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Neighborhood socioeconomic status and behavioral pathways to risks of colon and rectal cancer in women

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Abstract

Background—Neighborhood amenities and resources plausibly determine individual modifiable risk factors for colon and rectal cancer. Evidence on the associations between neighborhood socioeconomic status (SES) and incident colon and rectal cancer is limited.

Methods—We analyzed a prospective cohort of 111,129 women in the Nurses' Health Study with no history of cancer in 1986 followed to 2006. Neighborhood SES was based on Census-derived characteristics of block groups of residence. Cox models were used to estimate the multivariable-adjusted associations between neighborhood SES and incident colon and rectal cancer, and to examine for effect modification. For significant associations, path models were estimated with behavioral risk factors included as potential mediators.

Results—Neighborhood SES was unassociated with colon cancer among all women. However, among women with college or greater education, higher neighborhood SES was inversely related to colon cancer (p for trend = 0.01; p for interaction between neighborhood SES and education = 0.03). Path analysis suggested mediation by red meat intakes and body mass index (BMI). Higher neighborhood SES was inversely related to rectal cancer among all women (RR in highest quintile = 0.64; 95% CI = 0.44–0.93; p for trend = 0.08). Path analysis was consistent with mediation by multivitamin use and BMI.

Conclusion—These findings suggest that living in a higher-SES neighborhood may protect against rectal cancer in women and colon cancer in higher-educated women, mediated by selected behavioral risk factors. Risk factor differences between colon and rectal cancer may account for discrepancies in estimated neighborhood effects by cancer site.

Keywords

colon cancer; rectal cancer; behavior; epidemiology; public health

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Excluding non-melanotic skin cancer, colorectal cancer is the third most commonly diagnosed cancer among both women and men in the United States, accounting for an estimated 146,970 new cases (106,100 colon, 40,870 rectal cancer cases) and 49,920 deaths in both sexes combined in 2009.¹ A higher risk of colorectal cancer has been associated with a variety of modifiable behaviors, including diets high in red or processed meat, smoking, physical inactivity, and obesity.^{1,2} Notably, some evidence suggests differences in the behavioral risk factor epidemiology for colon and rectal cancer. Physical activity, for example, has been consistently inversely associated with colon cancer risk but not rectal cancer risk.³ In Japan, incidence rates of colon cancer have been observed to rise more rapidly than rates of rectal cancer.⁴

International variations in colon and rectal cancer incidence rates and migrant studies finding rapid changes in immigrant rates of colorectal cancer towards those of their host country populations implicate the importance of environmental influences.^{3,5,6} While there is growing empirical evidence for contextual effects of neighborhood socioeconomic environments (SES) on health outcomes such as coronary heart disease, few studies have specifically examined the relation between neighborhood SES and incident colon or rectal cancer. Plausibly, levels of amenities and resources across neighborhoods (e.g., the availability and cost of nutritious foods) may help to shape multiple individual-level behavioral risk factors for colon and rectal cancer, including diet and physical activity. Previous studies have identified relations between neighborhood SES and diet, physical activity, smoking, and body mass index (BMI).^{7–11}

Theoretical considerations and empirical data further suggest that the associations between neighborhood SES and colon and rectal cancer may be modified by individual characteristics such as age, educational attainment, and level of social integration. For example, risk factor behaviors of younger adults may be more malleable to features of the residential environment, and thus may exhibit stronger associations than in older adults.¹² Likewise, the uptake of healthy behaviors among higher- (vs. lower-) educated individuals may be greater in socioeconomic environments that facilitate such behaviors. In one study, among those living in high-SES neighborhoods, individuals of higher SES smoked less than lower-SES individuals, whereas in low-SES neighborhoods the two groups smoked at similar levels.⁷ Knowledge about healthy behaviors may also diffuse more rapidly among individuals who are more socially integrated.

In a large cohort of women, we explored the prospective relations between neighborhood SES and individual risks of colon and rectal cancer; and tested for differences in the associations according to age, educational attainment, and the number of close friends. To our knowledge, this is the first study to prospectively examine the associations between neighborhood SES and colon and rectal cancer. Furthermore, using path analysis, we investigated whether individual-level behavioral risk factors potentially mediated any observed significant associations between neighborhood SES and colon and rectal cancer risks.

MATERIALS AND METHODS

Study population

The study population was the Nurses' Health Study, a well-established, large, prospective cohort of women. The Nurses' Health Study began in 1976, when 121,700 female married registered nurses aged 30–55 residing in one of the 11 most populous US states were mailed and returned a detailed questionnaire on lifestyle factors and past medical history.¹³ 70% of those asked to participate completed the initial questionnaire. Follow-up questionnaires have since been mailed to cohort members every two years, to inquire and update information

about a variety of exposures along with the development of a number of medical conditions including cancer. A high response rate of 86% was achieved in 1986, and response rates of over 90% have been attained for the 1990 and subsequent questionnaires.¹³ After exclusion of those with a history of cancer prior to 1986 at any site (except for non-melanotic skin cancer), 111,129 participants geocoded (i.e., linked geographically) to the Census block group level formed the study cohort followed over the 1986 to 2006 period.

