given our prior findings for lung cancer mortality,[2][3] we also hypothesised that these associations would differ by sex and race. Lastly, we hypothesised that these associations would differ by smoking status since lung cancer death is markedly lower 10 years after quitting,[13] and the lung cancer screening guidelines use a cut-off of 15 years since quitting smoking.[14]

METHODS
Detailed methods of the SCCS[15] appear elsewhere. Briefly, the SCCS is comprised of 9842 white men and 15 463 white women, 22 905 black men and 32 457 black women, and 1566 men of other races and 2564 women of other races in 12 southeastern states aged 40–79 years who completed a baseline questionnaire between 2002 and 2009. Men and women were primarily low-income with the majority (86%) enrolled in person at community health centres and the remaining men and women randomly sampled from the general population. Depending on the enrolment site, in-person interviews or mailed questionnaires were completed. After enrolment, 1395 persons with incident lung cancer were identified through linkage with state cancer registries and the National Death Index. Information on lung cancer histology (squamous cell carcinoma, adenocarcinoma, small cell carcinoma, large cell carcinoma and other) was collected from the cancer registries. Approximately four controls were chosen by incidence density sampling and matched to each case on sex, race, age at diagnosis (±2 years increased to ±5 years if necessary), enrolment source (community health centre and general population) and year of recruitment for a total of 5580 controls. Controls were not matched to cases on recruitment site to avoid overmatching on residence. Exclusions included races other than white or black, and unknown neighbourhood deprivation index resulting in 1334 cases and 5315 controls for analysis.

In this multilevel nested case–control study, baseline surveys collected information on individual-level lung cancer risk factors including smoking status, total exposure to secondhand smoke, chronic obstructive pulmonary disease (COPD) and SES. Smoking status was categorised as never, former and current; within former was further stratified as time since last smoked, and current was categorised using number of cigarettes smoked per day as characterised by Blot et al.[16] The number of hours participants reported they were around the cigarette smoke of other people at home and at other indoor places including work was totaled and categorised as none and using tertiles among controls reporting more than none. COPD was identified using International Classification

of Diseases, Ninth Rivision, Clinical Modification (ICD9) codes from Medicaid or Medicare reports[17] and using self-report for the 1877 (28.2%) of cases and controls who were not enrolled in Medicaid or Medicare. Our decision to use claims data for the majority of participants was based on the finding of substantial under-reporting of COPD among those with claims data. Individual-level measures of SES included annual household income, education level, health insurance coverage and the Nam-Powers-Boyd (NPB) occupational status score,[18] which was defined using quartiles among controls. The NPB occupational status score was developed from the 2000 US Census as a measure of SES of occupations and ranged from 1 to 100 reflecting the lowest to highest socioeconomic standing. The score was based on responses to a question about the longest job held during adulthood in which we scored each occupation and used the average score within 20 distinct categories.

A multistage approach that included automated and interactive processes was used to maximise success of geocoding SCCS participants' addresses at baseline and follow-up.[19] A total of 99.96% of participant addresses have been geocoded with only 5.2% at the ZIP code centroid level (2.8% post office box and 2.3% non-post office box addresses). SCCS staff used Federal Information Processing Standard codes for geocoded participant addresses to link individual-level SCCS data with area-level data on deprivation detailed below. Information on neighbourhood deprivation was updated with each follow-up. However, participants' residence at study baseline was used for area-level data since nearly 65% of persons had identical neighbourhood deprivation index levels during follow-up. Values for the 35% of participants who had different neighbourhood deprivation index values at baseline and follow-up were somewhat more likely to become more deprived than less deprived (n=861 more deprived, n=610 less deprived). However, of those who became more deprived, there was no difference between cases and controls (cases n=115, mean change 0.99, SD 0.82; controls n=746, mean change 1.00, SD 0.86).

