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A Multilevel Analysis of Socioeconomic Status and Prostate Cancer Risk

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Abstract

PURPOSE—We investigated whether prostate cancer was associated with socioeconomic status (SES) at the individual level, area level, or a combination of both levels.

METHODS—This population-based case-control study of prostate cancer in men aged 65 to 79 years was conducted between 2000 and 2002 in South Carolina. Complete interviews were available for 407 incident prostate cancer cases and 393 controls (with respective response rates of 61% and 64%). We used educational level to measure individual-level SES and a composite variable capturing income and education from 2000 Census data to measure area-level SES.

RESULTS—After adjustment for race, age, geographic region, and prostate-specific antigen testing, men with some college were at reduced risk for prostate cancer (odds ratio [OR], 0.44; 95% confidence interval [CI], 0.27–0.72), as were men in the highest quartile of area-level SES (OR, 0.52; 95% CI, 0.34–0.80). When assessing individual-level and area-level SES simultaneously and accounting for their nonindependence, the independent negative associations persisted and appeared to be more striking for men with a diagnosis of localized disease, rather than advanced disease.

CONCLUSION—The independent effects of area-level and individual-level SES on prostate cancer risk seen in our study may help explain the conflicting results of previous studies conducted at both levels.

Keywords

Prostate Cancer; Socioeconomic Status; Multilevel Analysis; Case-Control Studies

INTRODUCTION

Prostate cancer is the most frequently diagnosed cancer in the United States and the second leading cause of cancer deaths among men. Little is understood about the cause of prostate cancer, and we do not know what factors might explain why African-American men are at

greater risk relative to white men. Several studies investigated prostate cancer incidence associated with individual-level socioeconomic status (SES) based on income, occupation, or educational level, with conflicting results. We limit our review to studies conducted in the United States because SES levels differ across countries. Two of the four studies that evaluated the association between individual-level SES and prostate cancer incidence in the United States reported positive associations (1, 2), whereas two studies reported no association (3, 4). Of the seven studies that investigated area-level SES and prostate cancer incidence in the United States, three studies each reported a positive association (5–7) or no association (8–10), whereas one study reported a negative association (11). Proposed mechanisms for explaining the positive association between individual-level and area-level SES and prostate cancer are consuming a healthy diet (4), engaging in exercise (4), and increased access to screening (12).

Studies of SES and prostate cancer must account for screening because the effect of high SES on prostate cancer risk may have differed before and after the advent of prostate-specific antigen (PSA) testing. Before PSA testing, men with higher SES were more likely to have lower rates of prostate cancer as a result of engaging in healthy behaviors (4). After PSA testing, men with higher SES were more likely to be screened annually (12) and thus the disease was more likely to be diagnosed, especially at an earlier stage (13). Using 1987 as the year that PSA testing became widespread, the majority of individual-level (1, 2, 4) and half the area-level (8–11) studies of SES and prostate cancer were conducted before screening, which may help explain the mixed results.

Along with the failure to account for PSA testing, another possible explanation for the mixed results of the SES and prostate cancer association is the failure to account for area-level SES in studies of individual-level SES, and vice versa. Several studies investigated the joint effects of individual-level and area-level SES and cardiovascular disease incidence (14, 15) and mortality (16, 17); however, few focused on cancer (17–19). Robert et al. (18) recently investigated the joint effect of individual-level and area-level SES on breast cancer incidence and found that area-level SES was associated positively with breast cancer after adjustment for individual-level SES, whereas the reverse was not true. Conversely, Steenland et al. (19) found little effect of area-level SES on prostate cancer mortality after adjustment for individual-level SES. Borrell et al. (17) found greater rates of cancer mortality among blacks and whites in the Atherosclerosis Risk in Communities Study who resided in neighborhoods with the lowest SES score that was weakened by adjustment for individual-level SES. To our knowledge, no other study simultaneously investigated the effect of individual-level and area-level measures of SES on prostate cancer risk. We assess joint effects of area-level and individual-level SES to indirectly determine whether conflicting results for prostate cancer incidence associated with individual-level SES may have been caused by the unmeasured influence of area-level SES.