Assessment of neighborhood SES

Census block groups of residence of study participants corresponding to addresses reported on each of the biennial questionnaires between 1986 and 2002 were subsequently linked to 1990 and 2000 US Census variables. A Census block group represents the smallest Census administrative unit, and contains on average 1000 residents.

Income, educational, and occupational data from the 1990 and 2000 Census were used to estimate the SES of Census block groups of residence. Six variables corresponding to dimensions of wealth and income (log of median household income, log of median value of housing units, and % of households receiving interest, dividend, or net rental income), education (% of adults ≥ 25 years who had completed high school and % of adults ≥ 25 years who had completed college), and occupation (% of employed persons ≥ 16 years in executive, managerial, or professional specialty occupations) were combined into a neighborhood SES summary score.¹⁴ For each variable, at the Census block group level, a standardized z score was derived by subtracting the overall mean and dividing by the standard deviation. Summary scores were then calculated by averaging the z scores for the six variables, with higher summary scores indicating a higher level of neighborhood SES. The six indicators were hypothesized to tap into the latent construct of neighborhood SES.

To attempt to capture more year-specific estimates of neighborhood exposure, neighborhood SES estimates were updated according to the Census block group of residence for a given year, and modeled as a time-varying covariate. We incorporated an approximate latency period between neighborhood SES and incident colon/rectal cancer of up to 10 years, given empirical evidence for a relatively long time lag between exposures and incident colorectal cancer.¹⁵ Neighborhood SES estimates for 1986 were derived from 1990 Census data, and analyzed in relation to cancer diagnoses between 1986 and 1996. Neighborhood SES estimates for 1988, 1990, and 1992 were also derived from 1990 Census data, and examined in relation to cancer diagnoses during the time periods 1996–98, 1998–2000, and 2000–2002, respectively. Neighborhood SES estimates for 1994 and 1996 were calculated by averaging 1990 and 2000 estimates (respectively derived from 1990 and 2000 Census data), and analyzed in relation to diagnoses during the periods 2002–2004 and 2004–2006, respectively.

Assessment of individual-level risk factors for colon and rectal cancer

Data from study participants on the following colon/rectal cancer risk factors were collected from the 1990 questionnaire (years in parentheses indicated where obtained from alternative biennial questionnaire years closest to 1990 for which the risk factor data were available, or at or prior to 1986 for family history covariate data): red and processed meat intakes (quartiles), calcium intakes (quartiles), alcohol intakes (0, 0.1–2, 2.1–8.2, >8.2 g/day), current daily multivitamin use (yes/no), physical activity (1988; quartiles), BMI (quartiles), pack-years of smoking (0, 1–10, 11–29, ≥ 30), oral contraceptive use (1984), family history of colorectal cancer (1982), history of polyp (1984, 1986), and aspirin use (never, past, 1 day/week, 2–5 days/week, 6+ days/week). Previous studies of this cohort have demonstrated reasonable levels of reliability and validity for risk factor measures, including dietary intakes, physical activity, and body weight.^{16–18}

Ascertainment of colon and rectal cancer

For study participants reporting a new incident case of colon or rectal cancer on a questionnaire, written permission was obtained to review medical records and pathology reports. Likewise, for deaths attributed to colon or rectal cancer, as identified through the National Death Index or next of kin, permission was obtained from the next of kin to review medical records. Trained physicians, blinded to the exposure information previously reported by study participants, then reviewed the medical records and pathology reports to confirm the diagnosis.¹³

Assessment of other covariates

Data from study participants on the following demographic and socioeconomic variables were gathered from the 1992 questionnaire when first asked (with the exception of age) and included as model covariates: age (continuous); race/ethnicity (Black, Asian, Hispanic, Other); educational attainment (RN, bachelor's degree, graduate degree); and husband's educational attainment (high school graduate, bachelor's degree, graduate degree). Information on the number of close friends (0–5, >5) was also obtained from the 1992 questionnaire.

Census block group-level covariates/potential confounders consisted of % Black, immigrant concentration (average of % of Hispanics and % of foreign-born residents), and residential stability (average of % living in the same house over the previous 5 years and % of housing occupied by owners). These were also modeled as time-varying covariates, and corresponded to the same years as neighborhood SES.

