Disparities in cancer incidence and mortality by area-level socioeconomic status: a multilevel analysis

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ABSTRACT

Background Disparities in cancer incidence and mortality have been observed by measures of area-level socioeconomic status (SES); however, the extent to which these disparities are explained by individual SES is unclear.

Methods Participants included 60 756 men and women in the VITamins And Lifestyle (VITAL) study cohort, aged 50–76 years at baseline (2000–2002) and followed through 2010. We constructed a block group SES index using the 2000 US Census and fit Cox proportional hazards models to estimate the association between area-level SES (by quintile) and total and site-specific cancer incidence and total cancer mortality, with and without household income and individual education in the models.

Results Lower area-level SES was weakly associated with higher total cancer incidence and lower prostate cancer risk, but was not associated with risk of breast cancer. Compared with the highest-SES areas, living in the lowest-SES areas was associated with higher lung (HR: 2.21, 95% CI 1.69 to 2.90) and colorectal cancer incidence (HR: 1.52, 95% CI 1.11 to 2.09) and total cancer mortality (HR: 1.68, 95% CI 1.47 to 1.93). Controlling for individual education and household income weakened the observed associations, but did not eliminate them (lung cancer HR: 1.43, 95% CI 1.07 to 1.91; colorectal cancer HR: 1.35, 95% CI 0.97 to 1.88; cancer mortality HR: 1.28, 95% CI 1.11 to 1.48).

Conclusions Area-level socioeconomic disparities exist for several cancer outcomes. These differences are not fully explained by individual SES, suggesting area-level factors may play a role.

INTRODUCTION

Associations have been reported between area-level socioeconomic status (SES) and several cancer outcomes—lower area-level SES has been associated with higher risk of colorectal,[1–4] lung,[3 5] prostate[6] and cervical cancer;[7 8] total[9 10] and site-specific cancer mortality;[10 11] later stage of diagnosis;[12–18] and more aggressive tumour characteristics[19]; while higher area-level SES has been associated with higher risk of breast[8 20–22] and prostate cancer[5 8 23]—however, the extent to which these observed associations are due to individual SES is rarely addressed.[6]

Understanding the extent to which observed associations between area-level SES and cancer outcomes are due to compositional factors (eg, if people living in lower-SES areas are themselves of lower SES and would be at increased risk of disease and mortality regardless of where they lived), or potentially influenced by contextual factors (eg, physical environment, neighbourhood resources, policies or social norms, which may contribute to disease risk independent of individual SES) is critical for appropriately targeting interventions to reduce socioeconomic disparities.[16 24]

The purpose of this paper is to estimate the association between area-level SES and total and site-specific cancer incidence and total cancer mortality, and to assess whether observed associations remain after control for individual educational attainment and household income. While the first approach estimates total area-level socioeconomic disparities in cancer outcomes, the second evaluates the degree of disparity that could be due to contextual effects of areas on cancer outcomes or their risk factors. To the best of our knowledge this is the first study to systematically examine whether observed associations between area-level SES and several cancer outcomes is due to individual socioeconomic characteristics by directly comparing those associations with and without control for individual SES.

MATERIALS AND METHODS

Study cohort

The VITamins And Lifestyle (VITAL) study is a prospective cohort study designed to investigate the associations of use of dietary supplements and other behaviours with cancer risk and mortality. It has previously been described in detail.[25] Participants were between ages 50 and 76 and lived in 1 of the 13 counties in the Western Washington Surveillance, Epidemiology and End Results (SEER) cancer registry at baseline. The Institutional Review Board at the Fred Hutchinson Cancer Research Center approved this research.

Using names purchased from a commercial mailing list, 364 418 sex-specific baseline questionnaires were mailed between October 2000 and December 2002 and were followed 2 weeks later by reminder postcards. A total of 79 300 questionnaires were returned, of which 77 719 passed quality control checks. Overall, 60 756 men and women were included in the cancer mortality analyses after excluding respondents whose baseline addresses were post office boxes (n=1137) or could not be geocoded (n=381) and respondents missing data on education (n=1333) or household income (n=15 443). Missing individual education and household income were not associated with area-level SES. Models of area-level SES, and total and site-specific cancer incidence further excluded respondents with a history of cancer other than non-melanoma skin cancer (n=11 259) or whose

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history of cancer was unknown (n=214). Numbers of exclusions reported are not mutually exclusive.

Area-level SES

Respondents' baseline addresses were geocoded using GPS Visualizer and Yahoo Maps. A 1% sample of addresses was geocoded again using Google Maps and more than 95% of the addresses in the validation sample were geocoded to within 400 m of one another using the two methods. Addresses were used to identify respondents' census block groups using TIGER/Line shapefiles for the 2000 US Census in ArcMap 10 (Esri, Redlands, California, USA).

Area-level SES was measured using a method developed by Diez-Roux *et al*[26] that has been used previously to examine associations between area-level SES and colon and rectal cancer.[2] Information from the 2000 Census was used to create a block group-level index of social disadvantage including log of median value of owner-occupied housing units; log of median household income; per cent of households receiving net rental, interest or dividend income; per cent of adults ages 25 and older who completed high school and who completed college; and per cent of employed persons ages 16 and older in professional and managerial occupations. Standardised z-scores were calculated for each variable based on the 3347 block groups in the Western Washington SEER catchment area and summed. Signs of the index scores were reversed so that higher values corresponded with lower area-level SES. Each participant was assigned the index value for their block group of residence. Index values ranged from −16.1 to 17.3 with a median value of −1.1 and mean of −1.3.

