Effects of individual and neighborhood socioeconomic status on outcomes following a colorectal cancer diagnosis

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ABSTRACT

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Evidence indicates inequalities in socioeconomic status (SES), especially those that result in differential access to early detection as well as to high-quality medical and supportive care, as the primary drivers of persistent disparities in outcomes following colorectal cancer (CRC) diagnosis. Yet research is limited on the independent and joint effects of individual SES (iSES) characteristics and neighborhood SES (nSES) on the likelihood of survival and health-related quality of life (HRQoL) following a CRC diagnosis. Further, no prior study of CRC outcomes has attempted to disentangle the effects of area-level SES from the effects of neighborhood contextual factors (e.g., population density, level of high-intensity development).

We used data from 3949 incident CRC cases (51% women) diagnosed between 1997-2018, who lived in the 13-county catchment area of the population-based Western Washington Surveillance, Epidemiology and End Results (SEER) cancer registry, and who participated in the Puget Sound Colorectal Cancer Cohort (PSCCC). We first focused on assessing the independent and joint effects of two self-reported iSES factors (i.e., educational attainment and household income) and census block group-level nSES on all-cause and disease-specific survival following a CRC diagnosis. We performed both overall and gender-specific analyses. In the same study population, we also evaluated nSES effects as well as the effects of two other neighborhood factors, population density and high-intensity development level, when all three factors were included in the same analytic model. Finally, using a subset of this study population – cases diagnosed between 2016-2018 – we investigated the possible

independent and joint effects of three iSES characteristics (i.e., self-reported educational attainment and household income, SEER-reported insurance type) and nSES on overall HRQoL in individuals recently diagnosed with CRC.

After a median 4.0 years of follow-up, 1591 cases died (844 due to CRC). After adjusting for iSES factors and nSES, lower household income was associated with poorer all-cause survival (p-trend: 0.04), especially in women (p-trend: <0.01); lower income effects in women were largest given the context of living in a low nSES neighborhood (HR: 1.61, 95% CI: 1.27-2.04). With respect to CRC-specific survival, lower educational attainment was related to higher mortality in men (p-trend 0.03) and living in a low nSES neighborhood was modestly associated with poorer survival in the overall study population (HR: 1.36, 95% CI: 1.02-1.80).

After additionally adjusting estimates for neighborhood population density and the neighborhood level of high-intensity development, living in a high nSES neighborhood remained marginally related to better CRC-specific survival (p-trend: 0.05). In addition, living in a densely populated neighborhood was associated with lower disease-specific mortality (p-trend: 0.02). When we stratified estimates by iSES factors, living in a high nSES neighborhood was modestly associated with survival only in cases reporting higher amounts of educational attainment; living in an intensely developed neighborhood was related to poorer survival only in cases reporting lower household income.

After adjusting for iSES factors and nSES, reporting a lower household income (p-trend:<0.01) and using Medicaid insurance versus private or other government-based insurance (p-value: <0.01) were each statistically and clinically significantly related to lower overall HRQoL after a CRC diagnosis. Low income effects were largest in the context of low nSES (β: -12.57, 95% CI: -16.90, -8.24), while Medicaid effects were roughly equivalent in high nSES (β: -9.81, 95% CI: -15.38, -4.25) and low nSES neighborhoods (β: -9.79, 95% CI: -15.66, -3.92).

Our findings indicate that the impacts of SES on outcomes following a CRC diagnosis are likely a mixture of iSES and nSES effects, and that there is likely something uniquely harmful about living in a low nSES neighborhood even after adjusting for other neighborhood contexts. Future research should investigate these associations in other study populations and geographic locations and also work to formally identify mediating mechanisms.

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DEDICATION

For my Gpa. Good goin', indeed. xo.

Also, for me. Specifically, for my twenty-year-old self, who decided that being on the receiving end of acts and threats of violence did not impede striving for a higher education; for my twenty-eight-year-old self, who decided to live; and for my thirty-year-old self, who decided that happiness was worth the effort.

PROJECT INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed invasive cancer and the third leading cause of cancer death in the United States (US).[1] Although localized disease has a relatively good prognosis in the general population, only 39% of new diagnoses are caught at this early stage and the overall 5-year relative survival following a CRC diagnosis remains poor (65%).[2,3] In addition, a CRC diagnosis and its treatment are associated with a litany of short-, long-, and late-term physical and psychosocial issues,[3,4] which likely affect the health-related quality of life (HRQoL) of CRC cases[5-9] and may result in substantial economic and psychosocial hardships for cases and their families.[4,9-11]

Critically, the likelihood of mortality and morbidity is not equitable across all new diagnoses, with African-American, American Indian/Alaska Native, and low income CRC cases experiencing greater odds of late-stage diagnosis,[1,11,12] lower HRQoL after diagnosis,[9,13-15] higher rates of disease recurrence,[1,16,17] and higher cancer mortality.[1,3] These disparities in CRC survival and HRQoL following a CRC diagnosis are thought to be largely motivated by individual- and area-level inequalities in socioeconomic status (SES),[1] especially those resulting in differential access to screening or high-quality medical and supportive care.[9-11,18,19]

Characteristics of individual SES (iSES) – such as educational attainment, household income, or other factors that represent an individual's social standing, wealth, and socioeconomic assets – are associated with a discretionary ability to access material (e.g., quality medical and supportive care, healthy foods and other goods) and social (e.g., opportunities for social participation or personal efficacy) resources that are critical to health and wellbeing following a CRC diagnosis. [20-25] Complementary, neighborhood SES (nSES) – a composite concept that includes a neighborhood's educational attainment, wealth, poverty, and employment opportunities – is related to the local availability of these critical material and social resources.[24,26-29] These two levels of SES may plausibly interact,[22,25,30-32] thereby modifying the likelihood of mortality and morbidity after CRC.[1,25] For example, a CRC case with low income living in a high nSES neighborhood may benefit from the greater availability of material and social resources in their area, or they may not be able to afford or access local services and goods due to higher costs in high nSES neighborhoods.[24,25,30] Additionally, apart from their influence on the accessibility or availability of

resources, iSES and nSES may each also affect CRC outcomes via stress response pathways,[23,25,30,33] since individuals reporting low iSES or who live in low nSES neighborhoods are more prone to exhibit dysregulation in stress-related biological processes[34,35] that are associated with cancer progression.[3,10,36]

Lower educational attainment and lower nSES have each previously been associated with greater CRC risk[27,28,37-39] as well as late-stage CRC diagnosis.[18,40-44] The few studies to evaluate the independent effects of area-level SES on CRC survival have also found that living in a socioeconomically deprived neighborhood or region is associated with increased mortality risk.[45-48] Additionally, among recently diagnosed CRC cases and CRC survivors, perceived or actual income limitations at the time of diagnosis have also been related to anxiety, depression, and stress, which all, in turn, affect cancer progression and survival duration[3,9,10,19,49,50] However, to our knowledge, no prior study of CRC outcomes has simultaneously assessed the independent effects of iSES characteristics and nSES in the same analysis. As such, it follows that no previous investigation has evaluated the joint effects of iSES factors and nSES on CRC mortality or wellbeing in CRC cases. Describing the independent and joint relationships of SES factors with CRC outcomes could make a substantive contribution towards a greater understanding of how SES inequalities affect quality of life and risk of death after a CRC diagnosis,[51,52] thereby enhancing the foundation for more effective interventions and policy-based solutions.[51-54]

Using data from a population-based cohort of CRC cases in the Seattle-Puget Sound region, the current project proposes to examine the independent and joint associations of iSES factors and nSES on CRC survival (Chapters 1 and 2) and HRQoL following a CRC diagnosis (Chapter 3). Because cross-level effects of iSES factors and nSES on mortality likely differ by gender, due to socially constructed SES-related gender norms for men and women,[25,28,30] we explored associations of SES with CRC survival both overall and by gender (Chapter 1); since prior evidence also indicates that nSES effects on cancer patient mortality may be due to other neighborhood contextual factors (e.g., the spatial concentration of people or buildings in the neighborhood),[38,55-57] we also simultaneously evaluated the independent effects of nSES, neighborhood population density, and the level of high-intensity (mixed use) development in the neighborhood on CRC survival (Chapter 2).

Chapter 1: Overall and gender-specific impacts of individual and neighborhood socioeconomic status on survival after a colorectal cancer diagnosis

ABSTRACT

Background. Evidence posits inequalities in socioeconomic status (SES) as primary drivers of persistent disparities in colorectal cancer (CRC) survival. Yet research is limited on the independent and joint effects of individual SES (iSES) characteristics and neighborhood SES (nSES) on survival after CRC.

Methods. We included data from 3949 population-based CRC cases (51% women) diagnosed 1997-2018 in the Seattle-Puget Sound region. We focused on the effects of two self-reported iSES factors, educational attainment and household income, and an nSES index constructed from US Census/American Community Survey block group-level data. We evaluated all-cause and CRC-specific survival using stage-stratified extended Cox models with robust standard errors to account for within-neighborhood dependence; we assessed overall and gender-specific effects separately.

Results. Over a median of 4.0 years follow-up, 1591 cases died (844 of CRC). After adjusting for iSES characteristics and nSES, lower income was associated with poorer all-cause survival (p-trend: 0.04), especially among women (p-trend: <0.01). Women with low income/low nSES had on average 1.6 times higher mortality compared to women with high income/high nSES (HR: 1.61, 95% CI: 1.27-2.04). With respect to CRC-specific survival, lower education was related to higher mortality in men (p-trend: 0.03) and low nSES was modestly associated with higher mortality in all cases (HR: 1.36, 95% CI: 1.02-1.80).

Conclusion. Different iSES factors and nSES are uniquely associated with CRC survival, and these relationships vary by gender. The extent to which these effects reflect gender-specific differences in access to care requires further study in other study populations and other geographic locations.

INTRODUCTION

In the United States, colorectal cancer (CRC) is the third most commonly diagnosed invasive cancer and the third leading cause of cancer death in women and men.[1] Although early stage disease has a fairly good prognosis in the general population, the overall 5-year relative survival following a CRC diagnosis remains poor (65%) and sociodemographic disparities in survival persist.[1] While prior evidence suggests that individual- and area-level socioeconomic status (SES) inequalities, specifically those that result in differential access to screening and treatment, are primary drivers of CRC survival disparities,[1,52,58] few prior studies have focused on SES factors as primary predictors of CRC mortality. [27,41,45-47,58-61] Exploring the effects of SES characteristics on CRC survival could facilitate a greater understanding of survival variability, thus improving the foundation for more effective interventions and policy-based solutions.[51,53] Characteristics of individual-level SES (iSES), such as educational attainment or income, may affect a CRC case's likelihood of survival by enabling their access to material (e.g., quality health care) and social (e.g., social participation) resources that shape health care-seeking and lifestyle behaviors.[20-22,25,29,53] Neighborhood SES (nSES) may also affect CRC survival over-and-above the effect of iSES characteristics by influencing physical (e.g., walkability features, environmental stressors) and social (e.g., social cohesion, community efficacy) environmental attributes, which impact area availability of material and social resources.[33,37,51,62-64] Further, these two levels of SES may interact and modify the likelihood of mortality following a CRC diagnosis.[22,25,28,65,66] A CRC case with low income residing in a high nSES neighborhood may benefit from the potentially greater collective availability of cancer care resources and have a lower risk of death than a CRC case with low income living in a low nSES neighborhood.[67,68] Conversely, a CRC case with low income and high nSES may experience a higher risk of death relative to cases with high income and high nSES because they are unable to meet the higher costs of the material and social resources in the area.[21,25,69-71]

Lower educational attainment and lower nSES have each been associated with greater CRC risk[28,37,38] as well as late-stage CRC diagnosis.[18,40,41] The few studies to investigate neighborhood effects on outcomes following a CRC diagnosis have also found that living in a neighborhood with lower nSES is associated with poorer survival.[45-47] Furthermore, in CRC cases and CRC survivors, perceived or actual income limitations at the time of diagnosis have been related to anxiety, depression, and stress, which all, in turn,

can affect cancer progression and survival duration.[3,10,36,49,50] However, to our knowledge, no prior CRC survival investigation has assessed the effects of iSES factors and nSES within the same analysis. The few existing studies exploring an independent association between nSES and CRC survival have all noted their limitation in not including, or being able to account for, any iSES characteristics.[45-47,58] Combining data from a population-based study of CRC cases in the Seattle-Puget Sound region with neighborhood data from the US Census/American Community Survey (ACS), we assessed the independent and joint associations of iSES and nSES with survival following a diagnosis of incident, invasive CRC. While CRC survival rates do not vary substantially by gender,[1] prior research suggests that iSES and nSES effects on health and mortality are highly gender-specific[25,30], likely due to socially constructed SES-related gender norms and roles. [21,25,30,53,72] Because of this evidence, we evaluated associations overall as well as by gender.

METHODS

Study design and population

Our study population included individuals aged 18-74 years who were diagnosed with incident, invasive CRC between 1998-2007 or 2016-2018 and participated in the Puget Sound Colorectal Cancer Cohort (PSCCC), a population-based cohort study of CRC risk and survival. We ascertained all CRC cases via the population-based Surveillance, Epidemiology, and End Results (SEER) cancer registry of the Seattle-Puget Sound region, which covers 13 counties in western Washington state.[73]

A detailed description of the PSCCC, including details of early recruitment phases and protocols for all years of recruitment, has been published elsewhere.[74] Briefly, eligible PSCCC participants included individuals who resided within the SEER catchment area and who, at the time of their diagnosis, were aged 20-74 (1998-2002, 2016-2018) or 18-49 years (2002-2007). The study was also concurrently enriched for postmenopausal women, aged 50-74 years, diagnosed with incident CRC between 1998-2002 and who resided in mostly rural counties within the SEER region (i.e., exclusive of King, Pierce, and Snohomish counties). After making initial contact with potentially eligible CRC cases via phone, mail, and/or email, we only enrolled cases who were able to complete the baseline survey in English and who resided in the catchment area. Over all recruitment phases, we identified a total of 6075 potentially

eligible participants through SEER, of whom 1963 (32%) refused participation, were deceased, or were lost to follow-up prior to the study interview.[74] Response rates were most favorable in earlier recruitment years (e.g., 1998-2002).

Measures

Data sources

According to PSCCC protocol, each participant completed a standardized baseline risk-factor survey at enrollment.[75] During Phase I of recruitment (1998-2002), surveys were administered an average of 8 months (median: 6.9 months) after a CRC diagnosis; in more recent recruitment phases (2016-2018), SEER electronic reporting enhancements shortened this average interval to ~3.5 months. The baseline survey, administered via structured telephone interview, online, or by paper form, collected information on iSES factors (e.g., educational attainment, household income), individual and family cancer history, current comorbidities (e.g., diabetes), physical attributes (i.e., height and weight), and limited lifestyle behaviors (e.g., CRC screening history, physical activity level, smoking status, alcohol consumption) that occurred before diagnosis.

Our other primary data source was the SEER cancer registry of the Seattle-Puget Sound region.[73] The registry requires reporting of an array of CRC case factors measured at or around the time of diagnosis, including demographic characteristics (e.g., gender, race/ethnicity, age, marital status), clinicopathologic features (e.g., stage at diagnosis), factors in the initial course of CRC treatment (e.g., surgery, radiation, chemotherapy), and residential address at diagnosis.

Residential address information from SEER was provided to our study in geocoded form. Geocoding protocol for the SEER registry stipulated that all home addresses were standardized to US postal service format and then geocoded to a latitude/longitude coordinate while employing, in order of priority, rooftop accuracy or street-level accuracy.[73,76] We reviewed addresses missing a SEER geocode and performed a second geocoding attempt using HERE data from 2017 Esri Business Analyst Desktop as the reference dataset (Redlands, CA).

Using the geocoded residential address at diagnosis, we assigned each CRC case a census block group.[77] Census block groups are relatively permanent statistical subdivisions of a county or county equivalent that generally contain between 600 – 3000 residents, with an optimal population of 1,500

individuals, and whose borders are often delineated with input from local residents.[77,78] Block groups are also the smallest geographic area for which most census information is available;[27,79,80] as such, epidemiologists and population health researchers commonly use block groups as proxy units for neighborhood effect studies.[81] Based on the year of their diagnosis, we mapped CRC cases to block group data from the 2000 US Decennial Census (cases diagnosed between 1998-2007) or from ACS 2013-2017 5-year estimates (cases diagnosed between 2016-2018).[63,77,81,82]

Exposure assessment

This study employed two characteristics of iSES (educational attainment and household income before diagnosis) and an index measure of nSES.

We measured iSES factors using responses from the PSCCC baseline survey.[22,65] For educational attainment, participants responded to the question "What is the highest level of education that you (have) completed?" and were provided with eight possible levels, including "Do Not Know/Prefer Not to Answer." These responses were collapsed into four categories: less than high school, high school degree or GED/high school equivalent, some college or a vocational school/technical school degree, and college degree or graduate school.[22,83] For household income before diagnosis, we asked participants "(As of) about two years ago, which of the following best describes your total annual household income (in USD) from all sources before taxes?" and were given seven possible responses, with a lowest category of <$15K/year, an uppermost category of ≥$70K/year, and categories for cases who did not know or declined to report their income. For analyses, we employed a six-category definition of annual household income: less than $15K, $15-29K, $30-44K, $45-69K, more than $70K, and "Missing" (cases who did not know or declined to report income).[9] While we did not report association estimates for this missing income category, we did include it in statistical models since these data may be missing not at random (MNAR) based on unmeasured social norms that may also impact CRC survival.[23,84]

To assess nSES, we used a census block group-level index measure previously detailed by Diez Roux and colleagues.[85] The index uses six aggregate census-based variables identified via factor analysis: median household income, median housing unit value, percentage of households earning income from investments, percentage of persons aged at least 25 years who have completed high school, percentage of persons aged at least 25 years who have completed a college degree, and percentage of persons

aged at least 16 years in a managerial or professional occupation. Income-based variables (i.e., median household income and median housing unit value) were transformed using the natural logarithm.[85] The standardized z-score for each census variable was calculated based on the 3,346 block groups in the 13-county SEER registry catchment area and then each z-score summed to create an index in which higher scores corresponded with lower nSES.[22,27] We assigned each CRC case the nSES index score of their census block group. The median nSES score in our study population (median: 15.97, interquartile range [IQR]: 7.19) was extremely similar to that in the underlying population of incident CRC cases in the Seattle-Puget Sound region (median: 16.44, IQR: 6.92). Despite this similarity, we created nSES quintiles for analytic models based on the distribution of nSES in the underlying case population so as to limit non-differential measurement error.[86]

To assess joint associations of iSES factors and nSES with CRC survival, we created two combination variables: one using binary indicators for education and nSES, and one using binary indicators for income and nSES.[22,25,52] Low education was defined as having a high school degree or less and high education as attending at least some college or having a vocational school/technical school degree. Low income included cases who reported a household income of less than $30K/year, while high income included CRC cases reporting at least $30K/year. Low nSES included quintiles 3-5 and high nSES quintiles 1-2.

Outcome assessment

Vital status, date of death, and cause of death data was available from SEER and its routine linkage to the National Death Index (NDI).[73] The registry performed their latest vital status assessment on 15 August 2019. In this study, we used two survival metrics: all-cause survival and disease-specific (i.e., CRC-specific) survival. We classified deaths with an underlying cause attributed to ICD-10 codes C18-C21 or C26 as CRC-specific deaths.[87,88]

Statistical analysis

To estimate hazard ratios (HR) and 95% confidence intervals (CI) for the independent and joint effects of iSES factors and nSES on CRC survival, we used extended Cox regression models with a time-varying coefficient for nSES[89-91] and robust standard errors to account for within-neighborhood dependence.[92] Based on prior evidence, it is likely that the effect of exposure to nSES will change for CRC cases over follow-up,[90,93] thereby potentially violating the proportional hazards assumption.[89] By allowing the effect of

nSES to vary over time, this assumption is relaxed.[89] Proportional hazards assumptions for educational attainment and household income were supported via testing for a nonzero slope of scale Schoenfeld residuals on ranked failure times. Of the 3346 block groups in the region, 2126 contained at least one participating CRC case and so were included in analyses; of those included, 1055 (50%) contained only a single participating CRC case, making true multilevel modeling infeasible.[81] The time axis was defined as days since diagnosis, with left censoring to account for the time-lag between diagnosis and PSCCC enrollment. We conducted separate analyses for all-cause and disease-specific survival, as well as for assessing overall and gender specific effects. We censored cases alive at the last vital status assessment at that date; in CRC-specific analyses, individuals who died from causes other than CRC were censored at the time of death.

We stratified the baseline hazards for all models by tumor stage at diagnosis.[94,95] Base models (i.e., models without mutual adjustment for iSES and nSES factors) adjusted estimates for age at diagnosis, year of diagnosis, gender, race/ethnicity, and marital status. Subsequent models estimated independent effects while mutually adjusting for educational attainment, household income, and nSES. We adjusted the joint effects of education and nSES for income, and the joint effects of income and nSES for education. Trends for iSES factors and nSES were examined by taking each predictor and performing a Wald test of the coefficient compared with zero; for nSES, we performed a Wald test on the measure's continuous form. We were cautious in our interpretation of linear trends, and, in the absence of main effects, only reported statistically significant p-trends given clear increasing or decreasing effect estimates across SES predictor levels.

To assess their relative impact on association estimates between SES factors and CRC survival, additional sets of prognostic factors that are hypothesized mediators were added sequentially to the model: 1) history of CRC screening; 2) factors in the initial course of CRC treatment (i.e., surgery, radiation, chemotherapy); 3) lifestyle behaviors occurring before diagnosis (i.e., cigarette smoking history, heavy alcohol consumption according to the American Cancer Society (ACS) definition[96], meeting ACS physical activity recommendations[3,96]); and comorbidities (i.e., body mass index [BMI, kg/m^2] two years before diagnosis, self-reported diabetes diagnosis). We created the order of these adjustment sets based on previous evidence for which factors mediate the largest proportion of the relationship between SES

characteristics and CRC survival.[1,11] However, we did not mean to formally investigate mediating mechanisms in this study, but instead to provide an initial description of the overall and gender-specific effects of iSES and nSES on survival following a CRC diagnosis.

All model covariates were defined as shown in Table 1. Two-sided tests were considered statistically significant at the α=0.05 level. We mapped CRC cases to block group-level data using R 3.5.3/3.6.1 (https://www.r-project.org/) and RStudio 1.2.1 (https://rstudio.com); we conducted all statistical analyses in STATA 15 (College Station, TX). This research was approved by the Institutional Review Board at the Fred Hutchinson Cancer Research Center.

RESULTS

Our analyses incorporated data from 3949 CRC cases, including 1937 men and 2012 women (Table 1). After a median of 4.0 years follow-up (IQR: 14.5 years), there were 1591 total deaths, with 844 deaths listing CRC as the underlying cause. The median age at diagnosis was 58 years (IQR: 18 years) and roughly 15% of cases were diagnosed at a distant stage of disease. Twenty-four percent of cases lived in a high nSES neighborhood (quintile 1), and over a third of cases had attended at least some college or reported an annual household income of at least $70K. Compared with men, women were more likely to live in a low nSES neighborhood (quintile 5, 20% versus 14%), have less than a college degree (67% versus 59%), report a household income below $30K/year (25% versus 16%), to be at least 70 years old at diagnosis (19% versus 14%), and to be widowed (10% versus 3%). Women were also more likely than men to report being a never-smoker (51% versus 43%) or a non-drinker (62% versus 41%), to report having met ACS weekly physical activity recommendations (64% versus 58%) in the decade before their CRC diagnosis, and to have a normal BMI (40% versus 22%) in the two years before diagnosis. The distributions of race/ethnicity, tumor stage at diagnosis, history of CRC screening, factors in the initial course of CRC treatment (i.e., surgery, radiation, chemotherapy), and self-reported past diagnosis of diabetes were roughly equal between men and women. The majority of the overall study population was non-Hispanic White (85%), had a history of CRC screening (82%), and had surgery as part of their initial CRC treatment (94%).

In the overall study population, educational attainment and household income were each weakly correlated with nSES as well as with each other (education/nSES: 0.35; income/nSES: 0.37; education/income: 0.39). While correlations between SES factors did not differ by gender, the joint distributions of iSES factors and nSES did vary somewhat between men and women. Men with higher levels of education and higher income were more likely to live in a high nSES neighborhood than women with similarly high iSES (Table 2). More women than men declined to report their level of household income; cases with missing income were more likely to live in high versus low nSES neighborhoods.

All-cause survival

Following adjustment for iSES factors and nSES, we found no evidence in our overall study population for independent associations of educational attainment with all-cause survival after a CRC diagnosis (Table 3). In contrast, lower annual household income was predictive of poorer survival in the overall study population (p-trend: 0.04), with individuals in the lowest income category (<$15K/year) experiencing poorest survival in comparison to those in the highest income category (≥$70K/year) (HR: 1.37, 95% CI:1.09-1.63). Among women, the risk of death also increased with decreasing income levels (p-trend: <0.01), with women in the lowest versus highest income bracket experiencing the highest mortality risk (HR: 1.86, 95% CI:1.47-2.35). In men, cases reporting moderate-high income ($45-69K) experienced poorer survival relative to cases in the highest income group (HR: 1.27, 95% CI: 1.07-1.50). We also observed lower educational attainment to be marginally associated with poorer survival in men (p-trend: 0.05) but low (<high school) versus high (≥college graduate) education marginally related to better survival in women (HR: 0.85, 95% CI: 0.69-1.04). Living in a low (quintile 5) versus high (quintile 1) nSES neighborhood was modestly, but not significantly, related to poorer survival in the overall analyses. Compared to cases with high education (≥some college) and high nSES (quintiles 1 and 2), cases with low education (≤high school degree) who lived in a low nSES neighborhood (quintiles 3-5) had a 1- to 1.2-fold modestly higher risk of all-cause mortality (overall population HR: 1.20 , 95%CI: 1.01-1.44) (Table 3). Relative to cases with high income (≥$30K) and high nSES, cases with low income (<$30K) and low nSES experienced a 1.2- to 1.6-fold increased risk of death (overall population HR: 1.22 , 95%CI: 1.02-1.46 ; women HR: 1.61 , 95%CI: 1.27-2.04). In addition, compared to women reporting high income and living in a high nSES neighborhood, we noted modestly poorer survival in women with high income and

low nSES (HR: 1.24, 95% CI: 0.99-1.57) and significantly poorer survival in women with low income and high nSES (HR: 1.52, 95% CI: 1.18-1.59).

Across overall and gender-specific analyses, we observed independent household income effects attenuating slightly after adjusting for factors in the initial course of CRC treatment (Table 4). While these findings persisted after limiting our analyses to individuals with complete data on all mediating factors (Supplementary Table 1), attenuations in effects were minor.

Disease-specific survival

After adjustment for iSES factors and nSES, we noted evidence in the overall study population of an independent relationship between living in a low versus high nSES neighborhood and poorer CRC-specific survival (HR: 1.36; 95% CI: 1.02-1.80), but no indication of educational attainment or household income effects (Table 5). Akin to gender-specific findings for all-cause survival, lower educational attainment in men was associated with a higher risk of CRC-specific mortality (p-trend: 0.03) and low education in women related to better CRC-specific survival (HR: 0.71, 95% CI: 0.52-0.97).

Relative to high education and high nSES, any other combination of educational attainment and nSES was associated with modestly poorer disease-specific survival in the overall study population (low education/low nSES HR: 1.25, 95% CI: 1.01-1.56) (Table 5). These associations were similar, but not statistically significant, in gender-specific models.

The effects of nSES – independent effects and joint associations with iSES characteristics – in the overall study population strengthened slightly in magnitude following adjustment for initial treatment factors (Table 6). These findings were consistent when we performed complete case analyses (Supplementary Table 2).

DISCUSSION

Within this population-based cohort of incident CRC cases in western Washington state, we found lower household income to be associated with poorer all-cause survival and living in a low nSES neighborhood to be at least marginally related to higher all-cause and disease-specific mortality. However, while the average effects of low nSES did not vary by gender, we observed clear gender differences in income effects, with lower income in women but moderate-high income in men strongly predicting worse survival.

Notably, too, lower income in women was a more significant prognostic factor given the context of living in a low nSES neighborhood. In contrast, we also noted gender-specific educational attainment effects on disease-specific survival that did not significantly differ by nSES; lower education was related to higher mortality in men irrespective of neighborhood socioeconomic context. Because these associations persisted after adjusting for all SES factors of interest, our findings indicate that the impacts of SES on CRC survival are likely a mixture of individual- and place-based effects. These results also highlight the importance of considering iSES effects within the contexts of the neighborhood socioeconomic environment, as well as the need to explore gender-specific associations of SES and CRC survival. Evidence from different populations across the US, as well as in Western Europe, indicate higher educational attainment as a predictor of adherence to preventative CRC screening guidelines[17,43,56,97,98] and subsequently of lower CRC risk.[28,37,99] In contrast, findings from studies of breast and prostate cancer survival show that education effects often completely attenuate after adjusting for other SES characteristics, including nSES.[22,38,65,100] These past findings suggest that while educational attainment might be a meaningful SES intervention target for cancer prevention,[25,43,66] other iSES factors that relate to socioeconomic assets just before diagnosis (e.g., income)[35,84] may have greater impacts on variations in access to resources critical to cancer survival.[23,64,101] Yet after mutual adjustment for iSES characteristics and nSES, we noted lower levels of education to be somewhat related to poorer all-cause survival and modestly related to disease-specific survival, but only in men. Conversely, in women, we consistently found low education to be associated with better survival. The basis for these findings is unclear. Although limited evidence indicates that the relationship between higher educational attainment and cancer care-seeking behaviors do not vary by social gender norms,[1,43] it is possible that our education results for men suggest an underlying unmeasured social mechanism[25,28,30] or an interaction between educational attainment and income (or wealth) that differentially enables men and women to access CRC medical and supportive care.[30,64,102,103] Observed education effects may also be due to differences between participating CRC cases in our study population and the underlying source population of CRC cases; in particular, this scenario seems a likely explanation for the noted relationship between low education and better survival in women. We find it likely that inadequate sample size and

statistical power are the likely explanations underlying our modest, but not significant, findings for gender-specific joint effects of education and nSES.