Statistical analysis

Using Cox proportional hazards models and adjusting standard errors for within-neighborhood clustering, the relative hazards of incident colon cancer for those in each of the higher vs. lowest quintile of neighborhood (Census block group-level) SES was estimated, controlling for individual-level sociodemographic and socioeconomic factors and neighborhood-level covariates. Missing values for continuous covariates (which comprised ~1% or less of all observations) were excluded from the models. A linear test for trend was performed by converting the neighborhood SES quintile categories into an ordinal continuous variable, and examining its corresponding p value. Cox proportional hazards models were similarly estimated for the outcome of incident rectal cancer.

For each cancer, we further tested for effect modification by each of individual-level age, educational attainment, and the number of close friends. Race/ethnicity could not be examined as an effect modifier because more than 90% of the cohort was White. The statistical significance of model terms corresponding to the interactions between neighborhood SES and the potential effect modifiers in their associations with colon/rectal cancer risk was tested using a likelihood ratio test, by comparing the changes in the values for $-2 \times$ maximum log-likelihood of the models with and without the interaction terms to a chi-square distribution.

The extent to which each of the individual-level behavioral risk factors for colon cancer mediated any observed significant associations of neighborhood SES with the risk of colon cancer was evaluated using path analysis. Neighborhood SES and neighborhood-level covariates were estimated for 1986, while the behavioral risk factor variables primarily corresponded to 1990. The outcome in the overall path model was any diagnosis of colon cancer over the follow-up period. All variables were first categorized to create ordinal variables (after excluding missing values), and a polychor correlation matrix was then estimated.¹⁹ To account for measurement error in neighborhood SES (that was derived from

six indicators) in the path model, correlation coefficients $\rho_{X_i,SES}$ for correlations between the neighborhood SES categorical variable and each other path model variable X_i were replaced by $\rho_{X_i,SES} / (0.93)^{1/2}$, where 0.93 was the value of Cronbach's coefficient α for the neighborhood SES measure constructed from the six neighborhood SES indicators as continuous variables (based on Spearman²⁰). The path analysis included direct (non-mediated) and indirect (mediated) paths between neighborhood SES and incident colon cancer. Correlations between residuals from equations of mediating factors with correlation coefficients of absolute value greater than 0.10 were specified in the models. Coefficient estimates were standardized to represent the standard deviation change in the dependent variable corresponding to a 1-standard deviation change in the independent variable along each pathway. Indirect effects between neighborhood SES and incident cancer mediated by a particular risk factor were estimated by the product of the component path coefficients (e.g., $\beta_1 * \beta_2$); the standard error of each estimate was approximated using the multivariate delta method,²¹ and statistical significance was assessed by dividing the estimated mediated effect by its standard error to produce a z score. A similar path analysis was conducted for rectal cancer.

The goodness-of-fit for each model containing both direct and mediated effects of neighborhood SES on colon/rectal cancer risk was evaluated using the Comparative Fit Index (CFI) and the Root Mean Square Error of Approximation (RMSEA).²²

For all analyses, statistical significance was assessed at a level of 0.05 (2-tailed). All models were estimated using SAS Version 9.1 software.

This study was approved by the institutional review board at the Brigham and Women's Hospital in Boston, Massachusetts.

RESULTS

Table 1 shows descriptive characteristics for the total sample of 111,129 women living in 49,102 Census block groups (analyzed in main effect and interaction models), and for the sub-sample of 46,128 women with behavioral risk factor data (analyzed in path models) at baseline in 1986. All six Census block group-level indicators used to construct the neighborhood socioeconomic score displayed a relatively wide range across neighborhood SES quintiles. For example, median household income ranged from an average value of \$22,700 in the lowest quintile to nearly threefold greater at \$65,300 in the highest quintile. Greater proportions of women in the higher quintiles of neighborhood SES were White, college-educated, taking multivitamins, and had lower red meat intakes and higher mean intakes of alcohol and levels of physical activity.

A total of 1223 cases of colon cancer was documented over 1,942,702 person-years of follow-up. Compared to women living in the lowest quintile of neighborhood SES, women in the highest quintile had a non-significantly lower risk of incident colon cancer, controlling for baseline demographic and socioeconomic neighborhood- and individual-level factors and a family history of colorectal cancer and history of polyp (multivariate RR = 0.91, 95% CI = 0.74–1.10; p for trend = 0.23; Table 2).

Among 24,678 women with college or greater educational attainment, living in a higher-SES neighborhood was significantly inversely related to individual colon cancer risk (multivariate RR in the highest vs. lowest quintile = 0.52, 95% CI = 0.33–0.80; p for trend = 0.01; Table 3). A non-significant positive association was seen among women with less than college education (multivariate RR in the highest quintile = 1.06, 95% CI = 0.83–1.34; p for trend = 0.90). The interaction between neighborhood SES and educational attainment in their associations with colon cancer was significant (p = 0.03). Age and the number of close

friends did not modify the association between neighborhood SES and colon cancer ($p > 0.30$ for each set of interaction terms; data not shown).