Block groups were chosen as an approximation of participants' neighbourhood environments because they are small, relatively permanent statistical subdivisions of counties and of census tracts designed to be relatively homogenous with respect to population characteristics, economic factors and living conditions,[27] and have been found to perform favourably in detecting socioeconomic gradients in cancer incidence and mortality.[8] Block groups in the catchment area covered a median of 3.3 square miles and included a median population of 1070.

Case ascertainment and censoring

In cancer incidence analyses, participants with no history of cancer at baseline were followed for their first incident, invasive cancer via annual linkage with SEER. This linkage is largely automated and based on ranking agreement between items common to both sets of data, such as Social Security number, name and date of birth. Matches with high concordance were linked automatically whereas visual inspection was used to adjudicate incomplete matches. A total of 6099 incident cancers were identified in an average of 8.1 years of follow-up.

Participants not diagnosed with cancer were right-censored at the date of the earliest of the following events: date they requested removal from the study (n=8), date they moved out of the SEER catchment area (n=3898), date of death (n=2214) or 31 December 2010 (n=39 967). Moves out of area were identified through linkage with the US National Change of Address System. For analyses of site-specific cancer incidence, participants diagnosed with cancers other than the one of interest were censored at the date of cancer diagnosis.

Cancer deaths were ascertained through annual linkage with the Washington State death file using procedures similar to those described above. In cancer mortality analyses, participants who did not die of cancer were right-censored at the date they requested removal from the study (n=9), date they moved out of Washington State (n=3536), date of death due to other causes (n=3116) or 31 December 2010 (n=51 608). A total of 2487 cancer deaths were observed in an average of 8.5 years of follow-up.

Statistical analyses

Area-level SES was divided into quintiles based on the distribution of participants' block group SES index values. Using these categories, cancer incidence and mortality rates were calculated and Cox proportional hazards models were used to calculate HRs and 95% CIs of cancer incidence and cancer mortality associated with living in areas in each of the lowest four quintiles of area-level SES compared with living in the highest-SES quintile. Participant age was used as the time scale, with participants entering the analysis at their age at baseline and exiting at age at outcome (cancer diagnosis; death due to cancer) or censoring event, as described above. Proportional hazards assumptions were examined using scaled Schoenfeld residuals. No significant deviations from proportionality were observed. All statistical tests were two sided with $p<0.05$ considered statistically significant.

Multivariable analyses included categorical variable adjustment for sex; additional adjustment for race/ethnicity and marital status (model 1) and further adjustment for individual education and household income (model 2). Although race/ethnicity and marital status are related to individual SES, the age and sex-adjusted model and model 1 yielded similar results for all cancer outcomes. p Values for trend are from the Wald test associated with area-level SES index modelled as a continuous variable. Statistical analyses were conducted using Stata 12.1 (StataCorp LP, College Station, Texas, USA). All models of area-level SES and cancer incidence and mortality utilise the cluster option to obtain SEs that account for correlation among residents of the same block groups.

Results of multilevel survival, or frailty, models with Weibull-distributed event times, γ frailty distributions and shared frailties by block group of residence are provided in online supplementary tables. These models use time since baseline as the time scale and include adjustment for baseline age. Results are nearly identical to the models presented here; however, not all frailty models converged successfully, therefore the Cox models are presented in the main tables.

RESULTS

Participants living in the lowest-SES areas tended to be older and a lower proportion was male, Caucasian, married or reported household incomes of at least $40 000 at baseline compared to those in the highest-SES areas (table 1). The median average household income for all block groups in the catchment area was $51 141 and the median proportion who completed college was 27.1%. By comparison, 51.9% of VITAL participants reported household incomes of less than $60 000 per year, and 42.3% completed college (data not shown).

Table 2 gives the mean, median and range of the measures included in the area-level SES index for all block groups in the 13 counties of the Western Washington SEER registry, and the block group-level measures for VITAL respondents. The overall catchment area and VITAL participants' block groups both represented a wide range of SES; however, on average, VITAL respondents' block groups had higher household incomes and home values, and a higher proportion of residents who completed high school and college, who were in professional and managerial occupations, and who lived in households that received net rental, interest or dividend income.

Table 1 Mean, SD and range of area-level socioeconomic status (SES) index values and baseline demographic factors by quintiles of area-level SES, The VITAL study cohort, Western Washington, USA, 2000–2002

		Area-level SES index				Demographic factors				
Quintiles of area-level SES index	N	Mean	SD	Range	Age Mean (SD)	Male Per cent	Caucasian Per cent	Married Per cent	College degree Per cent	Annual household income ≥$40 000 Per cent
Quintile 1 (high)	12 145	−8.4	2.21	−16.1, −5.6	60.3 (7.2)	52.2	94.1	78.4	67.9	86.9
Quintile 2	12 249	−3.8	−0.98	−5.6, −2.3	60.6 (7.3)	51.2	94.2	75.7	51.4	78.2
Quintile 3	12 018	−1.1	−0.73	−2.3, 0.3	61.0 (7.4)	51.9	94.1	76.1	41.8	72.3
Quintile 4	12 181	1.6	0.79	0.3, 3.0	61.2 (7.4)	49.4	92.7	73.0	31.4	63.4
Quintile 5 (low)	12 164	5.3	1.88	3.0, 17.3	61.6 (7.5)	47.4	90.6	66.4	23.3	52.6

VITAL, VITamins And Lifestyle.

Table 3 gives total and site-specific incidence rates per 10 000 person-years and HRs and 95% CIs by quintile of area-level SES. Total cancer incidence was 144/10 000 person-years, which is somewhat higher than in all of the Western Washington SEER catchment area (116.7/10 000), driven largely by higher prostate cancer incidence in VITAL (79.7/10 000 vs 47.8/10 000).[28] Total cancer incidence ranged from 135/10 000 in the highest-SES areas to 154.1 in the lowest-SES areas.