Previous studies of outcomes following a CRC diagnosis indicate that a large number of CRC cases experience some form of economic hardship, which often increases during the primary treatment period [49,104,105] and can lead to long-term financial instability.[35,84,106,107] Economic hardship, defined by low household income or unexpected income instability around the time of diagnosis, has also been observed as a predictor of both physical strain and psychosocial stress that, in turn, impact CRC prognosis.[10,34,36,104,105] In our study, lower annual household income was a strong predictor of poorer all-cause survival, especially in women. Our measure of household income pertained to a time period two years prior to CRC diagnosis, likely before the onset of cancer care-related costs.[35] As such, income effects in the overall study population effects may indicate how higher income levels can be leveraged to afford quality material and social resources – before and after diagnosis.[23,25,108] Additionally, the results for the independent effects of income suggest that, regardless of educational attainment and nSES, CRC cases with lower income at diagnosis may be susceptible to the short- and late-term effects of economic hardship,[9,84,105] which could affect the amount and quality of care received as well as levels of physical strain and psychosocial stress.[3,10,21,23,105]

Our findings for income also reflect how combined household earnings may be differently enabling for men and women depending on age.[66,83,109] A household income, due to marriage or cohabitation, is likely larger and more pertinent to treatment costs compared to individual earnings.[3,57] When CRC is diagnosed at an earlier age, the disease itself may be more severe and both individual and household earnings might be insufficient to cover the costs associated with intensive CRC care[35,41,61,84,107]; in our study, we found that men with moderate-high versus high income experienced poorer survival, and we also observed that of the CRC cases reporting higher household income, men were more likely than women to be younger at the time of CRC diagnosis. Conversely, when CRC is diagnosed at a later age, the accumulation of combined income has potentially already slowed or ceased, and economic hardship stemming from a CRC diagnosis and its treatment may significantly and permanently deplete existing savings.[35,84,106,107] This financial toxicity may be greatest for CRC cases living in low nSES neighborhoods, which may have a lower local availability of material and social resources that pushes

CRC cases to spend additional income to travel and purchase critical resources in other areas;[26,34,64,110-112] in contrast, toxicity may also be great for cases living in high nSES neighborhoods, since a case's income may not cover the costs of local resources.[33,52,84] This scenario could explain why we observed lower income levels to be strongly associated with poorer all-cause survival in women, and especially in women living in low nSES neighborhoods. These findings could also be partly due to the gender-specific joint distributions of income and nSES in our study, since women reporting an income of less than $30/year appeared more likely to live in higher nSES neighborhoods compared with men of the same income level. Sample size and statistical power are likely explanations for income effects observed for all-cause, but not CRC-specific, survival; we had adequate power to detect associations between household income and all-cause mortality because of the larger number of events, in overall and gender-specific models.

Although investigations to date are limited in number, population-based evidence suggests that the neighborhood socioeconomic environment is independently related to CRC stage at diagnosis and poorer CRC survival.[45-47,58] In the Seattle-Puget Sound region, recent evidence suggests that CRC mortality varies by census tract location and deprivation.[113] However, no prior CRC survival study had evaluated nSES effects while accounting for iSES characteristics. When we adjusted for iSES characteristics and nSES, the majority of nSES affects attenuated. Yet after mutual adjustment for all SES factors of interest, we found that living in a neighborhood with the lowest level of nSES was still independently associated with poorer survival in the overall study population. This finding may indicate that we lacked the necessary sample size and statistical power to explore gender-specific nSES effects. Alternatively, this result may suggest that, regardless of gender, CRC cases living in low nSES neighborhoods are less likely to have local access to quality medical care [18,22,47,64,114] , public places or venues to cultivate healthy lifestyle behaviors after diagnosis (e.g., physical activity after diagnosis),[33,38,52] and opportunities for social support and coping.[24,54,115,116] It is also possible that low nSES effects are entangled with the effects of densely populated, urban neighborhoods, where environmental hazards (e.g., air pollution, traffic congestion) can affect health care-seeking behaviors[33,116-118] and also provoke stress responses[34] that further cancer progression.[36] Finally, it may be that we found an effect for the lowest nSES category, versus a dose-reponse relationship between lower nSES levels and poorer CRC-specific survival, due to

the wealthier socioeconomic environment in the Seattle-Puget Sound region relative to other metropolitan areas.[119,120] Our findings may have been different given a region with greater variation in nSES. Although we noted minor attenuations in income effects and nSES effects after adjusting for factors in the initial course of CRC treatment (i.e., surgery, chemotherapy, radiation) as potential mediating factors, all effect estimate changes were within the range of variability. Thus, while these minor effect attenuations may add evidence that SES effects on CRC survival are mediated primarily by differences in treatment[11,18,61,121], these findings may also be due to chance or to the roughly equal distribution of treatment factors in this study population. Future research should explore whether the overall and gender-specific associations between SES factors and CRC survival are explained by more fine-grained aspects of CRC treatment (e.g., types of chemotherapy, distance or physical barriers to treatment, perceptions of physician engagement with initial treatment).[18,122]

There are several important limitations to the current study. First, participating CRC cases may be systematically different from the underlying CRC case population of the region with respect to the distributions of educational attainment, household income, and nSES. With nSES, we tried to limit the amount of bias in effect estimates by basing study quintile cutpoints on the quintile distribution of nSES in the underlying case population.[86] Similarly, for iSES factors, we used category definitions that appeared standard in recent literature; [22,83] however, even with these standard categorizations, we still had a large number of cases declining to report their household income, and there is likely some MNAR present in this variable.[23,30,84] A second drawback to this work is our use of administrative census block group boundaries to define neighborhoods; the boundaries of these administrative units may not align with a CRC case's perception of their neighborhood as a community nor with their perception of "local" material and social resources.[118,123,124] Because we were limited to using the residential address at diagnosis to link to neighborhood data, we also lacked information on each case's length of residency in their neighborhood. Moreover, we lacked the data to assess the effects of fine-grained iSES factors on CRC survival, including month to month financial precarity (e.g., living "paycheck to paycheck"[23]) at the time of diagnosis.[61] Finally, due to sample size limitations, we were limited in evaluating all effects in both overall and gender-specific analyses and we were unable to explore further demographic intersectionality (e.g., gender and race).

Despite these limitations, our findings make a substantive contribution to understanding the effects of iSES and nSES inequalities on survival following a CRC diagnosis, including how these relationships vary between men and women. While we had a large population-based sample of CRC cases,[52] our findings are relative to our region of study, and future research should be performed in other populations and other geographic locations, including areas with higher levels of rurality (Supplementary Tables 3 and 4). In addition, future studies will need to explore the gender-specific effects of fine-grained educational attainment measures and fine-grained income measures (e.g., financial precarity[23,53]) in the context of nSES, interactions between educational attainment and income,[30] and the difference in effects given a wider intersectional lens.[30,47] Crucially, future investigations should also work to formally identify the mediation mechanisms underlying associations of iSES factors and nSES with CRC mortality. Increasing this understanding will help to better inform interventions aimed at reducing long-standing disparities in CRC survival.[1,51,61,121]

Table 1. Characteristics of PSCCC CRC cases (N=3949), overall and by gender, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)			
		Gender	
	Overall	Male	Female
	N (%)	N (%)	N(%)
Total participants	3949 (-)	1937 (-)	2012 (-)
No. of deaths			
All-cause	1591 (-)	757 (-)	834 (-)
CRC-specific	*844 (53)*	*402 (53)*	*442 (53)*
Age at diagnosis, in years			
<40	284 (7)	577 (8)	607 (7)
40-49	816 (21)	146 (21)	138 (20)
50-59	1010 (25)	416 (27)	400 (24)
60-69	1184 (30)	526 (30)	484 (30)
≥70	655 (17)	272 (14)	383 (19)
Race/ethnicity			
Non-Hispanic white	3350 (85)	1607 (83)	1743 (87)
Other	599 (15)	330 (17)	269 (13)
Marital status at diagnosis			
Single, never married, or living unmarried	481 (12)	258 (13)	223 (11)
Married	2431 (62)	1277 (66)	1154 (58)
Separated or divorced	429 (11)	164 (9)	265 (13)
Widowed	264 (7)	57 (3)	207 (10)
Unknown	344 (8)	181 (9)	163 (8)
Tumor stage at diagnosis[a]			
Local	1491 (38)	722 (37)	769 (38)
Regional	1789 (45)	876 (45)	913 (45)
Distant	585 (15)	285 (15)	300 (15)
Unstaged/unknown	84 (2)	54 (3)	30 (1.5)
Educational attainment			
College graduate/graduate school	1436 (36)	783 (41)	653 (33)
Some college/vocational school	1370 (35)	644 (33)	726 (36)
High school completion or GED	886 (22)	396 (20)	490 (24)
<High school	257 (7)	114 (6)	143 (7)
Annual household income before diagnosis, in USD ($)[b]			
≥70K	1356 (34)	790 (41)	566 (28)
45-69K	818 (21)	438 (22)	380 (19)
30-44K	688 (17)	291 (15)	397 (20)
15-29K	505 (13)	190 (10)	315 (15)
<15K	319 (8)	120 (6)	199 (10)
Missing	263 (7)	108 (6)	155 (8)

Neighborhood socioeconomic status (nSES)[c]			
Quintile 1 (high nSES)	961 (24)	507 (26)	454 (23)
Quintile 2	789 (20)	403 (21)	386 (19)
Quintile 3	750 (19)	381 (20)	369 (18)
Quintile 4	772 (20)	364 (19)	408 (20)
Quintile 5 (low nSES)	677 (17)	282 (14)	395 (20)
Educational attainment and nSES[d]			
≥Some college & high nSES	*1429 (36)*	*758 (39)*	*671 (33)*
≥Some college & low nSES	*1377 (35)*	*669 (35)*	*708 (35)*
≤ High school & high nSES	*321 (8)*	*152 (8)*	*169 (9)*
≤ High school & low nSES	*822 (21)*	*358 (18)*	*464 (23)*
Household income and nSES[e]			
≥$30K & high nSES	*1430 (36)*	*779 (40)*	*651 (32)*
≥$30K & low nSES	*1432 (36)*	*740 (38)*	*692 (34)*
< $30K & high nSES	*197 (5)*	*78 (4)*	*119 (6)*
< $30K & low nSES	*627 (17)*	*232 (12)*	*395 (8)*
History of preventative CRC screening			
Never screened	722 (18)	352 (18)	370 (18)
First screening ≤2 years before diagnosis	1491 (38)	768 (40)	723 (36)
First screened >2 years before diagnosis	1732 (44)	816 (42)	916 (46)
Missing	4 (<1)	1 (<1)	3 (<1)
Surgery in initial course of CRC treatment			
No	233 (6)	142 (7)	91 (5)
Yes	3707 (94)	1792 (93)	1915 (95)
Unknown	9 (<1)	3 (<1)	6 (<1)
Radiation in initial course of CRC treatment			
No	3181 (81)	1525 (79)	1656 (82)
Yes	756 (19)	403 (21)	353 (18)
Unknown	12 (<1)	9 (<1)	3 (<1)
Chemotherapy in initial course of CRC treatment			
No	1682 (43)	836 (43)	846 (42)
Yes	2186 (55)	1061 (55)	1127 (56)
Unknown	81 (2)	40 (2)	41 (2)
Cigarette smoking history			
Never	1835 (46)	822 (43)	1013 (51)
Former	1681 (43)	895 (46)	786 (39)
Current	427 (11)	218 (11)	209 (10)
Missing	6 (<1)	2 (<1)	4 (<1)
Heavy alcohol consumption before diagnosis[f,g]			
Nondrinker	2032 (51)	791 (41)	1241 (62)
No	1161 (29)	712 (37)	449 (22)

Yes	531 (14)	311 (16)	220 (11)
Missing	225 (6)	123 (6)	102 (5)
Met physical activity recommendation before diagnosis[f,h]			
No	1028 (26)	485 (25)	543 (27)
Yes	1459 (37)	766 (40)	693 (34)
Missing	1462 (37)	686 (35)	776 (39)
Body mass index (kg/m^2) before diagnosis[b]			
<25.0	1214 (31)	421 (72)	793 (40)
25.0-29.9	1412 (36)	860 (44)	552 (27)
≥30.0	1285 (32)	642 (33)	643 (32)
Missing	38 (1)	14 (1)	24(1)
Diabetes[j]			
No	3405 (87)	1640 (85)	1765 (88)
Yes	537 (13)	291 (15)	246 (12)
Missing	7 (<1)	6 (<1)	1 (<1)

[a] Based on the 2000 (cases diagnosed between 1998-2007, 2016) and 2018 (cases diagnosed in 2018) versions of the SEER Summary Staging Manual
[b] Measured with respect to two years prior to CRC diagnosis
[c] Quintile cutpoints based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region
[d] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)
[e] Income collapsed as low (<$30K/year) and high ($≥30K/year); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Percentages will not add to 100% due to variable excluding cases missing income (N=263 [7%])
[f] Measured with respect to the decade prior to CRC diagnosis
[g] ACS heavy drinking definition: for women, ≥8 drinks per week; for men, ≥15 drinks per week
[h] ACS physical activity recommendation: ≥150 minutes of moderate intensity per week, 75 minutes of strenuous intensity per week, or an equivalent combination of moderate/strenuous activity per week
[j] Based on self-report of diabetes diagnosis

Table 2. Distributions of educational attainment, household income, and neighborhood SES for PSCCC CRC cases (N=3949), overall and by gender, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Neighborhood SES (nSES)[a]				
	Q1 (high nSES)	Q2	Q3	Q4	Q5 (low nSES)
	N (%)	N (%)	N (%)	N (%)	N (%)
			Overall		
Educational attainment					
College graduate/graduate school	577 (60)	330 (42)	249 (33)	184 (24)	96 (14)
Some college/vocational school	262 (27)	260 (33)	281 (38)	297 (38)	270 (40)
High school completion or GED	106 (11)	170 (21)	176 (23)	217 (28)	217 (32)
<High school	16 (2)	29 (4)	44 (6)	74 (10)	94 (14)
Household income[b]					
≥70K	538 (56)	324 (41)	240 (32)	164 (21)	90 (13)
45-69K	165 (17)	175 (22)	169 (21)	180 (23)	129 (19)
30-44K	95 (10)	133 (17)	141 (19)	179 (23)	140 (21)
15-29K	57 (6)	70 (9)	88 (12)	122 (16)	168 (25)
<15K	35 (4)	35 (4)	59 (8)	74 (10)	116 (17)
Missing	71 (7)	52 (7)	53 (7)	53 (7)	34 (5)
			Male		
Educational attainment					
College graduate/graduate school	319 (63)	191 (47)	125 (33)	100 (27)	48 (17)
Some college/vocational school	132 (26)	116 (29)	141 (37)	140 (38)	115 (41)
High school completion or GED	48 (9)	82 (20)	91 (24)	89 (25)	86 (30)
<High school	8 (2)	14 (3)	24 (6)	35 (10)	33 (12)
Household income[b]					
≥70K	308 (61)	197 (49)	140 (37)	93 (25)	52 (18)
45-69K	81 (16)	95 (24)	97 (25)	96 (26)	69 (25)
30-44K	40 (8)	58 (14)	56 (15)	82 (23)	55 (20)
15-29K	27 (5)	26 (6)	33 (9)	45 (12)	59 (21)
<15K	14 (3)	11 (3)	25 (6)	35 (10)	35 (12)
Missing	37 (7)	16 (4)	30 (8)	13 (4)	12 (4)
			Female		
Educational attainment					
College graduate/graduate school	258 (57)	139 (36)	124 (34)	84 (21)	48 (12)
Some college/vocational school	130 (28)	144 (37)	140 (38)	157 (38)	155 (39)
High school completion or GED	58 (13)	88 (23)	85 (23)	128 (31)	131 (33)
<High school	8 (2)	15 (4)	20 (5)	39 (10)	61 (16)
Household income[b]					
≥70K	230 (51)	127 (33)	100 (27)	71 (17)	38 (10)
45-69K	84 (18)	80 (21)	72 (20)	84 (20)	60 (15)
30-44K	55 (12)	75 (20)	85 (23)	97 (24)	85 (21)
15-29K	30 (7)	44 (11)	55 (15)	77 (19)	109 (28)
<15K	21 (5)	24 (6)	34 (9)	39 (10)	81 (20)

Missing	34 (7)	36 (9)	23 (6)	40 (10)	22 (6)

[a] Quintile cutpoints based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region
[b] Measured with respect to two years prior to CRC diagnosis

Table 3. Associations of educational attainment, household income, and neighborhood SES with all-cause survival, overall and by gender, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Overall			Male			Female		
	N=3949			N=1937			N=2012		
		Base model[a]	Base + all SES factors[b]		Base model[a]	Base + all SES factors[b]		Base model[a]	Base + all SES factors[b]
	N (deaths)	HR (95% CI)	HR (95% CI)	N (deaths)	HR (95% CI)	HR (95% CI)	N (deaths)	HR (95% CI)	HR (95% CI)
Educational attainment									
College graduate/graduate school	1436 (447)	1.00 (-)	1.00 (-)	783 (250)	1.00 (-)	1.00 (-)	653 (197)	1.00 (-)	1.00 (-)
Some college/vocational school	1370 (554)	1.13 (0.99-1.28)	1.05 (0.93-1.19)	644 (262)	**1.27 (1.07-1.51)**	**1.19 (1.01-1.40)**	726 (292)	0.97 (0.84-1.13)	0.89 (0.76-1.04)
High school completion	886 (424)	**1.20 (1.06-1.36)**	1.10 (0.97-1.25)	396 (173)	1.19 (0.99-1.44)	1.10 (0.91-1.34)	490 (251)	1.16 (0.99-1.35)	1.01 (0.86-1.19)
<High school	257 (166)	**1.18 (1.01-1.37)**	1.04 (0.89-1.23)	114 (72)	**1.32 (1.05-1.66)**	1.25 (0.99-1.59)	143 (94)	1.04 (0.86-1.26)	0.85 (0.69-1.04)
p-trend		***0.01***	*0.14*		***0.02***	*0.05*		*0.14*	*0.62*
Household income[c]									
≥70K	1356 (318)	1.00 (-)	1.00 (-)	790 (202)	1.00 (-)	1.00 (-)	566 (116)	1.00 (-)	1.00 (-)
45-69K	818 (344)	**1.20 (1.03-1.39)**	1.16 (0.99-1.34)	438 (196)	**1.36 (1.16-1.60)**	**1.27 (1.07-1.50)**	380 (148)	1.06 (0.84-1.34)	1.10 (0.88-1.38)
30-44K	688 (347)	**1.24 (1.09-1.42)**	**1.18 (1.03-1.36)**	291 (156)	**1.23 (1.03-1.47)**	1.13 (0.93-1.37)	397 (191)	**1.30 (1.09-1.56)**	**1.36 (1.12-1.65)**
15-29K	505 (290)	**1.27 (1.05-1.52)**	1.20 (0.98-1.46)	190 (110)	1.07 (0.80-1.45)	0.99 (0.73-1.36)	315 (180)	**1.51 (1.24-1.83)**	**1.54 (1.25-1.91)**
<15K	319 (180)	**1.46 (1.18-1.80)**	**1.37 (1.09-1.63)**	120 (56)	1.21 (0.84-1.72)	1.10 (0.76-1.58)	199 (124)	**1.78 (1.44-2.20)**	**1.86 (1.47-2.35)**
p-trend		***<0.01***	***0.04***		*0.51*	*0.85*		***<0.01***	***<0.01***
Neighborhood socioeconomic status (nSES)[d]									
Q1 (high nSES)	961 (278)	1.00 (-)	1.00 (-)	507 (150)	1.00 (-)	1.00 (-)	454 (128)	1.00 (-)	1.00 (-)
Q2	789 (266)	1.06 (0.86-1.30)	1.02 (0.83-1.26)	403 (131)	1.31 (0.99-1.73)	1.25 (0.95-1.63)	386 (135)	0.79 (0.59-1.05)	0.75 (0.56-1.00)
Q3	750 (307)	1.23 (0.99-1.52)	1.17 (0.94-1.46)	381 (152)	1.29 (0.95-1.76)	1.18 (0.87-1.60)	369 (155)	1.06 (0.78-1.43)	0.99 (0.74-1.35)
Q4	772 (358)	1.10 (0.89-1.37)	1.04 (0.83-1.29)	364 (169)	0.95 (0.70-1.29)	0.88 (0.66-1.18)	408 (189)	1.19 (0.90-1.58)	1.08 (0.81-1.44)
Q5 (low nSES)	677 (382)	**1.30 (1.04-1.61)**	1.21 (0.96-1.51)	282 (155)	1.25 (0.90-1.72)	1.16 (0.85-1.59)	395 (227)	1.21 (0.90-1.61)	1.06 (0.78-1.42)
p-trend		***0.02***	*0.20*		*0.02*	*0.16*		***0.10***	*0.84*
Education and nSES[e]									
≥Some college, High nSES	1429 (405)		1.00 (-)	758 (221)		1.00 (-)	671 (184)		1.00 (-)
≥Some college, Low nSES	1377 (596)		**1.20 (1.02-1.42)**	669 (291)		1.04 (0.82-1.30)	708 (305)		**1.30 (1.05-1.58)**
≤High school, High nSES	321 (139)		**1.24 (1.04 -1.46)**	152 (60)		1.15 (0.90-1.47)	169 (79)		1.24 (1.00-1.55)
≤High school , Low nSES	822 (451)		**1.20 (1.01-1.44)**	358 (185)		1.06 (0.82-1.38)	464 (266)		**1.27 (1.01-1.59)**
Household income and nSES[f]									
≥$30K, High nSES	1430 (411)		1.00 (-)	779 (235)		1.00 (-)	651 (176)		1.00 (-)

≥$30K, Low nSES	1432 (598)		1.08 (0.93-1.25)	740 (319)		0.89 (0.73-1.09)	692 (279)		1.24 (0.99-1.57)
<$30K, High nSES	197 (87)		0.96 (0.67-1.37)	78 (30)		0.58 (0.31-1.08)	119 (57)		**1.52 (1.18-1.95)**
<$30K, Low nSES	627 (383)		**1.22 (1.02-1.46)**	232 (136)		0.91 (0.71-1.17)	395 (247)		**1.61 (1.27-2.04)**

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), and gender (**male**, female). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends for SES factors come from a Wald test of continuous variables comparing the coefficient with zero; p-trends for income do not include cases missing income (N=263)

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends for SES factors come from a Wald test of continuous variables comparing the coefficient with zero, and do not include cases missing income (N=263)

[c] Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown

[d] Quintile cutpoints based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[e] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)

[f] Income collapsed as low (<$30K/year) and high ($≥30K/year); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263), so N=3686 for overall sample, N=1829 for males, and N=1857 for females

Table 4. Associations of educational attainment, household income, and neighborhood SES with all-cause survival, overall and by gender, adjusted for additional case characteristics, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Overall				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=3949	**N=3945**	**N=3924**	**N=2322**	**N=2297**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	1.05 (0.93-1.19)	1.05 (0.93-1.19)	1.06 (0.93-1.20)	1.04 (0.90-1.21)	1.01 (0.87-1.17)
High school completion	1.10 (0.97-1.25)	1.11 (0.97-1.26)	1.11 (0.98-1.26)	0.93 (0.78-1.11)	0.91 (0.76-1.09)
<High school	1.04 (0.89-1.23)	1.05 (0.89-1.23)	1.09 (0.93-1.27)	0.93 (0.73-1.18)	0.92 (0.73-1.16)
p-trend	*0.14*	*0.12*	*0.06*	*0.76*	*0.64*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	1.16 (0.99-1.34)	1.16 (1.00-1.34)	1.16 (1.00-1.35)	**1.25 (1.04-1.51)**	**1.25 (1.04-1.52)**
30-44K	**1.18 (1.03-1.36)**	**1.18 (1.02-1.36)**	1.15 (0.99-1.33)	1.09 (0.89-1.32)	1.09 (0.90-1.33)
15-29K	1.20 (0.98-1.46)	1.19 (0.97-1.46)	1.15 (0.93-1.42)	1.15 (0.87-1.51)	1.15 (0.87-1.51)
<15K	**1.37 (1.09-1.63)**	**1.37 (1.10-1.71)**	**1.30 (1.05-1.61)**	1.30 (0.99-1.71)	1.29 (0.98-1.69)
p-trend	***0.04***	***0.04***	*0.12*	*0.30*	*0.32*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	1.02 (0.83-1.26)	1.02 (0.82-1.26)	1.06 (0.86-1.32)	0.99 (0.73-1.33)	0.95 (0.71-1.28)
Q3	1.17 (0.94-1.46)	1.17 (0.94-1.46)	1.23 (0.98-1.55)	1.12 (0.80-1.58)	1.08 (0.76-1.52)
Q4	1.04 (0.83-1.29)	1.04 (0.84-1.30)	1.09 (0.88-1.36)	1.06 (0.78-1.45)	1.04 (0.76-1.41)
Q5 (low nSES)	1.21 (0.96-1.51)	1.21 (0.97-1.51)	**1.28 (1.02-1.61)**	1.32 (0.94-1.84)	1.27 (0.91-1.78)
p-trend	*0.20*	*0.17*	*0.08*	*0.06*	*0.10*
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	**1.20 (1.02-1.42)**	**1.21 (1.03-1.43)**	**1.25 (1.06-1.48)**	1.25 (1.00-1.56)	1.23 (0.99-1.54)
≤High school, High nSES	**1.24 (1.04 -1.46)**	**1.25 (1.05-1.47)**	**1.25 (1.06-1.47)**	1.09 (0.87-1.36)	1.09 (0.87-1.37)
≤High school , Low nSES	**1.20 (1.01-1.44)**	**1.22 (1.01-1.46)**	**1.27 (1.06-1.53)**	1.05 (0.81-1.35)	1.03 (0.80-1.33)

Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	1.08 (0.93-1.25)	1.08 (0.94-1.25)	1.11 (0.96-1.28)	1.12 (0.91-1.37)	1.11 (0.91-1.36)
<$30K, High nSES	0.96 (0.67-1.37)	0.96 (0.68-1.36)	0.90 (0.62-1.31)	0.91 (0.56-1.43)	0.92 (0.58-1.45)
<$30K, Low nSES	**1.22 (1.02-1.46)**	**1.23 (1.03-1.46)**	**1.23 (1.04-1.46)**	1.26 (1.00-1.58)	1.24 (0.98-1.55)
	Male				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=1937	**N=1936**	**N=1924**	**N=1152**	**N=1143**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	**1.19 (1.01-1.40)**	**1.20 (1.02-1.42)**	**1.19 (1.01-1.41)**	1.19 (0.95-1.48)	1.17 (0.94-1.45)
High school completion	1.10 (0.91-1.34)	1.12 (0.93-1.36)	1.11 (0.92-1.35)	0.87 (0.66-1.14)	0.88 (0.66-1.17)
<High school	1.25 (0.99-1.59)	**1.29 (1.02-1.64)**	**1.31 (1.03-1.67)**	1.08 (0.72-1.63)	1.03 (0.68-1.55)
p-trend	*0.05*	***0.03***	***0.02***	*0.73*	*0.82*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	**1.27 (1.07-1.50)**	**1.28 (1.08-1.52)**	**1.26 (1.06-1.50)**	**1.37 (1.08-1.74)**	**1.36 (1.07-1.73)**
30-44K	1.13 (0.93-1.37)	1.12 (0.93-1.36)	1.11 (0.91-1.34)	1.09 (0.85-1.41)	1.07 (0.83-1.38)
15-29K	0.99 (0.73-1.36)	1.00 (0.74-1.36)	0.96 (0.70-1.31)	1.03 (0.71-1.51)	1.07 (0.73-1.55)
<15K	1.10 (0.76-1.58)	1.11 (0.78-1.57)	1.07 (0.77-1.50)	**1.60 (1.04-2.45)**	**1.56 (1.01-2.40)**
p-trend	*0.85*	*0.88*	*0.66*	*0.44*	*0.39*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	1.25 (0.95-1.63)	1.21 (0.93-1.58)	1.28 (0.98-1.68)	1.11 (0.75-1.66)	1.03 (0.69-1.55)
Q3	1.18 (0.87-1.60)	1.16 (0.86-1.56)	1.22 (0.90-1.65)	0.99 (0.63-1.58)	0.95 (0.60-1.52)
Q4	0.88 (0.66-1.18)	0.88 (0.66-1.18)	0.92 (0.69-1.23)	0.77 (0.51-1.16)	0.76 (0.51-1.13)
Q5 (low nSES)	1.16 (0.85-1.59)	1.15 (0.84-1.57)	1.23 (0.90-1.67)	0.85 (0.55-1.31)	0.82 (0.53-1.28)
p-trend	*0.16*	*0.14*	*0.11*	*0.41*	*0.49*
Education and nSES[h]					

≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	1.04 (0.82-1.30)	1.03 (0.82-1.30)	1.06 (0.85-1.33)	0.88 (0.65-1.19)	0.88 (0.65-1.20)
≤High school, High nSES	1.15 (0.90-1.47)	1.16 (0.90-1.48)	1.14 (0.89-1.46)	0.94 (0.66-1.34)	0.95 (0.67-1.36)
≤High school , Low nSES	1.06 (0.82-1.38)	1.08 (0.83-1.40)	1.11 (0.85-1.43)	0.70 (0.49-1.02)	0.71 (0.49-1.03)
Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	0.89 (0.73-1.09)	0.90 (0.74-1.09)	0.92 (0.76-1.12)	0.84 (0.62-1.11)	0.83 (0.63-1.11)
<$30K, High nSES	0.58 (0.31-1.08)	0.59 (0.32-1.07)	0.53 (0.28-1.01)	0.72 (0.34-1.52)	0.79 (0.38-1.68)
<$30K, Low nSES	0.91 (0.71-1.17)	0.92 (0.71-1.18)	0.93 (0.72-1.19)	0.93 (0.67-1.29)	0.93 (0.67-1.29)
			Female		
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=2012	**N=2009**	**N=2000**	**N=1170**	**N=1154**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	0.89 (0.76-1.04)	0.88 (0.76-1.03)	0.90 (0.77-1.06)	0.95 (0.77-1.17)	0.91 (0.74-1.12)
High school completion	1.01 (0.86-1.19)	1.01 (0.85-1.18)	1.01 (0.86-1.19)	0.91 (0.70-1.17)	0.87 (0.67-1.12)
<High school	0.85 (0.69-1.04)	0.83 (0.68-1.02)	0.86 (0.70-1.05)	0.73 (0.54-1.00)	**0.72 (0.54-0.98)**
p-trend	*0.62*	*0.53*	*0.67*	*0.36*	*0.27*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	1.10 (0.88-1.38)	1.10 (0.88-1.38)	1.12 (0.89-1.41)	1.31 (0.98-1.75)	1.34 (1.00-1.78)
30-44K	**1.36 (1.12-1.65)**	**1.36 (1.12-1.65)**	**1.35 (1.11-1.64)**	1.27 (0.95-1.70)	1.28 (0.95-1.72)
15-29K	**1.54 (1.25-1.91)**	**1.54 (1.25-1.90)**	**1.53 (1.24-1.89)**	**1.43 (1.05-1.94)**	**1.43 (1.05-1.94)**
<15K	**1.86 (1.47-2.35)**	**1.86 (1.47-2.34)**	**1.77 (1.40-2.24)**	**1.60 (1.11-2.30)**	**1.59 (1.11-2.29)**
p-trend	***<0.01***	***<0.01***	***<0.01***	***0.03***	***0.03***
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	0.75 (0.56-1.00)	0.74 (0.56-1.00)	0.77 (0.57-1.04)	0.74 (0.49-1.12)	0.70 (0.47-1.06)
Q3	0.99 (0.74-1.35)	0.99 (0.73-1.34)	1.05 (0.76-1.43)	0.96 (0.60-1.53)	0.92 (0.58-1.46)