Figure 1 shows the standardized path coefficients for the path model between neighborhood SES and incident colon cancer with the inclusion of modifiable risk factors, among women with college or greater education. The overall goodness-of-fit of the model was reasonably good (RMSEA = 0.05; CFI = 0.97). Neighborhood SES was estimated to have a significant inverse direct effect on colon cancer ($\beta = -0.02$). Neighborhood SES was a relatively strong predictor of red meat and alcohol intakes, physical activity, and BMI. Of the modifiable risk factors, aspirin use was the strongest determinant of colon cancer ($\beta = -0.10$, corresponding to a 0.10 standard deviation decrease in the absolute risk of colon cancer with a 1-standard deviation increase in aspirin use). Red meat intakes were significantly positively related ($\beta = 0.02$) and calcium intakes significantly inversely related ($\beta = -0.05$) to colon cancer. Significant indirect paths between neighborhood SES and colon cancer were observed for red meat intakes, alcohol intakes, and BMI (with the strongest and most significant paths being for alcohol intakes and BMI); paths for red meat intakes and BMI contributed to the inverse association between neighborhood SES and colon cancer.

305 cases of rectal cancer were observed over 1,943,481 person-years of follow-up. Compared to women living in the lowest quintile of neighborhood SES, women in the highest quintile had a significantly lower risk of incident rectal cancer, adjusting for baseline factors (multivariate RR = 0.64; 95% CI = 0.44–0.93; Table 4; p for trend = 0.08). Age, educational attainment, and the number of close friends were not effect modifiers ($p > 0.30$ associated with each set of interaction terms; data not shown).

Figure 2 displays the standardized path coefficients for the path model between neighborhood SES and incident rectal cancer with the inclusion of modifiable risk factors among all women. The overall model goodness-of-fit was good (RMSEA = 0.04; CFI = 0.97). Neighborhood SES had a significant inverse direct effect on incident rectal cancer ($\beta = -0.03$). As was also found in the path analysis for colon cancer, neighborhood SES was a relatively strong predictor of red meat and alcohol intakes, physical activity, and BMI. Of the modifiable risk factors, multivitamin use and BMI were the strongest predictors of rectal cancer. In contrast to colon cancer, red meat intakes were significantly *inversely* related ($\beta = -0.02$) and calcium intakes significantly *positively* related ($\beta = 0.03$) to rectal cancer. In addition, alcohol intakes and smoking were less strongly positively associated with rectal cancer (compared to their associations with colon cancer), and aspirin use was weakly *positively* associated with rectal cancer. Significant indirect paths between neighborhood SES and rectal cancer were determined for red meat intakes, alcohol intakes, multivitamin use, smoking, and BMI (with the strongest and most significant path being for BMI); paths for multivitamin use and BMI contributed to the inverse association between neighborhood SES and rectal cancer.

DISCUSSION

In this large 20-year prospective study, we found that living in a higher SES neighborhood was significantly inversely related to individual colon cancer risk among women of college or greater (but not less than college) educational attainment. For rectal cancer, the significant associations were more generalized, with residence in a higher-SES neighborhood inversely related to individual rectal cancer risk among all women. For both relations, there was evidence consistent with mediation by selected behavioral risk factors.

In addition to the study's prospective design, a key strength of our study was its incorporation of a plausible latency period between neighborhood SES exposure and

incident cancer. Furthermore, path analysis enabled the examination of potential mediating risk factor pathways, including assessment of their relative magnitudes. Internal validity of our study was enhanced by medical confirmation of cancer diagnosis; use of validated behavioral risk factor measures; and selection of a cohort comprised of health professionals, who were more likely to have reported relatively accurate health information. We further controlled for multiple key neighborhood- and individual-level factors that reduced the potential for residual confounding.

To date, several studies (all of which have been cross-sectional in design) have investigated associations between neighborhood SES and incident colon and rectal cancer. In these studies, significant associations in the anticipated direction have been consistently demonstrated for rectal cancer and less consistently found for colon cancer. Using data from the Surveillance, Epidemiology, and End Results (SEER) Program, Baquet et al.²³ analyzed the ecological associations between Census tract-level median educational attainment, median household income, and age-adjusted incidence rates for colon and rectal cancer (stratified by population density and race/ethnicity). No clear relations were observed except for an inverse association between median household income and rectal cancer among Whites (p for trend = 0.06).

Among residents in four US urban areas, Gorey et al.²⁴ examined the associations between living in a high-poverty census tract and age-adjusted cumulative incidence of cancer, stratified by gender and race/ethnicity. For colon cancer, significant positive relations were observed in White women (relative risk, $RR = 1.48$; 95% confidence interval, $CI = 1.33$ – 1.65) and men, as well as in Black women and men. Positive associations of similar magnitudes and significance by gender and race/ethnicity were also seen for rectal cancer.