After controlling for demographics, living in the lowest-SES areas was marginally associated with higher total cancer incidence (HR: 1.08, 95% CI 0.99 to 1.17; $P_{trend}=0.067$) and with higher risk of lung (HR: 2.21, 95% CI 1.69 to 2.90; $P_{trend}<0.001$) and colorectal cancer (HR: 1.52, 95% CI 1.11 to 2.09; $P_{trend}=0.003$; table 2, model 1). Prostate cancer risk was inversely associated with area-level SES ($P_{trend}=0.015$). Area-level SES was not associated with incidence of breast cancer or of other cancers combined.

In models further adjusting for individual education and household income, the association between area-level SES and total cancer incidence attenuated (quintile 1 (Q1) vs quintile 5 (Q5) HR: 1.06, 95% CI 0.97 to 1.16; $P_{trend}=0.22$) and was eliminated for area-level SES and prostate cancer ($P_{trend}=0.66$) (table 2, Model 2). Living in the lowest-SES areas remained associated with higher lung cancer incidence (Q1 vs Q5 HR: 1.43, 95% CI 1.07 to 1.91) and marginally associated with higher colorectal cancer risk (Q1 vs Q5 HR: 1.35, 95% CI 0.97 to 1.88; $P_{trend}=0.062$), particularly among men (Q1 vs Q5 HR: 1.53, 95% CI 0.99 to 2.38; $P_{trend}=0.031$).

Table 4 gives cancer mortality rates, HRs and 95% CIs by quintile of area-level SES for total cancer mortality, and stratified by sex and by whether respondents were diagnosed with cancer before baseline. The overall cancer mortality rate was 48 deaths per 10 000 person-years and ranged from 33.6 in participants living in the highest-SES areas to 63.7 among those in the lowest-SES areas.

In models adjusted for demographics, living in lower-SES areas was associated with higher cancer mortality (Q1 vs Q5 HR: 1.68, 95% CI 1.47 to 1.93; $P_{trend}<0.001$; table 4, model 1). The association between area-level SES and cancer mortality was somewhat weaker in respondents who were diagnosed with cancer before baseline (Q1 vs Q5 HR: 1.54, 95% CI 1.26 to 1.87; $P_{trend}<0.001$) than among those not diagnosed before baseline (Q1 vs Q5 HR: 1.81, 95% CI 1.52 to 2.16; $P_{trend}<0.001$). Controlling for individual SES substantially weakened these results; however, living in lower-SES areas remained associated with higher cancer mortality among all respondents (Q1 vs Q5 HR: 1.28, 95% CI 1.11 to 1.48; $P_{trend}<0.001$) and particularly among those not diagnosed before (Q1 vs Q5 HR: 1.40, 95% CI 1.16 to 1.69; $P_{trend}<0.001$). These associations were similar among men and women.

DISCUSSION

The purpose of this study was to estimate the association between area-level SES and total and site-specific cancer incidence and total cancer mortality, and to assess whether observed associations remain after controlling for individual SES. Area-level SES was inversely associated with lung and colorectal cancer incidence and total cancer mortality. Controlling for individual SES weakened these associations; however, area-level SES remained associated with lung cancer incidence and total cancer

Table 2 Mean, median and range of area-level socioeconomic status measures for all block groups in the Western Washington SEER catchment area, and among participants in the VITAL study cohort, Western Washington, USA, 2000–2002

	All block groups in SEER catchment area			Block group values for VITAL participants		
	Mean	Median	Range	Mean	Median	Range
Median household income ($)*	53 700	51 200	7400–200 000	57 800	55 100	8700–200 000
Median home value ($)*	207 800	183 300	0–1 000 000	223 200	192 800	45 000–1 000 000
Per cent of adults ages 16 and older in professional or managerial occupations	37.0	35.2	0–87.8	40.1	38.7	1.9–87.8
Per cent of households receiving net rental, interest or dividend income	42.6	42.1	0–100.0	47.3	47.3	0–89.9
Per cent of adults ages 25 and older who graduated from high school	88.8	90.6	0–100.0	90.6	92.3	37.3–100.0
Per cent of adults ages 25 and older who graduated from college	30.8	27.1	0–100.0	34.5	31.4	0–91.1

*Median household income and median home price are both rounded to the nearest $100. The highest values reported by the Census were $200 000 for median household income and $1 000 000 for median home value.
SEER, Surveillance, Epidemiology and End Results; VITAL, VITamins And Lifestyle.

Table 3 Total and site-specific cancer incidence rates, HRs and 95% CIs associated with quintiles of area-level socioeconomic status, The VITAL study cohort, Western Washington, USA, 2000–2010

