Socioeconomic Inequalities in Premature Cancer Mortality Among U.S. Counties During 1999 to 2018

Suhang Song[1], Yuqi Duan[2,3], Junjie Huang[4], Martin C S Wong[2,4], Hongda Chen[5], Michael G. Trisolini[6], Kenneth A. Labresh[6], Sidney C. Smith Jr[7], Yinzi Jin[2,3], and Zhi-Jie Zheng[2,3]

ABSTRACT

Background: This study investigated socioeconomic inequalities in premature cancer mortality by cancer types, and evaluated the associations between socioeconomic status (SES) and premature cancer mortality by cancer types.

Methods: Using multiple databases, cancer mortality was linked to SES and other county characteristics. The outcome measure was cancer mortality among adults ages 25–64 years in 3,028 U.S. counties, from 1999 to 2018. Socioeconomic inequalities in mortality were calculated as a concentration index (CI) by income (annual median household income), educational attainment (% with bachelor's degree or higher), and unemployment rate. A hierarchical linear mixed model and dominance analyses were used to investigate SES associated with county-level mortality. The analyses were also conducted by cancer types.

Results: CIs of SES factors varied by cancer types. Low-SES counties showed increasing trends in mortality, while high-SES counties showed decreasing trends. Socioeconomic inequalities in mortality among high-SES counties were larger than those among low-SES counties. SES explained 25.73% of the mortality. County-level cancer mortality was associated with income, educational attainment, and unemployment rate, at −0.24 [95% (CI): −0.36 to −0.12], −0.68 (95% CI: −0.87 to −0.50), and 1.50 (95% CI: 0.92–2.07) deaths per 100,000 population with one-unit SES factors increase, respectively, after controlling for health care environment and population health.

Conclusions: SES acts as a key driver of premature cancer mortality, and socioeconomic inequalities differ by cancer types.

Impact: Focused efforts that target socioeconomic drivers of mortalities and inequalities are warranted for designing cancer-prevention implementation strategies and control programs and policies for socioeconomically underprivileged groups.

Introduction

Cancer is one of the leading causes of death in most U.S. states (1), and is expected to surpass heart disease as the first leading cause of death in that nation by 2020 (2). Socioeconomic inequalities currently contribute more to cancer mortality than to mortality from other noncommunicable chronic diseases (3). Compared with older adults, young and middle-aged adults experience widening socioeconomic inequalities and slower improvements in mortality rates (4). Premature cancer deaths may arguably have a greater and more substantial economic and social impact, and might induce significantly more productivity loss, than late-age cancer deaths (5, 6). Trends and patterns in premature cancer mortality can serve as a sentinel for future disease burden; hence, identifying adverse trends can inform the early implementation of cancer-control interventions (7, 8).

On the basis of a social determinants of health (SDOH) framework and prior studies, we built up a conceptual model: demographic composition, socioeconomic status (SES), health care environment, and population health will affect access to health care services, which will impact health outcomes, especially cancer mortality (9, 10). Some studies have indicated that, of these factors, SES is a significant predictor of cancer mortality, and individuals with lower incomes, less education, and greater unemployment are more likely to have higher mortality (11–14). Recent U.S.-based analyses have demonstrated inequalities in cancer mortality at the county level (15, 16), but few studies investigated the degree to which county-level mortality can be explained by the larger socioeconomic context of a county. Little is known about county-level inequality patterns in premature cancer mortality that consider different SES measures, such as income, educational attainment, and employment. It is still questionable whether the low and high SES groups have different socioeconomic inequalities.

In addition, SES is considered to be related to health care access and health risk profile, with income allowing easier access to quality healthcare, educational attainment capturing the knowledge-related health behaviors, and employment representing social standing with certain privileges (17). It is necessary to examine whether the associations between SES and cancer mortality persist after controlling for the major factors of health care access and health behaviors. Understanding such factors can help shed light on designing and implementing strategies for public health interventions and policies for the neediest counties (18).

The socioeconomic inequalities associated with mortality can vary substantially between specific cancer types, which highlights the need for different policy priorities to effectively tackle socioeconomic inequalities. For example, smoking-related cancers, particularly lung

[1]Taub Institute for Research in Alzheimer's Disease and the Aging Brain, Columbia University, New York, New York. [2]Department of Global Health, School of Public Health, Peking University, Beijing, P.R. China. [3]Institute for Global Health, Peking University, Beijing, P.R. China. [4]Jockey Club School of Public Health and Primary Care, Faculty of Medicine, Chinese University of Hong Kong, Hong Kong, P.R. China. [5]Office of Cancer Screening, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, P.R. China. [6]RTI International, Research Triangle Park, North Carolina. [7]School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

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Corresponding Author: Yinzi Jin, School of Public Health, Peking University, Beijing 100191, P.R. China. Phone: 8615-0010-81989; Fax: 8610-8280-2144; E-mail: yzjin@bjmu.edu.cn

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cancer, have accounted for much of the measured socioeconomic inequalities in premature smoking-related cancer mortality (19); colorectal cancer and breast cancer, which are responsive to screening, can also be important contributors to socioeconomic inequalities in premature mortality due to colorectal cancer and breast cancer (20, 21). However, no studies have examined the associations between SES and cancer type–specific premature mortality. Therefore, we examined these associations and investigated how SES explains the county-level premature mortality by cancer types.

To fill this gap, this study aimed to: (i) estimate socioeconomic inequalities in premature mortality caused by cancer among U.S. counties; and, (ii) investigate the associations between SES and premature cancer mortality.

Materials and Methods

Study design and data

This study linked the mortality and demographic data for each county to the county-level characteristics recorded in multiple databases; the methods used were introduced in our previous studies (22–24). The combined dataset was constructed to capture SES associated with mortality at the county level.

The outcome measure was county-level age-adjusted premature cancer mortality. This study defined premature cancer mortality as the number of deaths per 100,000 people attributable to cancers that occurred between the ages of 25 and 64 years (25). All causes of death from cancer were classified according to the International Classification of Diseases, Tenth Revision (ICD-10; Supplementary Data). County-level mortality and demographic data for 1999–2018 were obtained from death certificates from the U.S. Centers for Disease Control and Prevention. This database is available online (https://wonder.cdc.gov/; ref. 26); we included the following key data elements: age, sex, race, ethnicity, underlying cause of death, county, and year. To create stable units of analysis, county-level mortality data were pooled for 20 years from 1999 through 2018; 3,028 counties were included in the analysis.

The explanatory variables, SES, included three variables—county-level income (median household income in thousands of dollars), educational attainment (% with bachelor's degree or higher), and unemployment (percentage of county population ages 16 and older unemployed but seeking work, %). Controlled variables for this study consisted of three sets of correlates of county-level premature cancer mortality: demographic composition, health care environment, and population health (10). Data on those county-level factors were drawn from multiple databases, most of which were available for 2011–2018 (27–35). **Table 1** provides data sources and summary statistics for each factor. By combining mortality data for each county with county characteristics from multiple databases, the analyses for 2011–2018 were based on 2,912 counties. All data used in this study were deidentified; thus, Institutional Review Board approval was not required.