Information from the 2000 Census[20] for geocoded addresses was determined by spatial join to TIGER/Line Shapefiles[21] using ESRI ArcMap software (ESRI, Redlands, California, USA). Using formulas developed by Messer et al[22] and principal components analysis, Signorello et al[23] developed a neighbourhood deprivation index at the census tract level for SCCS participants comprising the following constructs: education, employment, occupation, housing and poverty. The 11 characteristics chosen from the Census to represent neighbourhood SES included: percentage of persons that did not graduate high school (age ≥25 years), percentage of males and females who are unemployed, percentage of males in professional occupations, percentage of housing units with ≥1 occupant per room, percentage of occupied housing units with renter/owner costs >50% of income, percentage of persons with income below the 1999 poverty status, percentage of female headed households

with dependent children, percentage of households with income <$30 000 per year, percentage of households with public assistance income, percentage of households with no car and median household value. Increasing values of neighbourhood deprivation index reflect increasing levels of deprivation. We used neighbourhood deprivation index at the block group level rather than the census tract level as used by Signorello *et al*[23] as has been recommended by Krieger *et al*.[5] Our index ranged from −2.29 to 5.88 and was modelled as quartiles among controls overall and within sex and race since there was no evidence of linearity based on likelihood ratio tests and cubic splines.

Statistical analyses were performed in SAS V.9.4. Conditional logistic regression was used to estimate the OR and 95% CI of lung cancer associated with area-level neighbourhood deprivation while accounting for effect modification and adjusting for confounding.[24] Effect modification by sex, race and smoking status was examined by adding product terms of the dichotomous exposure (upper two vs lower two quartiles among controls) and dichotomous putative effect modifiers to logistic regression models and performing likelihood ratio tests (p<0.1 provided evidence of statistically significant interaction). Smoking status was dichotomised as current and former smokers within 15 years since quitting (shorter term former smokers) and never smokers and former smokers who quit more than 15 years ago (longer term former smokers). There was evidence of effect modification of these associations by sex in whites but not in blacks and not by race. Nevertheless, we stratified by sex–race categories (205 white male cases, 492 black male cases, 276 white female cases, 361 black female cases, 817 white male controls, 1958 black male controls, 1097 white female controls and 1443 black female controls) since our findings on lung cancer mortality suggested distinct geographic patterns depending on sex and race. Nor was there evidence of effect modification by smoking status, but we stratified by smoking status since it is strongly related to neighbourhood deprivation and lung cancer risk.

Potential confounders of the association between neighbourhood deprivation and lung cancer included: age, annual household income, number of household members, education level, enrolment source, health insurance coverage, NPB occupational status score,[18] urban/rural residence defined as metro or nonmetro county using 2003 rural–urban continuum codes,[25] time at current residence, perceived indoor and outdoor air quality, family history of lung cancer, smoking status (in seven categories), total exposure to secondhand smoke, alcohol intake, COPD and lifetime maximum body mass index (BMI) as categorised in supplementary table 1. χ^2 tests were performed to assess statistically significant (two sided, p<0.05) differences between lung cancer cases and controls. Variables were considered confounders if their addition to the models changed the unadjusted OR by 10% or more. We adjusted for smoking status, COPD and total exposure to secondhand smoke, which met our criteria for model inclusion, and additionally adjusted for annual household income, education level, health insurance coverage and NPB occupational status score as measures of individual-level SES. Tests for trend across quartiles of exposure were performed by entering categorical variables as ordered categorical variables in the model.

We chose not to use multilevel modelling because relatively few participants were clustered within block groups. Of the 4084 block groups in the study, over two-thirds (67.7%) included one participant (85.8% cases, 70.7% controls), 16.4% included two participants (10.1% cases, 15.7% controls), 7.4% included three participants (2.2% cases, 7.2% controls), 3.8% included four participants (1.1% cases, 3.2% controls) and 4.7% included five or more participants (0.8% cases, 3.2% controls). Clarke[26] cautions against the use of multilevel modelling with fewer than five observations per group, which results in unreliable etimates.

Patient and public involvement
Neither patients nor the public were involved in development of the research question, study design, patient recruitment or study conduct; however, an annual newsletter is sent to study particicipants as a means of disseminating results.[27]

RESULTS
Online supplementary table 1 presents demographic and other characteristics of lung cancer cases and controls by sex and race. In comparison with controls, lung cancer cases across both sexes and races tended to have the following characteristics: lower household income, lower education level, Medicaid/Medicare, current smokers, exposed to secondhand smoke, COPD and lower maximum BMI. All cases other than white males tended to have a shorter time at current residence and to drink alcohol. White male and female cases tended to have lower NPB occupational status scores and to have a family history of lung cancer. Black male and female cases tended to have an urban residence. White and black female cases tended to have poor or fair indoor and outdoor air quality.

