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Contribution of health behaviors to the association between area-level socioeconomic status and cancer mortality

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Abstract

Cancer mortality is higher among residents of low-socioeconomic status (SES) areas than those of high-SES areas; however, the contribution of modifiable risk factors to this disparity is not known. We used data from 54,737 participants in the VITamins And Lifestyle (VITAL) Study, aged 50–76 with no history of cancer at baseline (2000–2002). Of these, 1,488 died of cancer over an average of 7.7 years of follow-up. Data on modifiable risk factors including body mass index (BMI), physical activity, diet, alcohol, smoking and screening were taken from baseline questionnaires. We constructed a block group-level SES index using data from the 2000 United States Census and fit Cox proportional hazards models estimating the association between area-level SES and total cancer mortality with and without control for modifiable risk factors. All statistical tests are 2-sided. Cancer mortality was 77% (95% CI: 50%, 111%) higher in the lowest-

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SES areas compared with the highest. Modifiable risk factors accounted for 45% (95% CI: 34%, 62%) of this association. Smoking explained the greatest proportion (29%; 95% CI: 22%, 40%) of the observed association, followed by diet (11%; 95% CI: 7%, 17%), physical activity (10%; 95% CI: 7%, 16%), screening (9%; 6%, 13%), and BMI (5%; 95% CI: 1%, 10%). Results were similar in models controlling for individual education and income. The association between area-level SES and cancer mortality is partially explained by modifiable risk factors, which could suggest the appropriate targets to reduce socioeconomic disparities.

Keywords

cancer mortality; socioeconomic status; neighborhood; screening; smoking; diet; physical activity; behavior

Previous work has suggested an inverse, dose-response association between area-level socioeconomic status (SES) and total cancer mortality such that cancer mortality was approximately 80% higher among residents of the lowest-SES areas compared with residents of the highest-SES areas (Hastert, Beresford, Sheppard, & White, 2015). This association partially attenuated after accounting for individual education and income; however, cancer mortality remained 40% higher in residents of the lowest-SES areas relative to the highest (Hastert et al., 2015). Modifiable risk factors including diet, physical activity, body mass index (BMI), alcohol consumption, smoking, and cancer screening are all associated with cancer outcomes (Ballard-Barbash, Friedenreich, Slattery, & Thune, 2006; Force, 2008; Hastert et al., 2015; Lee & Oguma, 2006; Marshall & Freudenheim, 2006; Nelson et al., 2009; Romaguera et al., 2012; Tang et al., 2010; Thun & Henley, 2006; Willett, 2006) and with SES, (Ball, Crawford, & Mishra, 2006; Black, Macinko, Dixon, & Fryer, 2010; Chaix & Chauvin, 2003; Diez-Roux, Link, & Northridge, 2000; Diez-Roux et al., 1999; Diez Roux, Merkin, Hannan, Jacobs, & Kiefe, 2003; Duncan, Jones, & Moon, 1999; Stafford et al., 2007; Zackrisson, Lindstrom, Moghaddassi, Andersson, & Janzon, 2007) and could contribute to the observed socioeconomic disparities in cancer mortality; however, their contribution to these socioeconomic disparities in cancer mortality is not clear.

Previous research has suggested that BMI, diet, physical activity, and smoking at least partially explained associations between individual SES and total mortality, (Stringhini et al., 2010) and between area-level SES and colorectal cancer incidence (Doubeni et al., 2012; Kim, Masyn, Kawachi, Laden, & Colditz, 2010). Although substantial disparities in cancer mortality have been observed by area-level SES (Hastert et al., 2015), no previous work has examined the potential contribution of modifiable risk factors to this association.

The purpose of this paper is to test whether and to what extent the observed association between area-level SES and cancer mortality is explained by six modifiable risk factors. Body mass index (BMI), physical activity, dietary factors (energy density and consumption of fruits and vegetables and red and processed meats), and alcohol consumption were identified from the cancer prevention recommendations of the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) ("Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective," 2007). Pack-years of smoking

and cancer screening behaviors including colonoscopy or sigmoidoscopy, mammography in women and prostate-specific antigen (PSA) testing in men were also considered based on their associations with cancer incidence and mortality (Nelson et al., 2009; "Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement, 2008"; Tang et al., 2010; Thun & Henley, 2006). Ascertaining modifiable risk factors that contribute to socioeconomic disparities in cancer mortality could help identify points of intervention to reduce those disparities.

METHODS

Study Cohort

The VITamins And Lifestyle (VITAL) study is a prospective cohort study designed to investigate associations between behaviors, including dietary supplement use, and cancer risk and mortality. It has previously been described in detail (White et al., 2004). Participants were eligible to join the cohort if they were between the ages of 50 and 76 and lived in one of the 13 counties included in the Western Washington Surveillance, Epidemiology and End Results (SEER) cancer registry at baseline. Using names purchased from a commercial mailing list, baseline questionnaires were mailed to 364,418 men and women between October, 2000 and December, 2002 and were followed two weeks later by reminder postcards. A total of 79,300 questionnaires were returned, of which 77,719 passed quality control checks.