Statistical analysis

To examine the trends in county-level age-adjusted premature cancer mortality rates from 1999 to 2018, we estimated the annual percentage change (APC) by using linear regression. The socioeconomic inequalities in mortality were calculated as the concentration index (CI) with standard error (SE) by county-level income, educational attainment, and unemployment. The CI is defined as follows (36):

$$\mathrm{CI} = \frac{2}{\mu} * cov(h, r)$$

In our study, h is the county-level premature cancer mortality rate, μ is the mean mortality across all counties, and r is the fractional rank of all counties according to income, educational attainment, or unemployment. The CI, ranging from -1 to $+1$, is a popular index that presents relative inequality by showing the mortality across counties, with each SES variable shown from lowest to highest (37–39). Negative values for income and educational attainment levels indicate that mortality is higher among counties with low-income/educational attainment levels; a positive value for unemployment rate indicates that mortality is higher among counties with higher unemployment rates. When there was no inequality, the CI was 0 and, in practice, a reasonably high level of inequality was represented by an absolute value of $0.2-0.3$ (40–42). We also assessed the trends in premature cancer mortality by groups of income, educational attainment, and unemployment. To assess the socioeconomic inequalities by cause of death and SES level, we calculated the CIs of the premature mortality for each cancer type and for the five cancer types (tracheal, bronchus, and lung cancer, colorectal cancer, breast cancer, pancreatic cancer and liver cancer) in 1999–2018 by low, middle, and high income, educational attainment, and unemployment tertiles.

To investigate the association between SES and county-level mortality, we fitted the hierarchical linear mixed model with state level as the second level. To quantify the extent to which SES was associated with mortality, we conducted a dominance analysis for decomposition by examining the relative importance of SES and three sets of controlled variables that contributed to the R-squared of the regression. We fitted four models by sequentially adding demographic composition (model 1), SES (including median household income, % with bachelor's degree or higher and unemployment rate; model 2), health care environment (model 3), and population health (model 4), thus structuring the analysis to account first for nonmodifiable factors and subsequently for modifiable factors.

By comparing the coefficients of SES in models 2, 3, and 4, the results could indicate whether health care environment and population health, as modifiable factors, might be linked to socioeconomic inequalities in mortality. Model 4 was also conducted for each type among five major contributing cancers, to investigate how SES explained the county-level premature cancer mortality by cancer types. Age-adjusted mortality rates were standardized by the direct method to the 2000 U.S. population. All analyses were conducted in Stata 14.1 (StataCorp LP).

Results

Socioeconomic inequalities in premature cancer mortality

Overall, the cancer mortality rate (per 100,000) decreased from 107.40 in 1999 to 76.60 in 2018 (APC $= -1.60$, $P < 0.001$) among adults ages 25–64 years. In 2018, cancers with the highest mortality rate (per 100,000) were tracheal, bronchus, and lung (16.1), colorectal (8.5), breast (8.1), pancreatic (5.3), and liver (4.3). For the socioeconomic inequalities, CIs were -0.085 (SE: 0.002), -0.074 (SE: 0.002), and 0.061 (SE: 0.003) by income, educational attainment, and unemployment, respectively, for overall cancer mortality from 1999 to 2018. CIs varied substantially by cancer types (**Table 2**).

Counties with high-income and educational attainment levels, and low unemployment rates had lower rates of premature cancer mortality during the 1999–2018 period. Counties with low-income and educational attainment levels, and high unemployment rates showed increasing trends in premature cancer mortality from 1999 to 2018; slopes of the fitted line were 0.48 (95% CI: 0.35–0.61), 0.55 (95% CI:

Table 1. Variables included in the regression analysis with summary statistics and bivariate regression results.

County characteristics	Definition	Data source	Mean (SD) [range]	Bivariate associations[d]	
				Coefficient	95% CI
Demographic composition					
Ages ≥65 years, %, 2011–2018	% of population ages 65 years or older.	ACS (27)	17.58 (4.33) [4.22–53.04]	0.78***	(0.57–0.98)
Female, %, 2011–2018	% of female.	ACS (27)	49.98 (2.21) [28.35–56.82]	0.76***	(0.35–1.17)
Non-Hispanic, Black or African American, %, 2011–2018	% of non-Hispanic African American population.	ACS (27)	9.19 (14.62) [0.00–86.05]	0.57***	(0.51–0.62)
Non-Hispanic, American Indian/Alaskan Native, %, 2011–2018	% of non-Hispanic American Indian/Alaskan Native population.	ACS (27)	1.66 (7.04) [0.00–94.33]	−0.06	(−0.19 to 0.08)
Non-Hispanic, Asian, %, 2011–2018	% of non-Hispanic Asian population.	ACS (27)	1.25 (2.57) [0.00–42.28]	−2.67***	(−2.99 to −2.35)
Non-Hispanic, Native Hawaiian/other Pacific Islander, %, 2011–2018	% of non-Hispanic Native Hawaiian/other Pacific Islander population.	ACS (27)	0.07 (0.38) [0.00–11.08]	−4.81***	(−6.99 to −2.63)
Non-Hispanic, Two or more races, %, 2011–2018	% of non-Hispanic population with two or more races.	ACS (27)	1.76 (1.59) [0.00–23.36]	−0.65**	(−1.19 to −0.10)
Hispanic, %, 2011–2018	% of Hispanic population.	ACS (27)	8.58 (13.21) [0.00–98.35]	−0.43***	(−0.50 to −0.37)
Socioeconomic status					
Median household income (thousands of dollars), 2011–2018	Annual median household income (thousands of dollars).	SAIPE (28)	47.97 (12.32) [23.48–126.98]	−1.12***	(−1.18 to −1.07)
Bachelor's degree or higher, %, 2011–2018	% of county population ages 25 and older received a bachelor's degree or higher.	ACS (29)	20.32 (9.03) [5.53–76.24]	−1.42***	(−1.50 to −1.35)
Unemployment rate, %, 2011–2017[b]	% of county population ages 16 and older unemployed but seeking work.	CHRR[a] (30)	6.30 (2.06) [1.92–23.97]	4.88***	(4.48–5.27)
Health care environment					
No. of primary care physicians per 100,000 population, 2011–2018	Ratio of population to primary care physicians.	CHRR[a] (30)	55.35 (34.95) [0.00–500.01]	−0.20***	(−0.22 to −0.18)
Medicare to Medicaid fee index, 2016	A computed ratio of the Medicaid fee for each service in each state to the Medicare fee for the same services. This is a state-level variable, updated by KFF in 2016.	KFF (31)	0.76 (0.13) [0.38–1.26]	−2.14	(−8.89 to 4.61)
Smoke-free law, 2018	27 states and DC enabled the statewide comprehensive smoke-free law before 2018.	MMWR (32)	0.42 (0.49) [0–1]	−19.03***	(−20.63 to −17.43)
Medicaid expansion, 2018	31 states and DC adopted Medicaid expansion before 2018.	KFF (33)	0.48 (0.50) [0–1]	−4.98***	(−6.70 to −3.26)
Food environment index, 2011–2016[b, c]	Index of factors that contribute to a healthy food environment, calculated as a composite score, ranging from 1 to 10, describing limits on access to healthy foods, with 1 indicating the lowest access to healthy foods, and 10 indicating the highest access to healthy foods.	CHRR[a] (30)	7.33 (1.12) [0.76–10.00]	−9.72***	(−10.42 to −9.02)
Health care quality index, 2011–2015[b]	Calculated by taking the mean of the z-scores for six variables related to primary care access and quality among Medicare enrollees: average annual percent of Medicare enrollees having at least one ambulatory visit to a primary care clinician, average annual percent of diabetic Medicare enrollees having hemoglobin A1c test, average annual percent of diabetic Medicare enrollees having eye examination, average annual percent of diabetic Medicare enrollees having blood lipids (LDL-C) test, average percent of female Medicare enrollees having at least one mammogram over a 2-year period and discharges for ambulatory care sensitive conditions per 1,000 Medicare enrollees.	DAHC (34)	0.01 (0.52) [−3.83–1.31]	−2.06**	(−3.76 to −0.37)