METHODS

Detailed methods of this population-based case–control study conducted in South Carolina from 2000 to 2002 appear elsewhere (20). Briefly, cases diagnosed with primary invasive prostate cancer between October 1999 and September 2001 were identified through the

South Carolina Central Cancer Registry. During this time, the South Carolina Central Cancer Registry was certified as silver by the North American Association of Central Cancer Registries, with a case ascertainment rate between 90% and 95% (21). Eligible cases were South Carolina residents who were Caucasian or African American, aged 65 to 79 years, and had histologically confirmed prostate cancer and for whom physicians had given permission for research staff to contact the patient. We selected all eligible cases with advanced disease (stages III and IV) and a random sample of men with localized disease (stages I and II). We had insufficient funding to study all men with localized disease. Because we wanted approximately equal numbers of men with localized disease by race, we performed stratified sampling by race and over-sampled African-American men by randomly selecting 82% of men with localized disease compared with 40% of Caucasian men with localized disease. Of 692 eligible prostate cancer cases, 425 (61.4%) completed a standardized telephone interview. Of the remaining eligible cases, 90 physicians refused (13.0%), 71 patients refused (10.3%), 24 patients died before the interview (3.5%), 59 patients were not located (8.5%), and 23 patients were too sick to participate (3.3%).

Control subjects were randomly sampled from the 1999 Health Care Financing Administration Medicare beneficiary file. Controls were frequency matched to cases for age (5-year age groups), race (Caucasian and African American), and geographic region (western 14 counties, middle 19 counties, and eastern 13 counties of the state). Eligible controls were South Carolina residents aged 65 to 79 years with no history of prostate cancer. Of 756 eligible controls, 482 (63.8%) completed the interview. Of the remaining eligible controls, 108 controls refused (14.3%), 22 controls died before the interview (2.9%), 112 controls were not located (14.8%), and 32 controls were too sick to participate (4.2%). We eliminated 59 subjects (7 cases and 52 controls) who upon review of medical records were determined to have prevalent prostate cancer. After excluding an additional 48 subjects (11 cases and 37 controls) who completed fewer than 10 questions, the final sample size was 800 subjects (407 cases and 393 controls).

Institutional Review Boards of the University of South Carolina, Centers for Disease Control and Prevention, and National Cancer Institute approved this project's data collection procedures. Interviewing began in June 2000 and was completed in August 2002. Trained interviewers from the University of South Carolina Survey Research Laboratory conducted computer-assisted telephone interviews with subjects who provided verbal consent with the understanding that written consent would be obtained. The questionnaire collected information on demographic characteristics, SES, stress, coping, alcohol and tobacco use, physical activity, diet, medical history, family history of cancer, history of sexually transmitted diseases, and farm-related work activities and exposures. Most exposures pertained to the period before a reference date, the date of diagnosis for cases and an assigned date for controls that was similar to the distribution of diagnosis dates among cases.

We used the generalized linear latent and mixed models macro in STATA 8 (StataCorp LP, College Station, Texas) to estimate the odds ratio (OR) of prostate cancer associated with individual-level and area-level SES while accounting for their nonindependence and controlling for potential confounding factors (22). We had a two-level hierarchical structure; therefore, we fit a two-random level intercepts logistic model and used RESET diagnostic

test to evaluate misspecification of error or inappropriate link function (23). Because the majority of men were retired, we used educational level to measure individual-level SES, rather than annual household income 1 year before diagnosis. There were five categories of educational level: (i) less than eighth grade, (ii) 9th to 11th grade, (iii) high school graduate, (iv) some college or technical school, and (v) college graduate or more. To measure area-level SES, we created a composite variable consisting of median household income, percentage of persons living below the poverty level, percentage unemployment, and percentage of college or higher educational attainment addressing four of the six domains thought to comprise socioeconomic position in the United States (24). Subjects' addresses were not geocoded; therefore, this information was available at the ZIP code level from the 2000 census (25). Of the total of 919 ZIP codes in South Carolina, 265 were represented in the study. To ensure sufficient sample sizes and minimize overdispersion of estimates, we collapsed ZIP codes of homogeneous geographic and demographic characteristics into groups with a minimum of 25 subjects in each. There were 21 groupings ranging from 29 to 57 subjects (median = 41). We reversed the coding of poverty level and unemployment, summed the four area-level measures of SES, and categorized the composite variable by using the quartile distribution among controls. Cronbach α for this composite variable was 0.83 among controls, indicating these items went together in measuring the area-level SES construct.