Table 1 presents ORs for the association between quartiles of neighbourhood deprivation index and lung cancer among all cases and controls and stratified by sex and race. After adjustment for smoking status and other confounders, and additional adjustment for annual household income, education level, health insurance coverage and NPB occupational status score, there was no monotonic increase in risk with worsening deprivation score overall or within sex and race groups. Black men in the third quartile of neighbourhood deprivation were at significantly increased risk of lung cancer relative to black men in the lowest quartile before (OR 1.52, 95% CI 1.08 to 2.14) and after (OR 1.49, 95% CI 1.05 to 2.12) adjustment

Table 1 OR for lung cancer associated with neighbourhood deprivation overall and stratified by sex and race, Southern Community Cohort Study, 2002–2009

Characteristic	Cases N	Controls N	OR* (95% CI)	P for interaction	OR† (95% CI)	P for interaction
			Overall			
Deprivation						
Quartile 1	272	1329	1.00 (referent)		1.00 (referent)	
Quartile 2	342	1329	1.08 (0.87 to 1.35)		1.08 (0.86 to 1.35)	
Quartile 3	314	1330	0.98 (0.78 to 1.23)		0.93 (0.73 to 1.18)	
Quartile 4	406	1327	1.25 (0.99 to 1.58)		1.16 (0.91 to 1.47)	
P for trend			0.09		0.39	
			White males			
Deprivation						
Quartile 1	37	206	1.00 (referent)		1.00 (referent)	
Quartile 2	38	202	0.68 (0.37 to 1.27)		0.65 (0.33 to 1.28)	
Quartile 3	66	203	1.37 (0.79 to 2.38)		1.43 (0.78 to 2.62)	
Quartile 4	64	206	1.27 (0.73 to 2.20)		1.26 (0.67 to 2.38)	
P for trend			0.12		0.11	
			Black males			
Deprivation				0.40‡		0.29‡
Quartile 1	103	490	1.00 (referent)		1.00 (Referent)	
Quartile 2	104	489	1.16 (0.82 to 1.64)		1.14 (0.80 to 1.63)	
Quartile 3	151	489	1.52 (1.08 to 2.14)		1.49 (1.05 to 2.12)	
Quartile 4	134	490	1.33 (0.95 to 1.87)		1.26 (0.89 to 1.79)	
P for trend			0.05		0.11	
			White females			
Deprivation				0.05§		0.04§
Quartile 1	53	274	1.00 (referent)		1.00 (Referent)	
Quartile 2	71	275	1.04 (0.63 to 1.72)		0.92 (0.54 to 1.58)	
Quartile 3	77	275	0.99 (0.61 to 1.61)		1.04 (0.62 to 1.73)	
Quartile 4	75	273	0.89 (0.54 to 1.47)		0.76 (0.44 to 1.30)	
P for trend			0.60		0.41	
			Black females			
Deprivation				0.38¶		0.44¶
				0.14**		0.11**
Quartile 1	79	361	1.00 (referent)		1.00 (Referent)	
Quartile 2	79	361	0.75 (0.48 to 1.17)		0.65 (0.41 to 1.04)	
Quartile 3	80	356	0.70 (0.46 to 1.09)		0.63 (0.40 to 1.00)	
Quartile 4	123	365	1.04 (0.69 to 1.57)		0.89 (0.57 to 1.38)	
P for trend			0.75		0.76	

*ORs and CI adjusted for smoking status, chronic obstructive pulmonary disease and exposure to secondhand smoke
†ORs and CI adjusted for smoking status, chronic obstructive pulmonary disease, exposure to secondhand smoke, annual household income, education level, health insurance coverage and NPB occupational status score.
‡P for interaction comparing white males with black males.
§P for interaction comparing white males with white females.
¶P for interaction comparing white females with black females.
**P for interaction comparing black males with black females.

for individual-level measures of SES. There was evidence of statistically significant interaction by sex among whites, but not blacks, in which the effect of worsening deprivation existed in males but not among females.