Overall, 54,736 men and women were included in the current analysis after excluding respondents with a history of cancer other than nonmelanoma skin cancer (n=11,259) or whose history of cancer was unknown (n=214) and respondents whose baseline addresses were post office boxes (n=1,137) or could not be geocoded (n=381). Respondents missing data for one or more potential mediators (n=8,716) were also excluded. Participants missing either individual educational attainment or annual household income remained in the analysis, but 977 respondents were excluded for missing both items. Additionally, the first year of follow-up (including 43 cancer deaths and 531 persons with other censoring events), was excluded to avoid potential reverse causality. Participants entered the survival analyses one year after the date of the completion of the baseline questionnaire, and were followed until the date of death due to cancer or a censoring event. Numbers of exclusions reported are not mutually exclusive, with participants meeting multiple exclusion criteria counted in the total excluded for each exclusion criterion.

Area-level Socioeconomic Status

Respondents' baseline addresses were geocoded using GPS Visualizer and Yahoo! Maps. Addresses were used to identify respondents' census block groups using TIGER/Line shapefiles for the 2000 Census in ArcMap 10 (Esri, Redlands, CA). In order to validate this geocoding method, a 1% sample of addresses was geocoded again using Google Maps and more than 95% of the addresses in the 1% validation sample were geocoded within 400 meters of one another using the two methods.

We measured area-level SES using a previously-developed index (Diez-Roux et al., 2001) which has been used in prior studies of area-level SES and cancer outcomes (Hastert et al., 2015; Kim et al., 2010). This index includes the log of median value of owner-occupied housing units; log of median household income; percent of households receiving net rental, interest or dividend income; percent of adults ages 25 and older who completed high school; percent of adults ages 25 and older who completed college; and percent of employed persons ages 16 and older in professional and managerial occupations. Standardized z-scores were calculated for each variable based on the 3,346 block groups in the 13 counties of the Western Washington SEER registry and summed to create an index such that higher values corresponded with lower SES. Index values of participants included in these analyses ranged from -16.1 to 16.7 with a median of -1.2 and mean of -1.5.

Census block groups were chosen as an approximation of participants' neighborhood environments. Block groups were used because they represent small, relatively permanent statistical subdivisions of counties and of census tracts that are designed such that their populations are relatively homogenous with respect to population characteristics, economic factors, and living conditions. They do not cross county, state or census tract boundaries and most were delineated with input from local participants. Block groups in the catchment area covered a median of 3.3 square miles and included a median population of 1,070. Block groups have been found to perform favorably in detecting socioeconomic gradients in cancer incidence and mortality (Krieger et al., 2002).

Data Collection

Sex-specific baseline questionnaires were used to collect self-reported information on medical history, height and weight, physical activity, diet, alcohol consumption, smoking, and cancer screening behaviors.

BMI (kg/m^2) was calculated using respondents' self-reported height and weight. Physical activity was assessed by a one-page questionnaire covering participation in 14 types of activities over the previous 10 years, including years and days per week, plus intensity for walking. These data were used to calculate a continuous measure of average MET-hours per week of moderate or fast walking and moderate or strenuous physical activity.

Dietary variables included energy density of the diet and consumption of fruits and vegetables and of red and processed meats, selected based on the dietary factors the WCRF/AICR found to be associated with cancer incidence and mortality (Arab et al., 2013; Hastert, Beresford, Patterson, Kristal, & White, 2013; Hastert, Beresford, Sheppard, & White, 2014; Inoue-Choi, Robien, & Lazovich, 2013; Romaguera et al., 2012; Vergnaud et al., 2013). Diet was assessed by a 126-item food frequency questionnaire (FFQ) covering the year before baseline. The FFQ was adapted from the questionnaire developed for use in the Women's Health Initiative and other studies. Measurement properties of earlier versions of the FFQ have been published previously (Patterson et al., 1999). The University of Minnesota's Nutrition Coordinating Center database was used to convert food frequency information into nutrients. Numbers of servings were based on the sex-specific medium portion size of each food and beverage (Schakel, Buzzard, & Gebhardt, 1997).

Energy density was calculated by dividing the energy (kcal) of foods consumed by the estimated weight (grams) of those foods. Beverages were excluded from the energy density calculations. Daily servings of fruits and vegetables included 25 foods and food groups, adjusted by portion size and by summary questions on total numbers of fruits and vegetables eaten to reduce over-estimation by participants and excluded fruit juices and potatoes. Ounces of red and processed meat consumed per week were estimated by multiplying the adjusted weekly frequencies of consumption of red or processed meat (including from mixed dishes) by sexspecific grams of meat per serving.

Alcohol consumption was measured in drinks per day where a drink was classified as 12 ounces of beer, 4 ounces of wine, 1.5 ounces of liquor, or one mixed drink. Pack-years of smoking was the product of the average number of cigarettes smoked per day and total years smoked. For screening behaviors, women were asked whether they received a mammogram and men were asked whether they received a PSA test within the two years before baseline. Both women and men were asked whether they received a sigmoidoscopy or colonoscopy in the ten years before baseline.

Case Ascertainment and Censoring

Deaths due to cancer were ascertained through December 31, 2010 by annual linkage with the Washington State death file. Linkage between VITAL and the death file 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. After excluding the first year of follow-up, a total of 1,488 cancer deaths were identified in an average of 7.7 years of follow-up.

Participants who did not die of cancer in Washington State were right-censored at the date of the earliest of the following events: date they requested removal from the study (n=14), date they moved out of Washington State (n=2,757), date of death due to other causes (n=2,295), or December 31, 2010 (n=48,182). Moves out of Washington State were identified through linkage with the National Change of Address System.