Individual-level variables assessed as confounders included marital status, family history of prostate cancer, body mass index, and frequency of PSA testing, as categorized in Table 1. Body mass index, defined as self-reported weight in kilograms before reference date divided by the square of self-reported height in meters, was categorized by using the quartile distribution among controls. PSA testing was categorized as frequency within the past 5 years, with men who reported they had a PSA test performed, but did not remember the number of tests, categorized as one to two tests (53 local cases, 10 advanced cases, 90 controls). Controls were frequency matched to cases on age, race, and geographic region; thus, we adjusted for these three factors based on the study design. We also adjusted for PSA testing because it was the only variable to materially change unadjusted ORs. Although PSA testing may be in the causal pathway between SES and prostate cancer, we adjusted for it to investigate the association between SES and prostate cancer, accounting for the effect of SES on PSA testing. In analyses by stage at diagnosis, men with stages I and II were classified as having localized disease, and men with stages III and IV were classified as having advanced disease. Stages I and II correspond to tumors that were clinically unapparent or confined within the prostate with no nodal involvement or metastases (26). Stages III and IV correspond to tumors that extended through the prostatic capsule or invaded adjacent structures with or without nodal involvement or metastases. Linear trend was assessed by treating categorical variables as continuous variables.

RESULTS

Table 1 lists cases by stage at diagnosis and controls for demographic and socioeconomic factors. Compared with controls, prostate cancer cases were more likely to be younger, reside in the middle portion of the state, be married or living as married, have a family history of prostate cancer, have undergone PSA testing, have a lower educational level

themselves, and live in a community with a lower composite SES. A greater percentage of men with a diagnosis of localized disease were African American and in the lowest quartile of body mass index than men with a diagnosis of advanced disease, whereas the reverse was true of men with a diagnosis with advanced disease.

ORs and 95% confidence intervals (CIs) for prostate cancer associated with individual-level and area-level SES are listed in Table 2. There were significant correlations between PSA testing and individual-level (Spearman $r = 0.30$; $p < 0.0001$) and area-level (Spearman $r = 0.09$; $p = 0.007$) SES (data not shown). After adjustment for race, age, geographic region, and PSA testing, men with some college or technical school were at significantly reduced risk (OR, 0.44; 95% CI, 0.27–0.72) and college graduates were at borderline reduced risk (OR, 0.67; 95% CI, 0.42–1.05) for prostate cancer. Combining these upper two categories resulted in a significantly reduced risk for prostate cancer (OR, 0.55; 95% CI, 0.35–0.87). Similarly, men in the highest quartile of area-level SES (OR, 0.52; 95% CI, 0.34–0.80) were at reduced prostate cancer risk. In both measures of SES, there was a trend of decreasing risk with increasing educational level. Although the trend test was significant for individual-level SES, it must be noted that the referent group was markedly higher than all other educational groups and the trend test is driven by this group. Additional adjusting for individual-level or area-level SES and accounting for the nonindependence of these measures resulted in independent negative associations for prostate cancer in men with some college (OR, 0.45; 95% CI, 0.27–0.78) and men in the highest quartile of area-level SES (OR, 0.52; 95% CI, 0.25–1.10).

Risk for prostate cancer associated with socioeconomic factors by stage at diagnosis is listed in Table 3. With one exception, the third quartile of area-level SES in men diagnosed with advanced disease, there were reductions in risk associated with individual-level and area-level SES regardless of stage at diagnosis. The decreased risk for men with some college or technical school and men who lived in the highest quartile of area-level SES was weaker for men with a diagnosis of advanced cancer than those with a diagnosis of localized cancer, but remained reduced even after adjustment for the other level measure of SES.