Table 2 presents ORs for the association between quartiles of neighbourhood deprivation index and lung cancer stratified by smoking status. After adjustment for smoking status and other confounders, but prior to adjustment

Table 2 OR for lung cancer associated with neighbourhood deprivation stratified by smoking status at baseline, Southern Community Cohort Study, 2002–2009

Characteristic	Cases N	Controls N	OR* (95% CI)	P for interaction	OR† (95% CI)	P for interaction
			Never and former smokers ≥15 years			
Deprivation						
Quartile 1	34	683	1.00 (referent)		1.00 (referent)	
Quartile 2	39	684	1.10 (0.59 to 2.08)		1.10 (0.55 to 2.21)	
Quartile 3	37	686	1.09 (0.56 to 2.13)		1.13 (0.54 to 2.37)	
Quartile 4	46	680	1.45 (0.73 to 2.90)		1.32 (0.62 to 2.81)	
P for trend			0.30		0.48	
			Current and former smokers <15 years			
Deprivation				0.23‡		0.29‡
Quartile 1	263	625	1.00 (referent)		1.00 (referent)	
Quartile 2	308	627	1.14 (0.89 to 1.45)		1.14 (0.89 to 1.46)	
Quartile 3	300	625	1.36 (1.05 to 1.76)		1.31 (1.00 to 1.70)	
Quartile 4	287	626	1.29 (0.99 to 1.68)		1.19 (0.91 to 1.57)	
P for trend			0.04		0.17	

*OR and CI adjusted for chronic obstructive pulmonary disease and exposure to secondhand smoke.
†OR and CI adjusted for chronic obstructive pulmonary disease, exposure to secondhand smoke, annual household income, education level, health insurance coverage and NPB occupational status score.
‡P for interaction comparing never and former smokers ≥15 years with current and former smokers <15 years.
NPB, Nam-Powers-Boyd.

for annual household income, education level, health insurance coverage and NPB occupational status score, there was a monotonic increase in risk with worsening deprivation score among current and short-term former smokers (p=0.04) but not among never and longer term former smokers. Current and short-term former smokers in the third quartile of neighbourhood deprivation were at significantly increased risk of lung cancer relative to black men in the lowest quartile before (OR 1.36, 95% CI 1.05 to 1.76) adjustment for individual-level measures of SES. There was no evidence of effect modification by smoking status with or without adjustment for individual-level measures of SES.

DISCUSSION
We found no significantly increased risk of lung cancer associated with greatest neighbourhood deprivation after tight control of smoking overall or within sex and race groups, with a modest attenuation in the association after further adjustment for individual-level SES measures. Similar analyses performed in a more heterogeneous population may differ since the individual-level SES of our population was fairly homogeneous. Most participants reported an annual household income of less than $25 000 (60.0% white males, 80.3% black males, 74.5% white females and 81.3% black females) (supplementary table 1). However, a previous analysis of the SCCS found similar positive associations between neighbourhood deprivation and death due to cardiovascular disease,

non-malignant diseases and cancer, while positive associations for individual-level SES were restricted to death from cardiovascular disease and non-malignant diseases.[23] The authors postulated there may be 'neighborhood environmental influences on cancer risk above those associated with low SES'.

The somewhat elevated lung cancer risk among those living in the most deprived neighbourhoods was only seen in men, with a significant interaction by sex in whites but not in blacks. A recent review of 36 studies reported that the impact of individual and area level SES on all health outcomes except heart disease was greater for men than for women.[28] Geronimus et al[29] studied telomere length as a measure of biological ageing due to stress and found that poor whites had shorter telomeres than non-poor whites, which was not the case for blacks or Mexicans. They surmised that some whites may be more affected by socioeconomic difficulties. In a study of early-stage non-small cell lung cancer conducted in Georgia among patients with higher neighbourhood deprivation, blacks were more likely to die but whites were not, even after controlling for surgery.[30] These authors posited that blacks and whites may experience area-level poverty differently, resulting in different impacts on adverse health outcomes. Our cross-sectional observations might therefore have been influenced by differences in cohort effects which, in turn, could have reflected initial levels rather than magnitudes of deprivation change according to sex and race.