Area-level SES	VITAL cohort N	Incident cancers N	Incidence rate*	Age- and sex-adjusted HR	Age- and sex-adjusted 95% CI	Model 1† Demographics only HR	Model 1† Demographics only 95% CI	Model 2‡ Demographics and individual SES HR	Model 2‡ Demographics and individual SES 95% CI
Total cancer incidence									
All respondents	52 186	6099	144.0						
Quintile 5 (high)	10 410	1160	135.0	1.00	ref	1.00	ref	1.00	ref
Quintile 4	10 407	1154	136.6	1.00	0.92 to 1.09	1.00	0.92 to 1.08	1.00	0.91 to 1.08
Quintile 3	10 480	1242	146.3	1.04	0.96 to 1.13	1.04	0.96 to 1.13	1.04	0.95 to 1.13
Quintile 2	10 402	1250	148.1	1.06	0.98 to 1.15	1.06	0.97 to 1.15	1.05	0.96 to 1.14
Quintile 1 (low)	10 487	1293	154.1	1.08	1.00 to 1.18	1.08	0.99 to 1.17	1.06	0.97 to 1.16
P_{trend}§					0.042		0.067		0.22
Women	25 260	2421	116.0						
Quintile 5 (high)	4863	432	106.1	1.00	ref	1.00	ref	1.00	ref
Quintile 4	4955	443	107.7	0.99	0.86 to 1.13	0.98	0.86 to 1.13	0.97	0.85 to 1.11
Quintile 3	4953	486	119.1	1.07	0.94 to 1.22	1.06	0.93 to 1.21	1.04	0.91 to 1.19
Quintile 2	5146	510	120.0	1.06	0.93 to 1.21	1.06	0.93 to 1.20	1.03	0.90 to 1.18
Quintile 1 (low)	5343	550	126.1	1.09	0.96 to 1.24	1.08	0.95 to 1.23	1.04	0.90 to 1.19
P_{trend}§					0.14		0.20		0.60
Men	26 926	3678	171.1						
Quintile 5 (high)	5547	728	160.9	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5452	711	163.9	1.01	0.91 to 1.12	1.01	0.91 to 1.12	1.01	0.91 to 1.12
Quintile 3	5527	756	171.6	1.03	0.93 to 1.14	1.03	0.93 to 1.14	1.03	0.93 to 1.15
Quintile 2	5256	740	176.5	1.06	0.96 to 1.18	1.06	0.95 to 1.17	1.06	0.95 to 1.18
Quintile 1 (low)	5144	743	184.3	1.09	0.98 to 1.20	1.08	0.97 to 1.20	1.07	0.96 to 1.20
P_{trend}§					0.11		0.15		0.26
Prostate cancer									
Men	26 926	1712	79.7						
Quintile 5 (high)	5547	394	87.1	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5452	333	76.7	0.88	0.76 to 1.01	0.88	0.76 to 1.01	0.92	0.80 to 1.06
Quintile 3	5527	349	79.2	0.88	0.77 to 1.02	0.88	0.77 to 1.02	0.95	0.82 to 1.10
Quintile 2	5256	318	75.9	0.85	0.73 to 0.98	0.85	0.73 to 0.98	0.94	0.81 to 1.10
Quintile 1 (low)	5144	318	78.9	0.87	0.75 to 1.01	0.88	0.76 to 1.02	1.01	0.86 to 1.18
P_{trend}§					0.012		0.015		0.66
Breast cancer									
Women	25 260	856	41.0						
Quintile 5 (high)	4863	159	39.1	1.00	ref	1.00	ref	1.00	ref
Quintile 4	4955	147	35.8	0.90	0.72 to 1.13	0.90	0.72 to 1.14	0.91	0.72 to 1.14
Quintile 3	4953	182	44.6	1.11	0.89 to 1.38	1.11	0.89 to 1.38	1.12	0.90 to 1.40
Quintile 2	5146	189	44.4	1.10	0.89 to 1.36	1.10	0.89 to 1.36	1.11	0.90 to 1.39
Quintile 1 (low)	5343	179	41.0	1.00	0.80 to 1.24	1.00	0.80 to 1.25	1.02	0.81 to 1.29
P_{trend}§					0.67		0.64		0.53
Lung cancer									
All respondents	52 186	676	16.0						
Quintile 5 (high)	10 410	74	8.6	1.00	ref	1.00	ref	1.00	ref
Quintile 4	10 407	123	14.6	1.64	1.22 to 2.19	1.62	1.21 to 2.17	1.37	1.02 to 1.85
Quintile 3	10 480	130	15.3	1.65	1.24 to 2.19	1.64	1.22 to 2.19	1.26	0.93 to 1.71
Quintile 2	10 402	160	19.0	2.04	1.55 to 2.70	2.00	1.51 to 2.65	1.41	1.05 to 1.89
Quintile 1 (low)	10 487	189	22.5	2.34	1.79 to 3.07	2.21	1.69 to 2.90	1.43	1.07 to 1.91
P_{trend}§					<0.001		<0.001		0.041
Women	25 260	292	14.0						
Quintile 5 (high)	4863	32	7.9	1.00	ref	1.00	ref	1.00	ref
Quintile 4	4955	49	11.9	1.44	0.92 to 2.25	1.43	0.91 to 2.22	1.28	0.82 to 2.00
Quintile 3	4953	50	12.3	1.43	0.92 to 2.21	1.41	0.91 to 2.19	1.17	0.74 to 1.84
Quintile 2	5146	75	17.6	2.01	1.33 to 3.03	1.94	1.29 to 2.93	1.51	0.97 to 2.35
Quintile 1 (low)	5343	86	19.7	2.15	1.43 to 3.22	2.02	1.34 to 3.02	1.46	0.94 to 2.26
P_{trend}§					<0.001		<0.001		0.078