DISCUSSION

We found a significantly reduced risk for prostate cancer associated with having some college or technical school and a borderline reduced risk for the highest category of our individual-level SES measure, educational level. In addition, there was a significant trend of decreasing risk with increasing educational level. A possible explanation for the trend is the greater percentage of cases (especially those with localized disease) with an elementary education than controls. Although not limited to men with a diagnosis of localized disease, the reduction in risk in the two highest SES categories was more pronounced for this group. Our results are in conflict with the majority of studies of individual-level SES and prostate cancer risk, which reported a positive (1, 2) or no association (3, 4). Possible explanations for our findings relate to the educational level and race of men in our study. Men in our study had a fairly low SES; 36.8% of our controls aged 65 and older had less than a high school education in comparison to 31.2% of men in the United States in 1999 (27). The only study of individual-level SES and prostate cancer conducted since the advent of PSA testing

found no association after adjustment for PSA testing for the highly educated, younger American Cancer Society Nutrition Cohort Study; 8% of their participants aged 55 years and older had less than a high school education (3) compared with 26% of men in the United States in 1999 (27). A large percentage of men in our study were African American (40.8% of cases; 42.2% of controls). Yu et al. (2) reported a weak positive association between college education and prostate cancer risk for Caucasian men, but not African-American men.

Similarly, prostate cancer was associated negatively with area-level SES measured by using our composite variable. Again, the reduction in risk was stronger for men with a diagnosis of localized disease than those with a diagnosis of advanced disease. The negative association we found was in contrast to most previous studies of area-level SES and prostate cancer that reported a positive association (5–7) or no association (8–10). In their study of area-level SES and prostate cancer mortality using the American Cancer Society Nutrition Cohort Study, Steenland et al. (K. Steenland, personal communication, February 9, 2006) found a positive association. Possible explanations for our findings relate to the race of men in our study and the different measures of area-level SES used by different studies. As indicated, more than 40% of our participants were African American. One study identified a positive association in all racial groups except whites (6), another study found a positive association in all racial groups except Asians (8), and another study reported no association in African-American or Caucasian men (9). Studies of area-level SES used a variety of measures, including a combination of occupation and poverty level (5), median household income (6), a combination of median household income and educational attainment (7), and a combination of household income, home value, occupation, and education (19).

After performing a multilevel analysis, there was little effect on either measure of SES with approximately the same reduction in prostate cancer risk associated with the two highest levels of individual-level SES combined (OR, 0.55; 95% CI, 0.35–0.87) as the highest quartile of area-level SES (OR, 0.52; 95% CI, 0.25–1.10). These results were evident for men with a diagnosis of localized and advanced disease; however, the association was more pronounced for men with localized disease. This is in contrast to the majority of studies of SES and cardiovascular disease incidence and mortality, which reported stronger associations for individual-level SES than area-level SES after simultaneous adjustment (14–17). In the American Cancer Society Nutrition Cohort Study, Steenland et al. (K. Steenland, personal communication, February 9, 2006) found no association between individual-level SES and prostate cancer mortality after adjustment for area-level SES and vice versa. However, the only study of cancer incidence to examine the joint effects of individual-level and area-level SES reported a stronger effect of area-level SES than individual-level SES (18). These investigators hypothesized that the stronger positive effect of area-level than individual-level SES they saw on breast cancer risk may have been caused by greater access to mammograms in higher SES areas (28) or to physical and environmental characteristics common in the community that may increase a woman's breast cancer risk. One possible explanation for the reduced prostate cancer risk associated with higher individual-level and area-level SES we saw is that men with higher SES and those living in higher SES areas are less likely to undergo PSA testing. This was not the case in our study in which PSA testing positively and significantly correlated with both measures of SES (individual-level SES,

Spearman $r = 0.30$, $p < 0.0001$; area-level SES, Spearman $r = 0.09$, $p = 0.007$). An alternative explanation for the reduced risk for prostate cancer associated with high individual-level and area-level SES is that men with higher SES and those from higher SES areas have greater access to healthful diets and physical activity.