(Continued on the following page)

Table 1. Variables included in the regression analysis with summary statistics and bivariate regression results. (Cont'd)

County characteristics	Definition	Data source	Mean (SD) [range]	Bivariate associations[d]	
				Coefficient	95% CI
Population health					
Smoker, %, 2011–2018	% of adults who are current smokers.	CHRR[a] (30)	19.87 (4.58) [5.10–46.18]	3.14***	(2.98–3.30)
Obesity, %, 2011–2018	% of adults that report a BMI ≥ 30.	CHRR[a] (30)	30.60 (4.00) [12.65–46.18]	3.47***	(3.30–3.64)
Total Medicare reimbursements per enrollee, thousands of dollars, 2011–2016[b]	Total Medicare reimbursements per enrollee price, age, sex, and race-adjusted (thousands of dollars).	DAHC (35)	9.70 (1.41) [5.85–18.42]	7.65***	(7.10–8.21)

Note: ***, $P < 0.01$; **, $P < 0.05$; *, $P < 0.10$.
Abbreviations: 95%CI, 95% Confidence Interval; ACS, American Community Survey; CHRR, County Health Rankings & Roadmaps; DAHC, Dartmouth Atlas of Health Care; DC, District of Columbia; KFF, Kaiser Family Foundation; MMWR, Morbidity and Mortality Weekly Report; SAIPE, Small Area Income and Poverty Estimates; SD, Standard Deviation.
[a]CHRR provides a model to help communities understand the factors influencing healthy residents. It summarizes many health outcomes and health factors from other databases each year.
[b]For those variables restricted to year range, we conducted an ordinary least squares regression model to predict the missing values.
[c]The 2014–2019 County Health Rankings & Roadmaps databases were used to summarize this variable from the U.S. Department of Agriculture Food Environment Atlas, Map the Meal Gap (DAFEA) from 2011–2016.
[d]The dependent variable for the bivariate association is county-level age-adjusted cancer mortality (deaths per 100,000 population) in U.S. residents ages 25–64 years, 2011–2018.

`0.42–0.68), and 0.40 (95% CI: 0.27–0.52); while counties with high SES showed decreasing trends in mortality (**Fig. 1**).

SES inequalities in mortality among counties with high-income and educational attainment levels, and low unemployment rates were larger than those among low-SES counties. For the total premature cancer mortality, CIs for counties with high, middle, and low income were −0.054 (SE: 0.004), −0.020 (SE: 0.003), and −0.031 (SE: 0.004); CIs for counties with high, middle, and low educational attainment levels were −0.062 (SE: 0.003), −0.015 (SE: 0.002), and −0.026 (SE: 0.003); and CIs for counties with high, middle, and low unemployment rates were 0.015 (SE: 0.004), 0.017 (SE: 0.004), and 0.035 (SE: 0.005). Taking lung cancer as an example, CIs for counties with high-income and educational attainment levels, and low unemployment rates were −0.085 (SE: 0.006), −0.096 (SE: 0.005), and 0.066 (SE: 0.007), respectively, the absolute values of which were higher than those for low-SES counties at −0.044 (SE: 0.006), −0.050 (SE: 0.004), and 0.023 (SE: 0.007), respectively (**Fig. 2**; Supplementary Data).

SES associated with premature cancer mortality

For overall cancer mortality during the period 2011–2018, dominance analysis showed that demographic composition and SES were the dominant factors associated with premature cancer mortality at a magnitude of 36.69% and 25.73%, respectively, followed by population health (24.23%), and health care environment (13.35%; **Table 3**).

In model 1, associations between mortality (deaths per 100,000 population) and the ethnic groups, non-Hispanic black or African American, non-Hispanic American Indian/Alaskan Native, non-Hispanic Asian, non-Hispanic Native Hawaiian/other Pacific Islander and non-Hispanic two or more races, were 0.58 (95% CI: 0.50–0.66), 0.37 (95% CI: 0.22–0.51), −2.92 (95% CI: −3.37 to −2.47), 4.90 (95% CI: 1.30–8.49), and 0.32 (95% CI: −0.55 to 1.19), respectively. Accounting for SES affected associations between demographic composition and mortality (model 2). The association between non-Hispanic black or African American and mortality was attenuated; the associations between non-Hispanic American Indian/Alaskan Native and non-Hispanic Native Hawaiian/other Pacific Islander and mortality showed reversed directions; the association between non-Hispanic Asian and mortality did not reach statistical significance; the association between non-Hispanic two or more races and mortality was intensified and reached statistical significance.

In model 2, mortality was negatively associated with an increase in median household income (in thousands of dollars) at −0.45 (95% CI: −0.56 to −0.35) per 100,000 population, and negatively associated with a one-unit increase in the percentage with bachelor's degree or higher at −1.14 (95% CI: −1.28 to −1.00) per 100,000. For each one-unit increase in unemployment rate, mortality increased by 2.44 (95% CI: 1.86–3.02) per 100,000, indicating unemployment rate had the highest association with mortality, compared with income and educational attainment levels.

In model 3, associations between mortality and median household income and unemployment rate were attenuated at −0.38 (95% CI: −0.50 to −0.26), and 2.20 (95% CI: 1.60–2.80) per 100,000, respectively, after controlling for health care environment. For health care environment, Medicare and Medicaid fee index, smoke-free law, food environment index, and health care quality index were inversely associated with mortality at −17.10 (95% CI: −32.50 to −1.70), −8.89 (95% CI: −13.90 to −3.91), −1.22 (95% CI: −2.45 to 0.02) and −2.71 (95% CI: −4.68 to −0.75), respectively.