Continued

Table 3 Continued

Area-level SES	VITAL cohort N	Incident cancers N	Incidence rate*	Age- and sex-adjusted HR	95% CI	Model 1† Demographics only HR	95% CI	Model 2‡ Demographics and individual SES HR	95% CI
Men	26 926	384	17.9						
Quintile 5 (high)	5547	42	9.3	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5452	74	17.1	1.79	1.25 to 2.58	1.77	1.23 to 2.55	1.46	1.01 to 2.12
Quintile 3	5527	80	18.2	1.83	1.26 to 2.67	1.81	1.24 to 2.66	1.34	0.90 to 1.98
Quintile 2	5256	85	20.3	2.07	1.44 to 2.96	2.03	1.42 to 2.92	1.34	0.91 to 1.97
Quintile 1 (low)	5144	103	25.6	2.51	1.77 to 3.57	2.37	1.66 to 3.37	1.43	0.97 to 2.09
P_{trend}§					<0.001		<0.001		0.23
Colorectal cancer									
All respondents	52 186	461	10.8						
Quintile 5 (high)	10 410	64	7.4	1.00	ref	1.00	ref	1.00	ref
Quintile 4	10 407	86	10.2	1.33	0.96 to 1.84	1.33	0.96 to 1.84	1.29	0.93 to 1.78
Quintile 3	10 480	94	11.1	1.40	1.02 to 1.92	1.39	1.01 to 1.91	1.32	0.96 to 1.81
Quintile 2	10 402	106	12.6	1.58	1.15 to 2.16	1.55	1.13 to 2.12	1.43	1.03 to 1.98
Quintile 1 (low)	10 487	111	13.2	1.61	1.18 to 2.20	1.52	1.11 to 2.09	1.35	0.97 to 1.88
P_{trend}§					0.001		0.003		0.062
Women	25 260	217	10.4						
Quintile 5 (high)	4863	30	7.4	1.00	ref	1.00	ref	1.00	ref
Quintile 4	4955	41	10.0	1.29	0.80 to 2.08	1.28	0.79 to 2.07	1.27	0.78 to 2.07
Quintile 3	4953	43	10.5	1.31	0.82 to 2.10	1.30	0.81 to 2.08	1.24	0.77 to 2.01
Quintile 2	5146	51	12.0	1.46	0.93 to 2.30	1.42	0.90 to 2.23	1.34	0.82 to 2.17
Quintile 1 (low)	5343	52	11.9	1.40	0.89 to 2.20	1.31	0.83 to 2.06	1.18	0.72 to 1.93
P_{trend}§					0.14		0.27		0.66
Men	26 926	244	11.4						
Quintile 5 (high)	5547	34	7.5	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5452	45	10.4	1.36	0.87 to 2.13	1.37	0.88 to 2.16	1.32	0.84 to 2.06
Quintile 3	5527	51	11.6	1.48	0.96 to 2.28	1.48	0.95 to 2.28	1.38	0.90 to 2.13
Quintile 2	5256	55	13.1	1.68	1.10 to 2.57	1.65	1.08 to 2.53	1.49	0.96 to 2.31
Quintile 1 (low)	5144	59	14.6	1.83	1.19 to 2.81	1.75	1.14 to 2.70	1.53	0.99 to 2.38
P_{trend}§					0.001		0.003		0.031
Other cancers									
All respondents	52 186	2389	56.4						
Quintile 5 (high)	10 410	469	54.6	1.00	ref	1.00	ref	1.00	ref
Quintile 4	10 407	465	55.0	0.99	0.88 to 1.12	0.99	0.87 to 1.12	0.99	0.87 to 1.12
Quintile 3	10 480	486	57.3	1.00	0.89 to 1.13	1.00	0.89 to 1.13	1.00	0.88 to 1.13
Quintile 2	10 402	476	56.4	0.99	0.87 to 1.12	0.99	0.88 to 1.13	0.98	0.86 to 1.12
Quintile 1 (low)	10 487	493	58.7	1.01	0.89 to 1.15	1.01	0.89 to 1.15	1.00	0.87 to 1.15
P_{trend}§					0.83		0.76		0.99
Women	25 260	1056	50.6						
Quintile 5 (high)	4863	211	51.8	1.00	ref	1.00	ref	1.00	ref
Quintile 4	4955	206	50.1	0.94	0.78 to 1.13	0.94	0.78 to 1.13	0.93	0.77 to 1.13
Quintile 3	4953	211	51.7	0.95	0.79 to 1.14	0.94	0.78 to 1.14	0.94	0.77 to 1.14
Quintile 2	5146	195	45.9	0.83	0.69 to 1.01	0.84	0.69 to 1.01	0.83	0.68 to 1.02
Quintile 1 (low)	5343	233	53.4	0.95	0.79 to 1.14	0.95	0.79 to 1.15	0.95	0.77 to 1.16
P_{trend}§					0.33		0.35		0.38
Men	26 926	1333	62.0						
Quintile 5 (high)	5547	258	57.0	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5452	259	59.7	1.03	0.87 to 1.22	1.03	0.87 to 1.22	1.03	0.87 to 1.23
Quintile 3	5527	275	62.4	1.05	0.89 to 1.24	1.05	0.90 to 1.24	1.05	0.89 to 1.24
Quintile 2	5256	281	67.0	1.14	0.96 to 1.35	1.14	0.96 to 1.35	1.12	0.94 to 1.34
Quintile 1 (low)	5144	260	64.5	1.07	0.90 to 1.27	1.07	0.90 to 1.27	1.04	0.86 to 1.26
P_{trend}§					0.21		0.21		0.42

*Per 10 000 person-years.
†Model 1: Adjusted for age (as the time scale in the Cox models), sex, race/ethnicity (Caucasian, Hispanic, African-American, American Indian/Alaska Native, Asian/Pacific Islander, other/missing) and marital status (married, living with partner, never married, separated/divorced, widowed).
‡Model 2: Adjusted for all factors in Model 1, plus education (high school graduate/ General Educational Development (GED) or below, some college/technical school, college graduate, advanced degree) and annual household income (<$20 000, $20 000–39 999, $40 000–59 999, $60 000–79 999 and $80 000 or more) at baseline.
§p Value associated with continuous area-level SES index.
SES, socioeconomic status; VITAL, VITamins And Lifestyle.