Statistical Analysis

We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of death due to cancer associated with quintile of area-level SES. These quintiles were based on the distribution of the area-level SES index values among VITAL participants included in the analyses. We used participant age as the time scale, with participants entering the analysis at their age one year after completing the baseline questionnaire and exiting at age at death due to cancer or age at censoring event. Proportional hazards assumptions were examined using scaled Schoenfeld residuals and no significant ($p<0.05$) deviations from proportionality were observed. All statistical tests were two-sided.

Multivariable analyses included categorical variable adjustment for potential confounders selected *a priori*, including sex, race/ethnicity (white, Hispanic, African-American,

American Indian/Alaska Native, Asian/Pacific Islander, other/missing), marital status (married, living with partner, never married, separated/divorced, widowed), and number of cancers diagnosed in first-degree relatives (0, 1, 2+) (Model 1). Models further controlling for individual SES included adjustment for education (high school graduate/GED or below, some college/technical school, college graduate, advanced degree) and household income (< \$20,000, \$20,000–39,999, \$40,000–59,999, \$60,000–79,999 and \$80,000 or more) (Model 2). Participants with missing data were treated as their own category for each potential confounder, including individual education and household income.

In order to estimate what proportion of the association between area-level SES and cancer mortality could be explained by modifiable risk factors, we used the continuous area-level SES index values. The proportion of the association explained by modifiable risk factors was assessed by calculating the percent reduction in the Model 1 coefficient for continuous area-level SES when health behaviors were added to the model using the formula: $(\beta_{\text{Model 1 + health behavior}} - \beta_{\text{Model 1}}) / (\beta_{\text{Model 1}})$. Each health behavior was included individually and then all behaviors were included in one model. The same procedure was used for Model 2. Ninety-five percent confidence intervals around the percent reduction in the association were calculated using a biascorrected bootstrap procedure with 2000 replications and including re-sampling. (DiCiccio & Efron, 1996) This approach to mediation analysis is approximately equivalent to the product of coefficients method commonly used in the social sciences in Cox models with a rare outcome (VanderWeele, 2011).

Statistical analyses were conducted using Stata 12.1 and SAS 9.3. Individual participants are the unit of analysis in each model. Data include one baseline measurement of each participant's home address, sociodemographic characteristics and modifiable risk factors. Models of area-level SES and cancer mortality utilize the cluster option in Stata to account for correlation among VITAL participants living in the same block groups. Two separate sensitivity analyses were conducted. The first fit multilevel frailty models instead of Cox models with standard errors adjusted to account for correlation between residents of the same block groups. The second sensitivity analysis fit Cox models accounting for competing risks of death due to a cause other than cancer.

RESULTS

Table 1 presents baseline demographic characteristics of the study population as well as the modifiable risk factors considered as potential mediators, stratified by area-level SES. Residents of lower-SES areas were older, and a lower proportion were male, white, college-educated or had annual household incomes of at least \$40,000 compared with residents of higher-SES areas. A socioeconomic gradient is evident for all modifiable risk factors considered such that living in lower-SES areas was associated with higher BMI, energy density, meat consumption, and pack-years of smoking, and with lower levels of physical activity, fruit and vegetable consumption, and receipt of screening. Living in lower-SES areas was also associated with lower alcohol intake.

Table 2 gives associations between the modifiable risk factors considered and cancer mortality. Higher BMI, energy density, alcohol consumption and smoking were all positively associated with cancer mortality, while physical activity, fruit and vegetable consumption and screening were inversely associated. Associations changed very little when individual SES was added to the models.

In Table 3, we present our analyses in which we first fit models estimating the association between area-level SES and total cancer mortality controlling for demographic factors (Model 1), and then, additionally, for individual education and household income (Model 2). Modifiable risk factors were then added to each of these models to estimate the proportion of the observed association between area-level SES and cancer mortality they explained individually, and then in combination.

Compared with residents of the highest-SES areas, cancer mortality was 77% higher among residents of the lowest-SES areas accounting for demographics and family history of cancer (Model 1, HR for quintile 5 (Q5) vs. quintile 1 (Q1): 1.77, 95% CI: 1.50, 2.11; $P_{\text{trend}} < 0.001$). In all models of the association between quintiles of area-level SES and cancer mortality, cancer mortality increased monotonically with decreasing area-level SES (Supplementary Table 1).

In Model 1, smoking accounted for the greatest proportion of the association between area-level SES and cancer mortality (29%), followed by diet (11%) physical activity (10%), screening (9%), and BMI (5%). Adding alcohol consumption did not change the association between area-level SES and cancer mortality. Adding all modifiable risk factors accounted for 45% of the observed association between area-level SES and cancer mortality; however, cancer mortality remained 38% (95% CI: 16%, 64%) higher in residents of the lowest-SES areas.

Adding individual education and income to the model including demographics and family history of cancer (but no modifiable risk factors) reduced the association between area-level SES and cancer mortality by 46% (95% CI: 32%, 68%; Model 2; data not shown), however, living in the lowest-SES areas remained associated with 37% higher cancer mortality (HR: 1.37, 95% CI: 1.14, 1.65; $P_{\text{trend}} < 0.001$).

When adding modifiable risk factors to Model 2, smoking again explained the greatest proportion of the remaining association (23%) followed by diet (9%), screening (8%), and physical activity (7%). Adding BMI did not significantly change the observed association between area-level SES and cancer mortality. Adding alcohol strengthened the association by 3%. Together these factors explained 37% of the association; however, cancer mortality remained 22% (95% CI: 2%, 48%) higher among residents of the lowest-SES areas than among those living in the highest-SES areas after accounting for modifiable risk factors and individual SES.