In model 4, associations between mortality and median household income, % with bachelor's degree or higher, and unemployment rate were further attenuated at −0.24 (95% CI: −0.36 to −0.12), −0.68 (95% CI: −0.87 to −0.50), and 1.50 (95% CI: 0.92–2.07) per 100,000, respectively, after controlling for health care environment and population health. For population health, mortality was positively associated with rates of tobacco smoking and obesity at 1.49 (95% CI: 1.22–1.76) and 0.82 (95% CI: 0.43–1.22) per 100,000, respectively. An additional increase in the total Medicare reimbursements per enrollee (in thousands of dollars) was positively associated with mortality at 1.70 (95% CI: 0.96–2.44) per 100,000.

Factors associated with site-specific mortality varied and showed different strengths for explaining premature cancer mortality. Demographic composition dominated the mortality across all the five cancer types. SES was the second most dominant factor associated with mortality for pancreatic (26.53%), liver (25.81%), and colorectal (25.16%) cancers. For lung and breast cancers, SES explained 25.06% and 16.54%, respectively, of the mortality, as the third dominant factor. (**Table 4**).

Table 2. Trends and socioeconomic inequalities in age-adjusted site-specific premature cancer mortality (deaths per 100,000 population) in U.S. residents ages 25–64 years, 1999–2018.

	Mortality rate[a] (deaths per 100,000 population)				Socioeconomic inequalities in mortality rate (CI[b])		
Cause of death	1999 (SE)	2018 (SE)	Annual percentage change	*P*	Income inequality (SE)	Educational attainment inequality (SE)	Employment inequality (SE)
Total	107.40 (0.30)	76.60 (0.20)	−1.600	<0.001	−0.085 (0.002)	−0.074 (0.002)	0.061 (0.003)
Lip and oral cavity cancer	1.00 (0.01)	0.90 (0.01)	−0.010	0.003	−0.126 (0.012)	−0.130 (0.013)	0.071 (0.013)
Nasopharynx cancer	0.20 (0.01)	0.20 (0.01)	0.000	NA	−0.031 (0.032)	−0.042 (0.030)	−0.001 (0.033)
Other pharynx cancer	0.50 (0.01)	0.50 (0.01)	0.002	0.269	−0.170 (0.016)	−0.158 (0.016)	0.090 (0.017)
Esophageal cancer	2.90 (0.01)	2.30 (0.01)	−0.030	<0.001	−0.102 (0.006)	−0.104 (0.004)	0.065 (0.006)
Stomach cancer	2.50 (0.01)	1.90 (0.01)	−0.030	<0.001	−0.115 (0.010)	−0.122 (0.008)	0.105 (0.012)
Colorectal cancer	9.60 (0.10)	8.50 (0.10)	−0.050	0.001	−0.106 (0.004)	−0.093 (0.003)	0.064 (0.004)
Liver cancer	2.90 (0.01)	4.30 (0.01)	0.100	<0.001	−0.102 (0.006)	−0.093 (0.004)	0.070 (0.006)
Gallbladder and biliary tract cancer	0.50 (0.01)	0.50 (0.01)	−0.002	0.420	−0.076 (0.017)	−0.091 (0.016)	0.057 (0.017)
Pancreatic cancer	5.40 (0.10)	5.30 (0.10)	0.010	0.070	−0.072 (0.004)	−0.067 (0.003)	0.046 (0.004)
Larynx cancer	1.00 (0.01)	0.60 (0.01)	−0.020	<0.001	−0.213 (0.013)	−0.201 (0.014)	0.124 (0.015)
Tracheal, bronchus, and lung cancer	30.90 (0.10)	16.10 (0.10)	−0.800	<0.001	−0.132 (0.004)	−0.125 (0.003)	0.088 (0.004)
Malignant skin melanoma	2.30 (0.01)	1.30 (0.01)	−0.050	<0.001	−0.064 (0.007)	−0.089 (0.006)	0.017 (0.007)
Nonmelanoma skin cancer	0.40 (0.01)	0.40 (0.01)	0.003	0.089	−0.123 (0.016)	−0.117 (0.018)	−0.002 (0.018)
Breast cancer	11.80 (0.10)	8.10 (0.10)	−0.200	<0.001	−0.061 (0.004)	−0.041 (0.003)	0.043 (0.004)
Cervical cancer	1.80 (0.01)	1.50 (0.01)	−0.010	<0.001	−0.172 (0.009)	−0.174 (0.007)	0.101 (0.009)
Ovarian cancer	3.20 (0.01)	2.20 (0.01)	−0.060	<0.001	−0.048 (0.006)	−0.048 (0.004)	0.031 (0.006)
Prostate cancer	1.70 (0.01)	1.40 (0.01)	−0.020	<0.001	−0.140 (0.010)	−0.124 (0.007)	0.094 (0.010)
Testicular cancer	0.20 (0.01)	0.20 (0.01)	0.000	NA	−0.081 (0.023)	−0.133 (0.026)	0.092 (0.029)
Uterine cancer	0.50 (0.01)	0.90 (0.01)	0.010	<0.001	−0.069 (0.011)	−0.081 (0.011)	0.038 (0.012)
Kidney cancer	2.60 (0.01)	1.90 (0.01)	−0.040	<0.001	−0.107 (0.006)	−0.122 (0.005)	0.058 (0.006)
Bladder cancer	1.30 (0.01)	1.10 (0.01)	−0.010	<0.001	−0.105 (0.009)	−0.119 (0.007)	0.073 (0.010)
Brain and nervous system cancer	4.10 (0.10)	3.60 (0.01)	−0.020	0.001	−0.027 (0.005)	−0.040 (0.004)	−0.005 (0.005)
Thyroid cancer	0.30 (0.01)	0.20 (0.01)	−0.001	0.502	−0.035 (0.017)	−0.056 (0.015)	0.025 (0.018)
Mesothelioma	0.40 (0.01)	0.20 (0.01)	−0.010	<0.001	−0.079 (0.024)	−0.128 (0.025)	0.063 (0.028)
Hodgkin lymphoma	0.50 (0.01)	0.20 (0.01)	−0.010	<0.001	−0.076 (0.015)	−0.08 (0.016)	0.057 (0.016)
Non-Hodgkin lymphoma	4.20 (0.10)	2.00 (0.01)	−0.100	<0.001	−0.081 (0.005)	−0.093 (0.005)	0.047 (0.006)
Multiple myeloma	1.90 (0.01)	1.20 (0.01)	−0.030	<0.001	−0.100 (0.008)	−0.091 (0.008)	0.064 (0.008)
Leukemia	3.90 (0.10)	2.60 (0.01)	−0.070	<0.001	−0.076 (0.005)	−0.085 (0.004)	0.039 (0.006)
Acute lymphoid leukemia	0.40 (0.01)	0.40 (0.01)	−0.002	0.359	−0.050 (0.015)	−0.087 (0.014)	0.041 (0.016)
Chronic lymphoid leukemia	0.50 (0.01)	0.10 (0.01)	−0.010	<0.001	−0.102 (0.019)	−0.098 (0.019)	0.055 (0.019)
Acute myeloid leukemia	1.50 (0.01)	1.30 (0.01)	−0.010	<0.001	−0.062 (0.007)	−0.082 (0.006)	0.024 (0.008)
Chronic myeloid leukemia	0.50 (0.01)	0.10 (0.01)	−0.020	<0.001	−0.105 (0.021)	−0.105 (0.022)	0.063 (0.025)
Other neoplasms	23.10 (0.10)	17.80 (0.10)	−0.300	<0.001	−0.097 (0.003)	−0.082 (0.002)	0.066 (0.003)