Table 4 Cancer-specific mortality rates, HRs and 95% CIs associated with quintiles of area-level socioeconomic status, The VITAL study cohort, Western Washington, USA, 2000–2010

Area-level SES	VITAL cohort N	Cancer deaths N	Cancer mortality rate*	Age and sex adjusted HR	Age and sex adjusted 95% CI	Model 1† Demographics only HR	Model 1† Demographics only 95% CI	Model 2‡ Demographics and individual SES HR	Model 2‡ Demographics and individual SES 95% CI
All respondents									
Women and men	60 756	2487	48.0						
Quintile 5 (high)	12 145	354	33.6	1.00	ref	1.00	ref	1.00	ref
Quintile 4	12 249	421	40.3	1.18	1.02 to 1.37	1.17	1.01 to 1.36	1.06	0.91 to 1.23
Quintile 3	12 018	507	49.4	1.40	1.22 to 1.60	1.38	1.20 to 1.58	1.18	1.02 to 1.36
Quintile 2	12 180	553	53.3	1.51	1.32 to 1.73	1.48	1.30 to 1.70	1.20	1.04 to 1.38
Quintile 1 (low)	12 164	652	63.7	1.75	1.53 to 2.00	1.68	1.47 to 1.93	1.28	1.11 to 1.48
P_{trend}§					<0.001		<0.001		<0.001
Women	30 095	1062	41.0						
Quintile 5 (high)	5810	139	27.5	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5974	179	34.7	1.22	0.97 to 1.53	1.20	0.95 to 1.50	1.10	0.88 to 1.40
Quintile 3	5787	204	41.1	1.41	1.13 to 1.75	1.38	1.11 to 1.73	1.22	0.97 to 1.54
Quintile 2	6158	245	46.2	1.54	1.25 to 1.91	1.51	1.22 to 1.86	1.27	1.02 to 1.59
Quintile 1 (low)	6366	295	54.5	1.75	1.43 to 2.15	1.67	1.36 to 2.06	1.33	1.06 to 1.67
P_{trend}§					<0.001		<0.001		0.006
Men	30 661	1425	54.9						
Quintile 5 (high)	6335	215	39.3	1.00	ref	1.00	ref	1.00	ref
Quintile 4	6275	242	45.8	1.16	0.96 to 1.41	1.15	0.95 to 1.40	1.03	0.85 to 1.25
Quintile 3	6231	303	57.3	1.39	1.16 to 1.66	1.38	1.15 to 1.65	1.15	0.96 to 1.39
Quintile 2	6022	308	60.7	1.49	1.25 to 1.77	1.49	1.23 to 1.75	1.15	0.95 to 1.38
Quintile 1 (low)	5798	357	74.2	1.75	1.48 to 2.08	1.75	1.43 to 2.02	1.24	1.03 to 1.50
P_{trend}§					<0.001		<0.001		0.002
Respondents diagnosed with cancer before baseline									
Women and men	8557	979	142.2						
Quintile 5 (high)	1657	152	110.5	1.00	ref	1.00	ref	1.00	ref
Quintile 4	1612	162	125.8	1.15	0.92 to 1.44	1.13	0.91 to 1.42	1.01	0.80 to 1.27
Quintile 3	1670	197	145.1	1.30	1.06 to 1.60	1.28	1.04 to 1.58	1.10	0.88 to 1.37
Quintile 2	1775	216	152.2	1.38	1.13 to 1.69	1.35	1.10 to 1.66	1.09	0.88 to 1.35
Quintile 1 (low)	1843	252	174.2	1.58	1.30 to 1.93	1.54	1.26 to 1.87	1.17	0.94 to 1.45
P_{trend}§					<0.001		<0.001		0.14
Women	4829	441	111.0						
Quintile 5 (high)	905	61	79.5	1.00	ref	1.00	ref	1.00	ref
Quintile 4	902	72	97.1	1.20	0.85 to 1.70	1.18	0.84 to 1.68	1.10	0.77 to 1.57
Quintile 3	910	96	128.4	1.60	1.15 to 2.21	1.57	1.13 to 2.18	1.42	1.01 to 1.99
Quintile 2	1005	99	121.0	1.50	1.09 to 2.08	1.45	1.05 to 2.01	1.27	0.90 to 1.80
Quintile 1 (low)	1107	113	125.8	1.54	1.12 to 2.11	1.45	1.06 to 1.99	1.19	0.84 to 1.67
P_{trend}§					0.002		0.009		0.31
Men	3728	538	184.7						
Quintile 5 (high)	752	91	149.7	1.00	ref	1.00	ref	1.00	ref
Quintile 4	710	90	164.8	1.11	0.82 to 1.50	1.10	0.81 to 1.48	0.93	0.69 to 1.27
Quintile 3	760	101	165.5	1.10	0.83 to 1.44	1.09	0.83 to 1.44	0.89	0.66 to 1.19
Quintile 2	770	117	194.7	1.30	0.99 to 1.70	1.27	0.97 to 1.67	0.96	0.72 to 1.28
Quintile 1 (low)	736	139	253.6	1.64	1.26 to 2.15	1.65	1.26 to 2.17	1.17	0.87 to 1.57
P_{trend}§					<0.001		<0.001		0.30
Respondents not diagnosed with cancer before baseline									
Women and men	52 199	1508	33.5						
Quintile 5 (high)	10 488	202	22.0	1.00	ref	1.00	ref	1.00	ref
Quintile 4	10 637	259	28.3	1.25	1.03 to 1.52	1.24	1.02 to 1.50	1.13	0.93 to 1.38
Quintile 3	10 348	310	34.8	1.48	1.24 to 1.77	1.47	1.23 to 1.76	1.28	1.06 to 1.53
Quintile 2	10 405	337	37.6	1.60	1.34 to 1.91	1.58	1.32 to 1.89	1.29	1.07 to 1.56
Quintile 1 (low)	10 321	400	45.6	1.87	1.57 to 2.23	1.81	1.52 to 2.16	1.40	1.16 to 1.69
P_{trend}§					<0.001		<0.001		<0.001