Fitting multilevel frailty models rather than Cox models with standard errors adjusted to account for correlation between residents of the same block groups did not alter the results. In separate models accounting for competing risks of death due to causes other than cancer the results were similar, although the overall association between area-level SES and cancer

mortality attenuated somewhat. The hazard ratio and 95% confidence interval of cancer mortality among residents of the lowest-SES compared with the highest-SES block groups was 1.71 (1.44, 2.03) in Model 1 and 1.33 (1.10, 1.60) in Model 2 (data not shown). However, in the competing risk models, modifiable risk factors explained a greater proportion of the association between area-level SES and cancer mortality, 47.3% in Model 1 and 43% in Model 2, driven by a higher proportion of the association explained by smoking (31.5% in Model 1 and 28.6% in Model 2).

DISCUSSION

The purpose of this study was to determine whether disparities in cancer mortality by area-level SES can be explained by modifiable risk factors. Our results suggest that health behaviors, particularly smoking, physical activity, diet, and screening, account for a substantial proportion of the observed association between area-level SES and cancer mortality; however, living in low-SES areas remains associated with higher cancer mortality even after accounting for BMI, health behaviors, and individual SES.

This is the first study to examine the role of modifiable risk factors in the association between area-level SES and cancer mortality. In a similar study examining the role of behavioral risk factors in the association between SES and colorectal cancer incidence, Doubeni et al. found that adherence to a Mediterranean diet, BMI, physical activity, and smoking each explained between 9% and 15% of the observed association, and that all behaviors and BMI together explained 36% of the association in a model not accounting for individual SES (Doubeni et al., 2012). In a previous study utilizing data from the Nurses' Health Study, Kim et al. reported an association between area-level SES and rectal cancer that was mediated by multivitamin use and BMI, but did not observe an overall association between area-level SES and colon cancer (Kim et al., 2010). Stringhini et al. reported that smoking status at baseline explained 32% (95% CI: 21%, 70%) of the association between individual SES and total mortality in the Whitehall II cohort study; however, they did not observe an overall association between individual SES and cancer mortality (Stringhini et al., 2010).

In the NIH-AARP Diet and Health Study, Major et al. reported higher cancer mortality in residents of census tracts in the lowest quintile of area-level SES relative to the highest (Q5 vs. Q1 HR_{men} : 1.44, 95% CI: 1.32, 1.57; HR_{women} : 1.27, 95% CI: 1.15, 1.40) (Major et al., 2010). These associations attenuated substantially in adjusted analyses (to HR_{men} : 1.09, 95% CI: 1.00, 1.20; HR_{women} : 1.09, 95% CI: 0.99, 1.22); however, the adjusted models included education as well as several modifiable risk factors including BMI, physical activity, smoking, and several dietary behaviors simultaneously, and do not indicate the proportion of the association explained by behaviors apart from SES.

Although we observed a strong relationship between area-level SES and cancer mortality (Hastert et al., 2015), using the ACS Nutrition Cohort, Steenland et al. found no association between area-level SES in women and an association in men that was no longer evident after controlling for educational attainment, other demographic factors, and health behaviors (Steenland, Henley, Calle, & Thun, 2004). Differences in methodology could partially

explain differences in observed results. Our analyses were limited to individuals with no history of cancer at baseline, and deaths due to rapidly-fatal cancers (e.g. lung, pancreatic, and hematologic cancers) account for a large proportion of the cancer deaths included here, while breast and prostate cancer account for relatively few. While lower SES is associated with higher incidence and mortality for most cancers, this association is less strong for breast and prostate cancers (Hastert et al., 2015; Kawachi & Kroenke, 2006; Steenland, Henley, & Thun, 2002), and including relatively few deaths due to breast and prostate cancer could contribute to the stronger observed association between area-level SES and cancer mortality compared to previous work.

Individual SES and health behaviors both account for some, but not all, of the association between area-level SES and cancer mortality. The attenuation of the association when individual SES and behaviors are added to the models suggests that some of the effect is compositional; however, even after accounting for age, race, gender, individual SES, and all of the modifiable risk factors considered, cancer mortality remained 22% higher in residents of low-SES areas. This remaining association could be due at least in part to mediation by factors not included in the models, such as access to health care, or contextual or area-level factors, such as environmental exposures, that could influence cancer mortality through pathways other than those considered here.

Although including measures of screening (mammography, PSA, colonoscopy or sigmoidoscopy) reduced the observed association between area-level SES and total cancer mortality by approximately 8%, breast, prostate, and colorectal cancers accounted for only a small proportion of the cancer deaths observed (2.9%, 2.2% and 6.9%, respectively). These screening measures may be capturing dimensions of access to care more broadly rather than representing the benefits of these individual screening tests.

The remaining association could also be due to measurement error in the factors adjusted for. Data on area-level SES and the modifiable risk factors considered were measured at only one point in time. Measurement error in factors measured at baseline is unlikely to be associated with future health outcomes and would lead to non-differential misclassification of those factors with respect to cancer mortality and an underestimation of the proportion of the association they explain (assuming that the measured mean values of those behaviors increased monotonically with the true values (White, Armstrong, & Saracci, 2008)). Further, this sample was drawn from one region of the United States and included predominantly white respondents, which may limit its generalizability to other populations. VITAL received completed baseline questionnaires from approximately 21.3% of invited participants. To the extent that the non-responders differed from VITAL participants, this could also limit the generalizability of our findings and suggest an opportunity for future investigation.