Abbreviations: CI, Concentration Index; SE, Standard Error.
[a]Mortality data were obtained from CDC WONDER.
[b]The CI, ranging from −1 to +1, presents the relative inequality by showing mortality across counties ranking from low-income/educational attainment levels and unemployment rate to high. Negative values for income and educational attainment levels indicate that mortality was higher among counties with lower income/educational attainment levels; a positive value for unemployment rate indicates that mortality was higher among counties with higher unemployment rates.

Discussion

To our knowledge, this is the first study to investigate county-level socioeconomic inequalities related to premature cancer mortality across U.S. counties as a function of income, educational attainment, and unemployment. We reported considerable inequalities in the scale of mortality among different SES levels, and illustrated the heterogeneity of cancer types. Our findings indicate that, overall, SES acts as a key modifiable driver of mortality, and that socioeconomic inequalities differ by cancer types. The findings also imply that SES may be related to health care access and health risk profile, given that associations between mortality and SES were attenuated after controlling for major factors relating to health care access and health risk. Our study suggests the need to design public health interventions and policies for counties with low-income and educational attainment levels, and high

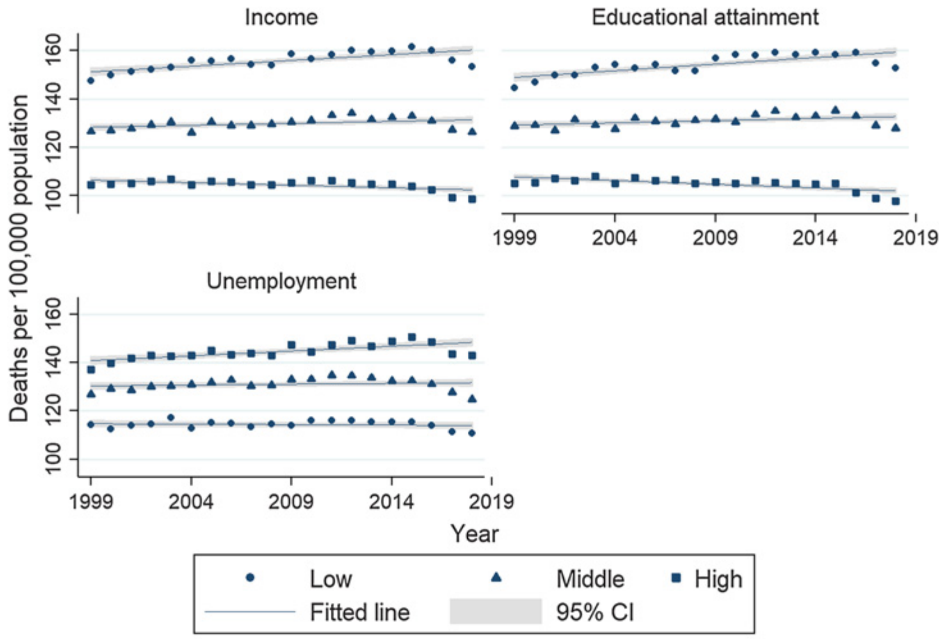

Figure 1.

Change in premature cancer mortality, by groups of income, educational attainment, and unemployment, 1999–2018. Note: We combined the CDC WONDER mortality data and data on county-level income, educational attainment, and unemployment from the Small Area Income and Poverty Estimates, the American Community Survey, and County Health Rankings & Roadmaps. The low, middle, and high levels of income, educational attainment and unemployment variables were categorized by the tertile of each variable. Income groups: The slopes of the fitted line in low/middle/higher groups were 0.48 ($P < 0.01$, 95% CI = 0.35–0.61), 0.16 ($P < 0.01$, 95% CI = 0.065–0.26) and −0.21 ($P < 0.01$, 95% CI = −0.29 to −0.13), respectively. Educational attainment groups: The slopes of the fitted line in low/middle/higher groups were 0.55 ($P < 0.01$, 95% CI = 0.42–0.68), 0.18 ($P < 0.01$, 95% CI = 0.083–0.29) and −0.30 ($P < 0.01$, 95% CI = −0.38 to −0.23), respectively. Unemployment groups: The slopes of the fitted line in low/middle/higher groups were -0.039 ($P = 0.48$, 95% CI = −0.15 to 0.07), 0.07 ($P = 0.21$, 95% CI = −0.04 to 0.18) and 0.40 ($P < 0.01$, 95% CI = 0.27–0.52), respectively.

unemployment rates, and highlights the need for different policy priorities to tackle socioeconomic inequalities according to cancer type.

The primary findings are that county-level premature cancer mortality decreased continuously as income and educational attainment increased; the premature cancer mortality increased with the increase of unemployment rate, and the socioeconomic inequalities among high-SES counties were larger than those among low-SES counties. These findings support the prior study, which showed that inequality was more negatively correlated with health for individuals in the highest income quartile (43). This may be attributable to the increased stress experienced by low-income individuals living in high-SES counties, who are exposed to relatively greater inequalities in health care environment or social welfare (44). In addition, low-SES counties evidenced increasing trends in mortality in contrast to decreasing trends in high-SES counties. We identified, moreover, a decline in mortality for cancer types that showed a stronger association between socioeconomic inequalities and mortality, which is compatible with previous studies, showing that most U.S. states with relatively higher regional inequalities had slower mortality declines (23). This finding indicates that widening socioeconomic inequalities may be strongly related to the poor overall progress in reducing premature cancer mortality, which was consistent with evidence from the previous review (45).

Building on the SDOH conceptual framework, previous studies and available datasets, our findings—associations between mortality and SES and three other sets of county-level factors—identify potential modifiable county-level health care delivery and risk factors worthy of policy makers' attention. Prior studies have reported the marked heterogeneity in these potentially modifiable factors across counties, and this heterogeneity may have partially contributed to socioeconomic inequalities in mortality (46, 47). Results of correlation analysis imply that these modifiable factors were linked to socioeconomic inequalities in mortality. When we adjusted for health care environment and health risk factors, the associations between SES and mortality were attenuated, with the most attenuation in the association between unemployment rate and mortality. This finding accords with prior work showing that health care access and health care behaviors have strong associations with socioeconomic factors, especially with unemployment rate, and corrective measures mitigating adverse consequences of socioeconomic factors can improve both access to health care and health outcomes (48, 49). Therefore, cancer-control public health interventions targeting health care delivery and the risk factors identified in this study are urgently needed in low-SES counties to reduce the growing mortality gap. Interventions related to improving SES may also help decrease mortality, such as minimum wage increases policy and publicly funded pre-kindergarten programs (50, 51).