Continued

Table 4 Continued

Area-level SES	VITAL cohort N	Cancer deaths N	Cancer mortality rate*	Age and sex adjusted HR	Age and sex adjusted 95% CI	Model 1† Demographics only HR	Model 1† Demographics only 95% CI	Model 2‡ Demographics and individual SES HR	Model 2‡ Demographics and individual SES 95% CI
Women	25 266	621	28.3						
Quintile 5 (high)	4905	78	18.2	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5072	107	24.2	1.27	0.93 to 1.73	1.25	0.92 to 1.71	1.16	0.85 to 1.59
Quintile 3	4877	108	25.6	1.30	0.97 to 1.75	1.28	0.95 to 1.73	1.13	0.83 to 1.54
Quintile 2	5153	146	32.5	1.60	1.20 to 2.13	1.58	1.19 to 2.09	1.33	0.98 to 1.81
Quintile 1 (low)	5259	182	40.3	1.90	1.43 to 2.51	1.83	1.38 to 2.42	1.47	1.09 to 1.99
P_{trend}§					<0.001		<0.001		0.009
Men	26 933	887	38.5						
Quintile 5 (high)	5583	124	25.5	1.00	ref	1.00	ref	1.00	ref
Quintile 4	5565	152	32.1	1.24	0.98 to 1.57	1.24	0.98 to 1.57	1.12	0.88 to 1.43
Quintile 3	5471	202	43.2	1.60	1.28 to 2.00	1.59	1.27 to 1.99	1.36	1.08 to 1.72
Quintile 2	5252	191	42.7	1.60	1.28 to 2.01	1.58	1.26 to 1.98	1.26	0.99 to 1.61
Quintile 1 (low)	5062	218	51.1	1.85	1.49 to 2.30	1.78	1.43 to 2.21	1.34	1.05 to 1.69
P_{trend}§					<0.001		<0.001		0.001

*Per 10 000 person-years.
†Model 1: Adjusted for age (as the time scale in the Cox models), sex, race/ethnicity (Caucasian, Hispanic, African-American, American Indian/Alaska Native, Asian/Pacific Islander, other/missing) and marital status (married, living with partner, never married, separated/divorced, widowed).
‡Model 2: Adjusted for all factors in Model 1, plus education (high school graduate/GED or below, some college/technical school, college graduate, advanced degree) and annual household income (<$20 000, $20 000–39 999, $40 000–59 999, $60 000–79 999 and $80 000 or more) at baseline.
§p Value associated with continuous area-level SES index.
SES, socioeconomic status; VITAL, VITamins And Lifestyle.

mortality, and marginally associated with colorectal cancer risk, suggesting that there are moderate-to-large associations between area-level SES and specific cancer outcomes, which are not completely explained by individual SES.

While measures of area-level SES should summarise information about socioeconomic conditions in a given area in a meaningful way and use data that can be compared between different locations and at different times,[8] there are no established standards for measuring area-level SES, making it difficult to directly compare results between studies. However, previous studies have also used categorical area-level SES measures, allowing for comparisons of relative SES and cancer outcomes.

Several prior studies have included measures of individual SES in multivariate-adjusted models of area-level socioeconomic factors and cancer outcomes;[1 2 5 6 9 10 20–22] however, very little prior work has directly compared these associations with and without control for individual socioeconomic factors,[6 10] or presented results controlling for individual SES without simultaneously adding several additional risk factors.[5 20] In a case–control study of area-level SES and prostate cancer among Caucasian and African-American men in South Carolina, Sanderson *et al*[6] reported an OR of 0.52 (95% CI 0.34 to 0.80) associated with living in ZIP codes in the highest quartile of area-level SES relative to the lowest. Adding individual educational attainment resulted in wider CIs but had little impact on the effect estimates. These results differed from our findings of lower prostate cancer incidence in lower-SES areas before accounting for individual SES, but no association once individual education and income were included. These differences may be due to the higher proportion of African-American men included in the Sanderson *et al* study, and possibly to high levels of screening in VITAL.

A previous study of area-level SES and premature cancer mortality among individuals ages 25–64 in Australia reported an age-adjusted rate ratio (RR) of 1.69 (95% CI 1.54 to 1.84) comparing the most disadvantaged quintiles of Statistical Local Areas to the least in men, which attenuated to 1.48 (95% CI 1.35 to 1.63) after adding individual occupation, similar to our results.[10] Associations between area deprivation and cancer mortality were much weaker among women (RR: 1.31, 95% CI 1.19 to 1.44) and did not change when including individual occupation.

In analyses adding parish-level unemployment to models already accounting for individual demographics and SES, proportion unemployed was inversely associated with lung cancer incidence in Denmark, similar to our results, and positively associated with prostate cancer incidence, unlike our findings of no association after including individual SES; however, results without controlling for individual SES were not presented.[5]

A case–control study in Wisconsin reported an OR of breast cancer of 1.23 (95% CI 1.09 to 1.39) for women in the highest quintile of census tract-level SES relative to those in the lowest quintile accounting for individual educational attainment.[20] In contrast, we observed no association between area-level SES and breast cancer incidence when accounting for individual SES, consistent with other previous findings of no association between area-level SES and breast cancer risk after including individual education and other risk factors.[21 22]

Analyses in the Nurses' Health Study found lower incidence of rectal cancer in women living in the highest-SES areas (using quintiles of the same index as in this study) relative to women in the lowest-SES areas when accounting for educational attainment and several other area-level characteristics and individual risk factors (relative risk: 0.64, 95% CI 0.44 to 0.93).[2] This same study reported no association between area-level SES and colon cancer overall.[2] We found no association between area-level SES and combined risk of colon and rectal cancer in women; however, we did not have sufficient numbers of cases to examine colon and rectal cancer separately.