This study features several important strengths including its large sample size and prospective design. The detailed information collected at baseline allowed us to successfully geocode almost all respondents; to examine several individual-level modifiable risk factors as potential mediators of the association between area-level SES and cancer mortality; to adjust for individual income and education; and to control for several potential confounding

factors. Linkage with the Washington State death file provided accurate and near-complete ascertainment of cancer mortality outcomes in this population. Reverse causality was minimized by excluding participants with a history of cancer at baseline (which could influence health behaviors) and the first year of follow-up (to avoid pre-diagnosis cancer symptoms leading to changes in behaviors); however, our results did not differ in sensitivity analyses including the first year of follow-up. Additionally, in our analyses we controlled for two measures of individual SES (annual household income and individual educational attainment), reducing the potential for residual confounding that exists when including only one measure of individual SES (Blakely & Subramanian, 2006). A previous review of multilevel studies of area-level socioeconomic context and health outcomes found that studies including more than one measure of individual-level SES reported smaller measures of association than studies including only one measure of individual SES (Pickett & Pearl, 2001).

The results presented here suggest that cancer mortality can be affected by social circumstances and that even after accounting for several modifiable risk factors and individual education and income, living in a lower-SES area remained associated with higher cancer mortality. This remaining association lends support to the idea of low socioeconomic status as a “fundamental cause” of cancer mortality, such that living in impoverished areas could increase risk of death due to cancer on its own, apart from differences in modifiable risk factors (Link & Phelan, 1995).

In identifying modifiable risk factors that contribute to disparities in cancer mortality by area-level SES, there is a risk of exacerbating those disparities to the extent that individuals with the most resources utilize information about health behaviors and disease risk, improving their outcomes, while those with the fewest resources are unable to utilize the information in the same way due to limited information, social, or financial resources (Heymann & Fischer, 2003). It is important to recognize that individuals living in the lowest-SES areas face constrained choices with regard to health behaviors that can impact disease risk and that although these results point to particular areas where interventions could be targeted to reduce socioeconomic disparities in cancer mortality (particularly around smoking, screening, diet, and physical activity): broader policy level interventions may be required to fully address these disparities. Further study is warranted into the potential for public policies to make improved health behaviors easier, particularly for those from the lowest-SES areas, and the effect of those policies on broader population health.

In summary, substantial socioeconomic disparities exist such that living in lower-SES areas is associated with higher cancer mortality. Our results suggest that several behaviors, particularly smoking, diet, screening, and physical activity could be effective targets of interventions aimed at reducing these disparities, but that area-level SES remains associated with cancer mortality even after accounting for these risk factors in addition to individual SES.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Arab L, Su J, Steck SE, Ang A, Fontham ET, Bensen JT, Mohler JL. Adherence to World Cancer Research Fund/American Institute for Cancer Research lifestyle recommendations reduces prostate cancer aggressiveness among African and Caucasian Americans. *Nutr Cancer*. 2013; 65(5):633–643. [PubMed: 23859030]
- Ball K, Crawford D, Mishra G. Socio-economic inequalities in women's fruit and vegetable intakes: a multilevel study of individual, social and environmental mediators. *Public Health Nutr*. 2006; 9(5): 623–630. doi: S1368980006001030 [pii]. [PubMed: 16923294]
- Ballard-Barbash, R.; Friedenreich, C.; Slaterry, M.; Thune, I. Obesity and Body Composition. In: Schottenfeld, D.; Fraumeni, JF., Jr, editors. *Cancer Epidemiology and Prevention*. 3rd ed.. New York, NY: Oxford University Press; 2006. p. 423-448.
- Black JL, Macinko J, Dixon LB, Fryer GE Jr. Neighborhoods and obesity in New York City. *Health Place*. 2010; 16(3):489–499. doi: S1353-8292(09)00151-8 [pii] 10.1016/j.healthplace.2009.12.007. [PubMed: 20106710]
- Blakely, T.; Subramanian, SV. Multilevel studies. In: Oakes, JM.; Kaufman, JS., editors. *Methods in Social Epidemiology*. San Francisco, CA: Jossey-Bass; 2006. p. 316-340.
- Chaix B, Chauvin P. Tobacco and alcohol consumption, sedentary lifestyle and overweightness in France: a multilevel analysis of individual and area-level determinants. *Eur J Epidemiol*. 2003; 18(6):531–538. [PubMed: 12908718]
- DiCiccio TJ, Efron B. Bootstrap confidence intervals. *Statistical Science*. 1996; 11(3):189–228.
- Diez-Roux AV, Kiefe CI, Jacobs DR Jr, Haan M, Jackson SA, Nieto FJ, Schulz R. Area characteristics and individual-level socioeconomic position indicators in three population-based epidemiologic studies. *Ann Epidemiol*. 2001; 11(6):395–405. [PubMed: 11454499]
- Diez-Roux AV, Link BG, Northridge ME. A multilevel analysis of income inequality and cardiovascular disease risk factors. *Soc Sci Med*. 2000; 50(5):673–687. doi: S0277953699003202 [pii]. [PubMed: 10658848]
- Diez-Roux AV, Nieto FJ, Caulfield L, Tyroler HA, Watson RL, Szklo M. Neighbourhood differences in diet: the Atherosclerosis Risk in Communities (ARIC) Study. *J Epidemiol Community Health*. 1999; 53(1):55–63. [PubMed: 10326055]
- Diez Roux AV, Merkin SS, Hannan P, Jacobs DR, Kiefe CI. Area characteristics, individual-level socioeconomic indicators, and smoking in young adults: the coronary artery disease risk development in young adults study. *Am J Epidemiol*. 2003; 157(4):315–326. [PubMed: 12578802]
- Doubeni CA, Major JM, Laiyemo AO, Schootman M, Zuber AG, Hollenbeck AR, Allison J. Contribution of behavioral risk factors and obesity to socioeconomic differences in colorectal cancer incidence. *J Natl Cancer Inst*. 2012; 104(18):1353–1362. [PubMed: 22952311]
- Duncan C, Jones K, Moon G. Smoking and deprivation: are there neighbourhood effects? *Soc Sci Med*. 1999; 48(4):497–505. doi: S0277953698003608 [pii]. [PubMed: 10075175]

- Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: World Cancer Research Fund/American Institute for Cancer Research; 2007.
- Force USPST. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2008; 149(9):627–637. [PubMed: 18838716]
- Hastert TA, Beresford SA, Patterson RE, Kristal AR, White E. Adherence to WCRF/AICR cancer prevention recommendations and risk of postmenopausal breast cancer. *Cancer Epidemiol Biomarkers Prev.* 2013; 22(9):1498–1508. [PubMed: 23780838]
- Hastert TA, Beresford SA, Sheppard L, White E. Adherence to the WCRF/AICR cancer prevention recommendations and cancer-specific mortality: results from the Vitamins and Lifestyle (VITAL) Study. *Cancer Causes Control.* 2014; 25(5):541–552. [PubMed: 24557428]
- Hastert TA, Beresford SA, Sheppard L, White E. Disparities in cancer incidence and mortality by area-level socioeconomic status: a multilevel analysis. *J Epidemiol Community Health.* 2015; 69(2):168–176. [PubMed: 25288143]
- Heymann, J.; Fischer, A. Neighborhoods, health research, and its relevance to public policy. In: Kawachi, I.; Berkman, LF., editors. *Neighborhoods and Health.* New York, NY: Oxford University Press; 2003. p. 335–347.
- Inoue-Choi M, Robien K, Lazovich D. Adherence to the WCRF/AICR guidelines for cancer prevention is associated with lower mortality among older female cancer survivors. *Cancer Epidemiol Biomarkers Prev.* 2013; 22(5):792–802. [PubMed: 23462914]
- Kawachi, I.; Kroenke, C. Socioeconomic disparities in cancer incidence and mortality. In: Schottenfeld, D.; Fraumeni, JF., Jr, editors. *Cancer Epidemiology and Prevention.* New York, NY: Oxford University Press; 2006. p. 174–188.
- Kim D, Masyn KE, Kawachi I, Laden F, Colditz GA. Neighborhood socioeconomic status and behavioral pathways to risks of colon and rectal cancer in women. *Cancer.* 2010; 116(17):4187–4196. [PubMed: 20544839]
- Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, Carson R. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. *Am J Epidemiol.* 2002; 156(5):471–482. [PubMed: 12196317]
- Lee, IM.; Oguma, Y. Physical Activity. In: Schottenfeld, D.; Fraumeni, JF., Jr, editors. *Cancer Epidemiology and Prevention.* 3rd ed.. New York, NY: Oxford University Press; 2006. p. 449–467.
- Link BG, Phelan J. Social conditions as fundamental causes of disease. *J Health Soc Behav, Spec No.* 1995:80–94.
- Major JM, Doubeni CA, Freedman ND, Park Y, Lian M, Hollenbeck AR, Sinha R. Neighborhood socioeconomic deprivation and mortality: NIH-AARP diet and health study. *PLoS One.* 2010; 5(11):e15538. [PubMed: 21124858]
- Marshall, JR.; Freudenheim, JL. Alcohol. In: Schottenfeld, D.; Fraumeni, JF., Jr, editors. *Cancer Epidemiology and Prevention.* 3rd ed.. New York, NY: Oxford University Press; 2006. p. 243–258.
- Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L, Force USPST. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2009; 151(10):727–737. W237–W742. [PubMed: 19920273]
- Patterson RE, Kristal AR, Tinker LF, Carter RA, Bolton MP, Agurs-Collins T. Measurement characteristics of the Women's Health Initiative food frequency questionnaire. *Ann Epidemiol.* 1999; 9(3):178–187. doi: S1047279798000556 [pii]. [PubMed: 10192650]
- Pickett KE, Pearl M. Multilevel analyses of neighbourhood socioeconomic context and health outcomes: a critical review. *J Epidemiol Community Health.* 2001; 55(2):111–122. [PubMed: 11154250]
- Romaguera D, Vergnaud AC, Peeters PH, van Gils CH, Chan DS, Ferrari P, Norat T. Is concordance with World Cancer Research Fund/American Institute for Cancer Research guidelines for cancer prevention related to subsequent risk of cancer? Results from the EPIC study. *Am J Clin Nutr.* 2012; 96(1):150–163. [PubMed: 22592101]