Q4	1.08 (0.81-1.44)	1.07 (0.81-1.43)	1.11 (0.83-1.48)	1.18 (0.77-1.80)	1.13 (0.74-1.72)
Q5 (low nSES)	1.06 (0.78-1.42)	1.05 (0.78-1.41)	1.11 (0.82-1.49)	1.38 (0.87-2.20)	1.33 (0.84-2.10)
p-trend	*0.84*	*0.88*	*0.72*	*0.25*	*0.35*
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	**1.30 (1.05-1.58)**	**1.30 (1.05-1.59)**	**1.33 (1.07-1.65)**	**1.46 (1.08-1.96)**	**1.43 (1.07-1.93)**
≤High school, High nSES	1.24 (1.00-1.55)	1.23 (0.99-1.53)	1.23 (1.00-1.52)	1.14 (0.85-1.53)	1.11 (0.82-1.51)
≤High school , Low nSES	**1.27 (1.01-1.59)**	1.26 (1.00-1.57)	**1.29 (1.02-1.62)**	1.19 (0.86-1.64)	1.16 (0.85-1.60)
Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	1.24 (0.99-1.57)	1.24 (0.99-1.55)	1.26 (1.00-1.59)	1.29 (0.95-1.75)	1.27 (0.94-1.72)
<$30K, High nSES	**1.52 (1.18-1.95)**	**1.52 (1.19-1.95)**	**1.47 (1.14-1.89)**	1.33 (0.94-1.88)	1.31 (0.93-1.85)
<$30K, Low nSES	**1.61 (1.27-2.04)**	**1.59 (1.26-2.02)**	**1.60 (1.26-2.03)**	**1.50 (1.08-2.07)**	**1.46 (1.05-2.02)**

[a]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[b]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[c]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[d]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[e]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes)**.** Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[f]Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown

[g]Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2018) in the region

[h]Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)

[i]Income collapsed as low (<$30K) and high ($≥30K); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263) and in base + SES N=3686, N=1829 for males, and N=1857 for females

Table 5. Associations of educational attainment, household income, and neighborhood SES with disease-specific survival, overall and by gender, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Overall N=3949			Male N=1937			Female N=2012		
		Base model[a]	Base + all SES factors[b]		Base model[a]	Base + all SES factors[b]		Base model[a]	Base + all SES factors[b]
	N (deaths)	HR (95% CI)	HR (95% CI)	N (deaths)	HR (95% CI)	HR (95% CI)	N (deaths)	HR (95% CI)	HR (95% CI)
Educational attainment									
College graduate/graduate school	1436 (249)	1.00 (-)	1.00 (-)	783 (128)	1.00 (-)	1.00 (-)	653 (121)	1.00 (-)	1.00 (-)
Some college/vocational school	1370 (315)	1.08 (0.93-1.26)	1.04 (0.89-1.22)	644 (153)	1.27 (1.00-1.61)	**1.29 (1.03-1.62)**	726 (162)	0.90 (0.75-1.08)	0.85 (0.69-1.04)
High school completion	886 (207)	1.09 (0.92-1.30)	1.06 (0.89-1.26)	396 (86)	1.08 (0.83-1.40)	1.13 (0.87-1.45)	490 (121)	1.06 (0.86-1.30)	0.98 (0.78-1.23)
<High school	257 (73)	1.05 (0.85-1.31)	1.05 (0.82-1.33)	114 (35)	**1.42 (1.03-1.96)**	**1.65 (1.17-2.32)**	143 (38)	0.82 (0.62-1.09)	**0.71 (0.52-0.97)**
p-trend		*0.38*	*0.34*		*0.19*	***0.03***		*0.68*	*0.39*
Household income[c]									
≥70K	1356 (221)	1.00 (-)	1.00 (-)	790 (133)	1.00 (-)	1.00 (-)	566 (88)	1.00 (-)	1.00 (-)
45-69K	818 (200)	1.15 (0.98-1.35)	1.12 (0.94-1.32)	438 (112)	**1.32 (1.06-1.63)**	1.22 (0.97-1.53)	380 (88)	0.95 (0.75-1.21)	0.97 (0.75-1.24)
30-44K	688 (153)	0.96 (0.80-1.15)	0.93 (0.76-1.12)	291 (56)	0.80 (0.60-1.07)	0.74 (0.54-1.00)	397 (97)	1.07 (0.85-1.34)	1.10 (0.86-1.41)
15-29K	505 (140)	0.94 (0.74-1.19)	0.88 (0.68-1.14)	190 (52)	0.78 (0.53-1.15)	0.72 (0.48-1.06)	315 (88)	1.06 (0.82-1.35)	1.03 (0.78-1.37)
<15K	319 (79)	0.98 (0.74-1.29)	0.92 (0.68-1.24)	120 (29)	1.03 (0.60-1.76)	0.96 (0.58-1.59)	199 (50)	1.04 (0.78-1.38)	1.05 (0.76-1.45)
p-trend		*0.36*	*0.14*		*0.14*	*0.08*		*0.58*	*0.70*
Neighborhood socioeconomic status (nSES)[d]									
Q1 (high nSES)	961 (161)	1.00 (-)	1.00 (-)	507 (90)	1.00 (-)	1.00 (-)	454 (71)	1.00 (-)	1.00 (-)
Q2	789 (137)	0.95 (0.72-1.25)	0.93 (0.71-1.23)	403 (68)	0.97 (0.67-1.42)	0.93 (0.65-1.33)	386 (69)	0.89 (0.62-1.28)	0.93 (0.63-1.37)
Q3	750 (162)	1.19 (0.90-1.57)	1.16 (0.88-1.48)	381 (79)	1.49 (0.99-2.25)	1.33 (0.90-1.97)	369 (83)	0.91 (0.63-1.32)	0.95 (0.64-1.39)
Q4	772 (192)	1.01 (0.75-1.33)	0.99 (0.75-1.28)	364 (85)	0.91 (0.59-1.40)	0.81 (0.54-1.23)	408 (107)	1.04 (0.72-1.49)	1.09 (0.75-1.59)
Q5 (low nSES)	677 (192)	**1.34 (1.02-1.76)**	**1.36 (1.02-1.80)**	282 (80)	1.26 (0.83-1.91)	1.20 (0.80-1.80)	395 (112)	1.21 (0.86-1.71)	1.31 (0.89-1.91)
p-trend		*0.08*	*0.07*		*0.69*	*0.50*		*0.20*	*0.40*
Education and nSES[e]									
≥Some college, High nSES	1429 (226)		1.00 (-)	758 (124)		1.00 (-)	671 (102)		1.00 (-)
≥Some college, Low nSES	1377 (338)		**1.29 (1.05-1.58)**	669 (157)		1.25 (0.92-1.68)	708 (181)		1.21 (0.94-1.57)
≤High school, High nSES	321 (72)		1.22 (0.96-1.54)	152 (34)		1.18 (0.85-1.65)	169 (38)		1.22 (0.90-1.66)
≤High school , Low nSES	822 (208)		**1.25 (1.01-1.56)**	358 (87)		1.27 (0.93-1.74)	464 (121)		1.16 (0.88-1.54)
Household income and nSES[f]									

≥$30K, High nSES	1430 (237)		1.00 (-)	779 (133)		1.00 (-)	651 (104)		1.00 (-)
≥$30K, Low nSES	1432 (337)		1.17 (0.97-1.42)	740 (168)		1.11 (0.85-1.46)	692 (169)		1.16 (0.89-1.52)
<$30K, High nSES	197 (43)		0.81 (0.52-1.24)	78 (17)		0.54 (0.27-1.09)	119 (26)		1.21 (0.86-1.70)
<$30K, Low nSES	627 (176)		1.06 (0.84-1.33)	232 (64)		0.95 (0.65-1.38)	395 (112)		1.15 (0.85-1.54)

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), and gender (**male**, female). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends for SES factors come from a Wald test of continuous variables comparing the coefficient with zero; p-trends for income do not include cases missing income (N=263)

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends for SES factors come from a Wald test of continuous variables comparing the coefficient with zero, and do not include cases missing income (N=263)

[c] Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown

[d] Quintile cutpoints based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[e] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)

[f] Income collapsed as low (<$30K/year) and high ($≥30K/year); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263), so N=3686 for overall sample, N=1829 for males, and N=1857 for females

Table 6. Associations of educational attainment, household income, and neighborhood SES with disease-specific survival, overall and by gender, with additional adjustment factors, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Overall				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=3949	**N=3945**	**N=3924**	**N=2322**	**N=2297**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	1.04 (0.89-1.22)	1.05 (0.90-1.22)	1.06 (0.90-1.24)	1.14 (0.94-1.40)	1.14 (0.93-1.39)
High school completion	1.06 (0.89-1.26)	1.06 (0.89-1.27)	1.08 (0.90-1.29)	1.17 (0.92-1.47)	1.16 (0.92-1.47)
<High school	1.05 (0.82-1.33)	1.04 (0.81-1.32)	1.06 (0.83-1.34)	1.06 (0.72-1.56)	1.08 (0.73-1.59)
p-trend	*0.34*	*0.33*	*0.24*	*0.25*	*0.22*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	1.12 (0.94-1.32)	1.12 (0.94-1.32)	1.13 (0.96-1.35)	1.13 (0.91-1.41)	1.14 (0.91-1.42)
30-44K	0.93 (0.76-1.12)	0.92 (0.76-1.12)	0.91 (0.74-1.10)	0.76 (0.58-1.00)	0.78 (0.60-1.02)
15-29K	0.88 (0.68-1.14)	0.88 (0.68-1.13)	0.85 (0.65-1.12)	0.74 (0.52-1.04)	0.75 (0.54-1.06)
<15K	0.92 (0.68-1.24)	0.91 (0.67-1.24)	0.90 (0.67-1.21)	0.89 (0.61-1.31)	0.92 (0.63-1.34)
p-trend	*0.14*	*0.14*	*0.10*	*0.05*	*0.06*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	0.93 (0.71-1.23)	0.94 (0.71-1.23)	0.95 (0.72-1.25)	0.89 (0.62-1.28)	0.90 (0.63-1.29)
Q3	1.16 (0.88-1.48)	1.17 (0.89-1.54)	1.26 (0.95-1.67)	1.33 (0.90-1.96)	1.32 (0.90-1.94)
Q4	0.99 (0.75-1.28)	1.01 (0.76-1.33)	1.04 (0.79-1.38)	1.02 (0.69-1.52)	1.02 (0.69-1.52)
Q5 (low nSES)	**1.36 (1.02-1.80)**	**1.37 (1.04-1.82)**	**1.46 (1.10-1.94)**	**1.63 (1.05-2.53)**	**1.64 (1.06-2.55)**
p-trend	*0.07*	*0.06*	***0.02***	***0.02***	***0.02***
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	**1.29 (1.05-1.58)**	**1.29 (1.06-1.59)**	**1.37 (1.11-1.68)**	**1.52 (1.15-1.99)**	**1.51 (1.15-1.98)**

≤High school, High nSES	1.22 (0.96-1.54)	1.22 (0.96-1.54)	**1.24 (0.98-1.57)**	**1.35 (1.02-1.80)**	**1.35 (1.02-1.80)**
≤High school , Low nSES	1.25 (1.00-1.56)	1.25 (1.00-1.57)	**1.33 (1.06-1.68)**	**1.43 (1.04-1.95)**	**1.42 (1.04-1.94)**
Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	1.17 (0.97-1.42)	1.18 (0.98-1.43)	**1.22 (1.01-1.47)**	**1.31 (1.03-1.68)**	**1.32 (1.03-1.69)**
<$30K, High nSES	0.81 (0.52-1.24)	0.80 (0.52-1.23)	0.71 (0.44-1.15)	0.66 (0.34-1.30)	0.67 (0.34-1.32)
<$30K, Low nSES	1.06 (0.84-1.33)	1.06 (0.84-1.34)	1.11 (0.88-1.40)	1.19 (0.89-1.60)	1.19 (0.88-1.61)
	Male				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=1937	**N=1936**	**N=1924**	**N=1152**	**N=1143**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	**1.29 (1.03-1.62)**	**1.30 (1.03-1.63)**	**1.33 (1.06-1.66)**	1.31 (0.95-1.79)	1.31 (0.96-1.80)
High school completion	1.13 (0.87-1.45)	1.14 (0.88-1.47)	1.15 (0.87-1.48)	1.05 (0.72-1.52)	1.03 (0.70-1.50)
<High school	**1.65 (1.17-2.32)**	**1.66 (1.18-2.34)**	**1.71 (1.20-2.43)**	1.39 (0.73-2.66)	1.42 (0.74-2.72)
p-trend	***0.03***	***0.03***	***0.02***	*0.22*	*0.22*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	1.22 (0.97-1.53)	1.21 (0.97-1.52)	1.21 (0.96-1.52)	1.16 (0.84-1.61)	1.17 (0.84-1.63)
30-44K	0.74 (0.54-1.00)	0.73 (0.53-1.00)	0.73 (0.53-1.00)	**0.64 (0.43-0.95)**	**0.65 (0.44-0.97)**
15-29K	0.72 (0.48-1.06)	0.71 (0.48-1.06)	0.66 (0.44-1.01)	0.60 (0.36-1.01)	0.60 (0.36-1.01)
<15K	0.96 (0.58-1.59)	0.96 (0.58-1.57)	0.93 (0.58-1.49)	1.31 (0.72-2.38)	1.32 (0.72-2.41)
p-trend	*0.08*	*0.09*	*0.05*	*0.10*	*0.09*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	0.93 (0.65-1.33)	0.92 (0.64-1.32)	0.97 (0.67-1.40)	1.04 (0.64-1.69)	1.04 (0.64-1.68)
Q3	1.33 (0.90-1.97)	1.32 (0.90-1.96)	1.40 (0.94-2.08)	1.70 (0.98-2.96)	1.68 (0.96-2.92)
Q4	0.81 (0.54-1.23)	0.81 (0.54-1.23)	0.88 (0.59-1.32)	0.96 (0.54-1.70)	0.97 (0.55-1.72)
Q5 (low nSES)	1.20 (0.80-1.80)	1.19 (0.79-1.77)	1.27 (0.84-1.94)	1.21 (0.62-2.36)	1.22 (0.63-2.36)

p-trend	*0.50*	*0.23*	*0.11*	*0.20*	*0.17*
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	1.25 (0.92-1.68)	1.24 (0.92-1.67)	1.32 (0.98-1.78)	1.33 (0.86-2.00)	1.34 (0.89-2.02)
≤High school, High nSES	1.18 (0.85-1.65)	1.19 (0.86-1.66)	1.20 (0.86-1.69)	1.10 (0.70-1.73)	1.11 (0.69-1.76)
≤High school , Low nSES	1.27 (0.93-1.74)	1.28 (0.94-1.74)	1.33 (0.96-1.83)	1.20 (0.74-1.96)	1.20 (0.73-1.95)
Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	1.11 (0.85-1.46)	1.11 (0.85-1.46)	1.17 (0.90-1.53)	1.25 (0.85-1.84)	1.27 (0.86-1.87)
<$30K, High nSES	0.54 (0.27-1.09)	0.54 (0.27-1.08)	0.46 (0.21-1.03)	0.49 (0.16-1.54)	0.46 (0.14-1.50)
<$30K, Low nSES	0.95 (0.65-1.38)	0.95 (0.66-1.38)	0.97 (0.67-1.39)	1.10 (0.68-1.79)	1.09 (0.67-1.78)
	Female				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=2012	**N=2009**	**N=2000**	**N=1170**	**N=1154**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	0.85 (0.69-1.04)	0.85 (0.69-1.04)	0.87 (0.71-1.07)	1.05 (0.80-1.37)	1.03 (0.78-1.36)
High school completion	0.98 (0.78-1.23)	0.98 (0.78-1.23)	0.99 (0.78-1.25)	1.17 (0.86-1.61)	1.17 (0.85-1.61)
<High school	**0.71 (0.52-0.97)**	**0.69 (0.50-0.95)**	**0.71 (0.82-0.97)**	0.73 (0.44-1.20)	0.77 (0.47-1.27)
p-trend	*0.39*	*0.31*	*0.38*	*0.85*	*0.78*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	0.97 (0.75-1.24)	0.97 (0.76-1.24)	0.99 (0.77-1.27)	1.13 (0.82-1.56)	1.14 (0.82-1.59)
30-44K	1.10 (0.86-1.41)	1.09 (0.85-1.40)	1.11 (0.86-1.42)	0.92 (0.62-1.36)	0.92 (0.62-1.35)
15-29K	1.03 (0.78-1.37)	1.02 (0.77-1.34)	1.03 (0.78-1.37)	0.83 (0.55-1.23)	0.84 (0.57-1.25)
<15K	1.05 (0.76-1.45)	1.04 (0.76-1.44)	1.02 (0.74-1.41)	0.80 (0.47-1.37)	0.82 (0.48-1.40)
p-trend	*0.70*	*0.80*	*0.86*	*0.24*	*0.27*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	0.93 (0.63-1.37)	0.93 (0.63-1.37)	0.94 (0.63-1.39)	0.72 (0.42-1.23)	0.72 (0.42-1.24)

Q3	0.95 (0.64-1.39)	0.95 (0.65-1.40)	1.03 (0.69-1.54)	0.84 (0.48-1.48)	0.83 (0.47-1.48)
Q4	1.09 (0.75-1.59)	1.10 (0.75-1.60)	1.13 (0.77-1.65)	0.85 (0.48-1.52)	0.85 (0.48-1.52)
Q5 (low nSES)	1.31 (0.89-1.91)	1.33 (0.91-1.95)	1.37 (0.93-2.02)	1.65 (0.91-2.99)	1.61 (0.87-2.96)
p-trend	*0.40*	*0.21*	*0.16*	*0.11*	*0.15*
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	1.21 (0.94-1.57)	1.22 (0.95-1.58)	1.27 (0.98-1.65)	1.39 (0.97-1.99)	1.38 (0.95-2.01)
≤High school, High nSES	1.22 (0.90-1.66)	1.23 (0.90-1.67)	1.22 (0.90-1.65)	**1.52 (1.04-2.23)**	**1.56 (1.05-2.31)**
≤High school , Low nSES	1.16 (0.88-1.54)	1.18 (0.89-1.56)	1.22 (0.91-1.62)	1.27 (0.84-1.91)	1.27 (0.83-1.94)
Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	1.16 (0.89-1.52)	1.17 (0.90-1.53)	1.19 (0.91-1.56)	1.39 (0.97-1.99)	1.27 (0.88-1.82)
<$30K, High nSES	1.21 (0.86-1.70)	1.21 (0.86-1.70)	1.16 (0.81-1.67)	**1.52 (1.04-2.23)**	1.35 (0.85-2.14)
<$30K, Low nSES	1.15 (0.85-1.54)	1.15 (0.85-1.54)	1.17 (0.86-1.58)	1.27 (0.84-1.91)	1.07 (0.70-1.63)

[a]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[b]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[c]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (never screened, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[d]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[e]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes)**.** Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[f]Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown

[g]Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2018) in the region

[h]Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)

[i]Income collapsed as low (<$30K) and high ($≥30K); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263) and in base + SES N=3686, N=1829 for males, and N=1857 for females

Supplementary Table 1. Associations between educational attainment, household income, and neighborhood SES and all-cause survival with additional adjustment factors in a complete case analysis of the overall study population (N=2297), Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Overall				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	1.02 (0.88-1.19)	1.03 (0.88-1.18)	1.05 (0.91-1.21)	1.04 (0.90-1.20)	1.02 (0.88-1.17)
High school completion	0.91 (0.76-1.08)	0.91 (0.76-1.08)	0.93 (0.78-1.11)	0.92 (0.77-1.10)	0.91 (0.76-1.09)
<High school	0.94 (0.74-1.19)	0.93 (0.73-1.18)	0.94 (0.74-1.19)	0.94 (0.74-1.20)	0.92 (0.73-1.17)
p-trend	*0.67*	*0.64*	*0.85*	*0.77*	*0.64*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	**1.27 (1.05-1.54)**	**1.27 (1.05-1.54)**	**1.25 (1.03-1.50)**	**1.24 (1.03-1.50)**	**1.26 (1.04-1.51)**
30-44K	1.15 (0.93-1.41)	1.15 (0.94-1.54)	1.10 (0.91-1.34)	1.10 (0.90-1.34)	1.10 (0.90-1.33)
15-29K	1.21 (0.91-1.61)	1.21 (0.92-1.60)	1.15 (0.88-1.51)	1.15 (0.88-1.52)	1.15 (0.87-1.51)
<15K	**1.37 (1.03-1.83)**	**1.37 (1.02-1.83)**	**1.32 (1.01-1.73)**	1.30 (0.99-1.71)	1.28 (0.98-1.68)
p-trend	*0.16*	***0.15***	*0.25*	*0.27*	*0.32*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	0.97 (0.71-1.32)	0.97 (0.71-1.32)	1.01 (0.74-1.35)	1.01 (0.74-1.35)	0.96 (0.71-1.30)
Q3	1.10 (0.78-1.55)	1.10 (0.78-1.54)	1.11 (0.79-1.57)	1.12 (0.79-1.57)	1.08 (0.77-1.52)
Q4	1.01 (0.73-1.41)	1.01 (0.73-1.39)	1.06 (0.78-1.44)	1.06 (0.78-1.44)	1.04 (0.77-1.41)
Q5 (low nSES)	1.27 (0.89-1.80)	1.26 (0.89-1.78)	1.31 (0.94-1.83)	1.31 (0.94-1.83)	1.27 (0.91-1.77)
p-trend	*0.12*	*0.11*	*0.07*	*0.07*	*0.10*
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	1.21 (0.97-1.53)	1.21 (0.97-1.51)	**1.24 (1.01-1.54)**	**1.24 (1.01-1.55)**	1.23 (0.99-1.54)
≤High school, High nSES	1.08 (0.86-1.36)	1.08 (0.86-1.36)	1.10 (0.88-1.37)	1.10 (0.88-1.38)	1.10 (0.87-1.38)
≤High school , Low nSES	1.02 (0.79-1.32)	1.01 (0.79-1.30)	1.04 (0.82-1.33)	1.04 (0.81-1.34)	1.03 (0.80-1.33)

Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	1.10 (0.90-1.34)	1.10 (0.90-1.33)	1.10 (0.90-1.33)	1.11 (0.91-1.36)	1.11 (0.91-1.35)
<$30K, High nSES	1.01 (0.64-1.58)	1.01 (0.64-1.58)	0.91 (0.57-1.44)	0.92 (0.58-1.44)	0.92 (0.58-1.44)
<$30K, Low nSES	1.23 (0.99-1.54)	1.24 (0.99-1.54)	1.24 (0.99-1.55)	**1.25 (1.01-1.57)**	1.23 (0.98-1.54)

[a]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[b]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[c]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (never screened, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[d]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[e]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes)**.** Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[f]Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown

[g]Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2018) in the region

[h]Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)

[i]Income collapsed as low (<$30K) and high ($≥30K); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263) and in base + SES N=3686, N=1829 for males, and N=1857 for females

Supplementary Table 2. Associations between educational attainment, household income, and neighborhood SES and disease-specific survival with additional adjustment factors in a complete case analysis of the overall study population (N=2297), Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Overall				
	Base + SES[a]	**Base + SES + Screening[b]**	**Base + SES + Screening + Treatment[c]**	**Base + SES + Screening + Treatment + Lifestyle[d]**	**Base + SES + Screening + Treatment + Lifestyle + Comorbidities[e]**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Educational attainment					
College graduate/graduate school	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Some college/vocational school	1.06 (0.87-1.29)	1.05 (0.86-1.28)	1.09 (0.89-1.33)	1.14 (0.93-1.39)	1.14 (0.94-1.40)
High school completion	1.07 (0.84-1.35)	1.06 (0.83-1.34)	1.10 (0.87-1.40)	1.16 (0.92-1.47)	1.17 (0.92-1.48)
<High school	0.97 (0.66-1.42)	0.95 (0.65-1.40)	0.99 (0.68-1.44)	1.08 (0.74-1.60)	1.08 (0.73-1.60)
p-trend	*0.57*	*0.61*	*0.38*	*0.24*	*0.22*
Household income[f]					
≥70K	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
45-69K	1.18 (0.94-1.48)	1.18 (0.94-1.48)	1.15 (0.92-1.43)	1.14 (0.91-1.41)	1.14 (0.92-1.42)
30-44K	0.82 (0.62-1.08)	0.83 (0.63-1.09)	0.77 (0.59-1.01)	0.78 (0.59-1.02)	0.78 (0.60-1.02)
15-29K	0.81 (0.56-1.16)	0.82 (0.58-1.17)	0.78 (0.55-1.10)	0.75 (0.53-1.06)	0.76 (0.54-1.06)
<15K	0.92 (0.62-1.38)	0.92 (0.65-1.37)	0.91 (0.62-1.32)	0.90 (0.61-1.33)	0.91 (0.62-1.34)
p-trend	*0.15*	*0.15*	*0.08*	*0.06*	*0.06*
Neighborhood socioeconomic status (nSES)[g]					
Q1 (high nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Q2	0.91 (0.63-1.32)	0.91 (0.63-1.32)	0.92 (0.64-1.33)	0.90 (0.62-1.29)	0.90 (0.63-1.29)
Q3	1.32 (0.90-1.94)	1.34 (0.91-1.96)	1.33 (0.90-1.96)	1.33 (0.90-1.95)	1.32 (0.90-1.95)
Q4	1.01 (0.67-1.52)	1.01 (0.67-1.51)	1.04 (0.70-1.55)	1.02 (0.69-1.51)	1.02 (0.69-1.52)
Q5 (low nSES)	**1.70 (1.10-2.64)**	**1.73 (1.11-2.67)**	**1.79 (1.17-2.76)**	**1.63 (1.05-2.53)**	**1.64 (1.06-1.25)**
p-trend	***0.03***	***0.02***	***0.01***	***0.02***	***0.02***
Education and nSES[h]					
≥Some college, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥Some college, Low nSES	**1.49 (1.12-1.98)**	**1.49 (1.13-1.97)**	**1.53 (1.16-2.02)**	**1.51 (1.15-1.99)**	**1.51 (1.15-1.98)**
≤High school, High nSES	1.30 (0.95-1.76)	1.29 (0.95-1.75)	1.33 (0.99-1.78)	**1.36 (1.02-1.82)**	**1.36 (1.02-1.81)**
≤High school , Low nSES	1.35 (0.98-1.86)	1.34 (0.98-1.85)	**1.41 (1.02-1.93)**	**1.43 (1.04-1.95)**	**1.42 (1.04-1.94)**
Household income and nSES[i]					
≥$30K, High nSES	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
≥$30K, Low nSES	**1.33 (1.04-1.71)**	**1.34 (1.05-1.72)**	**1.33 (1.04-1.70)**	**1.32 (1.03-1.68)**	**1.32 (1.03-1.69)**

<$30K, High nSES	0.79 (0.39-1.59)	0.79 (0.40-1.57)	0.70 (0.32-1.38)	0.67 (0.34-1.33)	0.68 (0.35-1.33)
<$30K, Low nSES	1.18 (0.88-1.59)	1.20 (0.90-1.61)	1.24 (0.93-1.67)	1.18 (0.88-1.59)	1.19 (0.88-1.61)

[a]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[b]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[c]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (never screened, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[d]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[e]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), all SES factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes)**.** Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. Gender-specific models not adjusted for gender. P-trends, from Wald tests of coefficients compared with zero, do not include cases missing income (N=263)

[f]Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown

[g]Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2018) in the region

[h]Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)

[i]Income collapsed as low (<$30K) and high ($≥30K); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263) and in base + SES N=3686, N=1829 for males, and N=1857 for females

Supplementary Table 3. Associations of educational attainment, household income, and neighborhood SES with all-cause survival by urbanicity/rurality of residential neighborhood, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)[a]

	Urbanicity/rurality					
	100% Urban n=3111		Mixed urban/rural n=507		100% Rural n=331	
	N (deaths)	HR (95% CI)	N (deaths)	HR (95% CI)	N(deaths)	HR (95% CI)
Educational attainment						
College graduate/graduate school	1185 (377)	1.00 (-)	156 (40)	1.00 (-)	95 (30)	1.00 (-)
Some college/vocational school	1068 (452)	1.07 (0.93-1.23)	189 (67)	0.83 (0.55-1.26)	113 (35)	0.82 (0.49-1.38)
High school completion	669 (334)	1.09 (0.95-1.27)	118 (45)	0.84 (0.53-1.32)	99 (45)	1.13 (0.72-1.77)
<High school	189 (128)	1.02 (0.86-1.23)	44 (26)	0.74 (0.41-1.34)	24 (12)	0.89 (0.40-1.97)
p-trend		*0.31*		*0.72*		*0.60*
Household income[b]						
≥70K	1076 (266)	1.00 (-)	188 (36)	1.00 (-)	92 (16)	1.00 (-)
45-69K	648 (276)	1.13 (0.96-1.34)	103 (43)	1.22 (0.77-1.91)	67 (25)	1.82 (0.97-3.42)
30-44K	529 (270)	1.16 (0.99-1.36)	84 (41)	0.93 (0.57-1.52)	75 (36)	1.46 (0.80-2.68)
15-29K	400 (236)	1.19 (0.94-1.50)	58 (29)	1.13 (0.65-1.99)	47 (25)	1.41 (0.74-2.68)
<15K	249 (151)	**1.51 (1.22-1.87)**	44 (18)	0.75 (0.36-1.54)	26 (11)	1.69 (0.68-4.23)
p-trend		***0.02***		*0.20*		*0.39*
Neighborhood socioeconomic status (nSES)[c]						
Q1 (high nSES)	845 (250)	1.00 (-)	72 (17)	1.00 (-)	44 (11)	1.00 (-)
Q2	597 (219)	1.05 (0.84-1.32)	122 (28)	0.60 (0.26-1.41)	70 (19)	1.66 (0.58-4.72)
Q3	556 (245)	1.25 (0.98-1.59)	120 (38)	0.60 (0.29-1.25)	74 (24)	1.98 (0.73-5.37)
Q4	566 (258)	1.02 (0.80-1.30)	123 (61)	0.82 (0.39-1.71)	83 (39)	1.75 (0.70-4.35)
Q5 (low nSES)	547 (319)	1.22 (0.96-1.56)	70 (34)	0.70 (0.31-1.61)	60 (29)	1.98 (0.64-6.15)
p-trend		*0.11*		*0.56*		*0.36*
Education and nSES[d]						
≥Some college, High nSES	1186 (349)	1.00 (-)	152 (33)	1.00 (-)	91 (23)	1.00 (-)
≥Some college, Low nSES	1067 (480)	**1.24 (1.03-1.48)**	193 (74)	0.76 (0.42-1.37)	117 (42)	1.62 (0.88-2.99)
≤High school, High nSES	256 (120)	**1.26 (1.06-1.50)**	42 (12)	0.59 (0.29-1.23)	23 (7)	2.70 (0.93-7.85)
≤High school , Low nSES	602 (342)	1.19 (0.97-1.46)	120 (59)	0.74 (0.40-1.36)	100 (50)	1.63 (0.91-2.91)
Household income and nSES[e]						
≥$30K, High nSES	1171 (350)	1.00 (-)	159 (35)	1.00 (-)	100 (26)	1.00 (-)
≥$30K, Low nSES	1082 (462)	1.08 (0.92-1.28)	216 (85)	0.86 (0.51-1.45)	134 (51)	1.41 (0.69-2.87)
<$30K, High nSES	165 (77)	0.95 (0.65-1.37)	24 (7)	1.03 (0.46-2.33)	8 (3)	2.19 (0.71-6.72)
<$30K, Low nSES	484 (310)	**1.32 (1.09-1.59)**	78 (40)	0.72 (0.37-1.39)	65 (33)	1.33 (0.57-3.11)