Kee et al.²⁵ explored the association between neighborhood socioeconomic deprivation for electoral wards in Northern Ireland and colorectal cancer (controlling for age and gender), and determined that living in a successively higher deprivation quintile was significantly related to higher rectal cancer risk ($OR = 1.09$; 95% $CI = 1.01$ – 1.18) and marginally non-significantly related to higher colon cancer risk ($OR = 1.05$; 95% $CI = 0.99$ – 1.10).

Gorey et al.²⁶ conducted an ecological analysis between residence in a low- (vs. high-) income census tract in a large Canadian metropolitan area and cancer incidence. For colon cancer, a null association was found among women ($RR = 0.99$; 95% $CI = 0.97$ – 1.01), while a significant positive association was observed among men. In contrast, for rectal cancer, significant positive associations were seen among both women ($RR = 1.04$; 95% $CI = 1.01$ – 1.07) and men ($RR = 1.25$; 95% $CI = 1.08$ – 1.44).

In the current study, the presence of effects of neighborhood SES on incident colon cancer among higher-educated women and on incident rectal cancer among all women was supported by statistical evidence of dose-response (reaching significance and approaching significance for colon and rectal cancer, respectively), as well as evidence of mediation by behavioral risk factors including BMI. This is in keeping with a growing literature documenting associations between neighborhood socioeconomic environments and these risk factors.

Our results suggested differences in the effects of neighborhood socioeconomic environments on colorectal cancer by cancer site. The lack of significant associations for colon cancer among lower-educated women might signify a higher threshold for neighborhood effects as compared to rectal cancer. This might be attributed to differences in the behavioral risk factor epidemiology for the two sites (which in turn might be the long-term sequelae of morphologic, physiologic, and biochemical differences between the colon and rectum e.g., average crypt length and pH of the mucin coating the mucosa²⁷). For

example, we determined that alcohol intakes (observed to be *higher* in higher-SES neighborhoods) were more strongly positively associated with colon cancer than rectal cancer, and hence may have attenuated any overall protective effects of neighborhood SES on colon cancer risk. As found in our study, an investigation in Japan (a country in which the incidence rates of colon cancer have risen more rapidly than rates of rectal cancer⁴) further observed that calcium intakes were significantly inversely associated with colon cancer but not rectal cancer, while meat intakes were significantly inversely related to rectal cancer but not colon cancer.²⁸ A large prospective analysis using data from the Nurses' Health Study and the Health Professionals' Follow-up Study also observed unique patterns of risk factor associations between these sites in both women and men.²⁹ Moreover, higher-educated (vs. lower-educated) women may be more likely to favorably adapt their behaviors in response to their neighborhood socioeconomic environments, such that significant associations were present for these women (but not for lower-educated women). Studies on the associations between individual SES and colon and rectal cancer have further demonstrated divergent patterns, with protective associations between higher SES and rectal cancer but not colon cancer.^{30,31}

This study had several limitations. First, we estimated neighborhood SES using 1990 and 2000 Census data. Exposure misclassification in neighborhood SES may have been present in the inter-Censal estimates, although such misclassification is likely to have been non-differential with respect to cancer status and contributed to underestimation of the magnitude of the associations. In addition, there is evidence that both neighborhood poverty and relative rank orders for neighborhood poverty remain relatively stable over time, even over several decades.³² Second, it is possible that the use of administratively-defined Census block groups could have led to misclassification error (more likely to have been non-differential), if they are not good proxies for neighborhoods. However, one comparison of associations for Census-defined neighborhoods vs. 'ecologically meaningful' neighborhoods (as defined by local knowledge, historical data, and local perceptions of neighborhood boundaries) with self-reported health reported similar results,³³ suggesting that the associated misclassification error may not be substantial. Third, due to limitations of the path analysis statistical procedure which does not allow updating of covariates, behavioral risk factors were predominantly modeled based on measures at a fixed intermediate timepoint in 1990 (shortly after baseline), and hence corresponded in time to after diagnosis in some instances. Nevertheless, the vast majority of incident cancers (82.6% for colon cancer, 84.9% for rectal cancer) were diagnosed after 1990. Some exposure misclassification may have been present due to the lack of updating of risk factors in our path analysis findings, although is unlikely to have been differential. Fourth, because study participants in the Nurses' Health Study were not randomly sampled from the US population, our results may not be generalizable to all US women. Nonetheless, the participants' relative homogeneity with respect to individual age, SES, and race/ethnicity should have reduced potential confounding by these factors, and thereby increased internal validity. Finally, given the relatively higher education of study participants (with all possessing at least a registered nurse degree), it is possible that in the general population stronger effect modification might be demonstrated due to wider variations in educational attainment e.g., comparing those with college or greater education to those with less than high school education.