- Schakel SF, Buzzard IM, Gebhardt SE. Procedures for estimating nutrient values for food composition databases. *J Food Composition Anal.* 1997; 10:102–114.
- Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2008; 149(9):627–637. [PubMed: 18838716]
- Stafford M, Cummins S, Ellaway A, Sacker A, Wiggins R, Macintyre S. Pathways to obesity: identifying local, modifiable determinants of physical activity and diet. *Soc Sci Med.* 2007; 65(9): 1882–1897. doi: S0277-9536(07)00304-8 [pii] 10.1016/j.socscimed.2007.05.042. [PubMed: 17640787]
- Steenland K, Henley J, Calle E, Thun M. Individual- and area-level socioeconomic status variables as predictors of mortality in a cohort of 179,383 persons. *Am J Epidemiol.* 2004; 159(11):1047–1056. doi: 10.1093/aje/kwh129. 159/11/1047 [pii]. [PubMed: 15155289]
- Steenland K, Henley J, Thun M. All-cause and cause-specific death rates by educational status for two million people in two American Cancer Society cohorts, 1959–1996. *Am J Epidemiol.* 2002; 156(1):11–21. [PubMed: 12076884]
- Stringhini S, Sabia S, Shipley M, Brunner E, Nabi H, Kivimaki M, Singh-Manoux A. Association of socioeconomic position with health behaviors and mortality. *JAMA.* 2010; 303(12):1159–1166. doi:303/12/1159 [pii] 10.1001/jama.2010.297. [PubMed: 20332401]
- Tang P, Sun L, Uhlman MA, Polascik TJ, Freedland SJ, Moul JW. Baseline PSA as a predictor of prostate cancer-specific mortality over the past 2 decades: Duke University experience. *Cancer.* 2010; 116(20):4711–4717. [PubMed: 20589748]
- Thun, MJ.; Henley, SJ. Tobacco. In: Schottenfeld, D.; Fraumeni, JF., Jr, editors. *Cancer Epidemiology and Prevention*. 3rd ed.. New York, NY: Oxford University Press; 2006. p. 217-242.
- VanderWeele TJ. Causal mediation analysis with survival data. *Epidemiology.* 2011; 22(4):582–585. [PubMed: 21642779]
- Vergnaud AC, Romaguera D, Peeters PH, van Gils CH, Chan DS, Romieu I, Norat T. Adherence to the World Cancer Research Fund/American Institute for Cancer Research guidelines and risk of death in Europe: results from the European Prospective Investigation into Nutrition and Cancer cohort study1,4. *Am J Clin Nutr.* 2013; 97(5):1107–1120. [PubMed: 23553166]
- White, E.; Armstrong, BK.; Saracci, R. *Principles of exposure measurement in epidemiology: Collecting, evaluating, and improving measures of disease risk factors*. 2nd ed.. New York: Oxford University Press; 2008.
- White E, Patterson RE, Kristal AR, Thornquist M, King I, Shattuck AL, Potter JD. VITamins And Lifestyle cohort study: study design and characteristics of supplement users. *Am J Epidemiol.* 2004; 159(1):83–93. [PubMed: 14693663]
- Willett, WC. Diet and Nutrition. In: Schottenfeld, D.; Fraumeni, JF., Jr, editors. *Cancer Epidemiology and Prevention*. 3rd ed.. New York, NY: Oxford University Press; 2006. p. 405-421.
- Zackrisson S, Lindstrom M, Moghaddassi M, Andersson I, Janzon L. Social predictors of non-attendance in an urban mammographic screening programme: a multilevel analysis. *Scand J Public Health.* 2007; 35(5):548–554. doi:778365316 [pii] 10.1080/14034940701291716. [PubMed: 17852976]

Highlights

- Area-level socioeconomic status (SES) is associated with cancer mortality
- We examined whether modifiable risk factors explain this association
- Smoking, diet, physical activity, and screening each weakened the association
- Area-level SES remained associated with cancer mortality outside of behavior

Table 1
Baseline demographic factors and modifiable risk factors by area-level socioeconomic status (SES)

	Area-level SES				
	Quintile 1 (High SES) (N=10,971)	Quintile 2 (N=10,921)	Quintile 3 (N=10,950)	Quintile 4 (N=10,919)	Quintile 5 (Low SES) (N=10,975)
Area-level SES index range	-16.1, -5.7	-5.7, -2.5	-2.5, 0.0	0.0, 2.8	2.8, 16.7
Demographic factors					
Age, mean (SD)	60.6 (7.1)	60.9 (7.3)	61.3 (7.2)	61.4 (7.3)	61.7 (7.4)
Male, %	51.8	51.0	51.0	49.7	48.0
White, %	94.1	94.4	94.8	93.6	91.9
College degree, %	68.4	52.5	43.0	32.7	24.7
Annual household income of at least \$40,000, %	88.5	80.9	75.7	67.0	57.3
Health behaviors					
Body mass index (kg/m ²), mean (SD)	26.2 (4.5)	27.1 (4.9)	27.5 (5.1)	28.0 (5.3)	28.4 (5.6)
Moderate/strenuous activity (MET-hours/week), mean (SD)	11.4 (14.4)	9.5 (13.5)	8.4 (12.9)	7.4 (11.9)	6.6 (11.4)
Energy density (kcal/g), mean (SD)	1.69 (0.44)	1.73 (0.48)	1.76 (0.48)	1.78 (0.53)	1.81 (0.54)
Fruits and vegetables (servings/day), mean (SD)	4.2 (2.5)	3.9 (2.4)	3.7 (2.4)	3.6 (2.4)	3.4 (2.4)
Red and processed meat (ounces/week), mean (SD)	17.9 (14.7)	19.3 (15.9)	20.4 (16.3)	21.1 (16.8)	21.4 (17.5)
Alcohol (drinks/week), mean (SD)	6.1 (8.7)	5.1 (8.5)	4.7 (8.4)	4.3 (8.4)	3.8 (8.5)
Smoking (pack-years), mean (SD)	9.1 (16.9)	12.1 (19.8)	13.3 (20.7)	14.4 (21.6)	16.5 (23.6)
Mammogram in previous 2 years (women only), %	93.6	92.0	91.5	90.6	89.4
Prostate-specific antigen test in previous 2 years (men only), %	75.5	73.2	70.1	69.1	71.9
Colonoscopy or sigmoidoscopy in previous 10 years, %	61.2	57.4	54.7	52.9	55.5