Urbanicity/rurality measure created using block group-level data from the 2000 US Decennial Census/ACS 5-year 2013-2017 estimates
[a]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends do not include cases missing income (N=263)
[b]Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown
[c]Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (diagnosed 1998-2007, 2016-2018) in the region
[d]Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)
[e]Income collapsed as low (<$30K) and high ($≥30K); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263), so N=3686 for overall sample

Supplementary Table 4. Associations of educational attainment, household income, and neighborhood SES with disease-specific survival by urbanicity/rurality of residential neighborhood, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)[a]

	Urbanicity/rurality					
	100% Urban n=3111		Mixed urban/rural n=507		100% Rural n=331	
	N (deaths)	HR (95% CI)	N (deaths)	HR (95% CI)	N (deaths)	HR (95% CI)
Educational attainment						
College graduate/graduate school	1185 (203)	1.00 (-)	156 (28)	1.00 (-)	95 (18)	1.00 (-)
Some college/vocational school	1068 (260)	1.12 (0.94-1.33)	189 (39)	0.65 (0.37-1.12)	113 (16)	0.70 (0.35-1.36)
High school completion	669 (159)	1.06 (0.87-1.30)	118 (25)	0.86 (0.47-1.58)	99 (23)	1.32 (0.69-2.54)
<High school	189 (58)	1.03 (0.79-1.35)	44 (9)	0.50 (0.21-1.22)	24 (6)	0.92 (0.16-5.28)
p-trend		*0.44*		*0.51*		*0.15*
Household income[b]						
≥70K	1076 (181)	1.00 (-)	188 (30)	1.00 (-)	92 (10)	1.00 (-)
45-69K	648 (161)	1.12 (0.92-1.35)	103 (23)	1.04 (0.57-1.87)	67 (16)	2.11 (0.84-5.32)
30-44K	529 (117)	0.90 (0.72-1.12)	84 (19)	0.87 (0.45-1.69)	75 (17)	1.38 (0.52-3.65)
15-29K	400 (115)	0.89 (0.66-1.19)	58 (15)	0.75 (0.37-1.54)	47 (10)	1.14 (0.42-3.11)
<15K	249 (66)	1.08 (0.81-1.44)	44 (8)	**0.41 (0.17-0.98)**	26 (5)	1.71 (0.49-6.04)
p-trend		*0.40*		***0.04***		*0.68*
Neighborhood socioeconomic status (nSES)[c]						
Q1 (high nSES)	845 (143)	1.00 (-)	72 (12)	1.00 (-)	44 (6)	1.00 (-)
Q2	597 (110)	0.94 (0.70-1.27)	122 (17)	0.64 (0.22-1.90)	70 (10)	0.85 (0.06-11.31)
Q3	556 (128)	1.22 (0.89-1.66)	120 (19)	0.53 (0.21-1.32)	74 (15)	2.93 (0.38-22.68)
Q4	566 (136)	0.97 (0.70-1.33)	123 (36)	0.86 (0.32-2.29)	83 (20)	2.63 (0.34-20.24)
Q5 (low nSES)	547 (163)	1.35 (0.99-1.84)	70 (17)	1.25 (0.40-3.96)	60 (12)	5.58 (0.60-51.88)
p-trend		*0.10*		*0.99*		*0.04*
Education and nSES[d]						
≥Some college, High nSES	1186 (193)	1.00 (-)	152 (21)	1.00 (-)	91 (12)	1.00 (-)
≥Some college, Low nSES	1067 (270)	**1.32 (1.05-1.66)**	193 (46)	0.78 (0.36-1.69)	117 (22)	**7.65 (1.38-42.31)**
≤High school, High nSES	256 (60)	1.23 (0.95-1.59)	42 (8)	0.74 (0.32-1.74)	23 (4)	**6.05 (1.22-30.03)**
≤High school , Low nSES	602 (157)	1.20 (0.93-1.55)	120 (26)	0.75 (0.33-1.72)	100 (25)	**7.76 (1.61-37.34)**
Household income and nSES[e]						
≥$30K, High nSES	1171 (199)	1.00 (-)	159 (24)	1.00 (-)	100 (14)	1.00 (-)
≥$30K, Low nSES	1082 (260)	1.18 (0.96-1.45)	216 (48)	0.79 (0.41-1.54)	134 (29)	**5.07 (1.14-22.49)**
<$30K, High nSES	165 (38)	0.82 (0.52-1.30)	24 (4)	0.69 (0.19-2.55)	8 (1)	0.90 (0.18-4.59)
<$30K, Low nSES	484 (143)	1.14 (0.89-1.46)	78 (19)	0.44 (0.18-1.03)	65 (14)	4.17 (0.93-18.81)

Urbanicity/rurality measure created using block group-level data from the 2000 US Decennial Census/ACS 5-year 2013-2017 estimates
[a]Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), and all SES factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends do not include cases missing income (N=263)
[b]Measured with respect to two years prior to CRC diagnosis. Category for cases with missing income (N=263) included in statistical models, but estimate for missing category not shown
[c]Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (diagnosed 1998-2007, 2016-2018) in the region
[d]Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)
[e]Income collapsed as low (<$30K) and high ($≥30K); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Estimates exclude cases missing income (N=263), so N=3686 for overall sample

Chapter 2: Differentiating between the effects of neighborhood socioeconomic status, neighborhood population density, and neighborhood level of high-intensity development on survival after colorectal cancer

ABSTRACT

Background. Evidence posits inequalities in socioeconomic status (SES), including differences in neighborhood SES (nSES), as primary drivers of persistent disparities in colorectal cancer (CRC) survival. However, no prior CRC survival study has attempted to disentangle nSES effects from the effects of other neighborhood factors, such as population density and high-intensity development.

Methods. We included data from 3949 population-based CRC cases diagnosed 1997-2018 in the Seattle-Puget Sound region. We constructed an nSES index and a population density measure using Census-based block group-level data, and created a block group-level proportion high-intensity development measure using data from the US Geological Survey's National Land Cover Database. We assessed neighborhood factor effects on CRC survival using Cox proportional hazards models with robust standard errors to account for within-neighborhood dependence. We adjusted primary model estimates for individual SES (iSES) factors (i.e., education, household income), and used separate analyses to stratify by these factors.

Results. Over a median of 4.0 years follow-up, 1591 cases died (844 of CRC). After mutual adjustment, living in a high nSES neighborhood was marginally related to lower all-cause (HR: 0.83, 95% CI: 0.73-1.01) and lower CRC-specific mortality (HR: 0.85, 95% CI: 0.69-1.05); following stratification by iSES factors, this effect was only observed in cases reporting greater educational attainment. Living in a highly populated neighborhood was associated with better disease-specific survival (p-trend: 0.02). Living in an intensely developed neighborhood was related to poorer all-cause (HR: 1.62, 95% CI: 1.09-2.41) and CRC-specific survival (HR: 1.73, 95% CI: 1.01-3.08) only in CRC cases reporting lower income.

Conclusion. When assessed simultaneously, neighborhood SES, population density, and the level of high-intensity development are each modestly associated with survival after CRC. These effects vary across iSES subgroups.

INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed invasive cancer and the third leading cancer cause of death in the United States (US).[1] Despite significant improvements in CRC survival over the last four decades, sociodemographic disparities persist, with African-American, American Indian/Alaska Native, and low income CRC cases experiencing higher mortality after diagnosis.[1,18,41,61,121,125] Prior evidence indicates that these disparities in CRC survival are largely due to socioeconomic status (SES) inequalities,[121] including inequalities in neighborhood socioeconomic status (nSES), that result in differential access to screening and high-quality treatment.[1,11,18,121] Yet the impact of nSES on CRC survival may actually proxy for the effects of other neighborhood characteristics, [52,56,126] such as the number of people living in the neighborhood (population density)[38,55,56] or the amount of residential and commercial development present in the neighborhood physical environment (high-intensity development).[38,47,100,127] Differentiating between the influences of these neighborhood characteristics would aid health researchers and policy creators in deciding which of these factors should be used as a meaningful identifier of higher mortality neighborhoods for CRC cases.[51,57]

Neighborhood SES, neighborhood population density, and neighborhood high-intensity development may all affect the likelihood of CRC survival by influencing the area availability of material (e.g., screening facilities, high-quality treatment) and social (e.g., opportunities for social participation and support) resources that are critical to early detection and appropriate care.[24,33,57,78,128] Although the effects of these neighborhood factors likely operate on CRC mortality through similar mediating mechanisms, the impact of each factor would presumably be unique for two reasons. First, each factor is a theoretically distinct construct with an independent definition. Neighborhood SES refers to the level of socioeconomic resources within a neighborhood (e.g., housing value, employment opportunities, poverty level),[64,85] population density to the spatial concentration of neighborhood residents,[47,55] and high-intensity development to the spatial concentration of mixed-use buildings (i.e., residential and commercial) and other man-made physical infrastructure.[33,129,130] Second, because each factor is a distinct construct, there may be different social meanings in the common set of mediating factors. For example, although the local availability of medical services might impact health care accessing behaviors in CRC cases, cases living in high nSES neighborhoods may possess the individual economic means to cover costs and, thus, may

receive or seek care further recommendations from their provider irrespective of the distance to health services.[18,61] Likewise, CRC cases living in neighborhoods with greater levels of high-intensity development likely have more opportunities for social interaction and social ties, which may encourage them in health care accessing behaviors.[33,115,116] Conversely, cases living in densely populated neighborhoods might experience lower social support levels, and can be exposed to environmental stressors (e.g., poor air quality, traffic congestion) that may lower the likelihood of regular health care accessing behaviors[117,118,131] and may also directly impact stress-related biological processes associated with cancer progression.[26,34,36,57,132-134]

Because the constructs of nSES, population density, and high-intensity development are theoretically distinct, it is possible to simultaneously assess their independent effects in CRC cases. Further, since complex associations likely exist between all three factors, it is also imperative to mutually adjust their effects for each other.[55-57] However, to our knowledge, no prior study of CRC survival has evaluated these factors in the same analysis.

Combining data from a population-based study of CRC cases in the Seattle-Puget Sound region with data on neighborhood characteristics from the US Census/American Community Survey (ACS) and US Geological Survey (USGS), we assessed the independent associations of neighborhood nSES, population density, and high-intensity development with CRC survival, and explored whether effects attenuated when we evaluated factors concurrently. We adjusted effect estimates for two characteristics of individual SES (iSES; i.e., educational attainment, household income) given that the distributions of these iSES factors may vary across neighborhood factors.[18,33,47,57,133] In addition, since the effects of neighborhood factors may plausibly differ by educational attainment or household income, [22,47]we also explored stratifying associations by iSES characteristics.

METHODS

Study design and population

Our study population included individuals aged 18-74 years who were diagnosed with incident, invasive CRC between 1998-2007 or 2016-2018 and participated in the Puget Sound Colorectal Cancer Cohort (PSCCC), a population-based cohort study of CRC risk and survival.[135] We ascertained all CRC cases via

the population-based Surveillance, Epidemiology, and End Results (SEER) cancer registry of the Seattle-Puget Sound region, which covers 13 counties in western Washington state.[73]

A detailed description of the PSCCC, including details of early recruitment phases and protocols for all years of recruitment, has been published elsewhere.[74] Briefly, eligible PSCCC participants included individuals who resided within the SEER catchment area and who, at the time of their diagnosis, were aged 20-74 (1998-2002, 2016-2018) or 18-49 years (2002-2007). The study was also concurrently enriched for postmenopausal women, aged 50-74 years, diagnosed with incident CRC between 1998-2002 and who resided in mostly rural counties within the SEER region (i.e., exclusive of King, Pierce, and Snohomish counties). After making initial contact with potentially eligible CRC cases via phone, mail, and/or email, we only enrolled cases who were able to complete the baseline survey in English and who resided in the catchment area. Over all recruitment phases, a total of 6075 potentially eligible participants were identified through SEER, of whom 1963 (32%) refused participation, were deceased, or were lost to follow-up prior to the study interview.[74] Response rates were most favorable in earlier recruitment years (i.e.,1998-2002).

Measures

Data sources

According to PSCCC protocol, each participant completed a standardized baseline risk-factor survey at enrollment.[75] During Phase I of recruitment (1998-2002), surveys were administered an average of 8 months (median: 6.9 months) after a CRC diagnosis; in more recent recruitment phases (2016-2018), SEER electronic reporting enhancements shortened this average interval to ~3.5 months. The baseline survey, administered via structured telephone interview, online, or by paper form, collected information on iSES factors (e.g., educational attainment, household income), individual and family cancer history, current comorbidities (e.g., diabetes), physical attributes (i.e., height and weight), and limited lifestyle behaviors (e.g., CRC screening history, physical activity level, smoking status, alcohol consumption) that occurred before diagnosis.

Our other primary data source was the SEER cancer registry of the Seattle-Puget Sound region.[73] The registry requires reporting of an array of CRC case factors measured at or around the time of diagnosis, including demographic characteristics (e.g., gender, race/ethnicity, age, marital status), clinicopathologic

features (e.g., stage at diagnosis), factors in the initial course of CRC treatment (e.g., surgery, radiation, chemotherapy), and residential address at diagnosis.

Residential address information from SEER was provided to our study in geocoded form. Geocoding protocol for the SEER registry stipulated that all home addresses were standardized to US postal service format and then geocoded to a latitude/longitude coordinate while employing, in order of priority, rooftop accuracy or street-level accuracy.[73,76] We reviewed addresses missing a SEER geocode and performed a second geocoding attempt using HERE data from 2017 Esri Business Analyst Desktop as the reference dataset (Redlands, CA).

Using the geocoded residential address at diagnosis, we assigned each CRC case a census block group.[78,85] Census block groups are relatively permanent statistical subdivisions of a county or county equivalent that generally contain between 600 – 3000 residents, with an optimal population of 1,500 individuals, and whose borders are often delineated with input from local residents.[77,82] Block groups are also the smallest geographic area for which most census information is available;[27] as such, epidemiologists and population health researchers commonly use block groups as proxy units for neighborhood effect studies. [52,81] Based on the year of their diagnosis, we mapped CRC cases to block group data from the 2000 US Decennial Census and the 2001 USGS National Land Cover Database (NLCD) 2001 (cases diagnosed between 1998-2007), and to ACS 2013-2017 5-year estimates and the NLCD 2011 (cases diagnosed between 2016-2018). [63,77,81,82,136]

Exposure assessment

We assessed three neighborhood factors as exposures in this study: nSES, population density, and high-intensity development.

For *nSES*, we used a block group-level index measure previously detailed by Diez Roux and colleagues.[85] The index uses six aggregate census/ACS-based variables identified via factor analysis: median household income, median housing unit value, percentage of households earning income from investments, percentage of persons aged at least 25 years who have completed high school, percentage of persons aged at least 25 years who have completed a college degree, and percentage of persons aged at least 16 years in a managerial or professional occupation. Income-based variables (i.e., median household income and median housing unit value) were transformed using the natural logarithm.[85] The

standardized z-score for each census variable was calculated based on the 3,346 block groups in the 13-county SEER registry catchment area and then each z-score summed to create an index in which lower scores corresponded with lower nSES.[22,27] We assigned each CRC case the nSES index score of their census block group. The median nSES score in our study population (median: 15.97, interquartile range [IQR]: 7.19) was extremely similar to that in the underlying population of incident CRC cases in the Seattle-Puget Sound region (median: 16.44, IQR: 6.92).

Using census/ACS data, we estimated *population density* of each block group as the number of people per square mile.[22,38,55,128] We assigned each CRC case the population density for their census block group. The median population density in our CRC cases (median: 2987.9 persons/mi^2, IQR: 4543.1 persons/mi^2) was slightly higher than in the underlying CRC case population (median: 2841.3 persons/mi^2, IQR: 4773.8 persons/mi^2).

To characterize a neighborhood's level of *high-intensity development*, we used data from the NLCD 16-category land cover classification schema, which codes satellite imagery of land cover types to a 30-m resolution.[33,136] We fitted land cover data to block groups by performing a spatial join with a block group polygon shapefile and assessed the proportion of each block group allocated to each land cover classification. The NLCD classified land cover as highly developed if impervious surfaces (e.g., buildings, pavement) constituted 80-100% of the total cover.[136] We assigned each CRC case the percentage of their residential block group covered by high-intensity development. Use of this satellite-based measure enabled us to look at land cover for the entire SEER catchment area rather than only the Seattle Metropolitan area.[33,128,137] The median level of high-intensity development in our study population's block groups (median: 2.0% , IQR: 6.8%) was nearly identical to that in the underlying CRC case population's block groups (median: 2.0%, IQR: 7.5%).

Outcome assessment

Vital status, date of death, and cause of death data was available from SEER and its routine linkage to the National Death Index (NDI).[73] The registry performed its latest vital status linkage for this study population on 15 August 2019. In this study, we used two survival metrics: all-cause survival and disease-specific (i.e., CRC-specific) survival. We classified deaths with an underlying cause attributed to ICD-10 codes C18-C21 or C26 as CRC-specific deaths.[87,88]

Covariate assessment

We measured iSES factors (i.e., educational attainment, household income) using responses from the PSCCC baseline survey.[22,75]

For educational attainment, participants responded to the question "What is the highest level of education that you (have) completed?" and were provided with eight possible levels, including "Do Not Know/Prefer Not to Answer." We collapsed these responses into a measure with three categories: high school degree or less, some college or vocational/technical school degree, at least a college degree.[22,83]

For household income before diagnosis, we asked participants "(As of) about two years ago, which of the following best describes your total annual household income (in USD) from all sources before taxes?" and were given seven possible responses, with a lowest category of <$15K/year, an uppermost category of ≥$70K/year, and categories for cases who did not know or declined to report their income. For analyses, we employed a four-category definition of annual household income: $30K or less/year, $30-69K/year, at least $70K/year, and "missing" (cases who did not know or declined to report income).[9,22,41] We included this missing category in statistical models since these data may be missing not at random (MNAR) based on unmeasured factors which likely also impact CRC survival.[9,41]

For analyses stratified by iSES characteristics, we used binary indicators for educational attainment and household income.[22,25] Low education was defined as having a high school degree or less and high education as attending at least some college or having a vocational school/technical school degree. Low income included cases who reported a household income of less than $30K/year, while high included CRC cases reporting at least $30K/year.

Statistical analysis

To estimate hazard ratios (HR) and 95% confidence intervals (CI) for the independent effects of nSES, population density, and high-intensity development on CRC survival, we used Cox proportional hazards regression with robust standard errors to account for within-neighborhood dependence.[92] Of the 3346 block groups in the region, 2126 contained at least one participating CRC case and so were included in analyses; of those included, 1055 (50%) only contained a single participating CRC case, making true multilevel modeling infeasible.[52,81] We defined the time axis as days since diagnosis, with left censoring to account for the time-lag between diagnosis and PSCCC enrollment. We conducted separate analyses for

all-cause and disease-specific survival; we also performed separate stratified analyses according to educational attainment levels and household income levels. Cases alive at the last vital status assessment were censored at that date; in CRC-specific analyses, we censored individuals who died from causes other than CRC at their date of death. Proportional hazards assumptions for neighborhood factors were supported via testing for a nonzero slope of scaled Schoenfeld residuals on ranked failure times.

We stratified the baseline hazards for all models by tumor stage at diagnosis.[94,95] Through a series of five models, we evaluated the independent effects of neighborhood factors first separately (Model 1) and then in different combinations: nSES and population density (Model 2); nSES and high-intensity development (Model 3); population density and high-intensity development (Model 4); and nSES, population density, and high-intensity development (Model 5). We used Model 5 as our primary model form for subsequent analyses. We also adjusted all estimates for age at diagnosis, year of diagnosis, gender, race/ethnicity, marital status, educational attainment, and household income. Trends for neighborhood factors were examined by taking the continuous form of each factor and performing a Wald test of the coefficient compared with zero. We were cautious in our interpretation of linear trends, and, in the absence of main effects, only reported statistically significant p-trends given clear increasing or decreasing effect estimates across predictor levels. We conducted a sensitivity analysis of neighborhood factor effects by additionally adjusting for other neighborhood characteristics: proportion of open-space development, proportion of households living in poverty, racial/ethnic composition, and the density of street nodes (intersections).

To assess their relative impact on association estimates between neighborhood factors and CRC survival, additional sets of prognostic factors that are hypothesized mediators were added sequentially to the model: 1) history of CRC screening; 2) factors in the initial course of CRC treatment (i.e., surgery, radiation, chemotherapy); 3) lifestyle behaviors occurring before diagnosis (i.e., cigarette smoking history, heavy alcohol consumption according to the American Cancer Society (ACS) definition[96], meeting ACS physical activity recommendations[96]); and comorbidities (i.e., body mass index [BMI, kg/m^2] two years before diagnosis, self-reported diabetes diagnosis). We created the order of these adjustment sets based on previous evidence for which factors mediate the largest proportion of the relationship between SES characteristics and CRC survival,[1,52,78] and which hypothetically explain associations between all of our

neighborhood factors and CRC mortality.[33,57] However, we did not mean to formally investigate mediating mechanisms in this study, but instead to provide substantive description on the independent effects of these three neighborhood factors on survival following a CRC diagnosis.

All model covariates were defined as shown in Table 1. Two-sided tests were considered statistically significant at the α=0.05 level. We joined raster data to block group polygons and mapped CRC cases to block group-level NLCD and census/ACS data using R 3.5.3/3.6.1 (https://www.r-project.org/) and RStudio 1.2.1 (https://rstudio.com); we conducted all statistical analyses in STATA 15 (College Station, TX). This research was approved by the Institutional Review Board at the Fred Hutchinson Cancer Research Center.

RESULTS

Our analyses included 3,949 incident, invasive CRC cases who were followed for a median of 4.0 years (IQR: 14.5 years) after their baseline interview (Table 1). By the end of follow-up, there were 1,591 deaths, of which 844 (53%) had CRC listed as the underlying cause of death on their death certificate. The median age at diagnosis was 58 years (IQR: 18 years) and just under half of CRC cases (45%) were diagnosed at a regional stage of disease. The majority of cases were non-Hispanic white, married, had a household income before diagnosis of at least $30K/year, and had received surgery as part of the initial course of CRC treatment. Additionally, most cases reported having first screened for CRC more than two years prior to their diagnosis, being never smokers or non-drinkers, and being overweight or obese according to their BMI. The study population had roughly equal proportions of men and women, as well as college graduates and cases with some college. Approximately 38% of cases lived in highly developed neighborhoods (high-intensity development quintiles 4 and 5), 41% in densely populated neighborhoods (quintiles 4 and 5), and 44% in high nSES neighborhoods (quintiles 4 and 5).

We found a moderate linear correlation between the level of high-intensity development in a neighborhood and the level of population density in a neighborhood (r=0.52) (Table 2). Both high-intensity development and population density were weakly correlated with the level of nSES in a neighborhood (high-intensity development/nSES r:-0.19; population density/nSES r: 0.01). The joint distributions of high-intensity development and population density with nSES illustrated that, for the neighborhoods

represented in this analysis, high nSES (quintile 5) neighborhoods were more likely to have lower levels of high-intensity development and high versus low population density. In contrast, low nSES (quintile 1) neighborhoods showed greater levels of high-intensity development as well as higher levels of population density.

All-cause survival

After adjustment for case demographics and individual-level socioeconomic characteristics, we did not find evidence for any independent linear relationships between our neighborhood factors of interest and all-cause survival following a CRC diagnosis (Table 3). However, we noted a relationship between living in a high versus low nSES neighborhood and modestly better survival (Model 5 HR: 0.86, 95% CI: 0.73-1.01). Mutual adjustment for all three neighborhood factors produced little-to-no change in effect estimates (Models 1-5). Additional adjustment for other neighborhood factors also had little impact (Supplementary Table 1).

Adjusting for initial CRC treatment course factors and lifestyle behaviors slightly attenuated the effects of high-intensity development and slightly strengthened nSES effects (Table 4). These findings persisted after limiting our analyses to cases with complete information on all possible mediating factors (Supplementary Table 2).

Among CRC cases with high educational attainment (≥some college), living in a high nSES neighborhood remained related to better survival (HR: 0.76, 95% CI: 0.62-0.93) and living in a neighborhood with moderate-low (quintile 2) versus low (quintile) high-intensity development was associated with poorer survival (HR: 1.24, 95% CI: 1.02-1.51) (Table 5). Conversely, in cases with low education (≤high school degree), we noted that living in a high nSES neighborhood was associated with a higher risk of death relative to living in a low nSES neighborhood (HR: 1.26, 95% CI: 1.01-1.60). In cases with low income (<$30K/year), we noted a relationship between living in a neighborhood with a greater level of high-intensity development and an increased risk of death (quintile 5 HR: 1.62, 95% CI: 1.09-2.41); this association was not present in CRC cases reporting high household income (≥$30K/year).

Colorectal cancer-specific survival

Akin to findings for all-cause survival, living in a neighborhood with high nSES was modestly related to better CRC-specific survival (Model 5 quintile 5 HR: 0.85, 95% CI: 0.69-1.05) (Table 6). Additionally, we

noted a lower risk of CRC death for cases living in a neighborhood with greater population density (p-trend: 0.02). And, as observed with all-cause survival, mutual adjustment for our neighborhood factors of interest (Models 1-5) and additional adjustment for other neighborhood factors (Supplementary Table 3) had little impact on effect estimates. Effects also did not attenuate after being adjusted for a history of CRC screening, factors in the initial CRC treatment course, lifestyle behaviors before diagnosis, and comorbidities, either in the full study population (Table 6) or after limiting analyses to cases with complete information on all possible mediating factors (Supplementary Table 4).

Again, comparable to all-cause survival findings, the modest CRC-specific survival benefit of living in a high nSES neighborhood was present only for cases with high educational attainment (quintile 5 HR: 0.77, 95% CI: 0.59-0.99) (Table 7). Additionally analogous, we found that CRC cases who reported low household income and lived in an intensely developed neighborhood experienced poorer survival (quintile 4 HR: 2.15, 95% CI: 1.23-3.79; quintile 5 HR: 1.73, 95% CI: 1.01-3.08).

DISCUSSION

The purpose of the current study was to determine whether and to what extent three neighborhood factors (i.e., nSES, population density, high-intensity development) were associated with CRC survival when evaluated concurrently. Within this population-based cohort of CRC cases in western Washington state, we found that mutually adjusting for these three neighborhood factors had little to no impact on their observed effects. Instead, across analyses, living in a high nSES neighborhood had a modest beneficial effect on both all-cause and disease-specific survival, particularly among cases with higher levels of educational attainment, while residing in a densely populated neighborhood had a modest beneficial impact on disease-specific survival. Conversely, living in a highly developed neighborhood was associated with poorer all-cause and CRC-specific survival, but only among cases reporting low annual household income. These persistent findings indicate that no singular neighborhood factor dominates the influence of neighborhood environment on CRC survival, and, as such, it is crucial to consider multiple dimensions of neighborhood context in these analyses.[52,57]

Prior studies of CRC cases have shown living in a lower nSES neighborhood, or a neighborhood with higher levels of socioeconomic deprivation, to be associated with greater odds of late stage CRC

diagnosis[18,44,52] and a higher likelihood of poorer survival following a CRC diagnosis.[45-47,58] In the Seattle Puget-Sound region, evidence suggests that CRC mortality is substantially greater in economically deprived census tracts.[113] Past investigations have also found an area's population density to be related to late-stage CRC diagnosis[18,55,138] and CRC survival.[47,55,56,122] However, unlike the linear relationship observed between increasing population density and poorer disease-specific survival in other cancer survival investigations,[56,65,129,139] the few studies of CRC to explore the effects of area population density have often found U-shape associations,[52,55] in which high and low population density were both related to greater odds of late-stage diagnosis or higher mortality.[52] To our knowledge, no prior study of CRC survival has explored the effects of living in a highly developed neighborhood.

Similar to past evidence, we also found a survival benefit to living in a high nSES neighborhood. We additionally noted that this effect was present only in CRC cases reporting higher educational attainment; in cases reporting lower educational attainment, we found living in a high nSES neighborhood to be associated with a higher mortality risk. These findings may indicate that CRC cases with more education could better leverage their wealthy socioeconomic environment to cultivate healthy behaviors, seek out further knowledge of their disease, or to avoid financial hardship and other sources of stress.[30,43,102,103] These results also may also be partly driven by the joint distribution of education and income in our study population, since CRC cases with higher educational attainment were also likely to report high household income (≥$70K/year).[25,30]

Dissimilar to the limited prior CRC research on population density effects, we noted a linear association between increasing levels of neighborhood population density and better CRC-specific survival. This finding may be explained by densely populated neighborhoods often having greater resource density,[33,64] including material (e.g., supportive care) and social (e.g., opportunities for social interaction) resources that aid in improving quality of life after a CRC diagnosis.[64,104,140] However, in comparison to previous findings, our population density findings, as well as results for nSES and high-intensity development, were also relatively modest.[52] This difference from past evidence might be due to evaluating all three neighborhood factors in tandem,[57] but more likely suggests that our findings are relative to the geographical scale of our analysis (i.e., block groups) and the study region.[57] Because we focused on residential neighborhood effects, we employed a relatively small administrative unit, while previous

studies have employed larger units – census tracts, zip code tabulation areas, or counties.[52,55,56] In addition, Census-based evidence indicates that the distribution of nSES, population density, and high-intensity development in the Seattle-Puget Sound area may differ from distributions in other geographic regions.[90,141] Over the last two decades, the Seattle-Puget Sound region has been one of the fastest growing regions in the US, with respect to population growth and to increased construction of high-intensity development,[119] and has become one of the wealthiest metropolitan areas in the country.[120,141] The majority of our CRC cases (79%) lived in neighborhoods classified as 100% urban.[122] Also, in our study population, high nSES neighborhoods were more densely populated, and so the limited beneficial effect of population density on CRC-specific survival may be explained by living in a wealthier socioeconomic environment.[18,122] We likely would have found different results given a different area unit size or a different US metropolitan region.