This study was not without limitations. Our response rates were less than desired, and we sampled men with localized disease, somewhat limiting the generalizability of our results and possibly resulting in some nonsignificant reductions in prostate cancer risk. African-American men with advanced disease were less likely to participate than African-American men with localized disease, which limited study power to statistically assess effect modification by race and stage. We were unable to determine whether nonparticipation rates of cases and controls differed by SES. However, similar percentages of nonrespondents (22.6%) and respondents (25.2%) had diagnoses of advanced disease, which would argue against selective survival of cases. The average time between diagnosis and interview was 8.7 months, which may have led to misclassification. Another source of misclassification was the memory problems common in men aged 65 years and older. Our study power was limited for some joint effects because of small numbers. We were unable to assess race as an effect modifier of the association between SES and prostate cancer because of small numbers. Analysis at the grouped ZIP code level in our study may not reflect the area-level SES accurately because SES of block groups and census tracts within ZIP codes tend to vary substantially (24). Although block groups and census tracts may better represent area-level SES than grouped ZIP codes, we chose to group ZIP codes to provide stable estimates.

Our study is the first population-based case-control study of prostate cancer to simultaneously assess the effect of individual-level and area-level SES on prostate cancer risk. Additional strengths of the study include the fairly large number of men with advanced disease, which allowed us to perform analyses by stage at diagnosis, and use of an accepted measure of area-level SES (24). We adjusted for the frequency of PSA testing in an attempt to isolate the effect of SES apart from its influence on access to care. Area-level 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 (29). The independent effects of area-level and individual-level SES on prostate cancer risk seen in our study may help explain the conflicting results of previous studies conducted at both levels and would argue for the measurement of both levels in future studies.

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Selected Abbreviations and Acronyms

CI	confidence interval
OR	odds ratio
PSA	prostate-specific antigen

SES socioeconomic status

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TABLE 1

Comparison of cases by stage at diagnosis and controls for demographic and socioeconomic factors

	Localized cases (n = 314)N (%)	Advanced cases (n = 102)N (%)	Controls (n = 429)N (%)
Race			
Caucasian	175 (55.7)	70 (68.6)	258 (60.1)
African-American	139 (44.3)	32 (31.4)	171 (39.9)
Age (years)			
65–69	138 (44.0)	54 (52.9)	186 (43.4)
70–74	102 (32.5)	32 (31.4)	125 (29.1)
75–79	74 (23.5)	16 (15.7)	118 (27.5)
Geographic region			
Eastern counties	180 (57.3)	55 (53.9)	243 (56.6)
Middle counties	81 (25.8)	26 (25.5)	92 (21.5)
Western counties	53 (16.9)	21 (20.6)	94 (21.9)
Marital status ^a			
Single/separated/divorced/widowed	56 (18.6)	17 (17.0)	80 (20.6)
Married/living as married	245 (81.4)	83 (83.0)	308 (79.4)
Missing	5	1	5
Family history ^a			
None	212 (70.9)	66 (66.7)	329 (84.6)
First-degree	63 (21.1)	23 (23.2)	43 (11.0)
Second-degree	24 (8.0)	10 (10.1)	17 (4.4)
Missing	7	2	4
Body mass index (quartiles) ^a			
<24.4	77 (25.9)	13 (13.1)	90 (23.5)
24.4–27.2	83 (28.0)	31 (31.3)	101 (26.3)
27.3–29.8	69 (23.2)	27 (27.3)	96 (25.1)
>29.9	68 (22.9)	28 (28.3)	96 (25.1)
Missing	9	2	10
No. of prostate-specific antigen tests in past 5 years			
0	43 (13.7)	18 (17.7)	98 (22.9)
1–2	102 (32.5)	29 (28.4)	154 (36.0)
3–4	48 (15.3)	19 (18.6)	66 (15.4)
5	121 (38.5)	36 (35.3)	110 (25.7)
Missing	1	0	0
Educational level			
Elementary education	84 (26.8)	22 (22.2)	89 (20.7)
Some high school	44 (14.1)	11 (11.1)	69 (16.1)
High school graduate	78 (24.9)	23 (23.2)	102 (23.8)
Some college or technical school	37 (11.8)	17 (17.2)	77 (18.0)
College graduate	70 (22.4)	26 (26.3)	92 (21.5)
Missing	1	3	0

	Localized cases (n = 314)N (%)	Advanced cases (n = 102)N (%)	Controls (n = 429)N (%)
Composite socioeconomic status (quartiles)			
Low	105 (33.4)	30 (29.4)	118 (27.5)
Medium	94 (29.9)	18 (17.7)	115 (26.8)
High	71 (22.6)	35 (34.3)	106 (24.7)
Very high	44 (14.0)	19 (18.6)	90 (21.0)

^aConsists of 306 local cases, 101 advanced cases, and 393 controls.