Table 2

Hazard ratios (HRs) and 95% confidence intervals (CIs) of cancer mortality associated with modifiable risk factors

Modifiable risk factors	Model 1 ^a Demographics and area-level SES HR (95% CI)	Model 2 ^b Demographics, area-level and individual SES HR (95% CI)
Body mass index (per 5 kg/m ²)	1.08 (1.02, 1.14)	1.06 (1.00, 1.11)
Moderate/strenuous activity (per 5 MET-hours/ week)	0.93 (0.90, 0.95)	0.94 (0.91, 0.97)
Energy density (per kcal/g)	1.22 (1.15, 1.31)	1.17 (1.09, 1.26)
Fruits and vegetables (per serving/day)	0.95 (0.93, 0.98)	0.97 (0.95, 1.00)
Red and processed meat (per 5 ounces/week)	1.04 (1.02, 1.05)	1.03 (1.02, 1.05)
Alcohol (per drink/day)	1.04 (1.00, 1.08)	1.04 (1.00, 1.09)
Smoking (per 10 pack-years)	1.20 (1.18, 1.22)	1.19 (1.17, 1.21)
Mammogram in previous 2 years (vs. none; women only) ^d	0.59 (0.47, 0.74)	0.62 (0.49, 0.77)
Prostate-specific antigen test in previous 2 years (vs. none; men only) ^e	0.63 (0.54, 0.74)	0.66 (0.56, 0.76)
Colonoscopy or sigmoidoscopy in previous 10 years (vs. none)	0.75 (0.68, 0.84)	0.78 (0.70, 0.87)

All models include 54,736 respondents and 1,488 cancer deaths, unless otherwise noted.

^aModel 1: Adjusted for age, sex, race/ethnicity, marital status, family history of cancer, and area-level SES index.

^bModel 2: Adjusted for Model 1 covariates, individual education and annual household income.

^dModel includes 27,213 women and 647 cancer deaths

^eModel includes 27,523 men and 841 cancer deaths

Table 3

Role of modifiable risk factors in explaining the association between area-level socioeconomic status (SES) and cancer mortality

	Model 1 ^a Demographics only		Model 2 ^b Demographics and individual SES	
	Q1 vs. Q5 (categorical) HR (95% CI) ^c	Percent change (continuous) (95% CI) ^d	Q1 vs. Q5 (categorical) HR (95% CI) ^c	Percent change (continuous) (95% CI) ^e
Model 1 or 2, covariates only	1.77 (1.50, 2.11)	--	1.37 (1.14, 1.65)	--
Plus body mass index	1.72 (1.45, 2.05)	-5.1 (-9.9, -1.2)	1.35 (1.12, 1.62)	-5.0 (-14.4, 0.2)
Plus physical activity	1.68 (1.41, 1.99)	-10.4 (-16.1, -6.6)	1.34 (1.12, 1.62)	-7.1 (-16.5, -3.4)
Plus diet ^f	1.67 (1.40, 1.98)	-11.1 (-17.3, -7.0)	1.33 (1.11, 1.60)	-8.8 (-22.3, -4.2)
Plus alcohol	1.79 (1.51, 2.13)	2.0 (-0.4, 4.4)	1.38 (1.15, 1.66)	2.8 (0.1, 7.9)
Plus pack-years of smoking	1.50 (1.26, 1.79)	-28.6 (-40.0, -21.9)	1.27 (1.06, 1.53)	-23.2 (-53.5, -13.0)
Plus screening ^g	1.70 (1.43, 2.01)	-8.9 (-13.3, -5.8)	1.34 (1.12, 1.62)	-8.0 (-18.7, -3.8)
All modifiable risk factors^h	1.38 (1.16, 1.64)	-44.6 (-62.4, -33.7)	1.22 (1.02, 1.48)	-37.1 (-62.6, -20.3)

All models include 54,736 respondents, and 1,488 cancer deaths

^aModel 1: Adjusted for age, sex, race/ethnicity, marital status, family history of cancer

^bModel 2: Adjusted for all factors in Model 1, plus education and annual household income

^cHazard ratio (HR) and 95% confidence interval (CI) associated with the lowest (Q1) vs. highest quintile (Q5) of area-level SES

^dPercent change in continuous $\beta = 100 \times (\beta_{\text{Model 1+ health behavior}} - \beta_{\text{Model 1}}) / (\beta_{\text{Model 1}})$; 95% CI based on bias-corrected bootstrap estimation with 2,000 repetitions

^ePercent change in continuous $\beta = 100 \times (\beta_{\text{Model 2+ health behavior}} - \beta_{\text{Model 2}}) / (\beta_{\text{Model 2}})$; 95% CI based on bias-corrected bootstrap estimation with 2,000 repetitions

^fDiet model includes energy density, servings of fruits and vegetables, and red and processed meat intake.

^gScreening model includes mammogram in the previous two years (women), prostate-specific antigen screening in the previous two years (men) and colonoscopy or sigmoidoscopy in the previous 10 years.