Our geographic scale and the characteristics of our study region likely also explain our limited findings for high-intensity development effects. Neighborhoods with greater levels of high-intensity development – typified by mixed-use buildings, street connectivity, and other physical environment infrastructure – often attract a greater number of quality resources, including primary- and specialty-care physicians and walkable destinations (e.g., restaurants, parks, stores). [64,115,116,142] By placing commercial spots near housing, high-intensity development may also deter crime and social disorder by increasing the level of "eyes on the street," a type of social interaction where neighborhood residents observe and actively participate in their surroundings.[33,63,143-145] Opportunities for social participation and interaction may also promote regular health-seeking behaviors that increase the likelihood of survival in CRC cases.[33,64,128] Apart from an extremely modest relationship between moderate-low high-intensity development and poorer all-cause survival, we did not find evidence for high-intensity development effects in our overall study population. Yet among CRC cases reporting low household income, living in a highly developed neighborhood was associated with higher all-cause and disease-specific mortality. It may be that, in our study population, neighborhoods with increased levels of mixed-use development also had greater levels of traffic congestion,[33,38] air pollution,[117,131] or social decohesion and isolation.[57,118,146] We did find that the highly developed neighborhoods represented by our study also had a moderate-low to low level of nSES, indicating these neighborhoods may not have a greater availability of material and social resources as we

had initially presumed. In this scenario, CRC cases with higher iSES, including income, might have sought needed resources in neighborhoods other than their area of residence;[64,147,148] low income cases in our study may not have had this option.[18,41]

Although we noted minor attenuations in neighborhood effects on all-cause survival after adjusting for factors in the initial course of CRC treatment and lifestyle behaviors as potential mediating factors, all effect estimate changes were well within the range of variability. Future research should explore whether the effects of nSES, population density, and high-intensity development on CRC survival are explained by more fine-grained aspects of CRC treatment (e.g., types of chemotherapy, distance or physical barriers to treatment, perceptions of physician engagement with initial treatment)[9,18,61,148] and of lifestyle behaviors (e.g., daily physical activity patterns before and after diagnosis).[1,38,52]

There are several key limitations to the current study. First, CRC cases participating in the study cohort may be systematically different from the underlying population of incident CRC cases, including if cases with more severe forms of the disease were more likely to live in specific neighborhoods and were unable to participate. We tried to limit the amount that participation could bias our effect estimates by basing study quintile cutpoints for neighborhood factors on the quintile distribution of those factors in the underlying case population.[86] A second drawback to this work is our use of administrative census block group boundaries to define neighborhoods; the boundaries of these administrative units may not align with a CRC case's perception of their neighborhood as a community nor with their perception of "local" material and social resources.[149] Because we were limited to using the residential address at diagnosis to link to neighborhood data, we also lacked information on each case's length of residency in their neighborhood and so there may have been some additional misclassification of exposure. A third limitation is our use of NLCD data to define a neighborhood's level of high-intensity development. While these data did enable us to study the spatial concentration of mixed-use development in the entire SEER catchment area rather than only the Seattle Metropolitan area, the satellite-based measure is limited in its ability to distinguish between different types of man-made infrastructure.[33,136] We lacked fine-grained information on specific commercial destinations, either related to medical care or to walkability and other lifestyle factors, that could have better characterized highly developed neighborhoods.[18,38,51,150] Moreover, despite evidence indicating substantial changes in the study region's socioeconomic and physical

environments,[141] we did not measure changes in nSES, population density, or high-intensity development over time, which could have affected our findings.

Despite these limitations, the findings of this study further the understanding of how three neighborhood factors are associated with CRC survival even when they are simultaneously considered. Our results are likely a combination of contextual effects – neighborhood effects that operate via resources or other area features and act independently of the individual-level demographics of residents – and compositional effects – neighborhood effects that are due to the demographic composition of the individuals living in the neighborhood.[51,52] However, by being able to control for iSES factors, our observed effects may represent truly contextual effects of nSES, population density, and high-intensity development on CRC outcomes.[22,25] Future CRC survival research including these three neighborhood factors and characteristics of iSES should be performed in other populations and other geographic locations. In addition, future studies should explore these associations given greater demographic intersectionality (e.g., jointly considering education and income and/or gender and race/ethnicity) and work to formally identify the mediation mechanisms underlying these associations. A better understanding of these complex relationships will help to pinpoint combinations of neighborhood contexts and individual-level demographics that can potentially serve as intervention targets to enhance CRC survival.[51,57,125]

Table 1. Characteristics of PSCCC CRC cases (N=3949), Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)	
	N (%)
Total participants	3949 (-)
Vital status	
Alive	2358 (60)
Deceased	1591 (40)
Colorectal cancer listed as underlying cause of death	*844 (53)*
Age at diagnosis, in years	
<40	284 (7)
40-49	816 (21)
50-59	1010 (26)
60-69	1184 (30)
≥70	655 (16)
Gender	
Male	1937 (49)
Female	2012 (51)
Race/ethnicity	
Non-Hispanic white	3350 (85)
Other	599 (15)
Marital status	
Single, never married, or unmarried	481 (12)
Married	2431 (61)
Separated or divorced	429 (11)
Widowed	264 (7)
Unknown	344 (9)
Tumor stage at diagnosis[a]	
Local	1491 (38)
Regional	1789 (45)
Distant	585 (15)
Unstaged/unknown	84 (2)
Educational attainment	
≤High school completion or GED	1143 (29)
Some college or vocational school	1370 (35)
≥College completion	1436 (36)
Household income before diagnosis, in USD ($)[b]	
≤$15-29K	824 (21)
$30-69K	1506 (38)
≥$70K	1356 (34)
Missing	263 (7)

Neighborhood socioeconomic status (nSES)[c]	
Quintile 1 (low nSES)	677 (17)
Quintile 2	772 (20)
Quintile 3	750 (19)
Quintile 4	789 (20)
Quintile 5 (high nSES)	961 (24)
Population density (people/mi^2) in neighborhood[d]	
Quintile 1 (low density)	669 (17)
Quintile 2	837 (21)
Quintile 3	832 (21)
Quintile 4	861 (22)
Quintile 5 (high density)	750 (19)
High-intensity development (%) in neighborhood[e]	
Quintile 1 (low percentage)	823 (21)
Quintile 2	807 (20)
Quintile 3	827 (21)
Quintile 4	789 (20)
Quintile 5 (high percentage)	703 (18)
History of CRC screening before diagnosis	
Never screened	722 (18)
First screening ≤2 years before diagnosis	1491 (38)
First screened >2 years before diagnosis	1732 (44)
Missing	4 (<1)
Surgery in initial course of CRC treatment	
No	233 (6)
Yes	3707 (94)
Missing	9 (<1)
Radiation in initial course of CRC treatment	
No	3181 (81)
Yes	756 (19)
Missing	12 (<1)
Chemotherapy in initial course of CRC treatment	
No	1682 (43)
Yes	2186 (55)
Unknown	81 (2)
Cigarette smoking status at diagnosis	
Never	1835 (46)
Former	1681 (43)
Current	427 (11)
Missing	6 (<1)

Heavy alcohol consumption before diagnosis[f,g]	
Nondrinker	2032 (52)
No	1161 (29)
Yes	531 (13)
Missing	225 (6)
Met physical activity recommendation before diagnosis[f,h]	
No	1028 (26)
Yes	1459 (37)
Missing	1462 (37)
Body mass index ([BMI], kg/m^2) before diagnosis[b]	
<25.0	1214 (31)
25.0-29.9	1412 (36)
≥30.0	1285 (32)
Missing	38 (1)
Diabetes[i]	
No	3405 (86)
Yes	537 (14)
Missing	7 (<1)

[a] Based on the 2000 (cases diagnosed between 1998-2016) and 2018 (cases diagnosed in 2018) versions of the SEER Summary Staging Manual
[b] Measured with respect to two years prior to CRC diagnosis
[c] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region
[d] Based on the quintile distribution for block-group level population density in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region
[e] Based on the quintile distribution for block-group level high-intensity development in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region
[f] Measured with respect to the decade prior to CRC diagnosis
[g] ACS heavy drinking definition: for women, ≥8 drinks/week; for men, ≥15 drinks/week
[h] ACS physical activity recommendation: ≥150 minutes of moderate intensity per week, 75 minutes of strenuous intensity per week, or an equivalent combination of moderate/strenuous activity per week
[i] Based on self-report of diabetes diagnosis

Table 2. Distributions of neighborhood SES, population density, and high-intensity development for PSCCC CRC cases (N=3949), Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	Neighborhood SES[a]				
	Q1 (low nSES)	Q2	Q3	Q4	Q5 (high nSES)
	N (%)	N (%)	N (%)	N (%)	N (%)
Total	677 (-)	772 (-)	750 (-)	789 (-)	961 (-)
Population density[b]					
Quintile 1 (low density)	107 (16)	171 (22)	161 (21)	135 (17)	95 (10)
Quintile 2	114 (17)	167 (21)	152 (20)	171 (22)	233 (24)
Quintile 3	135 (20)	145 (19)	139 (19)	175 (22)	238 (25)
Quintile 4	154 (23)	145 (19)	197 (26)	169 (21)	196 (20)
Quintile 5 (high density)	167 (24)	144 (19)	101 (14)	139 (18)	199 (21)
High-intensity development[c]					
Quintile 1 (low percentage)	86 (13)	144 (19)	147 (20)	183 (23)	263 (27)
Quintile 2	64 (9)	148 (19)	162 (22)	191 (24)	242 (25)
Quintile 3	103 (15)	151 (20)	190 (25)	174 (22)	209 (22)
Quintile 4	170 (25)	186 (24)	147 (19)	146 (19)	140 (15)
Quintile 5 (high percentage)	254 (38)	143 (18)	104 (14)	95 (12)	107 (11)

Linear correlations (r) between neighborhood factors: nSES/population density: 0.01; nSES/high-intensity development: -0.19; population density/high-intensity development: 0.52.

[a] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[b] Based on the quintile distribution for block-group level population density in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[c] Based on the quintile distribution for block-group level high-intensity development in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Table 3. Associations of neighborhood SES, population density, and high-intensity development with all-cause survival, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

	N (deaths)	Model 1[a] HR (95% CI)	Model 2[a] HR (95% CI)	Model 3[a] HR (95% CI)	Model 4[a] HR (95% CI)	Model 5[a] HR (95% CI)
Neighborhood socioeconomic status (nSES)[b]						
Quintile 1 (low nSES)	677 (382)	1.00 (-)	1.00 (-)	1.00 (-)		1.00 (-)
Quintile 2	772 (355)	0.92 (0.80-1.05)	0.92 (0.80-1.04)	0.92 (0.81-1.05)		0.92 (0.81-1.05)
Quintile 3	750 (310)	1.04 (0.91-1.17)	1.02 (0.90-1.15)	1.05 (0.93-1.18)		1.03 (0.92-1.16)
Quintile 4	789 (266)	0.95 (0.84-1.08)	0.94 (0.82-1.06)	0.95 (0.83-1.08)		0.94 (0.83-1.07)
Quintile 5 (high nSES)	961 (278)	0.84 (0.71-1.01)	**0.84 (0.70-0.99)**	0.85 (0.72-1.01)		0.86 (0.73-1.01)
p-trend		*0.13*	*0.13*	*0.14*		*0.17*
Population density[c]						
Quintile 1 (low density)	669 (261)	1.00 (-)	1.00 (-)		1.00 (-)	1.00 (-)
Quintile 2	837 (319)	1.01 (0.88-1.13)	1.01 (0.89-1.15)		0.97 (0.84-1.12)	0.99 (0.86-1.15)
Quintile 3	832 (343)	1.01 (0.88-1.15)	1.03 (0.90-1.17)		0.96 (0.81-1.15)	1.01 (0.84-1.19)
Quintile 4	861 (370)	**1.13 (1.01-1.26)**	**1.13 (1.01-1.26)**		1.08 (0.94-1.24)	1.10 (0.95-1.26)
Quintile 5 (high density)	750 (298)	0.90 (0.77-1.05)	0.91 (0.78-1.06)		0.86 (0.72-1.01)	0.88 (0.75-1.04)
p-trend		*0.38*	*0.35*		*0.19*	*0.23*
High-intensity development[d]						
Quintile 1 (low percentage)	823 (317)	1.00 (-)		1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	807 (312)	**1.18 (1.02-1.35)**		**1.18 (1.03-1.35)**	**1.17 (1.01-1.36)**	**1.16 (1.01-1.35)**
Quintile 3	827 (329)	1.02 (0.87-1.19)		1.01 (0.87-1.17)	1.02 (0.86-1.22)	1.01 (0.84-1.19)
Quintile 4	789 (315)	1.12 (0.96-1.29)		1.10 (0.95-1.26)	1.13 (0.95-1.35)	1.10 (0.93-1.30)
Quintile 5 (high percentage)	703 (318)	1.11 (0.95-1.30)		1.08 (0.93-1.26)	1.15 (0.96-1.38)	1.11 (0.93-1.32)
p-trend		*0.66*		*0.91*	*0.27*	*0.45*

Model 1: Separate models for each neighborhood contextual factor; Model 2: Model includes nSES and population density; Model 3: Model includes nSES and high-intensity development; Model 4: Model includes population density and high-intensity development; Model 5: Model includes all three neighborhood contextual factors.

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), and household income (**<$30K/year**, $30-69K/year, ≥$70K/year). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[c] Based on the quintile distribution for block-group level population density in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[d] Based on the quintile distribution for block-group level high-intensity development in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Table 4. Associations of neighborhood SES, population density, and high-intensity development with all-cause survival adjusted for additional case characteristics, Seattle-Puget Sound Region, 1998-3018 (with follow-up through 2019)

	Model 5 (Main Model)[a]	Model 5 + Screening[b]	Model 5 + Screening + Treatment[c]	Model 5 + Screening + Treatment + Lifestyle[d]	Model 5 + Screening + Treatment + Lifestyle + Comorbidities[e]
	N=3949	N=3945	N=3924	N=2322	N=2297
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Neighborhood socioeconomic status (nSES)[f]					
Quintile 1 (low nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	0.92 (0.81-1.05)	0.92 (0.81-1.05)	0.91 (0.80-1.03)	0.88 (0.74-1.05)	0.89 (0.75-1.06)
Quintile 3	1.03 (0.92-1.16)	1.04 (0.92-1.17)	1.02 (0.90-1.15)	0.92 (0.78-1.10)	0.92 (0.77-1.10)
Quintile 4	0.94 (0.83-1.07)	0.94 (0.83-1.06)	0.92 (0.81-1.04)	**0.82 (0.68-0.98)**	**0.81 (0.68-0.98)**
Quintile 5 (high nSES)	0.86 (0.73-1.01)	0.85 (0.73-1.01)	**0.83 (0.70-0.97)**	**0.78 (0.63-0.98)**	**0.80 (0.64-0.99)**
p-trend	*0.17*	*0.14*	*0.07*	*0.06*	*0.10*
Population density[g]					
Quintile 1 (low density)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	0.99 (0.86-1.15)	0.99 (0.86-1.16)	0.99 (0.87-1.17)	1.03 (0.84-1.26)	1.04 (0.85-1.27)
Quintile 3	1.01 (0.84-1.19)	1.01 (0.85-1.19)	1.02 (0.86-1.20)	1.07 (0.87-1.33)	1.07 (0.86-1.32)
Quintile 4	1.10 (0.95-1.26)	1.10 (0.96-1.27)	1.12 (0.97-1.28)	1.20 (0.98-1.46)	1.19 (0.98-1.46)
Quintile 5 (high density)	0.88 (0.75-1.04)	0.89 (0.76-1.04)	0.89 (0.75-1.04)	0.86 (0.68-1.09)	0.86 (0.68-1.09)
p-trend	*0.23*	*0.24*	*0.15*	*0.09*	*0.07*
High-intensity development[h]					
Quintile 1 (low percentage)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	**1.16 (1.01-1.35)**	**1.16 (1.01-1.34)**	1.14 (0.99-1.32)	1.07 (0.90-1.27)	1.06 (0.89-1.25)
Quintile 3	1.01 (0.84-1.19)	0.99 (0.84-1.18)	0.96 (0.80-1.15)	**0.79 (0.65-0.96)**	**0.79 (0.65-0.96)**
Quintile 4	1.10 (0.93-1.30)	1.10 (0.93-1.29)	1.07 (0.91-1.26)	0.91 (0.75-1.11)	0.91 (0.75-1.11)
Quintile 5 (high percentage)	1.11 (0.93-1.32)	1.10 (0.93-1.31)	1.11 (0.93-1.31)	0.88 (0.72-1.07)	0.87 (0.71-1.07)
p-trend	*0.45*	*0.47*	*0.36*	*0.96*	*0.94*

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[d] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[e] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends come from a Wald test of continuous predictors comparing the coefficient with zero

[f] Based on the quintile distribution for block-group nSES in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[g] Based on the quintile distribution for block-group population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[h] Based on the quintile distribution for block-group high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Table 5. Associations of neighborhood SES, population density, and high-intensity development with all-cause survival by educational attainment and household income, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

		Educational attainment			
	Model 5	Low (≤High school) N=1143		High (≥Some college) N=2806	
	HR (95% CI)[a]	N (deaths)	HR (95% CI)[b]	N (deaths)	HR (95% CI)[b]
Neighborhood socioeconomic status (nSES)[c]					
Quintile 1 (low nSES)	1.00 (-)	311 (189)	1.00 (-)	366 (193)	1.00 (-)
Quintile 2	0.92 (0.81-1.05)	289 (158)	0.98 (0.83-1.16)	478 (197)	0.87 (0.73-1.04)
Quintile 3	1.03 (0.92-1.16)	222 (104)	1.01 (0.84-1.21)	533 (206)	1.02 (0.86-1.20)
Quintile 4	0.94 (0.83-1.07)	199 (88)	1.03 (0.85-1.26)	590 (178)	0.87 (0.74-1.03)
Quintile 5 (high nSES)	0.86 (0.73-1.01)	122 (51)	**1.26 (1.01-1.60)**	839 (227)	**0.76 (0.62-0.93)**
p-trend	*0.17*		*0.30*		***0.04***
Population density[d]					
Quintile 1 (low density)	1.00 (-)	239 (111)	1.00 (-)	430 (150)	1.00 (-)
Quintile 2	0.99 (0.86-1.15)	236 (123)	1.04 (0.84-1.30)	601 (196)	0.95 (0.78-1.16)
Quintile 3	1.01 (0.84-1.19)	228 (109)	0.90 (0.71-1.15)	604 (234)	1.00 (0.81-1.24)
Quintile 4	1.10 (0.95-1.26)	258 (139)	1.03 (0.82-1.30)	603 (231)	1.10 (0.91-1.32)
Quintile 5 (high density)	0.88 (0.75-1.04)	182 (108)	0.94 (0.74-1.19)	568 (190)	0.84 (0.67-1.04)
p-trend	*0.23*		*0.53*		*0.12*
High-intensity development[e]					
Quintile 1 (low percentage)	1.00 (-)	228 (110)	1.00 (-)	595 (207)	1.00 (-)
Quintile 2	**1.16 (1.01-1.35)**	223 (103)	1.02 (0.83-1.26)	584 (209)	**1.24 (1.02-1.51)**
Quintile 3	1.01 (0.84-1.19)	234 (121)	0.92 (0.73-1.16)	593 (208)	1.06 (0.85-1.33)
Quintile 4	1.10 (0.93-1.30)	241 (130)	1.10 (0.87-1.39)	548 (185)	1.10 (0.88-1.37)
Quintile 5 (high percentage)	1.11 (0.93-1.32)	217 (126)	1.08 (0.85-1.37)	486 (192)	1.16 (0.92-1.45)
p-trend	*0.45*		*0.41*		*0.24*
		Household income[f]			
	Model 5	**Low (<$30K) N=824**		**High (≥$30K) N=2862**	
	HR (95% CI)[a]	**N (deaths)**	**HR (95% CI)[g]**	**N (deaths)**	**HR (95% CI)[g]**
Neighborhood socioeconomic status (nSES)[b]					
Quintile 1 (low nSES)	1.00 (-)	284 (186)	1.00 (-)	359 (183)	1.00 (-)

Quintile 2	0.92 (0.81-1.05)	195 (111)	**0.81 (0.66-0.99)**	521 (209)	0.94 (0.79-1.11)
Quintile 3	1.03 (0.92-1.16)	148 (86)	1.21 (0.98-1.49)	552 (206)	0.95 (0.81-1.11)
Quintile 4	0.94 (0.83-1.07)	105 (49)	0.99 (0.77-1.27)	632 (192)	0.90 (0.76-1.07)
Quintile 5 (high nSES)	0.86 (0.73-1.01)	92 (38)	0.82 (0.56-1.20)	798 (219)	**0.84 (0.69-1.01)**
p-trend	*0.17*		*0.33*		*0.12*
Population density[c]					
Quintile 1 (low density)	1.00 (-)	136 (70)	1.00 (-)	488 (175)	1.00 (-)
Quintile 2	0.99 (0.86-1.15)	156 (85)	0.82 (0.60-1.14)	632 (215)	1.02 (0.86-1.21)
Quintile 3	1.01 (0.84-1.19)	147 (89)	0.86 (0.59-1.25)	629 (231)	0.98 (0.83-1.16)
Quintile 4	1.10 (0.95-1.26)	180 (104)	0.87 (0.64-1.18)	620 (241)	1.09 (0.92-1.29)
Quintile 5 (high density)	0.88 (0.75-1.04)	205 (122)	0.82 (0.61-1.10)	493 (147)	0.86 (0.70-1.05)
p-trend	*0.23*		*0.24*		*0.45*
High-intensity development[d]					
Quintile 1 (low percentage)	1.00 (-)	127 (65)	1.00 (-)	643 (233)	1.00 (-)
Quintile 2	**1.16 (1.01-1.35)**	135 (74)	**1.43 (1.01-2.03)**	606 (207)	1.05 (0.91-1.22)
Quintile 3	1.01 (0.84-1.19)	148 (92)	1.36 (0.90-2.06)	629 (220)	0.95 (0.81-1.12)
Quintile 4	1.10 (0.93-1.30)	177 (96)	**1.58 (1.06-2.36)**	556 (189)	0.96 (0.81-1.13)
Quintile 5 (high percentage)	1.11 (0.93-1.32)	237 (143)	**1.62 (1.09-2.41)**	428 (160)	0.95 (0.80-1.14)
p-trend	*0.45*		*0.11*		*0.67*

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Based on the quintile distribution for block-group nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[d] Based on the quintile distribution for block-group population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[e] Based on the quintile distribution for block-group high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[f] Measured with respect to two years before diagnosis; estimates exclude 263 cases (7%) missing income

[g] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

Table 6. Associations of neighborhood SES, population density, and high-intensity development with disease-specific survival, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)						
		Model 1[a]	**Model 2[a]**	**Model 3[a]**	**Model 4[a]**	**Model 5[a]**
	N (deaths)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Neighborhood socioeconomic status (nSES)[b]						
Quintile 1 (low nSES)	677 (192)	1.00 (-)	1.00 (-)	1.00 (-)		1.00 (-)
Quintile 2	772 (191)	0.89 (0.75-1.05)	0.86 (0.73-1.03)	0.89 (0.75-1.06)		0.88 (0.74-1.04)
Quintile 3	750 (163)	0.97 (0.82-1.14)	0.94 (0.79-1.11)	0.98 (0.83-1.17)		0.97 (0.82-1.16)
Quintile 4	789 (137)	**0.84 (0.71-0.99)**	**0.82 (0.69-0.98)**	0.85 (0.71-1.02)		0.86 (0.72-1.02)
Quintile 5 (high nSES)	961 (161)	**0.82 (0.67-0.99)**	**0.81 (0.66-0.99)**	0.84 (0.68-1.03)		0.85 (0.69-1.05)
p-trend		***0.03***	***0.03***	***0.04***		*0.05*
Population density[c]						
Quintile 1 (low density)	669 (143)	1.00 (-)	1.00 (-)		1.00 (-)	1.00 (-)
Quintile 2	837 (178)	0.95 (0.79-1.15)	0.97 (0.80-1.17)		0.94 (0.76-1.15)	0.94 (0.76-1.17)
Quintile 3	832 (179)	0.91 (0.77-1.09)	0.93 (0.78-1.11)		0.86 (0.70-1.05)	0.87 (0.70-1.08)
Quintile 4	861 (195)	1.01 (0.85-1.19)	1.01 (0.85-1.19)		0.93 (0.76-1.15)	0.95 (0.77-1.17)
Quintile 5 (high density)	750 (149)	**0.79 (0.65-0.97)**	**0.79 (0.64-0.97)**		**0.73 (0.58-0.91)**	**0.73 (0.58-0.93)**
p-trend		*0.06*	*0.05*		***0.01***	***0.02***
High-intensity development[d]						
Quintile 1 (low percentage)	823 (175)	1.00 (-)		1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	807 (146)	0.99 (0.82-1.18)		0.99 (0.83-1.19)	1.01 (0.84-1.23)	1.02 (0.84-1.24)
Quintile 3	827 (179)	0.91 (0.75-1.11)		0.90 (0.74-1.10)	0.97 (0.78-1.21)	0.96 (0.77-1.20)
Quintile 4	789 (177)	1.14 (0.96-1.37)		1.10 (0.92-1.32)	**1.23 (1.01-1.52)**	1.22 (0.99-1.51)
Quintile 5 (high percentage)	703 (167)	1.04 (0.87-1.26)		1.01 (0.83-1.21)	1.17 (0.95-1.44)	1.13 (0.90-1.41)
p-trend		*0.62*		*0.95*	*0.05*	*0.16*

Model 1: Separate models for each neighborhood contextual factor; Model 2: Model includes nSES and population density; Model 3: Model includes nSES and high-intensity development; Model 4: Model includes population density and high-intensity development; Model 5: Model includes all three neighborhood contextual factors.