Furthermore, mortality inequalities varied substantially by cancer types. Factors associated with site-specific mortality varied and showed different strengths for explaining the socioeconomic inequalities in mortality. Although declines in tracheal, bronchus, and lung cancer mortality were observed, owing to substantial progress made in comprehensive tobacco control (8), socioeconomic inequalities have

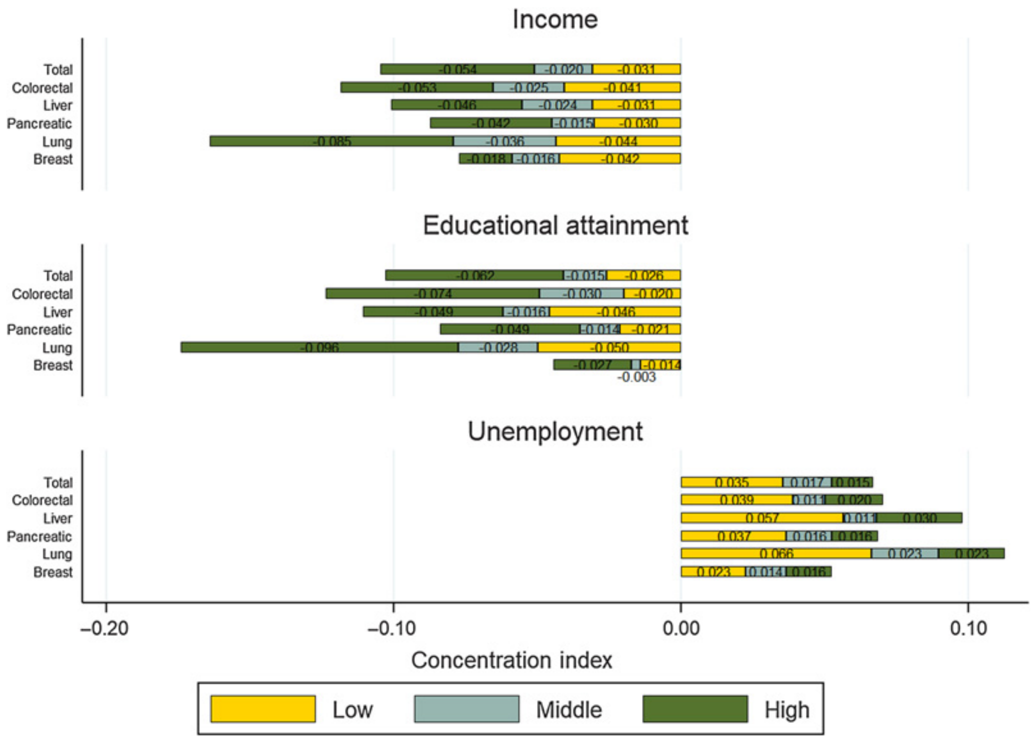

Figure 2.

Socioeconomic inequalities in site-specific premature cancer mortality, 1999–2018. Note: We combined CDC WONDER mortality data and data on county-level income, educational attainment, and unemployment from the Small Area Income and Poverty Estimates, the American Community Survey, and County Health Rankings & Roadmaps. The low, middle, and high levels of income, educational attainment and unemployment variables were categorized by the tertile of each variable.

widened over the past two decades and are now the largest inequality among the five major contributing cancers. Therefore, antitobacco public health policies should focus on expanding local programs targeting low-SES counties. There were 27 states and the District of Columbia enabled the statewide comprehensive smoke-free law by 2018, which was beneficial to nearly 50% of the U.S. population (33). Implementing smoke-free laws was negatively associated with the cancer mortality controlling for SES and demographic (demo-socioeconomic) factors with statistical significance, although the association was not statistically significant after additionally controlling for population health. It would be critical to promote the implementation of statewide and local smoke-free laws to improve people's health behaviors and to protect nonsmokers with continued efforts (33). State tobacco taxation varies widely, from 17 cents per pack in Missouri to $4.50 in the District of Columbia (52), highlighting the need for intensified efforts to link the taxation policy to income level.

Conversely, we observed increasing mortality trends in several cancers, including pancreatic and liver, which have been related to the prevalence of risk factors (e.g., obesity) in previous studies (7, 53). We found that demo-socioeconomic factors dominated in explaining county-level pancreatic and liver cancer mortality, while health risk factors were associated with only about 20% (pancreatic) and 10% (liver) of mortality. These results can be explained with evidence from previous studies: patterns of cancer risk factors as a function of demo-socioeconomic factors are complex and reflect demo-socioeconomic factors that influence behaviors as well as the heterogeneity of these broad categories (54). According to the latest National Health Insurance Survey, nearly 30% of non-Hispanic American Indians/Alaskan Natives and 12% of non-Hispanic black or African Americans are uninsured; and even the insured may face financial barriers to accessing healthcare (55, 56). Barriers to accessing healthcare hinder a variety of preventive services, including receipt of provider recommendations for weight loss and healthy diet as well as vaccinations and screenings (8). Therefore, reducing the inequalities in cancer risk factors should require targeted and tailored efforts for demo-socioeconomically deprived counties to apply local policies as well as behavioral interventions.

The most recent policy to address access to healthcare was the 2010 Affordable Care Act, which has led to increased insurance coverage and financial protection by expanding Medicaid eligibility to low-income populations through the federal marketplace (56). However, by the end of 2018, 19 states who had not adopted Medicaid expansion had 99 premature cancer deaths per 100,000 population, while the mortality among the states with Medicaid expansion was 91 deaths per 100,000 population in 2018 (26), indicating that Medicaid expansion will provide more affordable coverage to lower income families and individuals, which may reduce the mortality gap between those of higher and lower SES (52). Therefore, policy initiatives such as Medicaid expansions and health-care safety nets should target populations of low SES by applying broader strategies of national, state, and local policies, such as offering cancer screening services in alternative or nonclinical settings (e.g., mobile mammography vans at worksites or in residential communities; refs. 58, 59), strengthening local health departments and interventions of improving health care access and health behaviors.

Table 3. Factors associated with county-level premature cancer death rates in U.S. residents ages 25–64 years, 2011–2018.