TABLE 2

Odds ratios for prostate cancer associated with individual-level and area-level socioeconomic factors

	OR ^a (95% CI)	OR ^b (95% CI)	OR ^c (95% CI)
Educational level			
Elementary education	1.00 (Referent)	1.00 (Referent)	
Some high school	0.60 (0.37–0.95)	0.57 (0.34–0.94)	
High school graduate	0.69 (0.45–1.06)	0.70 (0.44–1.11)	
Some college or technical school	0.44 (0.27–0.72)	0.45 (0.27–0.78)	
College graduate	0.67 (0.42–1.05)	0.65 (0.39–1.07)	
<i>p</i> for trend	0.05	0.08	
Composite socioeconomic status (quartiles)			
Low	1.00 (Referent)		1.00 (Referent)
Medium	0.79 (0.53–1.17)		0.78 (0.38–1.59)
High	0.86 (0.58–1.28)		0.96 (0.42–2.23)
Very high	0.52 (0.34–0.80)		0.52 (0.25–1.10)
<i>p</i> for trend	< 0.01		0.13

OR = odds ratio; CI = confidence interval.

^a Adjusted for race, age, geographic region, and prostate-specific antigen testing.^b Adjusted for race, age, geographic region, composite socioeconomic status, and prostate-specific antigen testing.^c Adjusted for race, age, geographic region, educational level, and prostate-specific antigen testing.

TABLE 3

Odds ratios for prostate cancer associated with individual-level and area-level socioeconomic factors by stage at diagnosis

	OR ^a (95% CI)	OR ^b (95% CI)	OR ^c (95% CI)
Localized			
Educational level			
Elementary education	1.00 (Referent)	1.00 (Referent)	
Some high school	0.60 (0.36–0.98)	0.54 (0.31–0.93)	
High school graduate	0.70 (0.44–1.11)	0.70 (0.43–1.16)	
Some college or technical school	0.39 (0.22–0.67)	0.41 (0.23–0.73)	
College graduate	0.62 (0.38–1.02)	0.61 (0.35–1.05)	
<i>p</i> for trend	0.03	0.06	
Composite socioeconomic status (quartiles)			
Low	1.00 (Referent)		1.00 (Referent)
Medium	0.87 (0.58–1.32)		0.88 (0.40–1.96)
High	0.72 (0.47–1.11)		0.80 (0.35–1.83)
Very high	0.48 (0.30–0.76)		0.51 (0.21–1.21)
<i>p</i> for trend	< 0.01		0.10
Advanced			
Educational level			
Elementary education	1.00 (Referent)	1.00 (Referent)	
Some high school	0.54 (0.24–1.21)	0.61 (0.26–1.42)	
High school graduate	0.67 (0.33–1.34)	0.69 (0.32–1.45)	
Some college or technical school	0.58 (0.27–1.25)	0.54 (0.24–1.26)	
College graduate	0.77 (0.37–1.59)	0.74 (0.34–1.64)	
<i>p</i> for trend	0.62	0.49	
Composite socioeconomic status (quartiles)			
Low	1.00 (Referent)		1.00 (Referent)
Medium	0.56 (0.28–1.10)		0.57 (0.24–1.36)
High	1.32 (0.72–2.40)		1.41 (0.63–3.17)
Very high	0.72 (0.37–1.39)		0.66 (0.26–1.65)
<i>p</i> for trend	0.84		0.74

OR = odds ratio; CI = confidence interval.

^a Adjusted for race, age, geographic region, and prostate-specific antigen testing.

^b Adjusted for race, age, geographic region, composite socioeconomic status, and prostate-specific antigen testing.

^c Adjusted for race, age, geographic region, educational level, and prostate-specific antigen testing.