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), and household income (**<$30K/year**, $30-69K/year, ≥$70K/year). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[c] Based on the quintile distribution for block-group level population density in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[d] Based on the quintile distribution for block-group level high-intensity development in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Table 7. Associations of neighborhood SES, population density, and high-intensity development with disease-specific survival adjusted for additional case characteristics, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)					
	Model 5 (Main Model)[a]	**Model 5 + Screening[b]**	**Model 5 + Screening + Treatment[c]**	**Model 5 + Screening + Treatment + Lifestyle[d]**	**Model 5 + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N=3949	**N=3945**	**N=3924**	**N=2322**	**N=2297**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Neighborhood socioeconomic status (nSES)[f]					
Quintile 1 (low nSES)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	0.88 (0.74-1.04)	0.88 (0.74-1.05)	0.87 (0.73-1.03)	0.91 (0.70-1.17)	0.90 (0.70-1.16)
Quintile 3	0.97 (0.82-1.16)	0.98 (0.82-1.16)	0.95 (0.80-1.13)	0.91 (0.70-1.19)	0.90 (0.69-1.18)
Quintile 4	0.86 (0.72-1.02)	0.86 (0.72-1.02)	**0.83 (0.69-0.99)**	0.82 (0.63-1.06)	0.81 (0.63-1.05)
Quintile 5 (high nSES)	0.85 (0.69-1.05)	0.85 (0.69-1.05)	**0.82 (0.66-0.99)**	0.79 (0.58-1.08)	0.78 (0.57-1.07)
p-trend	*0.05*	*0.05*	***0.02***	***0.04***	***0.04***
Population density[g]					
Quintile 1 (low density)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	0.94 (0.76-1.17)	0.94 (0.76-1.16)	0.94 (0.76-1.17)	1.05 (0.76-1.43)	1.06 (0.77-1.46)
Quintile 3	0.87 (0.70-1.08)	0.87 (0.70-1.08)	0.87 (0.70-1.09)	1.01 (0.73-1.38)	1.01 (0.73-1.40)
Quintile 4	0.95 (0.77-1.17)	0.95 (0.77-1.17)	0.96 (0.78-1.18)	1.01 (0.81-1.49)	1.12 (0.82-1.52)
Quintile 5 (high density)	**0.73 (0.58-0.93)**	**0.73 (0.58-0.91)**	**0.72 (0.57-0.91)**	0.82 (0.60-1.12)	0.82 (0.59-1.13)
p-trend	***0.02***	***0.02***	***0.01***	*0.12*	*0.11*
High-intensity development[h]					
Quintile 1 (low percentage)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	1.02 (0.84-1.24)	1.02 (0.84-1.24)	0.98 (0.81-1.20)	0.81 (0.62-1.06)	0.80 (0.61-1.05)
Quintile 3	0.96 (0.77-1.20)	0.96 (0.77-1.20)	0.91 (0.73-1.15)	**0.72 (0.54-0.95)**	**0.72 (0.54-0.95)**
Quintile 4	1.22 (0.99-1.51)	1.23 (0.99-1.52)	1.17 (0.95-1.46)	0.97 (0.75-1.27)	0.96 (0.74-1.25)
Quintile 5 (high percentage)	1.13 (0.90-1.41)	1.14 (0.91-1.42)	1.12 (0.90-1.40)	0.94 (0.71-1.25)	0.93 (0.70-1.25)
p-trend	*0.16*	*0.16*	*0.14*	*0.51*	*0.46*

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[d] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[e] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for come from a Wald test of continuous predictors comparing the coefficient with zero

[f] Based on the quintile distribution for block-group nSES in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[g] Based on the quintile distribution for block-group population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[h] Based on the quintile distribution for block-group high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Table 8. Associations of neighborhood SES, population density, and high-intensity development with disease-specific survival by educational attainment and household income, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

		Educational attainment			
	Model 5	Low (≤High school) N=1143		High (≥Some college) N=2806	
	HR (95% CI)[a]	N (deaths)	HR (95% CI)[b]	N (deaths)	HR (95% CI)[b]
Neighborhood socioeconomic status (nSES)[c]					
Quintile 1 (low nSES)	1.00 (-)	311 (84)	1.00 (-)	366 (108)	1.00 (-)
Quintile 2	0.88 (0.74-1.04)	289 (76)	0.96 (0.73-1.26)	478 (115)	0.83 (0.66-1.03)
Quintile 3	0.97 (0.82-1.16)	222 (48)	0.93 (0.68-1.25)	533 (115)	0.96 (0.77-1.20)
Quintile 4	0.86 (0.72-1.02)	199 (45)	1.05 (0.74-1.48)	590 (92)	**0.76 (0.61-0.95)**
Quintile 5 (high nSES)	0.85 (0.69-1.05)	122 (27)	1.19 (0.85-1.67)	839 (134)	**0.77 (0.59-0.99)**
p-trend	*0.05*		*0.76*		*0.05*
Population density[d]					
Quintile 1 (low density)	1.00 (-)	239 (57)	1.00 (-)	430 (86)	1.00 (-)
Quintile 2	0.94 (0.76-1.17)	236 (59)	0.80 (0.56-1.13)	601 (119)	0.96 (0.73-1.27)
Quintile 3	0.87 (0.70-1.08)	228 (54)	0.69 (0.46-1.04)	604 (125)	0.89 (0.68-1.18)
Quintile 4	0.95 (0.77-1.17)	258 (70)	0.75 (0.52-1.09)	603 (125)	0.99 (0.76-1.30)
Quintile 5 (high density)	**0.73 (0.58-0.93)**	182 (40)	**0.59 (0.39-0.87)**	568 (109)	0.76 (0.57-1.02)
p-trend	***0.02***		***<0.01***		***0.04***
High-intensity development[e]					
Quintile 1 (low percentage)	1.00 (-)	228 (58)	1.00 (-)	595 (117)	1.00 (-)
Quintile 2	1.02 (0.84-1.24)	223 (39)	0.84 (0.58-1.22)	584 (107)	1.12 (0.88-1.44)
Quintile 3	0.96 (0.77-1.20)	234 (63)	0.95 (0.66-1.36)	593 (116)	1.02 (0.77-1.36)
Quintile 4	1.22 (0.99-1.51)	241 (64)	1.39 (0.95-2.03)	548 (113)	1.18 (0.90-1.55)
Quintile 5 (high percentage)	1.13 (0.90-1.41)	217 (56)	1.13 (0.76-1.69)	486 (111)	1.16 (0.88-1.54)
p-trend	*0.16*		*0.27*		*0.09*
		Household income[f]			
	Model 5	**Low (<$30K) N=824**		**High (≥$30K) N=2862**	
	HR (95% CI)[a]	**N (deaths)**	**HR (95% CI)[g]**	**N (deaths)**	**HR (95% CI)[g]**
Neighborhood socioeconomic status (nSES)[c]					
Quintile 1 (low nSES)	1.00 (-)	284 (84)	1.00 (-)	359 (101)	1.00 (-)

Quintile 2	0.88 (0.74-1.04)	195 (53)	0.74 (0.54-1.02)	521 (122)	0.88 (0.70-1.10)
Quintile 3	0.97 (0.82-1.16)	148 (39)	**1.39 (1.01-1.93)**	552 (114)	0.81 (0.64-1.02)
Quintile 4	0.86 (0.72-1.02)	105 (22)	0.88 (0.59-1.29)	632 (106)	0.82 (0.65-1.04)
Quintile 5 (high nSES)	0.85 (0.69-1.05)	92 (21)	1.14 (0.73-1.77)	798 (131)	0.80 (0.62-1.03)
p-trend	*0.05*		*0.83*		*0.05*
Population density[d]					
Quintile 1 (low density)	1.00 (-)	136 (30)	1.00 (-)	488 (103)	1.00 (-)
Quintile 2	0.94 (0.76-1.17)	156 (45)	0.93 (0.56-1.55)	632 (123)	0.99 (0.79-1.25)
Quintile 3	0.87 (0.70-1.08)	147 (35)	0.79 (0.44-1.42)	629 (135)	0.87 (0.69-1.11)
Quintile 4	0.95 (0.77-1.17)	180 (47)	0.87 (0.52-1.46)	620 (137)	0.93 (0.73-1.20)
Quintile 5 (high density)	**0.73 (0.58-0.93)**	205 (62)	0.69 (0.42-1.13)	493 (76)	**0.75 (0.57-0.98)**
p-trend	***0.02***		*0.12*		*0.12*
High-intensity development[e]					
Quintile 1 (low percentage)	1.00 (-)	127 (29)	1.00 (-)	643 (136)	1.00 (-)
Quintile 2	1.02 (0.84-1.24)	135 (29)	1.25 (0.75-2.07)	606 (106)	0.93 (0.75-1.16)
Quintile 3	0.96 (0.77-1.20)	148 (40)	1.35 (0.77-2.46)	629 (129)	0.92 (0.74-1.14)
Quintile 4	1.22 (0.99-1.51)	177 (50)	**2.15 (1.23-3.79)**	556 (113)	1.05 (0.83-1.32)
Quintile 5 (high percentage)	1.13 (0.90-1.41)	237 (71)	**1.73 (1.01-3.08)**	428 (90)	0.97 (0.75-1.27)
p-trend	*0.16*		*0.06*		*0.86*

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Based on the quintile distribution for block-group nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[d] Based on the quintile distribution for block-group population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[e] Based on the quintile distribution for block-group high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[f] Measured with respect to two years before diagnosis; estimates exclude 263 cases (7%) missing income

[g] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

Supplementary Table 1. Associations of neighborhood SES, population density, and high-intensity development with all-cause survival adjusted for additional neighborhood contextual and compositional factors, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

		Model 5[a]	Model 5 + Other neighborhood factors[b]
	N (deaths)	HR (95% CI)	HR (95% CI)
Neighborhood socioeconomic status (nSES)[c]			
Quintile 1 (low nSES)	677 (382)	1.00 (-)	1.00 (-)
Quintile 2	772 (355)	0.92 (0.81-1.05)	0.95 (0.82-1.09)
Quintile 3	750 (310)	1.03 (0.92-1.16)	1.08 (0.94-1.24)
Quintile 4	789 (266)	0.94 (0.83-1.07)	0.99 (0.85-1.16)
Quintile 5 (high nSES)	961 (278)	0.86 (0.73-1.01)	0.91 (0.75-1.09)
p-trend		*0.17*	***0.56***
Population density[d]			
Quintile 1 (low density)	669 (261)	1.00 (-)	1.00 (-)
Quintile 2	837 (319)	0.99 (0.86-1.15)	1.05 (0.87-1.27)
Quintile 3	832 (343)	1.01 (0.84-1.19)	1.06 (0.85-1.32)
Quintile 4	861 (370)	1.10 (0.95-1.26)	1.12 (0.90-1.40)
Quintile 5 (high density)	750 (298)	0.88 (0.75-1.04)	0.87 (0.68-1.11)
p-trend		*0.23*	***0.04***
High-intensity development[e]			
Quintile 1 (low percentage)	823 (317)	1.00 (-)	1.00 (-)
Quintile 2	807 (312)	**1.16 (1.01-1.35)**	**1.17 (1.01-1.35)**
Quintile 3	827 (329)	1.01 (0.84-1.19)	1.01 (0.83-1.19)
Quintile 4	789 (315)	1.10 (0.93-1.30)	1.10 (0.93-1.29)
Quintile 5 (high percentage)	703 (318)	1.11 (0.93-1.32)	1.07 (0.90-1.27)
p-trend		*0.45*	*0.57*

Open-space development (designed green areas, including public parks) level in neighborhood created by mapping NCLD 2001/2011 data to census block groups. Density of street nodes (intersections) was created by mapping OpenStreetMap data (OSM, data collected between 2007/2008-2019, https://www.openstreetmap.org) to census block groups and using these data to estimate the number of real nodes per square mile in each neighborhood; we eliminated any "dangle" nodes (e.g., nodes that refer to a cul-de-sac or dead end) and nodes pertaining to highway on- and off-ramps. Other neighborhood factors (percentage of households in neighborhood living in poverty, percentage of neighborhood population who were non-Hispanic White, percentage of neighborhood population who were non-Hispanic Black, percentage of neighborhood population who were non-Hispanic Asian, percentage of neighborhood population who were non-Hispanic other race, percentage of neighborhood population who were Hispanic) we created using block group-level data from the 2000 US Decennial Census/ACS 5-year 2013-2017 estimates.

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), nSES (in quintiles), population density (in quintiles), high-intensity development (in quintiles), open-space development (in quintiles), poverty (in quartiles), percentage non-Hispanic White (binary, cut at median), percentage non-Hispanic Black (binary, cut at median), percentage non-Hispanic Asian (binary, cut at median), percentage non-Hispanic other (binary, cut at median), percentage Hispanic (binary, cut at median), and street node (intersection) density (in quartiles). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[d] Based on the quintile distribution for block-group level population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[e] Based on the quintile distribution for block-group level high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Supplementary Table 2. Associations of neighborhood SES, population density, and high-intensity development with all-cause survival adjusted for additional case characteristics in a complete case analysis (N=2297), Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)						
		Model 5 (Main Model)[a]	**Model 5 + Screening[b]**	**Model 5 + Screening + Treatment[c]**	**Model 5 + Screening + Treatment + Lifestyle[d]**	**Model 5 + Screening + Treatment + Lifestyle + Comorbidities[e]**
	N (deaths)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Neighborhood socioeconomic status (nSES)[f]						
Quintile 1 (low nSES)	326 (169)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	401 (173)	0.88 (0.73-1.04)	0.88 (0.73-1.04)	0.88 (0.74-1.05)	0.88 (0.74-1.05)	0.89 (0.75-1.06)
Quintile 3	425 (158)	0.92 (0.77-1.08)	0.92 (0.77-1.09)	0.91 (0.77-1.08)	0.92 (0.76-1.09)	0.92 (0.78-1.10)
Quintile 4	492 (154)	**0.81 (0.67-0.97)**	**0.82 (0.68-0.98)**	**0.81 (0.68-0.97)**	**0.82 (0.68-0.99)**	**0.81 (0.68-0.98)**
Quintile 5 (high nSES)	653 (166)	**0.79 (0.63-0.99)**	**0.80 (0.64-0.99)**	**0.78 (0.63-0.97)**	**0.79 (0.63-0.98)**	**0.80 (0.64-0.99)**
p-trend		*0.08*	*0.09*	*0.06*	*0.07*	*0.10*
Population density[g]						
Quintile 1 (low density)	362 (119)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	495 (170)	1.04 (0.85-1.27)	1.03 (0.85-1.26)	1.03 (0.84-1.26)	1.03 (0.84-1.27)	1.04 (0.85-1.27)
Quintile 3	475 (166)	1.05 (0.85-1.30)	1.05 (0.85-1.30)	1.07 (0.86-1.32)	1.08 (0.87-1.33)	1.07 (0.86-1.32)
Quintile 4	515 (209)	1.19 (0.97-1.46)	1.19 (0.97-1.46)	1.20 (0.98-1.46)	1.20 (0.98-1.47)	1.19 (0.98-1.46)
Quintile 5 (high density)	450 (156)	0.85 (0.68-1.08)	0.85 (0.68-1.07)	0.86 (0.68-1.08)	0.86 (0.68-1.09)	0.86 (0.68-1.09)
p-trend		*0.11*	*0.11*	*0.07*	*0.08*	*0.07*
High-intensity development[h]						
Quintile 1 (low percentage)	497 (164)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	479 (165)	1.08 (0.91-1.27)	1.08 (0.91-1.28)	1.06 (0.90-1.26)	1.07 (0.90-1.27)	1.06 (0.89-1.25)
Quintile 3	480 (175)	**0.81 (0.67-0.99)**	**0.82 (0.67-0.99)**	**0.79 (0.65-0.97)**	**0.79 (0.65-0.96)**	**0.79 (0.65-0.96)**
Quintile 4	454 (167)	0.93 (0.77-1.13)	0.94 (0.77-1.13)	0.91 (0.75-1.11)	0.91 (0.74-1.10)	0.91 (0.75-1.11)
Quintile 5 (high percentage)	387 (149)	0.89 (0.73-1.09)	0.89 (0.74-1.09)	0.88 (0.72-1.08)	0.87 (0.72-1.07)	0.87 (0.71-1.06)
p-trend		*0.92*	*0.89*	*0.88*	*0.90*	*0.94*

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[d] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[e] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[f] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[g] Based on the quintile distribution for block-group level population density in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[h] Based on the quintile distribution for block-group level high-intensity development in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Supplementary Table 3. Associations of neighborhood SES, population density, and high-intensity development with disease-specific survival adjusted for additional neighborhood contextual and compositional factors , Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

		Model 5[a]	Model 5 + Other neighborhood factors[b]
	N (deaths)	HR (95% CI)	HR (95% CI)
Neighborhood socioeconomic status (nSES)[c]			
Quintile 1 (low nSES)	677 (192)	1.00 (-)	1.00 (-)
Quintile 2	772 (191)	0.90 (0.70-1.16)	0.89 (0.74-1.07)
Quintile 3	750 (163)	0.90 (0.69-1.18)	0.98 (0.80-1.20)
Quintile 4	789 (137)	0.81 (0.63-1.05)	0.86 (0.70-1.06)
Quintile 5 (high nSES)	961 (161)	0.78 (0.57-1.07)	0.87 (0.69-1.11)
p-trend		***0.04***	*0.16*
Population density[d]			
Quintile 1 (low density)	669 (143)	1.00 (-)	1.00 (-)
Quintile 2	837 (178)	1.06 (0.77-1.46)	0.96 (0.74-1.23)
Quintile 3	832 (179)	1.01 (0.73-1.40)	0.88 (0.63-1.20)
Quintile 4	861 (195)	1.12 (0.82-1.52)	0.98 (0.71-1.35)
Quintile 5 (high density)	750 (149)	0.82 (0.59-1.13)	0.81 (0.57-1.13)
p-trend		*0.11*	*0.10*
High-intensity development[e]			
Quintile 1 (low percentage)	823 (175)	1.00 (-)	1.00 (-)
Quintile 2	807 (146)	0.80 (0.61-1.05)	1.02 (0.85-1.24)
Quintile 3	827 (179)	**0.72 (0.54-0.95)**	0.97 (0.79-1.22)
Quintile 4	789 (177)	0.96 (0.74-1.25)	1.23 (0.99-1.55)
Quintile 5 (high percentage)	703 (167)	0.93 (0.70-1.25)	1.18 (0.94-1.51)
p-trend		*0.46*	*0.08*

Open-space development (designed green areas, including public parks) level in neighborhood created by mapping NCLD 2001/2011 data to census block groups. Density of street nodes (intersections) was created by mapping OpenStreetMap data (OSM, data collected between 2007/2008-2019, https://www.openstreetmap.org) to census block groups and using these data to estimate the number of real nodes per square mile in each neighborhood; we eliminated any "dangle" nodes (e.g., nodes that refer to a cul-de-sac or dead end) and nodes pertaining to highway on- and off-ramps. Other neighborhood factors (percentage of households in neighborhood living in poverty, percentage of neighborhood population who were non-Hispanic White, percentage of neighborhood population who were non-Hispanic Black, percentage of neighborhood population who were non-Hispanic Asian, percentage of neighborhood population who were non-Hispanic other race, percentage of neighborhood population who were Hispanic) we created using block group-level data from the 2000 US Decennial Census/ACS 5-year 2013-2017 estimates.

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), nSES (in quintiles), population density (in quintiles), high-intensity development (in quintiles), open-space development (in quintiles), poverty (in quartiles), percentage non-Hispanic White (binary, cut at median), percentage non-Hispanic Black (binary, cut at median), percentage non-Hispanic Asian (binary, cut at median), percentage non-Hispanic other (binary, cut at median), percentage Hispanic (binary, cut at median), and street node (intersection) density (in quartiles). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[d] Based on the quintile distribution for block-group level population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[e] Based on the quintile distribution for block-group level high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Supplementary Table 4. Associations of neighborhood SES, population density, and high-intensity development with disease-specific survival adjusted for additional case characteristics in a complete case analysis, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)

		Model 5 (Main Model)[a]	Model 5 + Screening[b]	Model 5 + Screening + Treatment[c]	Model 5 + Screening + Treatment + Lifestyle[d]	Model 5 + Screening + Treatment + Lifestyle + Comorbidities[e]
	N (deaths)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Neighborhood socioeconomic status (nSES)[f]						
Quintile 1 (low nSES)	326 (89)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	401 (102)	0.87 (0.68-1.12)	0.86 (0.67-1.11)	0.87 (0.68-1.12)	0.91 (0.70-1.17)	0.90 (0.70-1.16)
Quintile 3	425 (84)	0.91 (0.70-1.18)	0.91 (0.70-1.18)	0.88 (0.68-1.15)	0.91 (0.69-1.18)	0.90 (0.69-1.18)
Quintile 4	492 (87)	0.79 (0.61-1.02)	0.79 (0.61-1.02)	**0.78 (0.60-0.99)**	0.81 (0.63-1.05)	0.81 (0.63-1.05)
Quintile 5 (high nSES)	653 (93)	0.76 (0.56-1.04)	0.76 (0.56-1.04)	0.75 (0.55-1.01)	0.79 (0.58-1.08)	0.78 (0.57-1.07)
p-trend		***0.03***	***0.03***	***0.02***	***0.04***	***0.04***
Population density[g]						
Quintile 1 (low density)	362 (63)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	495 (98)	1.12 (0.82-1.54)	1.10 (0.80-1.51)	1.06 (0.77-1.47)	1.06 (0.77-1.45)	1.06 (0.77-1.46)
Quintile 3	475 (90)	1.03 (0.75-1.41)	1.01 (0.74-1.39)	1.02 (0.75-1.40)	1.01 (0.73-1.38)	1.01 (0.73-1.40)
Quintile 4	515 (118)	1.15 (0.85-1.56)	1.13 (0.84-1.54)	1.13 (0.83-1.53)	1.12 (0.82-1.51)	1.12 (0.82-1.52)
Quintile 5 (high density)	450 (86)	0.83 (0.60-1.14)	0.82 (0.59-1.12)	0.81 (0.59-1.10)	0.81 (0.59-1.11)	0.82 (0.59-1.13)
p-trend		*0.14*	*0.13*	*0.05*	*0.10*	*0.11*
High-intensity development[h]						
Quintile 1 (low percentage)	497 (95)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)	1.00 (-)
Quintile 2	479 (75)	0.84 (0.64-1.09)	0.84 (0.64-1.09)	0.80 (0.61-1.05)	0.80 (0.61-1.05)	0.80 (0.61-1.05)
Quintile 3	480 (96)	**0.71 (0.53-0.94)**	**0.71 (0.54-0.95)**	**0.69 (0.52-0.92)**	**0.72 (0.54-0.95)**	**0.72 (0.54-0.95)**
Quintile 4	454 (97)	0.98 (0.76-1.27)	0.99 (0.77-1.30)	0.95 (0.73-1.24)	0.96 (0.74-1.25)	0.96 (0.74-1.25)
Quintile 5 (high percentage)	387 (92)	0.91 (0.69-1.21)	0.92 (0.70-1.22)	0.90 (0.68-1.20)	0.94 (0.71-1.24)	0.93 (0.70-1.25)
p-trend		*0.63*	*0.56*	*0.52*	*0.48*	*0.46*

[a] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), and all three neighborhood contextual factors. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[b] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, and history of preventative CRC screening (**never screened,** first screening ≤2 years before diagnosis, first screening >2 years before diagnosis). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[c] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), and chemotherapy in initial course of CRC treatment (**no**, yes, unknown). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[d] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), and met ACS physical activity recommendation (**no**, yes) before diagnosis. Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[e] Estimates adjusted for age at diagnosis (<40, 40-49, 50-59, **60-69**, ≥70), year of diagnosis (continuous), race/ethnicity (**non-Hispanic White**, other), marital status (**single or never married or living unmarried**, married, separated or divorced, widowed, unknown), gender (**male**, female), educational attainment (**≤high school degree**, some college/vocational or technical school degree, ≥college degree), household income (**<$30K/year**, $30-69K/year, ≥$70K/year), all three neighborhood contextual factors, history of preventative CRC screening (**never screened**, first screening ≤2 years before diagnosis, first screening >2 years before diagnosis), surgery in initial course of CRC treatment (**no**, yes), radiation in initial course of CRC treatment (**no**, yes), chemotherapy in initial course of CRC treatment (**no**, yes, unknown), cigarette smoking history (**never**, former, current), heavy alcohol consumption before diagnosis as defined by the ACS (**nondrinker**, no, yes), met ACS physical activity recommendation (**no**, yes) before diagnosis, body mass index (BMI) before diagnosis (**<25**,25-29.9, ≥30), and self-report of diabetes diagnosis (**no**, yes). Baseline hazards stratified by 2000/2018 SEER Summary Stage (local, regional, distant, unknown/unstaged). Estimates included robust standard errors to account for within-neighborhood dependence. P-trends for contextual factors come from a Wald test of continuous variables comparing the coefficient with zero

[f] Based on the quintile distribution for block-group nSES in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[g] Based on the quintile distribution for block-group population density in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

[h] Based on the quintile distribution for block-group high-intensity development in the underlying case population (cases diagnosed between 1998-2007, 2016-2018) in the region

Chapter 3: Impacts of individual and neighborhood socioeconomic status on health-related quality of life following a colorectal cancer diagnosis

ABSTRACT

Background. Evidence indicates inequalities in socioeconomic status (SES) as primary drivers of persistent disparities in health-related quality of life (HRQoL) after a colorectal cancer (CRC) diagnosis. However, research evaluating the effects of multiple SES factors, including individual SES (iSES) characteristics and neighborhood SES (nSES), on HRQoL in CRC cases is limited.

Methods. We included data from 1320 population-based CRC cases diagnosed 2016-2018 in the Seattle-Puget Sound region. We focused on the independent and joint effects of three iSES factors (educational attainment, household income, insurance type) and an nSES index constructed from American Community Survey block group-level data. We measured overall HRQoL after a recent CRC diagnosis using the Functional Assessment of Cancer Therapy - Colorectal (FACT-C) survey. We evaluated SES effects on overall HRQoL using generalized linear models with robust standard errors to account for within-neighborhood dependence.

Results. After adjusting for iSES factors and nSES, having a lower income (p-trend: <0.01) and using Medicaid as the primary insurance payer (p-value: <0.01) were each related to lower overall HRQoL after CRC. Low income effects were largest given low nSES (β:-12.57, 95% CI:-16.90,-8.24), while Medicaid effects were strong in both high nSES (β:-9.81, 95% CI:-15.38,-4.25) and low nSES neighborhoods (β:-9.79, 95% CI:-15.66,-3.92). Education and nSES were not independently related to meaningful differences in HRQoL.

Conclusion. Lower income and Medicaid insurance are associated with poorer HRQoL in recently diagnosed CRC cases. Future research should evaluate these associations in other populations and other geographic locations so as to improve knowledge of potential intervention targets.

INTRODUCTION

Each year, nearly 135,000 individuals are diagnosed with colorectal cancer (CRC) in the United States (US).[1] Approximately two-thirds of CRC cases are living five years after diagnosis, reflecting advancements in early detection and the quality of treatment as well as the aging and growth of the US population.[1,3,61] However, a diagnosis of CRC, and the physical, psychosocial, and financial effects of its treatment, may still lead to substantial long-term hardships for CRC cases and their families.[3,10,11,84,106] Among cases, these hardships may result in progression or recurrence of CRC, development of second cancers, and a lower likelihood of survival.[3,10,36] Thus, as CRC treatment modalities continue to improve, adding to our understanding of factors associated with health-related quality of life (HRQoL) in CRC cases can potentially serve as intervention targets to enhance both survivorship and survival.[3,4,9,54,151]

In the US, CRC cases often report poorer quality of life and wellbeing relative to the general population.[3,5,9,152] Prior evidence suggests that HRQoL in CRC cases is impacted by a complex mix of factors, including patient demographics, initial treatment received, time since diagnosis, physical and social environment characteristics, and socioeconomic status (SES) factors.[3,9,54,153-155] In particular, disparities in HRQoL after a CRC diagnosis may be due to SES inequalities that result in differential access to supportive medical care,[9,35,52,54,61] defined as care intended to improve HRQoL for patients with serious or life-threatening illness.[156] Characteristics of individual-level SES (iSES), such as educational attainment, household income, and insurance type at diagnosis, may affect a CRC case's HRQoL by enabling their access to material (e.g., quality health and supportive care services, appropriate foods) or social (e.g., opportunities for social participation and interaction, coping) resources that, in turn, help them to cope with their disease, its treatment, and related morbidity.[21-25,31,53,54] Neighborhood SES (nSES) may also affect HRQoL by influencing the presence of elements in the physical (e.g., level of environmental pollutants, walkability features) and social (e.g., social cohesion and isolation, community efficacy) environments, thereby impacting the area availability of material and social resources.[24,29,33,63,64] Further, the effect of iSES factors may be different given the context of nSES, thereby modifying the likelihood of low HRQoL following a CRC diagnosis.[22,25,28,65,66] For example, a CRC case reporting low household income and living in a high nSES neighborhood may benefit from the potentially greater availability of cancer care services and other material resources and have higher HRQoL relative to a CRC case with

low income and low nSES.[24,67,68] Conversely, this example CRC case with low income and high nSES may also experience low HRQoL because they are unable to meet the higher costs of collective resources in their neighborhood.[21,23,25,70]

Although previous investigations are still limited in number, evidence consistently suggests associations between lower levels of iSES, including lower household income and Medicaid insurance, and poorer HRQoL in both recently diagnosed CRC cases and CRC survivors.[9,16,54,107,155,157-159] However, to our knowledge, only a single prior study of HRQoL in CRC cases has assessed the independent effects of multiple iSES factors within the same study,[9] and no previous work has examined the effects of iSES factors within the context of nSES.

Combining data from a population-based cohort of CRC cases in the Seattle-Puget Sound region with data on the neighborhood socioeconomic environment, we assessed the independent and joint effects of iSES factors (i.e., educational attainment, household income, insurance type) and nSES with self-reported HRQoL following a recent diagnosis of incident, invasive CRC. The findings from this study could make a substantive contribution to understanding the influence of individual and neighborhood socioeconomic resources on HRQoL,[3,34,84] thereby bettering the foundation for more effective interventions and policy-based solutions.[51,53]

METHODS

Study design and population

Our study population included individuals who were diagnosed with incident, invasive CRC between 2016-2018 and participated in the Puget Sound Colorectal Cancer Cohort (PSCCC), a population-based cohort study of CRC risk and survival.[74] We ascertained all CRC cases via the population-based Surveillance, Epidemiology, and End Results (SEER) cancer registry of the Seattle-Puget Sound region, which covers 13 counties in in western Washington state.[73]

Details of earlier recruitment phases and protocols (1997-2008) in the PSCCC have been published elsewhere.[74] Briefly, eligible PSCCC participants included individuals who resided within the SEER catchment area and were aged 20-74 years at the time of diagnosis. We made initial contact with potentially eligible CRC cases via phone, mail, and/or email, and only enrolled cases who were able to

complete the baseline survey in English and who maintained a residence in the catchment area. As of 20 August 2019, we identified a total of 3142 potentially eligible participants through SEER, of whom 1321 (42%) refused participation, were deceased, or were lost to follow-up prior to the study interview.

Measures

Data sources

According to PSCCC protocol, participants completed a risk factor survey at enrollment via structured phone interview, or by self-administered online or paper survey.[75] Baseline surveys were administered an average of 6.5 months after diagnosis (median: 5.5 months, IQR: 3.2 months). The baseline survey collected data on some iSES factors (e.g., educational attainment, household income) individual and family cancer history, current comorbidities (e.g., diabetes, colitis), physical attributes (e.g., height, weight), and limited lifestyle behaviors (e.g., CRC screening history, physical activity level, smoking status, alcohol use) that occurred before diagnosis.

Another primary data source was the SEER cancer registry of the Seattle-Puget Sound.[73] The registry requires reporting of an array of CRC case factors measured at or around the time of diagnosis, including demographic characteristics (e.g., gender, race/ethnicity, age, marital status), clinicopathologic features (e.g., stage at diagnosis), limited iSES factors (e.g., insurance type at diagnosis), first course of treatment (e.g., surgery, radiation, chemotherapy), and residential address at diagnosis.

The registry provided our study with residential address information for each CRC case in geocoded form. Geocoding protocol for SEER stipulated that all home addresses were standardized to US postal service format and then geocoded to a latitude/longitude coordinate while employing, in order of priority, rooftop accuracy or street-level accuracy.[73,76] We reviewed addresses missing a SEER geocode, and performed a second geocoding attempt using HERE data from 2017 Esri Business Analyst Desktop as the reference dataset (Redlands, CA).

Using the geocoded residential address at diagnosis, we assigned each CRC case a census block group and mapped them to block group data from the American Community Survey (ACS) 2013-2017 5-year estimates.[77,82] Census block groups are relatively permanent statistical subdivisions of a county or county equivalent that generally contain between 600 – 3000 residents, with an optimal population of 1,500 individuals, and whose borders are often delineated with input from local residents.[77,78] Block groups are

also the smallest geographic area for which most census information is available;[27] as such, epidemiologists and population health researchers commonly use block groups as proxy units for neighborhood effect studies.[52,81]

Exposure assessment

This study focused on four primary exposures – three dimensions of iSES (i.e., educational attainment, household income, insurance type) and an index measure of nSES.

We measured educational attainment and household income using responses from the PSCCC baseline survey.[75] For educational attainment, CRC cases responded to the question "What is the highest level of education that you (have) completed?" and were provided with eight possible levels, including "Do Not Know/Prefer Not to Answer." We collapsed these responses into three categories: high school degree or less, some college or a vocational school/technical school degree, and college degree or graduate school.[22,83] For household income, CRC cases were asked "(As of) about two years ago, which of the following best describes your total annual household income from all sources before taxes?" and were given seven possible responses, with a lowest category of <$15K, an uppermost category of ≥$70K, and categories for "Do Not Know" and "Prefer Not to Answer." For analyses, we employed a four-category definition of income: less than $30K/year, $30-69K/year, at least $70K/year, and missing (cases who did not know or declined to report).[9,22] While we did not report effect estimates for cases missing income (N=73), we included the group in analytic models since these data may be missing not at random (MNAR) based on unmeasured social norms that may also impact HRQoL in CRC cases.[22,30,84,102]

We measured insurance type using SEER data on primary payer/insurance carrier at CRC diagnosis, as obtained by the reporting facility.[160] We categorized these data into a three-category measure: private or government insurance (i.e., private insurance, Medicare, Veterans Affairs, TRICARE, Military, Indian/Public Health Service), Medicaid insurance, and unknown/uninsured.[9,16,44] While we did not report association estimates for the unknown/uninsured category (N=200), we chose to include it in statistical models because of possible MNAR data.[16] A total of 11 CRC cases reported being uninsured at diagnosis.