There was an increased trend of lung cancer among current and shorter term formers smokers that no longer existed after additional adjustment for individual-level measures of SES. Other studies have tended to find increased lung cancer risks associated with lower area-level SES, some without adjustment for smoking,[8 9 12] and others with weakened associations after smoking adjustment.[7 10 11] While the approximate 20%–30% increases in risk we find are small in comparison with the 1000% or greater increased risks we and others find among cigarette smokers,[16] these increased risks may be signalling the existence of neighborhood-related environmental exposures, social factors and/or behaviours correlated with where one lives that influence lung cancer risk.

Elevated age-adjusted lung cancer mortality rates have been observed in the southern USA for nearly five decades, with the excesses first becoming apparent in seaboard areas where ship manufacturing was common during World War II and then with high rates spreading across inland areas as smoking prevalence became higher in southern states than elsewhere in the USA.[2 3 31] Much of the excess risk of lung cancer is attributable to the region's higher prevalence of smoking, which has continued to the present[32] but contributory roles of other environmental factors are possible. The SCCS provided the opportunity to examine associations between social deprivation, as measured by socioeconomic indices recorded by the US Census Bureau for small area neighbourhoods, and individual-level education, income and occupational status, with risk of incident lung cancer. The SCCS population was particularly appropriate for such an analysis because many cohort participants were recruited from disadvantaged, underserved neighbourhoods where deprivation levels would be high. The study also enabled adjustment for smoking and other potential risk factors ascertained through detailed interviews and questionnaires completed by participants.

A potential limitation of our study is the neighbourhood deprivation index we used was developed at the census tract level rather than at the block group level.[23] However, use of block group-level neighbourhood deprivation rather than census tract-level neighbourhood deprivation has been recommended by others,[5] and the smaller block groups should be more homogenous and span a wider range of values enhancing our ability to detect trends. Another limitation is the use of a single-level analysis that did not account for random effects and was more prone to type I error even with limited data clustering.[26] A potentially more important limitation is our inability to completely rule out residual confounding by smoking. Smoking is strongly related to lung cancer risk and to SES. Indeed, within the SCCS, we have found that low SES, measured both at the individual level and the neighbourhood level, is associated with increasing smoking prevalence.[33] While we adjusted for current smoking using cigarettes smoked per day categories, and former smoking by years since quitting, minor perturbations in differences within these categories could impact

the small increases in risk we find with the deprivation indices. We did not see clear linear or monotonic trends in rising risk with increasing deprivation overall or when stratified by sex and race, suggesting further caution in interpretation of the study findings. The use of a socioeconomically homogeneous sample may limit its generalisability to other populations. A final limitation was the exclusion of races other than white or black (57 cases and 228 controls) whose lung cancer risk profile may differ substantially.

Strengths of our study include the large size and diversity of the cohort under observation, the relatively large numbers of lung cancer cases ascertained, the adjustment for individual-level smoking status using several dimensions of smoking exposure history, use of the NPB occupational status score and a comprehensive neighbourhood deprivation index encompassing education, employment, occupation, housing and poverty. Area-level measures of SES appear to impact lung cancer risk among black males only in this population after control for smoking and individual-level measures of SES. We adjusted for the NPB occupational status score, but the somewhat stronger link for men raises the possibility that occupational factors may be involved, since historically men have been more likely than women to be employed in heavy industries and since several occupational exposures in southern industries have long been recognised as lung carcinogens.[34] Asbestos exposure has been linked to increased lung cancer, but mesotheliomas, the signal of asbestos-induced cancer, have been rare among cohort members (to date five mesothelioma cases vs over 1300 lung cancers among SCCS participants) suggesting that exposures to this carcinogen are not likely to be widespread. Research in at least one southern state (South Carolina) found that socioeconomic deprivation was associated with elevated lifetime cancer risk by air toxics,[35] and a national US study identified significant positive associations between socioeconomic deprivation and respiratory and cancer hazardous air pollutants.[36]

Our findings may provide clues to further research of the contribution of area-level SES in lung cancer risk. These analyses address associations between high area-level deprivation and increased lung cancer risk but do not search for areas with high deprivation and low lung cancer incidence. If such discordant areas exist, they would provide additional evidence that area-level deprivation may be non-deterministic, even if it is a determinant. Identification of discordant areas in future studies could have important implications for public health policy.

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