In summary, our study's findings suggest that living in a higher-SES neighborhood may protect against the development of rectal cancer in women and colon cancer in higher-educated women, mediated by behavioral risk factors including BMI. Differences in the behavioral risk factor epidemiology for colon and rectal cancer may account for the discrepancies in estimated neighborhood effects by cancer site. Additional studies are needed to confirm these findings, including in more diverse populations. Ultimately,

identifying the presence of such neighborhood SES contextual effects on colon and rectal cancer risks may lend greater support to policies and interventions to reduce poverty concentration. In the case of colon cancer, the presence of effect modification by educational attainment may suggest the need for supplementary interventions tailored towards higher-educated women.

Condensed abstract

Living in a richer neighborhood may protect against rectal cancer in women and colon cancer in higher-educated women. These associations may be mediated by behavioral risk factors including body mass index.

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REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2009. American Cancer Society; Atlanta, GA: 2009.
2. Tomeo CA, Colditz GA, Willett WC, et al. Harvard Report on Cancer Prevention. Volume 3: prevention of colon cancer in the United States. *Cancer Causes Control*. 1999; 10(3):167–80. [PubMed: 10454062]
3. Potter JD. Colorectal cancer: molecules and populations. *J Natl Cancer Inst*. 1999; 91:916–932. [PubMed: 10359544]
4. The Research Group for Population-Based Cancer Registration in Japan. Cancer incidence in Japan. In: Tajima, K.; Kuroishi, T.; Oshima, A., editors. *Cancer mortality and morbidity statistics*. Japan Scientific Societies Press; Tokyo: 2004. p. 95-130.
5. Parkin, DM.; Muir, CS.; Whelan, SL.; Gao, JT.; Ferlay, J.; Powell, J. *Cancer incidence in five continents*. International Agency for Research on Cancer; Lyon (France): 1992.
6. Flood DM, Weiss NS, Cook LS, Emerson JC, Schwartz SM, Potter JD. Colorectal cancer incidence in Asian migrants to the United States and their descendants. *Cancer Causes Control*. 2000; 11:403–411. [PubMed: 10877333]
7. Chuang YC, Cubbin C, Ahn, Winkleby MA. Effects of neighborhood socioeconomic status and convenience store concentration on individual level smoking. *J Epidemiol Community Health*. 2005; 59:568–573. [PubMed: 15965140]
8. Diez Roux AV, Nieto FJ, Muntaner C, et al. Neighborhood environments and coronary heart disease: a multilevel analysis. *Am J Epidemiol*. 1997; 146(1):48–63. [PubMed: 9215223]
9. 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; 53:55–63. [PubMed: 10326055]
10. Cubbin C, Hadden WC, Winkleby MA. Neighborhood context and cardiovascular disease risk factors: the contribution of material deprivation. *Ethn Dis*. 2001; 11:687–700. [PubMed: 11763293]
11. Chuang YC, Ennett ST, Bauman KE, Foshee VA. Neighborhood influences on adolescent cigarette and alcohol use: mediating effects through parent and peer behaviors. *J Health Soc Behav*. 2005; 46:187–204. [PubMed: 16028457]
12. Kling JR, Liebman JB, Katz LF. Experimental analysis of neighborhood effects. *Econometrica*. 2007; 75:83–119.
13. Colditz GA. The Nurses' Health Study: a cohort of US women followed since 1976. *J Am Med Women's Assoc*. 1995; 50:40–44. [PubMed: 7722205]