For nSES, we used a census block group-level index measure previously detailed by Diez Roux and colleagues.[85] The index uses six aggregate census-based variables identified via factor analysis: median

household income, median housing unit value, percentage of households earning income from investments, percentage of persons aged ≥ 25 years who have completed high school, percentage of persons aged ≥ 25 years who have completed a college degree, and percentage of persons aged ≥ 16 years in a managerial or professional occupation. Income-based variables (i.e., median household income and median housing unit value) were transformed using the natural logarithm.[85] The standardized z-score for each census variable was calculated based on the 3,346 block groups in the SEER catchment area and then each z-score summed to create an index in which higher scores corresponded with lower nSES.[22,27] We assigned each CRC case the nSES index score of their census block group. The median nSES score in our study population (median: 13.91, interquartile range [IQR]: 6.74) was extremely similar to the median nSES score in the underlying case population containing all of the potentially eligible CRC cases identified via SEER (median: 14.89, IQR: 6.64). Despite this similarity, we created nSES quartiles based on the quartile distribution of nSES in this underlying case population so as to limit non-differential measurement error.[22,65,86]

To assess joint associations of iSES factors and nSES with CRC survival, we created three combination variables: one using indicators for education and nSES, one with indicators for income and nSES, and one consisting of indicators for insurance and nSES.[22,25,65] We defined low education as having a high school degree or less and high education as attending at least some college or having a vocational school/technical school degree. Low income included cases who reported an income of less than $30Kyear, while high income included CRC cases reporting at least $30K/year; we excluded cases missing income information from joint effect analyses (N=73). We grouped insurance as insured and Medicaid, and excluded cases with unknown insurance type from joint effect analyses (N=200). Low nSES included quartiles 3 and 4 and high nSES consisted of quartiles 1 and 2.

Outcome assessment

We assessed HRQoL using the Functional Assessment of Cancer Therapy - Colorectal (FACT-C) tool, which was included in the PSCCC baseline survey.[3,6,161,162] The tool is a version of the Functional Assessment of Cancer Therapy – General (FACT-G), a well validated measure of self-report HRQoL, specific to individuals undergoing treatment for CRC.[3,151,162] The FACT-C comprises five subdomains of wellbeing: physical (PWB, seven items), social/family (SWB, seven items), emotional (EWB, six items),

functional (FWB, seven items), and CRC-specific (CCS, seven items).[3,163] Subdomain items refer to the prior week and are scored on a scale of 0 ("not at all") to 4 ("very much"). We scored subdomains based on the predefined scoring guidelines, and, as per this protocol, participants were required to have answered at least half of a subdomain's items to have a score for that subdomain.[161,163] Subdomains are summed together to create overall HRQoL, but can also be analyzed separately.[151,152] The FACT-C has been found to be reproducible and comparable to other measures of HRQOL;[161,162] the tool has also been noted to be able to differentiate between clinically distinct groups and to have good psychometric properties.[3,151,152,163] A higher overall HRQoL score and higher subdomain scores indicate better HRQoL. Overall HRQoL has a possible score range of 0-136 points, and the subdomain scores range from 0-28 (PWB, SWB, FWB, CCS) or 0-24 (EWB).[151,162] A five-to-eight-point difference in overall HRQoL, and a two-point difference in subdomain HRQoL, is considered clinically meaningful for CRC cases, [151,152,162,164] and we used these definitions in our interpretations.

Statistical analysis

We used generalized linear models assuming a gaussian distribution to obtain adjusted estimates (β) and 95% confidence intervals (CI) for associations of iSES factors and nSES with differences in mean overall HRQoL. We employed robust standard errors to account for within-neighborhood dependence[92] and also to control for mild violation of the homoskedasticity and normal distribution assumptions of linear regression.[165,166] Of the 3346 block groups in the region, 1035 contained at least one participating CRC case and so were included in this analysis; of these, 808 (61%) block groups contained only a single participating CRC case, making true multilevel modeling infeasible.[81] In a secondary analysis, we also constructed separate models for each subdomain of HRQoL.

We mutually adjusted all estimates for all iSES characteristics (i.e., educational attainment, household income, insurance type) and nSES, as well as for gender, race/ethnicity, age at diagnosis, marital status, tumor stage at diagnosis,[94,95] and time since diagnosis (in days). Trends for SES factors (including a p-value rather than p-trend for insurance type) were examined by taking each primary predictor and performing a Wald test of the coefficient compared with zero; for nSES, we performed a Wald test on the measure's continuous form. We were cautious in our interpretation of linear trends, and, in the absence of a main association, only reported statistically significant P-trends given clear increasing or decreasing

effect estimates across the levels of the predictors. We used the variance inflation factors (VIF) and tolerances (1/VIF) to check for multicollinearity between terms in the final model. We used a tolerance value of <0.1, comparable to a VIF of 10, as the threshold for unacceptable multicollinearity;[9,163] no variables in the final regression analyses showed a tolerance value <0.1.

All model covariates were defined as shown in Table 1. Two-sided tests were considered statistically significant at the α=0.05 level. We mapped CRC cases to block group-level data using R 3.5.3/3.6.1 (https://www.r-project.org/) and RStudio 1.2.1 (https://rstudio.com); we conducted all statistical analyses in STATA 15 (College Station, TX). This research was approved by the Institutional Review Board at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

RESULTS

Study population

Our analyses included data from 1320 individuals recently diagnosed with incident, invasive CRC (Table 1). The median time from diagnosis to completing the ACCESS baseline survey was 165 days (IQR: 95 days). The median age at diagnosis was 59 years (IQR: 16 years), and only 36% of cases were diagnosed at a local stage of disease. Over half of the cases were male, were married, reported as non-Hispanic White, or had surgery or radiation as part of their initial course of CRC treatment. We observed that cases were more likely to report attaining at least a college degree versus attending some college (45% versus 35%), having a household income before diagnosis of at least $70K/year versus less than $70K/year (52% versus 43%), having private or other government insurance versus Medicaid as the primary payer at diagnosis (75% versus 9%), and living in a neighborhood with high (quartile 1) versus low (quartile 4) nSES (41% versus 11%).

In this study population, the mean overall HRQoL score was 103.1 (SD: 19.9) (Table 1), which is comparable to mean HRQoL scores from previous population-based studies of CRC cases.[5,6,9,154,162,164] We observed lower mean HRQoL scores in cases who were under 50 years old at diagnosis, not married, or living in a low nSES neighborhood, as well as in cases who had a regional or distant stage tumor, a high school degree or less, an income of less than $30K/year, Medicaid insurance, or chemotherapy or radiation as part of their initial treatment course. For cases with lower education, income, or with Medicaid

insurance, HRQoL scores appeared lowest given the context of living in a low nSES neighborhood. Overall mean HRQoL scores did not appear to vary by gender or by time since diagnosis. Educational attainment, household income, and insurance type were each weakly correlated with nSES as well as with each other (Table 2). Joint distributions of iSES factors and nSES illustrated that the majority of cases living in high nSES neighborhoods had attained a college degree or reported a household income of at least $70K/year, while the majority of cases in low nSES neighborhoods had attended some college and reported less than $70K/year in income. Moderate-high (quartile 2), moderate-low (quartile 3), and low nSES neighborhoods had roughly equal proportions of cases who had attended some college or obtained a vocational/technical school degree. At each level of nSES, the majority of cases had insurance other than Medicaid at diagnosis; however, the proportion of cases with Medicaid insurance in moderate-low and low nSES neighborhoods was roughly twice the percentage of Medicaid-presenting cases in moderate-high and high nSES neighborhoods.

Regression results

After adjusting for case and treatment characteristics, we observed evidence that annual household income and insurance type each had an independent effect on overall HRQoL score following a CRC diagnosis (Table 3). Compared to cases reporting an annual household income before diagnosis of at least $70K/year, cases with an income of less than $30K/year experienced significantly poorer HRQoL (β: -7.93, 95% CI: -11.50, -4.35). Likewise, cases presenting with Medicaid at diagnosis reported lower HRQoL relative to cases with other types of insurance (β: -7.82, 95% CI: -12.04, -3.60). Both of these effects increased in magnitude given the context of living in a low nSES neighborhood (quartiles 3 and 4) (low income/low nSES β: -12.57, 95% CI: -16.90, -8.24; Medicaid/low nSES β: -9.79, 95% CI: -15.66, -3.92). However, relative to insured cases who lived in a high nSES neighborhood, cases with Medicaid who resided in a high nSES neighborhood also experienced poorer HRQoL (β: -9.81, 95% CI: -15.38, -4.25). We also found indications that living in a low nSES neighborhood had a modest but not clinically significant independent effect on lower HRQoL (β: -4.58, 95% CI: -8.26, -0.91). Educational attainment was not a strong predictor of overall HRQoL in this study population.

With respect to subdomains of HRQoL, we noted lower household income to be significantly related to poorer social and functional wellbeing (SWB β: -2.68, 95% CI: -3.71, -1.65; FWB β: -2.30, 95% CI: -3.38, -

1.22), and Medicaid to be significantly related to poorer functional wellbeing and modestly associated with poorer physical wellbeing (FWB β: -2.23, 95% CI: -3.51, -0.95; PWB β: -1.88, 95% CI: -2.47, -0.69) (Table 4). Akin to findings for overall HRQoL, these effects were also strongest given the context of living in a low nSES neighborhood. In addition, relative to CRC cases with high income and high nSES, cases with low income and low nSES also reported poorer physical and CRC-specific wellbeing (PWB β: -2.48, 95% CI: -3.74, -1.22; CCS β: -2.29, 95% CI: -3.37, -1.21).

Our findings were consistent after using logistic regression to model the independent and joint effects of iSES factors and nSES on odds of very low HRQoL (Supplementary Table 1), as well as following additional adjustment for primary tumor site, comorbidities (i.e., body mass index [BMI, kg/m^2], self-report of diabetes diagnosis), and lifestyle behaviors (i.e., smoking status, heavy alcohol consumption, average daily sedentary activity) (Supplementary Table 2).

DISCUSSION

Within this population-based cohort of individuals recently diagnosed with incident CRC, we found clinically significant associations of two characteristics of iSES, annual household income and insurance type, with self-reported overall HRQoL. While lower nSES was not a meaningful independent predictor of HRQoL following a CRC diagnosis, we noted larger lower income effects given the context of living in a low nSES neighborhood. Conversely, compared to CRC cases with private or other government insurance, cases with Medicaid coverage reported lower HRQoL in both low and high nSES neighborhoods. In addition, Medicaid effects were enhanced when we considered the joint association of insurance and nSES with survival, suggesting that the mechanisms underlying the impact of Medicaid may be different between low and high nSES neighborhoods. Thus, our findings underscore the necessity of considering neighborhood socioeconomic context to better characterize iSES effects on HRQoL in CRC cases.

To the best of our knowledge, we are only the second investigation of HRQoL following a CRC diagnosis to simultaneously assess the independent effects of multiple iSES factors.[9] Our findings on the effects of income and insurance type are consistent with those from this recent population-based study of incident CRC diagnoses in New Mexico, which suggested that lower income and Medicaid insurance were each

independently associated with lower overall and functional HRQoL.[9] Our observation that lower income impacts overall HRQoL, as well as social and functional wellbeing, also mirrors results from a small but growing body of research that indicates lower income to be related to poorer physical and psychosocial functioning in recently diagnosed cases as well as in CRC survivors who have completed their initial course of treatment.[9,107,154,155,158] However, as far as we can tell, no prior study of HRQoL after a CRC diagnosis has explored the joint effects of iSES characteristics and nSES.

The mechanisms underlying our findings for low income effects are presumably complex.[9,19,23,167] Past research suggests that a large number of CRC cases experience some form of economic hardship after their diagnosis, including cancer- and treatment-related financial toxicity.[9,35,84,105,107,159] This toxicity often increases during the initial treatment period[49,105,111,112] and can lead to long-term financial instability in all CRC cases,[35,106,107] but especially in cases who reported a lower level of income prior to their diagnosis.[30,167] When defined by insufficient household income or unexpected income precarity (e.g., an event causing an individual to live "paycheck-to-paycheck"[23]) around the time of cancer diagnosis, economic hardship in cancer survivors has also been observed as a predictor of non-adherence to surveillance screening,[84,167] of delaying or forgoing medical and supportive care, [84,167] and of physical and psychosocial strain that may impact long-term prognosis [3,10] via stress-related biological processes influencing cancer progression.[10,36,104,105,167] Income can also be leveraged to purchase helpful and necessary material resources separate from health care (e.g., housing, transportation, healthy and non-irritating foods) and enable different options for social participation (e.g., support groups, access to commercial locations that involved social interaction) as well as an individual-level sense of security and personal control during a period of enormous strain.[9,24,54,64] Notably, using income to access any material and social resources important to CRC care and coping depends on the local resource availability, which is likely heavily influenced by nSES.[24,33,69,158] A final, probable contributor to our income-related findings is our cross-sectional study design, in which income and HQRoL were self-reported in the same baseline interview. Thus, even though the referent period for our income measure was two years prior to CRC diagnosis and the referent period for HRQoL was the week prior to PSCCC baseline interview, there is likely some influence of health and wellbeing on earnings and savings that slightly inflated our

estimates.[54,84,155] This may be particularly true with respect to the functional wellbeing subdomain, which includes two items asking about ability to work and satisfaction from work.[54,162]

Presenting with Medicaid insurance at diagnosis has been previously related to greater odds of late-stage CRC diagnosis[16,44] and higher risks of CRC recurrence and mortality.[9,16,45,168] Consistent with our findings, limited recent evidence also indicates that, compared to cases with other types of insurance, CRC cases with Medicaid insurance report poorer overall HRQoL and physical wellbeing.[9,84] Differences between Medicaid and other insurance types (e.g., private insurance, Medicare) in access to and reimbursement for health services, including supportive care, may help to explain our results.[9,11,114,140] When we explored joint associations between insurance type and nSES in the current study, we also found large Medicaid effects in both low and high nSES neighborhoods. Due to lower payment rates with Medicaid versus other insurance payers, health care services in high nSES neighborhoods may be less willing to accept and provide care to CRC cases with Medicaid versus other insurance types;[44,64,114,169,170] in contrast, low nSES neighborhoods may lack medical and supportive care altogether,[64] meaning that CRC cases with Medicaid would need to access services at a farther distance from their home.[18,114]

Evidence indicates higher educational attainment as a predictor of adherence to preventive CRC screening guidelines[17,43,56,97,98] as well as of lower CRC risk.[28,37,99] Our findings that lower education did not affect overall HRQoL in recently diagnosed CRC cases suggests that compared with income and insurance, or any iSES factor referring to a time period closer to diagnosis, educational attainment may not as meaningfully enable access to medical and supportive care services or to other critical material and social resources. [23,30,64,84,101]

Our study findings and interpretations should be read in light of key limitations. First, participating CRC cases may be systematically different from the underlying population of incident CRC cases,[9,54] including if cases with more severe forms of the disease and lower HRQoL were unable to participate, and so the distributions of iSES factors and nSES in our study may be different from those in the region. We tried to limit the amount that participation could bias our estimates by basing nSES quartile cutpoints on the distribution of quartiles in the underlying case population and by using categorizations of iSES factors standard to CRC survival and survivorship literature. However, more than 50% of participating CRC cases reported into our highest income category (≥$70K) and 41% were assigned to the high nSES

neighborhoods. A second potential drawback to this work is our use of administrative census block group boundaries to define neighborhoods. Compared to a CRC case's perception of their neighborhood, isolated census block groups may not align with perceived community and daily activity space, or a case's view of their "local" material and social resources.[26,123,171] Because we were limited to using the residential address at diagnosis to link to neighborhood data, we also lacked information on each case's length of residency in their neighborhood. Third, our observed effects are relative to our study region and our geographic unit of analysis (block groups).[57] The Seattle-Puget Sound area is one of the wealthiest regions in the US,[120,141] with a median household income of approximately $93K/year,[119] and our results would likely have been different in another region or across different sizes of geographic units (e.g., tracts, counties) within our region of study. Fourth, household income and insurance type were each measured at a single time point and are imperfect proxies for the complex financial and insurance-related factors that affect HRQoL after a CRC diagnosis.[84] A fifth limitation to this study is our lack of fine-grained detail for a few key variables (e.g., details of primary treatment elements) and our complete lack of data for other factors (e.g., month-to-month financial precarity, perceptions of social and physician support, supportive care access).[9,18,19] Finally, our analyses were limited by sample size, and we were unable to evaluate associations through a potentially important intersectionality lens (e.g., considering associations by intersections of gender and race/ethnicity).[3,25,30,52]

Despite these limitations, our results substantially contribute to the knowledge of how iSES factors and nSES can affect HRQoL following a CRC diagnosis. Future research will need to evaluate these associations in other populations and other geographic locations, to assess these effects across different demographic intersections (e.g., gender, race/ethnicity, other socioeconomic class factors), and to formally identify underlying mediation mechanisms. An increasingly better understanding of how SES inequalities shape life and death after a CRC diagnosis will better inform intervention targets for both CRC cases and their caregivers.[51,84]

Table 1. Characteristics and mean overall HRQoL scores in PSCCC CRC cases (N=1320), Seattle-Puget Sound Region, 2016-2018			
		Overall HRQoL[a]	
	N (%)	Mean	SD
Total participants	1320 (-)	103.1	19.9
Age at diagnosis, in years			
<50	284 (22)	98.4	19.8
50-59	414 (31)	102.0	21.1
60-69	430 (33)	105.2	18.3
≥70	192 (15)	107.7	19.3
Gender			
Male	718 (54)	103.4	19.9
Female	602 (46)	102.7	19.9
Race/ethnicity			
Non-Hispanic White	1005 (76)	103.2	19.6
Other	315 (24)	102.9	20.8
Marital status at diagnosis			
Married	705 (53)	105.6	18.8
Not married	384 (29)	98.7	21.3
Unknown	231 (18)	102.9	19.6
Surgery in initial course of CRC treatment			
No	160 (12)	96.5	20.4
Yes	1160 (88)	104.0	19.7
Radiation in initial course of CRC treatment			
No	1073 (81)	104.4	19.4
Yes	247 (19)	97.3	21.2
Chemotherapy in initial course of CRC treatment			
No	645 (49)	108.8	18.2
Yes	675 (51)	97.7	19.9
Tumor stage at diagnosis[b]			
Local	475 (36)	110.1	17.7
Regional	559 (42)	99.9	20.5
Distant	224 (17)	97.1	19.2
Unknown/unstaged	62 (5)	99.9	17.9
Time since diagnosis[c]			
Tercile 1 (85 – 144 days)	440 (33)	103.5	20.1
Tercile 2 (145 – 199 days)	440 (33)	102.1	18.9
Tercile 3 (≥200 days)	440 (33)	103.7	20.7
Educational attainment			
College graduate/graduate school	597 (45)	105.1	18.4
Some college/vocational school	454 (35)	102.6	20.6
≤High school completion or GED	269 (20)	99.3	21.3
Household income before diagnosis, in USD ($)[d]			
≥$70K	686 (52)	106.3	18.3
$30-69K	341 (26)	102.4	18.9

<$30K	220 (17)	93.8	22.4
Missing	73 (5)	104.3	22.2
Insurance type at diagnosis[e]			
Private/other government insurance	996 (75)	104.6	19.2
Medicaid	124 (9)	90.1	22.0
Unknown/Uninsured	200 (15)	103.8	18.9
Neighborhood socioeconomic status (nSES)[f]			
Quartile 1 (high nSES)	545 (41)	105.1	18.7
Quartile 2	367 (28)	104.4	20.4
Quartile 3	261 (20)	100.9	20.0
Quartile 4 (low nSES)	147 (11)	96.5	21.1
Educational attainment and nSES[g]			
≥Some college & high nSES	*766 (58)*	*105.3*	*19.1*
≥Some college & low nSES	*285 (22)*	*100.6*	*19.9*
≤ High school & high nSES	*146 (11)*	*102.0*	*20.8*
≤ High school & low nSES	*123 (9)*	*96.2*	*21.6*
Household income and nSES[h]			
≥$30K & high nSES	*761 (58)*	*105.5*	*18.6*
≥$30K & low nSES	*266 (20)*	*103.5*	*18.3*
<$30K & high nSES	*100 (7)*	*98.3*	*22.8*
<$30K & low nSES	*120 (9)*	*90.0*	*21.5*
Insurance type and nSES[i]			
Private/other gov insurance & high nSES	*716 (54)*	*106.1*	*18.7*
Private/other gov insurance & low nSES	*280 (21)*	*100.8*	*20.0*
Medicaid & high nSES	*69 (5)*	*90.5*	*22.6*
Medicaid & low nSES	*55 (4)*	*89.6*	*21.4*

[a]Measured using the Functional Assessment of Cancer Therapy – Colorectal (FACT-C) self-report tool
[b]Based on the 2000 (for diagnoses in 2016-2017) and 2018 (for diagnoses in 2018) versions of the SEER Summary Staging Manual
[c]Time since diagnosis is equivalent to the time between CRC diagnosis and ACCESS interview. Percentages may not add to 100% because this variable was cut into terciles
[d]Measured with respect to two years before CRC diagnosis
[e]Insured group includes cases with private insurance, Medicare, Veterans Affairs, Military, TRICARE, or Indian/Public Health Service as the primary payer at CRC diagnosis; unknown/uninsured group includes 11 uninsured cases
[f]Measured at the block group-level by combining six census variables into the index indicator identified by Diez Roux and colleagues (CITE). Quartile cutpoints based on the quartile distribution of nSES in census block groups for the underlying CRC case population in the 13-county catchment area in the Seattle Puget-Sound region
[g]Education levels collapsed as low (≤high school) and high (≥some college or vocational school). Neighborhood SES levels collapsed as low (Q3 and Q4) and high (Q1 and Q2)
[h]Household income levels collapsed as low (<$30K/year) and high (≥$30K). Neighborhood SES levels collapsed as low (Q3 and Q4) and high (Q1 and Q2). Percentages will not add to 100% because variable excludes cases missing income (N=73)
[i]Insurance defined as Medicaid and insured)=. Neighborhood SES levels collapsed as low (Q3 and Q4) and high (Q1 and Q2). Percentages will not add to 100% because variable excludes cases with unknown insurance or who were uninsured (N=200)

Table 2. Distributions of educational attainment, household income, insurance type, and neighborhood SES for PSCCC CRC cases (N=1320), Seattle-Puget Sound Region, 2016-2018

	Neighborhood socioeconomic status (nSES)[a]			
	Q1 (high nSES)	Q2	Q3	Q4 (low nSES)
	N (%)	N (%)	N (%)	N (%)
Educational attainment				
College graduate/graduate school	330 (61)	147 (40)	92 (35)	28 (19)
Some college/vocational school	148 (27)	141 (38)	102 (39)	63 (43)
≤High school completion or GED	67 (12)	79 (22)	67 (26)	56 (38)
Household income[b]				
≥$70K	359 (66)	191 (52)	99 (38)	37 (25)
$30-69K	105 (19)	106 (29)	80 (31)	50 (34)
<$30K	46 (9)	54 (15)	67 (26)	53 (36)
Missing	35 (6)	16 (4)	15 (6)	7 (5)
Insurance type[c]				
Private/other government insurance	430 (79)	286 (78)	179 (69)	101 (69)
Medicaid	4 (8)	25 (7)	34 (13)	21 (14)
Unknown/uninsured	71 (13)	56 (15)	48 (18)	25 (17)

[a] Quartile cutpoints based on the quartile distribution of nSES in census block groups for the underlying CRC case population in the 13-county catchment area in the Seattle Puget-Sound region
[b] Measured with respect to two years before CRC diagnosis
[c] Only 11 uninsured cases

Table 3. Associations of educational attainment, household income, insurance type, and neighborhood SES with difference in mean overall health-related quality of life (HRQoL) score, Seattle-Puget Sound Region, 2016-2018

	N (%)	Difference in mean overall HRQoL[a] β (95% CI)
Educational attainment		
College graduate/graduate school	597 (45)	(ref)
Some college/vocational school	454 (35)	-0.68 (-3.00, 1.64)
≤High school completion or GED	269 (20)	-1.37 (-4.22, 1.49)
p-trend		*0.89*
Household income[b]		
≥$70K	686 (52)	(ref)
$30-69K	341 (26)	-1.96 (-4.62, 0.69)
<$30K	220 (17)	**-7.93 (-11.50, -4.35)**
p-trend		***<0.01***
Insurance type[c]		
Private/other government insurance	996 (76)	(ref)
Medicaid	124 (9)	**-7.82 (-12.04, -3.60)**
p-value		***<0.01***
Neighborhood socioeconomic status (nSES)[d]		
Q1 (high nSES)	545 (41)	(ref)
Q2	367 (28)	-0.19 (-2.61, 2.22)
Q3	261 (20)	-2.07 (-4.87, 0.73)
Q4 (low nSES)	147 (11)	**-4.58 (-8.26, -0.91)**
p-trend		***0.04***
Educational attainment and nSES[e]		
≥Some college, High nSES	766 (58)	(ref)
≥Some college, Low nSES	285 (22)	**-2.97 (-5.52, -0.43)**
≤High school, High nSES	146 (11)	-1.27 (-4.64, 2.09)
≤High school , Low nSES	123 (9)	**-3.98 (-7.88, -0.07)**
Household income and nSES[f]		
≥$30K, High nSES	761 (58)	(ref)
≥$30K, Low nSES	266 (20)	-1.19 (-3.67, 1.29)
<$30K, High nSES	100 (8)	-3.71 (-8.22, 0.80)
<$30K, Low nSES	120 (9)	**-12.57 (-16.90, -8.24)**
Insurance type and nSES[g]		
Private/other gov insurance, High nSES	716 (54)	(ref)
Private/other gov insurance, Low nSES	280 (21)	**-3.23 (-5.94, -0.52)**
Medicaid, High nSES	69 (5)	**-9.81 (-15.38, -4.25)**
Medicaid, Low nSES	55 (4)	**-9.79 (-15.66, -3.92)**
Intercept[h]		***110.1 (104.9, 115.3)***

[a] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income (N=73) or with unknown insurance type (N=200)

[b] Measured with respect to two years before CRC diagnosis

[c] Insured group includes cases with private insurance, Medicare, Veterans Affairs, Military, TRICARE, or Indian/Public Health Service as the primary payer at CRC diagnosis; unknown/uninsured group includes 11 uninsured cases

[d] Quartile cutpoints based on the quartile distribution of nSES in census block groups for the underlying CRC case population in the 13-county catchment area in the Seattle Puget-Sound region

[e] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2)

[f] Income collapsed as low (<$30K/year) and high (≥$30K); nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing income excluded (N=73), so analysis includes N=1247

[g] Insurance defined as Medicaid and insured; nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing insurance excluded (N=200), so analysis includes N=1120

[h] The intercept from the linear regression model reflects mean overall HRQoL among (hypothetical) individuals in the referent category for all variables

Table 4. Associations of educational attainment, household income, insurance type, and neighborhood SES with difference in mean health-related quality of life (HRQoL) subdomain scores, Seattle-Puget Sound Region, 2016-2018

	Difference in mean PWB[a]	Difference in mean SWB[a]	Difference in mean EWB[a]	Difference in mean FWB[a]	Difference in mean CCS[a]
	N=1320	N=1320	N=1320	N=1319	N=1319
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Educational attainment					
College graduate/graduate school	(ref)	(ref)	(ref)	(ref)	(ref)
Some college/vocational school	-0.13 (-0.78, 0.51)	-0.01 (-0.67, 0.67)	0.02 (-0.49, 0.53)	-0.28 (-1.00, 0.44)	-0.21 (-0.76, 0.34)
≤High school completion or GED	-0.26 (-1.05, 0.54)	0.54 (-0.26, 1.33)	-0.19 (-0.85, 0.48)	-0.90 (-1.81, 0.01)	-0.56 (-1.32, 0.19)
p-trend	*0.78*	*0.05*	*0.97*	*0.27*	*0.56*
Household income[b]					
≥$70K	(ref)	(ref)	(ref)	(ref)	(ref)
$30-69K	-0.33 (-1.09, 0.42)	**-1.08 (-1.84, -0.32)**	0.41 (-0.19, 1.02)	-0.55 (-1.38, 0.29)	-0.44 (-1.11, 0.24)
<$30K	**-1.29 (-2.29, -0.29)**	**-2.68 (-3.71, -1.65)**	-0.41 (-1.22, 0.48)	**-2.30 (-3.38, -1.22)**	**-1.31 (-2.21, -0.41)**
p-trend	*0.05*	***<0.01***	*0.82*	***<0.01***	***0.03***
Insurance type[c]					
Private/other government insurance	(ref)	(ref)	(ref)	(ref)	(ref)
Medicaid	**-1.88 (-3.08, -0.69)**	-0.95 (-2.13, 0.23)	**-1.44 (-2.43, -0.44)**	**-2.23 (-3.51, -0.95)**	**-1.37 (-2.47, -0.27)**
p-value	***<0.01***	*0.14*	***<0.01***	***<0.01***	***<0.01***
Neighborhood socioeconomic status (nSES)[d]					
Q1 (high nSES)	(ref)	(ref)	(ref)	(ref)	(ref)
Q2	-0.48 (-1.16, 0.19)	-0.09 (-0.58, 0.76)	0.27 (-0.26, 0.80)	-0.35 (-1.11, 0.42)	0.38 (-0.31, 0.97)
Q3	-0.73(-1.56, 0.09)	-0.06 (-0.84, 0.72)	-0.14 (-0.75, 0.48)	**-0.96 (-1.83, -0.09)**	-0.18 (-0.87, 0.52)
Q4 (low nSES)	**-1.64(-2.65, -0.63)**	-0.34 (-1.42, 0.75)	-0.55 (-1.35, 0.24)	**-1.33 (-2.52, -0.14)**	-0.73 (-1.69, 0.22)
p-trend	***<0.01***	*0.69*	*0.39*	***0.03***	*0.40*
Educational attainment and nSES[e]					
≥Some college, High nSES	(ref)	(ref)	(ref)	(ref)	(ref)
≥Some college, Low nSES	**-0.76 (-1.50, -0.01)**	-0.25 (-0.99, 0.49)	-0.39 (-0.94, 0.16)	**-1.02 (-1.83, -0.21)**	-0.61 (-1.23, 0.02)
≤High school, High nSES	-0.12 (-1.04, 0.79)	0.44 (-0.46, 1.34)	-0.18 (-0.98, 0.61)	-0.91 (-1.98, 0.16)	-0.54 (-1.48, 0.39)