County characteristics	Dominance (%)	Model 1[a] Coefficient (95% CI)	Model 2[a] Coefficient (95% CI)	Model 3[a] Coefficient (95% CI)	Model 4[a] Coefficient (95% CI)
Demographic composition					
Ages ≥65 years, %	0.23 (36.69)	2.98*** (2.75–3.22)	1.70*** (1.48–1.93)	1.75*** (1.52–1.97)	2.34*** (2.10–2.57)
Female, %		0.93*** (0.52–1.34)	2.11*** (1.75–2.48)	2.14*** (1.77–2.51)	1.97*** (1.60–2.33)
Non-Hispanic, Black or African American, %		0.58*** (0.50–0.66)	0.21*** (0.13–0.29)	0.16*** (0.07–0.25)	0.14*** (0.05–0.23)
Non-Hispanic, American Indian/Alaskan Native, %		0.37*** (0.22–0.51)	−0.25*** (−0.39 to −0.12)	−0.35*** (−0.50 to −0.19)	−0.57*** (−0.72 to −0.42)
Non-Hispanic, Asian, %		−2.92*** (−3.37 to −2.47)	0.34 (−0.10 to 0.79)	0.24 (−0.21 to 0.69)	0.17 (−0.27 to 0.61)
Non-Hispanic, Native Hawaiian/other Pacific Islander, %		4.90*** (1.30–8.49)	−2.85* (−5.77 to 0.08)	−2.81* (-5.67 to 0.04)	−1.09 (−3.74 to 1.57)
Non-Hispanic, two or more races, %		0.32 (−0.55 to 1.19)	0.65* (−0.10 to 1.40)	0.66* (−0.08 to 1.40)	0.29 (−0.42 to 0.99)
Hispanic, %		−0.33*** (−0.42 to −0.23)	−0.69*** (−0.77 to −0.60)	−0.68*** (−0.76 to −0.59)	−0.50*** (−0.59 to −0.41)
Socioeconomic status					
Median household income (in thousands of dollars)	0.16 (25.73)		−0.45*** (−0.56 to −0.35)	−0.38*** (−0.50 to −0.26)	−0.24*** (−0.36 to −0.12)
Bachelor's degree or higher, %			−1.14*** (−1.28 to −1.00)	−1.16*** (−1.32 to −1.00)	−0.68*** (−0.87 to −0.50)
Unemployment rate, %[b]			2.44*** (1.86–3.02)	2.20*** (1.60–2.80)	1.50*** (0.92–2.07)
Health care environment					
No. of primary care physicians per 100,000 population	0.09 (13.35)			0.01 (−0.02 to 0.04)	0.01 (−0.02 to 0.03)
Medicare to Medicaid fee index[c]				−17.10** (−32.50 to −1.70)	−9.47 (−21.30 to 2.39)
Smoke-free law[c]				−8.89*** (−13.90 to −3.91)	−3.11 (−6.91 to 0.68)
Medicaid expansion[c]				3.70 (−1.32 to 8.73)	2.20 (−1.51 to 5.90)
Food environment index[b]				−1.22* (−2.45 to 0.02)	−1.60*** (−2.78 to −0.42)
Health care quality index[b]				−2.71*** (−4.68 to −0.75)	−2.91*** (−4.80 to −1.02)
Population health					
Smoker, %	0.15 (24.23)				1.49*** (1.22–1.76)
Obesity, %					0.82*** (0.43–1.22)
Total Medicare reimbursements per enrollee (in thousands of dollars)[b]					1.70*** (0.96–2.44)

Note: Dependent variable was the number of deaths from 2011–2018 per 100,000 population in each county. Other county-level variables included in the models were estimated as the mean of each year's value. ***, $P < 0.01$; **, $P < 0.05$; *, $P < 0.10$.

Abbreviation: 95%CI, 95% Confidence Interval.

[a]We combined CDC WONDER mortality data and data on county characteristics from multiple county-level databases from 2011–2018. For hierarchical linear mixed models, 116 counties were excluded owing to the lack of data from the multiple county-level databases.

[b]For those variables restricted to year range, we conducted an ordinary least squares regression model to predict the missing values.

[c]State-level variables. The Medicaid-to-Medicare fee index was updated by Kaiser Family Foundation in 2016. The smoke-free law variable refers to whether a state implemented a comprehensive smoke-free law before 2018 (Reference = states didn't implement a comprehensive smoke-free law before 2018). The Medicaid expansion variable refers to whether a state adopted Medicaid expansion before 2018 (Reference = states did not adopt Medicaid expansion before 2018).

This study had several limitations. First, the study's observational nature limited the ability to draw any causal inference from the findings. Second, there may have been other contributory factors not considered in this analysis that vary across counties. One such county-level factor is health policies (e.g., Medicaid payment rates). Third, some county-level factors could only be obtained for the 2011–2017 period, and access to data was limited for some variables. However, for those variables, we conducted an ordinary least squares regression model to predict the missing values. Finally, the cause-of-death information on the death certificates was not always validated by medical records or autopsy verification. Thus, misclassification of causes of deaths may have occurred. It is unknown

Table 4. Factors associated with county-level site-specific premature cancer mortality in U.S. residents ages 25–64 years, 2011–2018.