14. Diez Roux AV, Merkin SS, Arnett D, et al. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med*. 2001; 345:99–106. [PubMed: 11450679]
15. Jacobs EJ, Connell CJ, Chao A, et al. Multivitamin use and colorectal cancer incidence in a US cohort: does timing matter? *Am J Epidemiol*. 2003; 158:621–628. [PubMed: 14507597]
16. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol*. 1985; 122:51–65. [PubMed: 4014201]
17. Wolf AM, Hunter DJ, Colditz GA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol*. 1994; 23:991–999. [PubMed: 7860180]
18. Rimm EB, Stampfer MJ, Colditz GA, Chute CG, Litin LB, Willett WC. Validity of self-reported waist and hip circumferences in men and women. *Epidemiol*. 1990; 1:466–473.
19. Drasgow, F. Polychoric and polyserial correlations. In: Kotz, L.; Johnson, NL., editors. *Encyclopedia of statistical sciences*. Vol. Vol. 7. Wiley; New York: 1988. p. 69-74.
20. Spearman C. General intelligence: Objectively determined and measured. *Amer J Psychol*. 1904; 15:201–293.
21. Sobel ME. Asymptotic confidence intervals for other statistic by simply replacing the estimation portions indirect effects in structural equation models. with the desired computations. *Sociological Methodol*. 1982; 12:290–312.
22. Loehlin, JC. *Latent variable models: an introduction to factor, path, and structural equation analysis*. 4th ed.. L. Erlbaum Associates; Mahwah, NJ: 2004.
23. Baquet CR, Horm JW, Gibbs T, Greenwald P. Socioeconomic factors and cancer incidence among blacks and whites. *J Natl Cancer Inst*. 1991; 83:551–557. [PubMed: 2005640]
24. Gorey KM, Vena JE. The association of near poverty status with cancer incidence among black and white adults. *J Community Health*. 1995; 20:359–366. [PubMed: 7593741]
25. Kee F, Wilson R, Currie S, et al. Socioeconomic circumstances and the risk of bowel cancer in Northern Ireland. *J Epidemiol Community Health*. 1996; 50:640–644. [PubMed: 9039383]
26. Gorey KM, Holowaty EJ, Laukkanen E, Fehringer G, Richter NL. Association between socioeconomic status and cancer incidence in Toronto, Ontario: possible confounding of cancer mortality by incidence and survival. *Cancer Prev Control*. 1998; 2:236–241. [PubMed: 10093638]
27. Iacopetta B. Are there two sides to colorectal cancer? *Int J Cancer*. 2002; 101:403–408. [PubMed: 12216066]
28. Wakai K, Hirose K, Matsuo K, et al. Dietary risk factors for colon and rectal cancers: a comparative case-control study. *J Epidemiol*. 2006; 16:125–135. [PubMed: 16710081]
29. Wei EK, Giovannucci E, Wu K, et al. Comparison of risk factors for colon and rectal cancer. *Int J Cancer*. 2004; 108:433–442. [PubMed: 14648711]
30. Frederiksen BL, Osler M, Harling H, Danish Colorectal Cancer Group. Jorgensen T. Social inequalities in stage at diagnosis of rectal but not in colonic cancer: a nationwide study. *Br J Cancer*. 2008; 98:668–673. [PubMed: 18231103]
31. Burnley IH. Disadvantage and male cancer incidence and mortality in New South Wales 1985–1993. *Soc Sci Med*. 1997; 45:465–476. [PubMed: 9232740]
32. Sampson, RJ.; Morenoff, J. Durable inequality: spatial dynamics, social processes and the persistence of poverty in Chicago neighborhoods. In: Bowles, S.; Durlauf, S.; Hoff, K., editors. *Poverty Traps*. Princeton University Press; Princeton, N.J.: 2006. p. 176-203.
33. Ross NA, Tremblay SS, Graham K. Neighborhood influences on health in Montreal, Canada. *Soc Sci Med*. 2004; 59:1485–1494. [PubMed: 15246176]

Figure 1.

Path analysis diagram of associations between neighborhood SES and incident colon cancer with potential mediating factors among women with college or greater education and risk factor data (n = 13,896). *Significant at 0.05 level. †Significant indirect paths between neighborhood SES and colon cancer for red meat intakes, alcohol intakes, and BMI. RMSEA = 0.05; CFI = 0.97.

Figure 2.

Path analysis diagram of associations between neighborhood SES and incident rectal cancer with potential mediating factors among all women with risk factor data (n = 46,128).

*Significant at 0.05 level. †Significant indirect paths between neighborhood SES and rectal cancer for red meat intakes, alcohol intakes, multivitamin use, BMI, and smoking. RMSEA = 0.04; CFI = 0.97.

TABLE 1
Characteristics by quintile of neighborhood socioeconomic score among 111,129 women in the Nurses' Health Study in 1986

Neighborhood characteristics	Neighborhood socioeconomic score				
	Q1 (lowest SES) n = 9,820 neighborhoods	Q2 n = 9,820	Q3 n = 9,821	Q4 n = 9,820	Q5 (highest SES) n = 9,821
Socioeconomic deprivation					
Median household income (\$1,000 US)	22.7	30.8	37.8	45.2	65.3
Median house value (\$1,000 US)	56.4	86.8	118.6	156.5	254.0
% Households receiving interest, dividend, or rental income	30.4	42.6	49.4	56.8	67.9
% Adults high school+	64.5	76.0	82.0	87.5	93.4
% Adults college+	13.0	20.8	28.7	39.4	57.6
% in executive, managerial, professional occupations	15.6	22.0	28.5	36.4	50.3
Individual characteristics					
	n = 17,119 women*	n = 20,486*	n = 22,031*	n = 25,128*	n = 26,365*
Median age (y)	n = 6,667 women [†]	n = 8,521 [†]	n = 9,141 [†]	n = 10,460 [†]	n = 11,339 [†]
Race/ethnicity White (%)	52.6	52.4	52.0	51.8	51.6
Educational attainment (% college+)	90.0	93.4	94.1	94.7	94.8
Husband's educational attainment (% college+)	16.7	18.6	21.8	26.0	33.5
Red meat intakes (mean; servings/d)	33.9	40.6	48.9	58.0	75.3
Alcohol intakes (mean; g/day)	0.48	0.46	0.44	0.43	0.41
Calcium intakes (mean; mg/day)	3.6	4.0	4.6	5.5	7.0
Multivitamin use (%)	1013	1046	1063	1064	1087
Physical activity (mean; MET-hrs/wk)	35.3	36.3	37.5	38.5	40.0
BMI (mean; kg/m ²)	14.3	14.8	15.0	15.8	17.3
Smoking (mean; pack-yrs)	26.5	26.2	25.9	25.5	24.8
Ever oral contraceptive use (%)	12.4	12.5	13.0	13.0	12.2
Current aspirin use (%)	43.8	43.6	45.5	47.4	49.9
	47.1	46.7	46.8	46.8	46.7