≤High school , Low nSES	**-1.23 (-2.32, -0.14)**	0.41 (-0.60, 1.42)	-0.60 (-1.49, 0.29)	**-1.68 (-2.92, -0.44)**	-0.94 (-1.93, 0.05)
Household income and nSES[f]					
≥$30K, High nSES	(ref)	(ref)	(ref)	(ref)	(ref)
≥$30K, Low nSES	-0.53 (-1.26, 0.20)	-0.21 (-0.93, 0.51)	0.04 (-0.52, 0.59)	-0.57 (-1.36, 0.23)	0.08 (-0.56, 0.71)
<$30K, High nSES	-0.54 (-1.74, 0.67)	**-2.06 (-3.31, -0.81)**	0.06 (-0.91, 1.03)	-1.23 (-2.58, 0.12)	0.05 (-1.06, 1.17)
<$30K, Low nSES	**-2.48 (-3.74, -1.22)**	**-2.61 (-3.92, -1.30)**	**-1.46 (-2.48, -0.45)**	**-3.73 (-5.06, -2.40)**	**-2.29 (-3.37, -1.21)**
Insurance type and nSES[g]					
Private/other gov insurance, High nSES	(ref)	(ref)	(ref)	(ref)	(ref)
Private/other gov insurance, Low nSES	**-0.86 (-1.63, -0.09)**	-0.32 (-1.06, 0.42)	**-0.62 (-1.21, -0.02)**	**-1.13 (-1.97, -0.29)**	-0.37 (-1.04, 0.31)
Medicaid, High nSES	**-2.13 (-3.69, -0.56)**	-1.51 (-3.06, 0.04)	**-2.02 (-3.41, -0.62)**	**-3.12 (-4.78, -1.46)**	-1.14 (-2.39, 0.11)
Medicaid, Low nSES	**-2.48 (-4.25, -0.70)**	-0.67 (-2.23, 0.89)	**-1.49 (-2.72, -0.26)**	**-2.62 (-4.44, -0.81)**	**-2.63 (-4.32, -0.94)**
Intercept[h]	*22.1 (20.6, 23.6)*	*23.4 (21.9, 24.7)*	*19.4 (18.3, 20.5)*	*21.7 (20.1, 23.2)*	*23.4 (22.0, 24.7)*

PWB: Physical wellbeing; **SWB:** Social wellbeing; **EWB:** Emotional wellbeing; **FWB:** Functional wellbeing; **CCS:** Colorectal cancer-specific wellbeing

[a] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income (N=73) or with unknown insurance type (N=200)

[b] Measured with respect to two years before CRC diagnosis

[c] Insured group includes cases with private insurance, Medicare, Veterans Affairs, Military, TRICARE, or Indian/Public Health Service as the primary payer at CRC diagnosis; unknown/uninsured group includes 11 uninsured cases

[d] Quartile cutpoints based on the quartile distribution of nSES in census block groups for the underlying CRC case population in the 13-county catchment area in the Seattle Puget-Sound region

[e] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2)

[f] Income collapsed as low (<$30K/year) and high (≥$30K); nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing income excluded (N=73), so analysis includes N=1247

[g] Insurance defined as Medicaid and insured; nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing insurance excluded (N=200), so analysis includes N=1120

[h] The intercepts from linear regression models reflect mean subdomain HRQoL among (hypothetical) individuals in the referent category for all variables

Supplementary Table 1. Associations of educational attainment, household income, insurance type, and neighborhood SES with low health-related quality of life (HRQoL), Seattle-Puget Sound Region, 2016-2018		
		Low HRQoL[a]
	N (N with low HRQoL)	**OR (95% CI)**
Total	**1320 (218)**	**(-)**
Educational attainment		
College graduate/graduate school	597 (77)	1.00 (-)
Some college/vocational school	454 (88)	1.40 (0.96-2.03)
≤High school completion or GED	269 (53)	1.09 (0.70-1.70)
p-trend		*0.63*
Household income[b]		
≥$70K	686 (83)	1.00 (-)
$30-69K	341 (60)	1.26 (0.82-1.94)
<$30K	220 (63)	**1.95 (1.21-3.15)**
p-trend		***0.03***
Insurance type[c]		
Private/other government insurance	996 (140)	1.00 (-)
Medicaid	124 (45)	**2.02 (1.19, 3.44)**
p-value		***<0.01***
Neighborhood socioeconomic status (nSES)[d]		
Q1 (high nSES)	545 (77)	1.00 (-)
Q2	367 (55)	1.02 (0.70-1.49)
Q3	261 (47)	1.10 (0.72-1.68)
Q4 (low nSES)	147 (39)	1.59 (0.97-2.61)
p-trend		*0.38*
Educational attainment and nSES[e]		
≥Some college, High nSES	766 (107)	1.00 (-)
≥Some college, Low nSES	285 (58)	1.38 (0.96-2.00)
≤High school, High nSES	146 (25)	1.04 (0.63-1.72)
≤High school , Low nSES	123 (28)	1.12 (0.65-1.95)
Household income and nSES[f]		
≥$30K, High nSES	761 (106)	1.00 (-)
≥$30K, Low nSES	266 (37)	0.90 (0.59-1.37)
<$30K, High nSES	100 (20)	1.05 (0.57-1.94)
<$30K, Low nSES	120 (43)	**2.77 (1.61-4.74)**
Insurance type and nSES[g]		
Private/other gov insurance, High nSES	716 (87)	1.00 (-)
Private/other gov insurance, Low nSES	280 (53)	1.41 (0.95-2.09)
Medicaid, High nSES	69 (28)	**3.36 (1.77-6.36)**
Medicaid, Low nSES	55 (17)	1.90 (0.95-3.82)

Logistic regression models estimate odds ratios (OR) and 95% CIs, and use robust standard errors to account for within-neighborhood dependence. [92] Low HRQoL is categorized as any score at least one standard deviation below the mean HRQoL in the study population.[151,152,172]

[a] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income (N=73) or with unknown insurance type (N=200)

[b] Measured with respect to two years before CRC diagnosis

[c] Insured group includes cases with private insurance, Medicare, Veterans Affairs, Military, TRICARE, or Indian/Public Health Service as the primary payer at CRC diagnosis; unknown/uninsured group includes 11 uninsured cases

[d] Quartile cutpoints based on the quartile distribution of nSES in census block groups for the underlying CRC case population in the 13-county catchment area in the Seattle Puget-Sound region

[e] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2)

[f] Income collapsed as low (<$30K/year) and high (≥$30K); nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing income excluded (N=73), so analysis includes N=1247

[g] Insurance defined as Medicaid and insured; nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing insurance excluded (N=200), so analysis includes N=1120

Supplementary Table 2. Associations of educational attainment, household income, insurance type, and neighborhood SES with difference in mean overall health-related quality of life (HRQoL) score with additional adjustment variables, Seattle-Puget Sound Region, 2016-2018

	Main Model	Main Model + Primary tumor site	Main Model + Primary tumor site + Comorbidities	Main Model + Primary tumor site + Comorbidities + Lifestyle behaviors
	Difference in mean overall HRQoL[a]	Difference in mean overall HRQoL[b]	Difference in mean overall HRQoL[c]	Difference in mean overall HRQoL[d]
	N=1320 β (95% CI)	N=1303 β (95% CI)	N=1267 β (95% CI)	N=1245 β (95% CI)
Educational attainment				
College graduate/graduate school	(ref)	(ref)	(ref)	(ref)
Some college/vocational school	-0.68 (-3.00, 1.64)	-0.78 (-3.11, 1.54)	-0.52 (-2.86, 1.83)	-0.01 (-2.42, 2.39)
≤High school completion or GED	-1.37 (-4.22, 1.49)	-1.39 (-4.24, 1.46)	-0.74 (-3.64, 2.16)	-0.29 (-3.26, 2.67)
p-trend	*0.89*	*0.86*	*0.55*	*0.45*
Household income[e]				
≥$70K	(ref)	(ref)	(ref)	(ref)
$30-69K	-1.96 (-4.62, 0.69)	-1.84 (-4.52, 0.83)	-2.03 (-4.72, 0.67)	-1.29 (-4.01, 1.43)
<$30K	**-7.93 (-11.50, -4.35)**	**-7.74 (-11.34, -4.14)**	**-7.56 (-11.25, -3.86)**	**-5.91 (-9.66, -2.15)**
p-trend	***<0.01***	***<0.01***	***<0.01***	***0.02***
Insurance type[f]				
Private/other government insurance	(ref)	(ref)	(ref)	(ref)
Medicaid	**-7.82 (-12.04, -3.60)**	**-7.74 (-11.99, -3.48)**	**-8.14 (-12.54, -3.74)**	**-7.88 (-12.26, -3.49)**
p-value	***<0.01***	***<0.01***	***<0.01***	***<0.01***
Neighborhood socioeconomic status (nSES)[g]				
Q1 (high nSES)	(ref)	(ref)	(ref)	(ref)
Q2	-0.19 (-2.61, 2.22)	-0.32 (-2.75, 2.10)	0.54 (-1.90, 2.98)	0.64 (-1.80, 3.09)
Q3	-2.07 (-4.87, 0.73)	-2.12 (-4.93, 0.69)	-1.08 (-3.94, 1.77)	-1.01 (-3.90, 1.88)
Q4 (low nSES)	**-4.58 (-8.26, -0.91)**	**-4.78 (-8.51, -1.04)**	-3.15 (-7.11, 0.82)	-2.82 (-6.69, 1.06)
p-trend	***0.04***	***0.03***	*0.29*	*0.30*
Educational attainment and nSES[h]				
≥Some college, High nSES	(ref)	(ref)	(ref)	(ref)
≥Some college, Low nSES	**-2.97 (-5.52, -0.43)**	**-3.04 (-5.62, -0.46)**	-1.95 (-4.56, 0.67)	**-1.81 (-4.45, 0.82)**
≤High school, High nSES	-1.27 (-4.64, 2.09)	-1.28 (-4.64, -2.07)	-0.35 (-3.81, 3.11)	-0.17 (-3.61, 3.28))
≤High school , Low nSES	**-3.98 (-7.88, -0.07)**	**-4.01 (-7.90, -0.11)**	-2.74 (-6.73, 1.25)	**-2.40 (-6.46, 1.65)**
Household income and nSES[i]				

≥$30K, High nSES	(ref)	(ref)	(ref)	(ref)
≥$30K, Low nSES	-1.19 (-3.67, 1.29)	-1.23 (-3.73, 1.28)	-0.72 (-3.27, 1.83)	-0.49 (-3.07, 2.08)
<$30K, High nSES	-3.71 (-8.22, 0.80)	-3.54 (-8.04, 0.95)	-3.56 (-8.32, 1.20)	-1.97 (-6.69, 2.74)
<$30K, Low nSES	**-12.57 (-16.90, -8.24)**	**-12.61 (-16.98, -8.24)**	**-11.14 (-15.45, -6.82)**	**-9.86 (-14.22, -5.50)**
Insurance type and nSES[j]				
Private/other gov insurance, High nSES	(ref)	(ref)	(ref)	(ref)
Private/other gov insurance, Low nSES	**-3.23 (-5.94, -0.52)**	**-3.21 (-5.95, -0.47)**	-2.20 (-4.96, 0.57)	-2.31 (-5.05, 0.44)
Medicaid, High nSES	**-9.81 (-15.38, -4.25)**	**-9.36 (-14.94, -3.78)**	**-10.13 (-15.97, -4.29)**	**-9.95 (-15.79, -4.11)**
Medicaid, Low nSES	**-9.79 (-15.66, -3.92)**	**-10.03 (-15.97, -4.08)**	**-9.60 (-15.73, -3.46)**	**-9.08 (-15.01, -3.14)**
Intercept[k]	*110.1 (104.9, 115.3)*	*111.2 (105.2, 117.2)*	*112.2 (106.5, 118.0)*	*112.5 (106.5, 118.5)*

[a] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income (N=73) or with unknown insurance type (N=200)

[b] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), primary tumor site at diagnosis (**colon**, rectum), and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income or with unknown insurance type

[c] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), primary tumor site at diagnosis (**colon**, rectum), self-reported diagnosis of colorectal comorbidities (i.e., colitis, Crohn's disease, diverticulitis, or irritable bowel syndrome) (**none**, ≥1), self-reported diagnosis of diabetes (**no**, yes), body mass index (BMI, kg/m^2) two years before CRC diagnosis (**<25**, 25-29, ≥30), and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income or with unknown insurance type

[d] HRQoL measured using the FACT-C self-report tool. All estimates adjusted for gender (**male**, female), race/ethnicity (**non-Hispanic white**, other), age at diagnosis(**<50**,50-59,60-69,≥70), marital status (**married**, not married, unknown), tumor stage at diagnosis (**local**, regional, distant, unknown/unstaged), surgery (**no**, yes), radiation (**no**, yes), chemotherapy (**no**, yes), time since diagnosis (in terciles), primary tumor site at diagnosis (**colon**, rectum), self-reported diagnosis of colorectal comorbidities (i.e., colitis, Crohn's disease, diverticulitis, or irritable bowel syndrome) (**none**, ≥1), self-reported diagnosis of diabetes (**no**, yes), body mass index (BMI, kg/m^2) two years before CRC diagnosis (**<25**, 25-29, ≥30),cigarette smoking history (**never**, former, current), met the American Cancer Society (ACS) definition of regular heavy alcohol consumption (**nondrinker**, no, yes) in the decade before diagnosis (CITE), average daily sedentary activity **(<4 hours/day**, ≥4 hours/day, unknown/none)[3], and all SES factors (educational attainment, household income, insurance type, nSES). P-trends for education, income, and nSES come from a Wald test of continuous variables comparing the coefficient with zero; p-value for insurance comes from a Wald chi-square test. P-trends/p-values do not include cases missing income or with unknown insurance type

[e] Measured with respect to two years before CRC diagnosis

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[j] Insurance defined as Medicaid and insured; nSES collapsed as low (Q3 and Q4) and high (Q1 and Q2). Cases missing insurance excluded (N=200), so analysis includes N=1120

[k] Intercepts from the linear regression models reflect the mean overall HRQoL among (hypothetical) individuals in the referent category for all variables

PROJECT CONCLUSION

In this project, we aimed to assess the independent and joint associations of iSES factors (i.e., educational attainment and household income) and nSES on survival following a diagnosis of incident, invasive CRC; to evaluate whether observed nSES effects on CRC survival proxied for the effects of other neighborhood factors (i.e., neighborhood population density, neighborhood level of high-intensity development) or if these neighborhood contexts had unique impacts on mortality after CRC; and to estimate the independent and joint associations between iSES characteristics and nSES on HRQoL in recently diagnosed CRC cases.

After mutual adjustment for iSES factors and nSES, our findings indicate that lower income household income was associated with poorer all-cause survival after CRC, particularly in women and especially given the context of living in a low nSES neighborhood, and that lower educational attainment was independently related to higher all-cause and CRC-specific mortality in men. These findings were consistent across sensitivity analyses that explored shape differences in the neighborhood "unit" as well as different parameterizations of all SES factors. Our results also suggest that living in a low nSES neighborhood was independently associated with poorer survival irrespective of gender, although we may have lacked adequate sample size and statistical power to detect gender-specific effects.

When we included nSES, neighborhood population density, and the neighborhood level of high-intensity development in the same analytic model, our findings showed that living in a high nSES neighborhood remained modestly associated with better survival. In addition, living in a highly populated neighborhood was related to lower disease-specific mortality. When estimates were stratified by iSES characteristics, living in a high nSES neighborhood was modestly associated with lower all-cause and CRC-specific mortality among CRC cases with higher amounts of educational attainment, while living in an intensely developed neighborhood was strongly related to poorer all-cause and CRC-specific survival in cases reporting lower household income.

After mutual adjustment for iSES factors and nSES, our results suggest a clinically meaningful decrease in overall HRQoL after a CRC diagnosis given lower household income or when using Medicaid as the primary insurance payer. While the effects of low income and nSES appeared uniquely harmful on overall

HRQoL, low income effects were also strongest in the context of low nSES; Medicaid effects were equally strong across neighborhood socioeconomic contexts.

Previous evidence indicates inequalities in SES as the primary drivers of persistent demographic disparities in outcomes following a CRC diagnosis; our findings show that the impacts of these inequalities are likely a mixture of individual- and neighborhood- or place-based effects, and that SES effects on survival vary by gender. These results may also suggest that exploring further intersectionality of these SES factors with demographics could help to identify crucial intervention targets to enhance both the likelihood of survival and the quality of survivorship in all CRC cases.

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APPENDIX 1. Conceptual models

Figure 1. Conceptual model of the association between socioeconomic status (SES) factors and colorectal cancer (CRC) survival

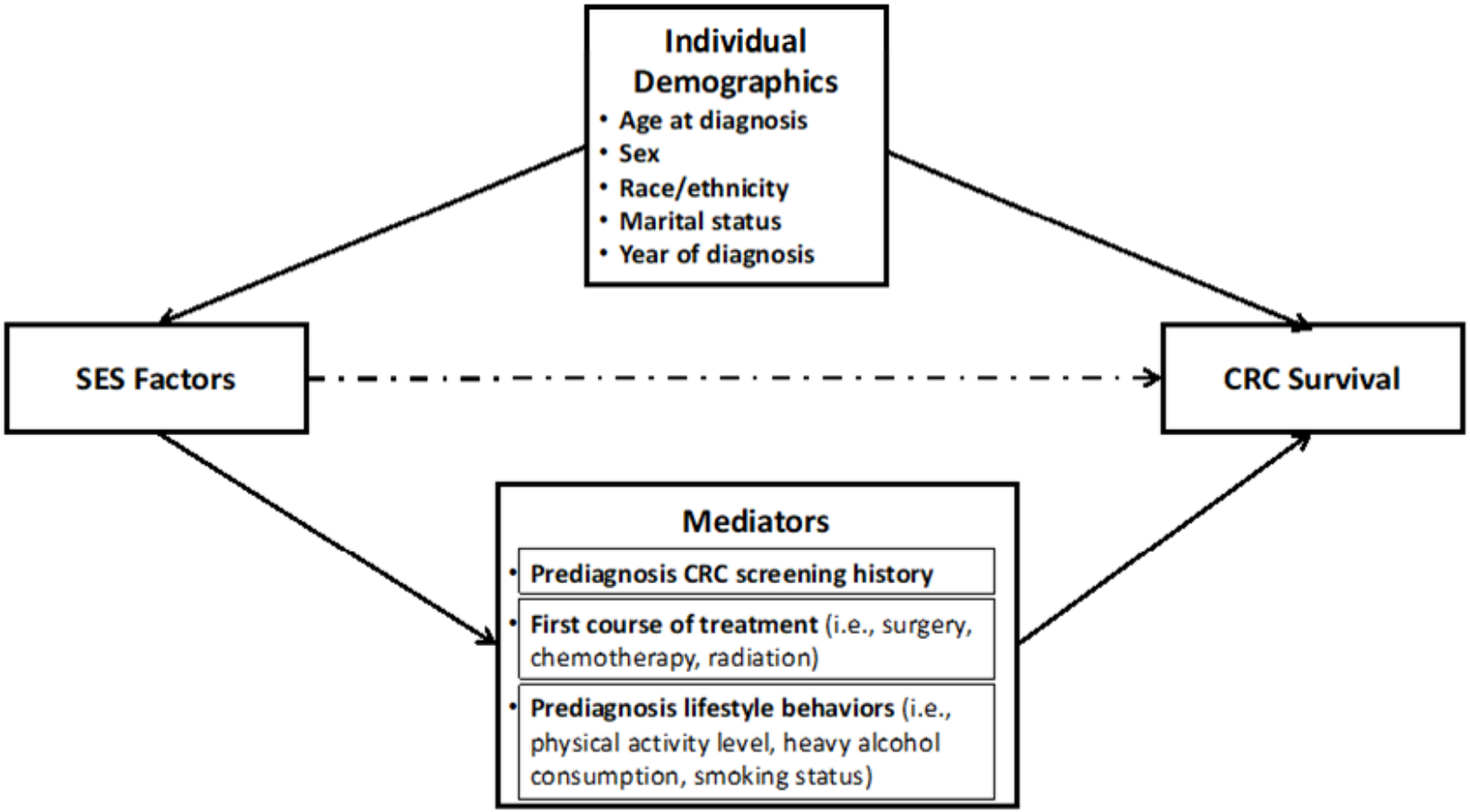


Figure 2. Conceptual model of the association between neighborhood factors (i.e., nSES, population density, and high-intensity development) and colorectal cancer (CRC) survival

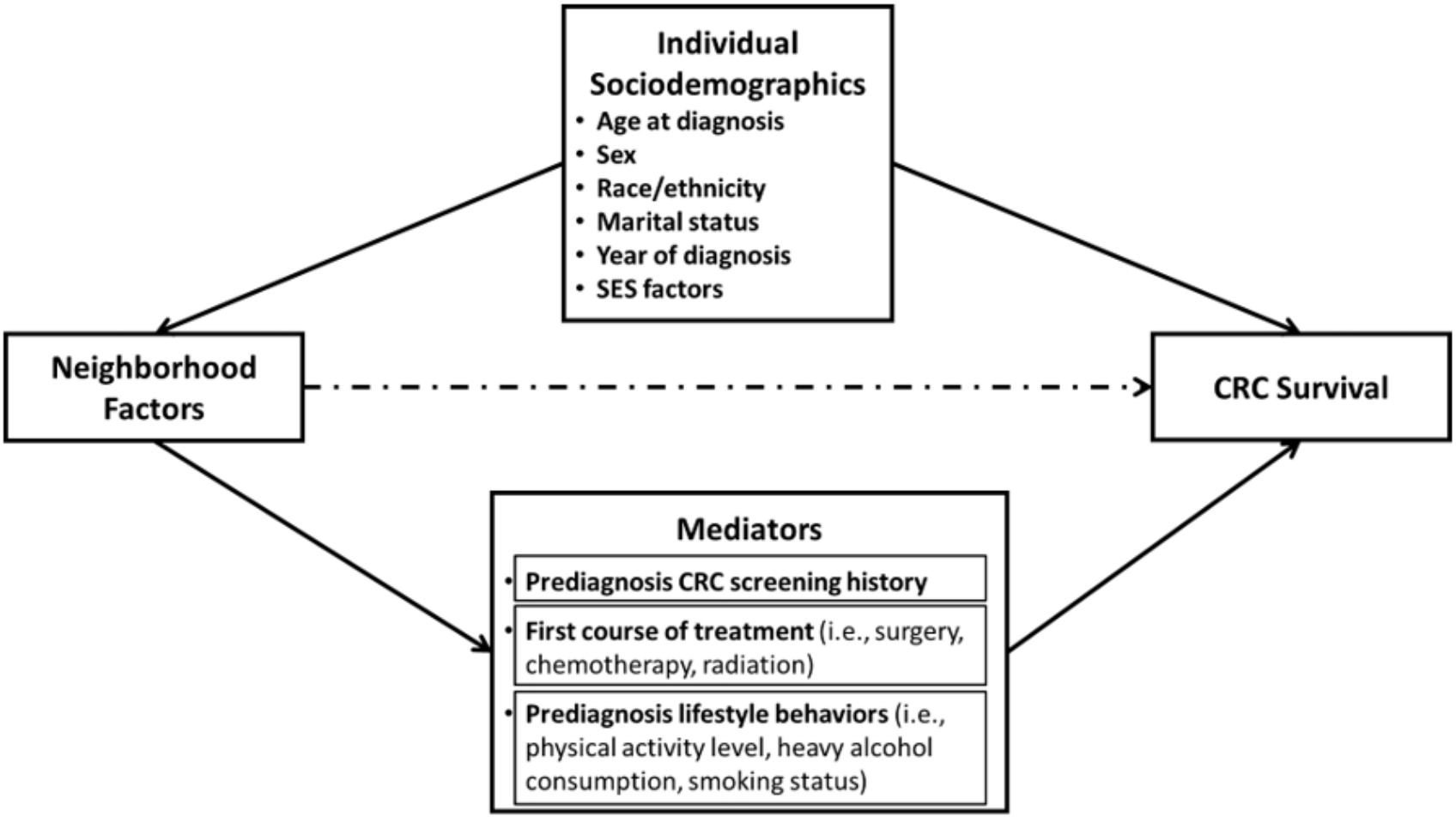
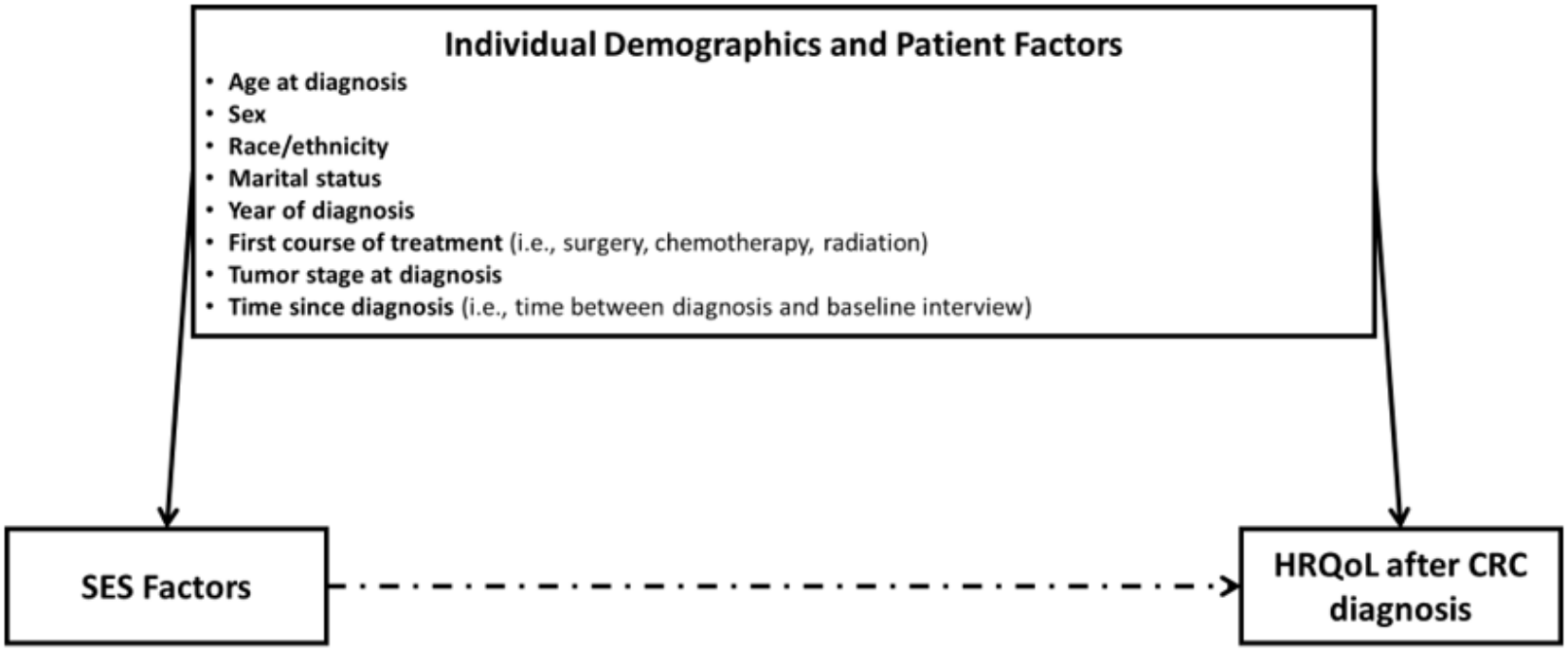


Figure 3. Conceptual model of the association between socioeconomic status (SES) factors and health related quality of life (HRQoL) following a colorectal cancer (CRC) diagnosis



APPENDIX 2. Characteristics of cases declining to report income

Table 1. Characteristics of PSCCC CRC cases declining to report income (N=263), overall and by gender, Seattle-Puget Sound Region, 1998-2018 (with follow-up through 2019)			
		Gender	
	Overall	Male	Female
	N (%)	N (%)	N(%)
Total participants	263 (-)	108 (-)	155 (-)
No. of deaths			
All-cause	112 (-)	37 (-)	75 (-)
CRC-specific	*51 (46)*	*20 (54)*	*31 (41)*
Age at diagnosis, in years			
<40	12 (5)	10 (9)	2 (1)
40-49	35 (13)	18 (17)	17 (11)
50-59	62 (24)	27 (25)	35 (23)
60-69	95 (36)	37 (34)	58 (37)
≥70	59 (22)	16 (15)	43 (28)
Race/ethnicity			
Non-Hispanic white	214 (81)	81 (75)	133 (86)
Other	49 (19)	27 (25)	22 (14)
Marital status at diagnosis			
Single, never married, or living unmarried	22 (8)	11 (10)	11 (7)
Married	177 (67)	75 (69)	102 (66)
Separated or divorced	17 (7)	8 (9)	9 (6)
Widowed	21 (8)	2 (2)	19 (12)
Unknown	26 (10)	2 (11)	14 (9)
Tumor stage at diagnosis[a]			
Local	109 (41)	46 (42)	63 (41)
Regional	118 (45)	44 (41)	74 (48)
Distant	31 (12)	15 (14)	16 (10)

Unstaged/unknown	5 (2)	3 (3)	2 (1)
Educational attainment			
College graduate/graduate school	85 (32)	43 (40)	42 (27)
Some college/vocational school	77 (29)	28 (26)	49 (32)
High school completion or GED	70 (27)	30 (28)	40 (26)
<High school	31 (12)	7 (6)	24 (15)
Neighborhood socioeconomic status (nSES)[c]			
Quintile 1 (high nSES)	71 (27)	37 (34)	34 (22)
Quintile 2	52 (20)	16 (15)	36 (23)
Quintile 3	53 (20)	30 (28)	23 (15)
Quintile 4	53 (20)	13 (12)	40 (26)
Quintile 5 (low nSES)	34 (13)	12 (11)	22 (14)
Educational attainment and nSES[d]			
≥*Some college & high nSES*	*93 (35)*	*42 (39)*	*51 (33)*
≥*Some college & low nSES*	*69 (26)*	*29 (27)*	*40 (26)*
≤ *High school & high nSES*	*30 (11)*	*11 (10)*	*19 (12)*
≤ *High school & low nSES*	*71 (27)*	*26 (24)*	*45 (29)*

[a] Based on the 2000 (cases diagnosed between 1998-2007, 2016) and 2018 (cases diagnosed in 2018) versions of the SEER Summary Staging Manual
[b] Measured with respect to two years prior to CRC diagnosis
[c] Quintile cutpoints based on the quintile distribution for block-group level nSES in the underlying incident CRC case population (cases diagnosed between 1998-2007, 2016-2018) in the region
[d] Education collapsed as low (≤high school) and high (≥some college); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2)
[e] Income collapsed as low (<$30K/year) and high ($≥30K/year); nSES collapsed as low (Q3-Q5) and high (Q1 and Q2). Percentages will not add to 100% due to variable excluding cases missing income (N=263 [7%])
[f] Measured with respect to the decade prior to CRC diagnosis
[g] ACS heavy drinking definition: for women, ≥8 drinks per week; for men, ≥15 drinks per week
[h] ACS physical activity recommendation: ≥150 minutes of moderate intensity per week, 75 minutes of strenuous intensity per week, or an equivalent combination of moderate/strenuous activity per week
[j] Based on self-report of diabetes diagnosis