County characteristics	Lung cancer[a] Coefficient (95% CI)	Lung cancer[a] Dominance (%)	Colorectal cancer[a] Coefficient (95% CI)	Colorectal cancer[a] Dominance (%)	Breast cancer[a] Coefficient (95% CI)	Breast cancer[a] Dominance (%)	Pancreatic cancer[a] Coefficient (95% CI)	Pancreatic cancer[a] Dominance (%)	Liver cancer[a] Coefficient (95% CI)	Liver cancer[a] Dominance (%)
Demographic composition										
Ages ≥65 years, %	0.76*** (0.65–0.88)	0.21 (31.32)	0.38*** (0.33–0.44)	0.16 (31.73)	0.31*** (0.26–0.36)	0.21 (52.59)	0.25*** (0.21–0.29)	0.18 (43.31)	0.31*** (0.26–0.36)	0.18 (42.48)
Female, %	0.29*** (0.11–0.47)		−0.16*** (−0.27 to −0.06)		0.22*** (0.12–0.32)		−0.16*** (−0.25 to −0.07)		−0.36*** (−0.46 to −0.26)	
Non-Hispanic, Black or African American, %	−0.09*** (−0.13 to −0.04)		0.06*** (0.04–0.09)		0.08*** (0.06–0.09)		0.02** (0.004–0.03)		0.05*** (0.03–0.07)	
Non-Hispanic, American Indian/Alaskan Native, %	−0.31*** (−0.41 to −0.22)		0.02 (−0.03 to 0.06)		−0.07*** (−0.11 to −0.03)		−0.05*** (−0.09 to −0.01)		−0.02 (−0.07 to 0.02)	
Non-Hispanic, Asian, %	0.32*** (0.12–0.52)		0.11** (0.02–0.19)		0.003 (−0.06 to 0.07)		0.01 (−0.05 to 0.07)		0.06* (−0.01 to 0.12)	
Non-Hispanic, Native Hawaiian/other Pacific Islander, %	−1.26* (−2.53 to 0.01)		0.44 (−0.10 to 0.98)		−0.11 (−0.53 to 0.30)		0.06 (−0.28 to 0.40)		−0.50** (−0.93 to −0.06)	
Non-Hispanic, two or more races, %	−0.05 (−0.40 to 0.31)		−0.33*** (−0.50 to −0.16)		−0.03 (−0.16 to 0.10)		−0.10* (−0.21 to 0.02)		0.14* (−0.01 to 0.30)	
Hispanic, %	−0.35*** (−0.40 to −0.31)		−0.06*** (−0.08 to −0.04)		−0.02** (−0.03 to −0.001)		−0.03*** (−0.05 to −0.02)		0.03*** (0.01–0.04)	
Socioeconomic status										
Median household income (in thousands of dollars)	−0.14*** (−0.20 to −0.08)	0.16 (25.06)	−0.03** (−0.06 to −0.003)	0.12 (25.16)	−0.01 (−0.03 to 0.02)	0.06 (16.54)	−0.01 (−0.03 to 0.01)	0.11 (26.53)	−0.03** (−0.05 to −0.01)	0.11 (25.81)
Bachelor's degree or higher, %	−0.29*** (−0.38 to −0.20)		−0.11*** (−0.15 to −0.06)		−0.02 (−0.06 to 0.01)		−0.06*** (−0.09 to −0.03)		−0.07*** (−0.11 to −0.03)	
Unemployment rate, %[b]	0.71*** (0.42–1.01)		0.04 (−0.10 to 0.19)		0.12** (0.01–0.24)		0.02 (−0.07 to 0.12)		−0.05 (−0.17 to 0.08)	
Health care environment										
No. of primary care physicians per 100,000 population	−0.01 (−0.02 to 0.005)	0.09 (13.89)	−0.004 (−0.01 to 0.003)	0.12 (24.33)	−0.003 (−0.01 to 0.003)	0.07 (17.88)	0.002 (−0.003 to 0.01)	0.04 (10.12)	0.004 (−0.003 to 0.01)	0.09 (21.27)
Medicare to Medicaid fee index[c]	−4.58 (−11.50 to 2.30)		3.84*** (1.39–6.29)		1.65* (−0.11 to 3.40)		1.39** (0.26–2.51)		1.09 (−1.04 to 3.22)	
Smoke-free law[c]	−1.06 (−3.28 to 1.16)		−0.65 (−1.42 to 0.13)		−0.10 (−0.64 to 0.45)		0.20 (−0.14 to 0.53)		−0.19 (−0.88 to 0.50)	
Medicaid expansion[c]	0.30 (−1.90 to 2.50)		−0.16 (−0.90 to 0.58)		0.03 (−0.49 to 0.56)		−0.10 (−0.40 to 0.20)		0.04 (−0.64 to 0.71)	
Food environment index[b]	−0.63* (−1.32 to 0.07)		−0.30* (−0.66 to 0.05)		−0.16 (−0.45 to 0.13)		−0.11 (−0.34 to 0.11)		0.01 (−0.32 to 0.35)	
Health care quality index[b]	−1.09** (−2.10 to −0.07)		−1.71*** (−2.24 to −1.18)		−1.28*** (−1.71 to −0.85)		−0.71*** (−1.09 to −0.34)		−1.09*** (−1.59 to −0.59)	

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Table 4. Factors associated with county-level site-specific premature cancer mortality in U.S. residents ages 25–64 years, 2011–2018. (Cont'd)

County characteristics	Lung cancer[a] Coefficient (95% CI)	Lung cancer[a] Dominance (%)	Colorectal cancer[a] Coefficient (95% CI)	Colorectal cancer[a] Dominance (%)	Breast cancer[a] Coefficient (95% CI)	Breast cancer[a] Dominance (%)	Pancreatic cancer[a] Coefficient (95% CI)	Pancreatic cancer[a] Dominance (%)	Liver cancer[a] Coefficient (95% CI)	Liver cancer[a] Dominance (%)
Population health										
Smoker, %	0.63*** (0.50–0.76)	0.20 (29.73)	−0.03 (−0.10 to 0.04)	0.09 (18.78)	−0.03 (−0.09 to 0.02)	0.05 (12.99)	0.02 (−0.04 to 0.07)	0.08 (20.04)	0.08** (0.01–0.15)	0.04 (10.44)
Obesity, %	0.33*** (0.14–0.52)		0.09** (0.01–0.18)		0.10*** (0.03 to 0.16)		0.12*** (0.06–0.18)		−0.03 (−0.11 to 0.05)	
Total Medicare reimbursements per enrollee (in thousands of dollars)[b]	1.38*** (0.99–1.77)		0.34*** (0.15–0.53)		−0.04 (−0.19 to 0.12)		0.003 (−0.12 to 0.13)		0.10 (−0.07 to 0.27)	

Note: Dependent variable was the number of deaths from 2011–2018 per 100,000 population in each county. Other county-level variables included in the models were estimated as the mean of each year's value. ***, $P < 0.01$; **, $P < 0.05$; *, $P < 0.10$.

Abbreviation: 95%CI, 95% Confidence Interval.

[a]We combined CDC WONDER mortality data and data on county characteristics from multiple county-level databases from 2011–2018. For hierarchical linear mixed models, 52–96 counties were excluded owing to the lack of data from the multiple county-level databases.

[b]For those variables restricted to year range, we conducted an ordinary least squares regression model to predict the missing values.

[c]State-level variables. The Medicaid-to-Medicare fee index was updated by Kaiser Family Foundation in 2016. The smoke-free law variable refers to whether a state implemented a comprehensive smoke-free law before 2018 (Reference = states didn't implement a comprehensive smoke-free law before 2018). The Medicaid expansion variable refers to whether a state adopted Medicaid expansion before 2018 (Reference = states did not adopt Medicaid expansion before 2018).

whether the use of death certificate-based methods and the use of ICD codes is an accurate method for identifying the number of death cases; however, annual trends and group comparisons of county, age, sex, and race should not be affected.

Conclusion

Socioeconomic inequalities relative to income, educational attainment, and unemployment were associated with premature cancer mortality across U.S. counties. Furthermore, SES acts as the key driver of premature cancer mortality; socioeconomic inequalities differ by cancer types. Focused efforts that target socioeconomic drivers of mortalities and inequalities are warranted for designing implementation strategies for cancer prevention and control programs and policies for underprivileged groups.

Authors' Disclosures

No disclosures were reported.

Authors' Contributions

S. Song: Conceptualization, resources, data curation, formal analysis, validation, visualization, methodology, writing–original draft, writing–review and editing. **Y. Duan:** Resources, data curation, writing–review and editing. **J. Huang:** Writing–review and editing. **M.C.S. Wong:** Writing–review and editing. **H. Chen:** Writing–review and editing. **M.G. Trisolini:** Writing–review and editing. **K.A. Labresh:** Writing–review and editing. **S.C. Smith Jr:** Writing–review and editing. **Y. Jin:** Conceptualization, resources, data curation, formal analysis, supervision, funding acquisition, validation, investigation, visualization, methodology, writing–original draft, project administration, writing–review and editing. **Z.-J. Zheng:** Conceptualization, project administration, writing–review and editing.

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