* For demographic and socioeconomic characteristics, number of women by quintile of neighborhood socioeconomic score.

[†] For behavioral risk factor data, number of women by quintile of neighborhood socioeconomic score.

TABLE 2

Relative risk of colon cancer by quintile of neighborhood socioeconomic score among 111,129 women in the Nurses' Health Study

		No. of cases/ person-years	Age-adjusted RR (95% CI)	Multivariate RR* (95% CI)
Neighborhood-level predictors				
Socioeconomic score	Q1 (lowest SES)	206/300 084	1.00	1.00
	Q2	242/358 014	1.01 (0.83–1.21)	1.02 (0.85–1.24)
	Q3	254/387 792	1.00 (0.83–1.21)	1.02 (0.85–1.23)
	Q4	265/438 539	0.95 (0.79–1.14)	0.97 (0.80–1.17)
	Q5 (highest SES)	256/458 273	0.90 (0.75–1.08)	0.91 (0.74–1.10)
	<i>P for trend</i>		<i>0.34</i>	<i>0.23</i>

* All models are adjusted for neighborhood % Black, immigrant concentration, and residential stability; and individual age, race/ethnicity, educational attainment, husband's educational attainment, family history of colorectal cancer, and history of polyp.

TABLE 3

Relative risk of colon cancer by quintile of neighborhood socioeconomic score, stratified by level of educational attainment*

		No. of cases/ person-years	Age-adjusted RR (95% CI)	Multivariate RR [†] (95% CI)
Less than college education (n = 73,232 women):				
Neighborhood-level predictors				
Socioeconomic score	Q1 (lowest SES)	137/216 976	1.00	1.00
	Q2	170/258 243	1.06 (0.84–1.33)	1.06 (0.85–1.34)
	Q3	181/268 657	1.12 (0.90–1.40)	1.12 (0.89–1.40)
	Q4	173/289 334	1.01 (0.81–1.27)	1.00 (0.80–1.26)
	Q5 (highest SES)	170/268 876	1.09 (0.87–1.37)	1.06 (0.83–1.34)
	<i>P for trend</i>		0.65	0.90
College+ education (n = 24,678 women):				
Neighborhood-level predictors				
Socioeconomic score	Q1 (lowest SES)	35/46 260	1.00	1.00
	Q2	38/63 426	0.77 (0.49–1.23)	0.81 (0.50–1.30)
	Q3	38/79 434	0.63 (0.40–1.00)	0.65 (0.40–1.04)
	Q4	63/106 686	0.79 (0.52–1.20)	0.82 (0.54–1.24)
	Q5 (highest SES)	53/145 318	0.50 (0.33–0.78)	0.52 (0.33–0.80)
	<i>P for trend</i>		0.01	0.01

* Educational attainment based on the 1992 Nurses' Health Study questionnaire.

[†] All models are adjusted for neighborhood % Black, immigrant concentration, and residential stability; and individual age, race/ethnicity, husband's educational attainment, family history of colorectal cancer, and history of polyp. P for interaction for multivariate model = 0.03.

TABLE 4

Relative risk of rectal cancer by quintile of neighborhood socioeconomic score among 111,129 women in the Nurses' Health Study

		No. of cases/ person-years	Age-adjusted RR (95% CI)	Multivariate RR* (95% CI)
Neighborhood-level predictors				
Socioeconomic score	Q1 (lowest SES)	65/300 205	1.00	1.00
	Q2	48/358 177	0.64 (0.44–0.92)	0.62 (0.43–0.91)
	Q3	65/387 932	0.80 (0.57–1.14)	0.79 (0.56–1.12)
	Q4	65/438 723	0.73 (0.52–1.03)	0.71 (0.50–1.01)
	Q5 (highest SES)	62/458 444	0.66 (0.47–0.94)	0.64 (0.44–0.93)
	<i>P for trend</i>		0.08	0.08

* All models are adjusted for neighborhood % Black, immigrant concentration, and residential stability; and individual age, race/ethnicity, educational attainment, husband's educational attainment, family history of colorectal cancer, and history of polyp.