Additional studies of area-level SES and cancer outcomes have included individual socioeconomic factors along with several modifiable risk factors (eg, diet, physical activity,

smoking, obesity, alcohol use) that are likely on the causal pathway between area-level SES and cancer outcomes.[1 9] Major *et al*[9] reported higher cancer mortality rates in quintiles of the lowest- relative to the highest-SES census tracts in the NIH-AARP Diet and Health Study. This association attenuated substantially in models including individual education; however, these models also included demographics, family history, and several behavioural risk factors that could be on the causal pathway between area-level SES and cancer mortality, making the contribution of individual-level SES unclear. Similarly, Doubeni *et al*[1] reported an inverse association between quintiles of area-level SES and colorectal cancer incidence that weakened when including individual education in addition to measures of diet, physical activity, body mass index, and smoking, which represent pathways through which area-level SES could impact colorectal cancer risk.[4]

Although previous work suggests that individual behaviours, such as smoking, alcohol consumption, diet and physical inactivity partially explain differences in cancer outcomes by area-level SES, the association between area-level SES and cancer mortality could also be due to higher incidence of more fatal types of cancer (eg, lung cancer, as found in this study); delay in seeking care for symptoms or less screening, both of which would lead to later stage at diagnosis; and/or less access to effective medical treatment or lower compliance with treatment, which could lead to poorer survival. Associations between area-level SES and cancer incidence and mortality that remain after controlling for individual SES (compositional factors) could indicate that there are also area-level (contextual) effects on these cancer outcomes, either directly or through influences on the factors noted above, suggesting that cancer prevention interventions may be important at the individual as well as area levels.

Limitations of this study should be noted. Although associations between area-level SES and cancer outcomes remained after controlling for two measures of individual SES, the remaining association could be at least partly due to residual confounding caused by measurement error in individual education and household income and by not including other measures of individual SES (eg, total assets; lifecourse socioeconomic factors) if they are more important. Our analysis of cancer mortality is limited because analyses of those diagnosed before baseline could be impacted by survival bias. Participants diagnosed before baseline had to survive long enough to be included in the study, and individuals from low-SES areas who are included here might not be representative of all individuals from lower-SES areas. There are differences in the types of cancer experienced in each group, with those diagnosed after baseline dying predominantly of rapidly-fatal cancers such as lung, pancreatic and haematological cancers and not breast, prostate or colorectal cancers. Additionally, models incorporating interaction terms between area-level SES and individual SES could add further insight into whether the relationship between area-level SES and cancer outcomes is consistent by different levels of individual SES.

VITAL recruited participants from only one region of the USA and a large majority of participants were Caucasian, which could limit its generalisability to other populations. Although baseline addresses were successfully geocoded for almost all VITAL respondents, misclassification of quintile of area-level SES index would occur to the extent that participants were placed in the wrong block group, and that particular block group was in a different quintile than the respondent's actual block group. Sensitivity analyses randomly reassigning quintiles of block group SES to 2% of VITAL participants resulted in only small alterations in the association between area-level SES and cancer incidence and mortality, suggesting that misclassification of area-level SES likely had only a small impact on our results. Area-level SES was assessed only at baseline and might not accurately reflect area-level SES at other aetiologically-relevant time points.

Strengths of this study include its prospective design, large sample size, and several years of follow-up, allowing for examination of several site-specific cancers as well as total cancer incidence and cancer mortality. Information collected from the detailed baseline questionnaires allowed us to control for demographic factors and to include two measures of individual-level SES. Linkage with SEER and the Washington State death file allowed for accurate and near-complete ascertainment of new cancer diagnoses and cancer deaths.

To the best of our knowledge this is the first study to systematically examine associations between area-level SES and total and site-specific cancer incidence and total cancer mortality with and without control for individual SES. Behaviours and other modifiable factors that affect cancer outcomes may be influenced by the socioeconomic characteristics of individuals as well as the socioeconomic and physical characteristics of the neighbourhoods in which they live. Future research should examine the causal pathways linking lower area-level SES to specific cancer outcomes to identify potential points of intervention to reduce these disparities.

What is already known on this subject

- Living in lower-socioeconomic status (SES) areas has been associated with higher incidence of some cancers and with higher cancer mortality.
- These associations vary by cancer site.
- The extent to which observed associations between area-level SES and cancer outcomes are due to individual socioeconomic factors is unclear.

What this study adds

- Living in low-socioeconomic status (SES) areas was associated with higher total, lung and colorectal cancer incidence, and higher total cancer mortality.
- After accounting for individual education and household income, living in lower-SES areas remained associated with higher lung and colorectal cancer incidence, and higher total cancer mortality.
- Associations between area-level SES, and cancer incidence and mortality, are partly explained by individual SES, but the places people live could also influence cancer outcomes, either directly or through other risk factors.

Contributors TAH and EW contributed to the conceptualisation of the study, acquisition of data and the interpretation of the results. TAH analysed the data and wrote the manuscript. TAH, SAAB, LS and EW contributed to the analysis plan, provided critical review and contributed to revising and finalising the manuscript.

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