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Neighborhood Deprivation and Clinical Outcomes among Head and Neck Cancer Patients

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Abstract

The unique effects of neighborhood-level economic deprivation on survival, recurrence, and second primary malignancy development were examined using adjusted Cox proportional hazards regression models among 1151 incident squamous cell carcinomas of the head and neck (SCCHN) patients. Cancer site was examined as a potential moderator. Main analyses yielded null results; however, interaction analyses indicated poorer overall survival [HR=1.59 (1.00-2.53)] and greater second primary malignancy development [HR=2.99 (1.46-6.11)] among oropharyngeal cancer patients from highly deprived neighborhoods relative to less deprived neighborhoods. Results suggest a dual focus on individual and neighborhood risk factors could help improve clinical outcomes among oropharyngeal cancer patients.

Keywords

neighborhood deprivation; head and neck cancer; survival; second primary malignancy; oropharyngeal cancer

Introduction

Squamous cell carcinomas of the head and neck (SCCHN) are cancers of the epithelial cells in the head and neck (excluding the eyes, ears, brain, thyroid, and esophagus), and are the main histological subtype of head and neck cancers. One of the strongest behavioral risk factors for SCCHN incidence is tobacco use, followed to a lesser extent by excessive alcohol use (Blot et al., 1988; Diaz, Holsinger, Zuniga, Roberts, & Sorensen, 2003; Lewin et al., 1998). Other factors related to SCCHN incidence include male gender, older age, African American race, and oncogenic human papillomavirus (HPV) status. Oncogenic HPV status

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is particularly relevant to oropharyngeal cancer (i.e., cancers that include the middle part of the throat including the soft palate, the base of tongue, the tonsils, and the back and side throat wall), with HPV-positive patients being younger, less likely to have a significant tobacco and alcohol use history, and more likely to have a better prognosis than HPV-negative patients (Chaturvedi, Engels, Anderson, & Gillison, 2008). In addition to these demographic and clinical factors, research suggests that individuals of lower socioeconomic status have higher rates of SCCHN incidence, even when controlling for tobacco and alcohol use status (S. Johnson, McDonald, & Corsten, 2008).

In total, SCCHN account for between 3% -5% of incident cancer cases in the US [cf. (NCI, 2011)], and approximately 6% of cancers worldwide (Lefebvre, 2005). Standard treatment options for SCCHN include surgery and/or radiotherapy for early stage or localized disease, with chemotherapy as an adjuvant treatment in advanced stages of disease (ACS, 2011). Despite relatively low incidence rates, treatment costs associated with SCCHN are significant, with recent estimates topping \$3.1 billion dollars annually in the US alone [cf. (NCI, 2011)]. Survival rates for SCHN vary based on disease stage at clinical presentation, and disease stage at presentation does not appear to be related to patients' socioeconomic status (S. Johnson, Corsten, McDonald, & Chun, 2010). Stage I and II disease represent localized cancers, Stages III, IVa, and IVb represent locally advanced disease with metastasis to local lymph nodes, and Stage IVc represents distant metastasis. Five-year survival rates for patients with SCCHN are about 91% for Stage I disease, 77% for Stage II, 61% for Stage III, 32% for Stage IVa, 25% for Stage IVb, and <4% for Stage IVc. [cf. (Lefebvre, 2005)]. Although 5-year survival rates for SCCHN are relatively high, patients with SCCHN frequently suffer mortality from comorbid illnesses and relatively high rates of second primary malignancy development [4% , cf. (Lefebvre, 2005)]. In addition, functional morbidities resulting from treatment that affects speech, swallowing, and facial aesthetics may result in social and occupational impairments and a potentially lower quality of life (Bonanno, Esmali, Fingeret, Nelson, & Weber, 2010; Buckwalter, Karnell, Smith, Christensen, & Funk, 2007; Givens et al., 2009; Goldstein, Hynds Karnell, Christensen, & Funk, 2007; Mowry, Tang, Sadeghi, & Wang, 2010; Terrell, Fisher, & Wolf, 1998; Teymoortash, Hoch, Eivazi, & Werner, 2010; Yao et al., 2007). Thus, the fiscal, social, and clinical consequences of SCCHN are significant, warranting the need to comprehensively understand the factors that affect treatment outcome among these patients.

Thus far, studies have cited a number of sociodemographic and clinical factors that affect SCCHN clinical outcomes (i.e., prognosis and survival), including age, sex, race/ethnicity, tumor stage, tobacco use, comorbidity (Piccirillo, Tierney, Costas, Grove, & Spitznagel, 2004), HPV status, treatment modality (Chaturvedi et al., 2008; Fakhry et al., 2008; Molina et al., 2008; Pytynia et al., 2004; Schrank, Han, Weiss, & Resto, 2011), and cancer site (Chaturvedi et al., 2008; Schrank et al., 2011). A number of studies have also focused on the significant relations of socioeconomic status (SES) with SCCHN outcomes, with lower SES predicting poorer clinical outcomes [e.g., (Arbes et al., 1999; Chu et al., 2011; Molina et al., 2008)]. However, these studies have relied on neighborhood-level SES as a proxy for patient-level SES, largely because individual-level SES information is often unavailable within population-based survival databases (e.g., cancer registries). As a result, the true influence of neighborhood SES on SCCHN outcomes, over and above the influence of individual-level SES, remains unstudied. Clarifying whether neighborhood-level SES plays a unique role in SCCHN outcomes is important to improving interventions, as significant associations would suggest that a dual focus on individual and neighborhood factors would be desirable for improving outcomes (Winkleby, Cubbin, & Ahn, 2006). Also, the clinical landscape of head and neck cancers has been changing in recent years, with rising rates of oropharyngeal cancers and declining rates of non-oropharyngeal cancers (Sturgis & Ang, 2011). A better understanding of contextual influences on SCCHN by cancer site is needed,

as site is associated with prognosis and survival outcomes (Chaturvedi et al., 2008; Schrank et al., 2011).

The purpose of the current study was to examine the unique effect of neighborhood-level SES on survival, recurrence, and the development of second primary malignancies among patients from Texas and Louisiana who were assessed and treated for incident SCCHN at a single, large multidisciplinary cancer center in the southwest. To our knowledge, this is the first study to examine the associations between neighborhood-level SES and SCCHN outcomes, while controlling for individual-level income as well as other sociodemographic and clinical variables. In addition to examining relations of neighborhood-level SES with clinical outcomes among all SCCHN patients, the potential for moderation by cancer site was also examined.

Materials and Methods

Study Design

The current study was a retrospective analysis of an ongoing epidemiological study of SCCHN patients at The University of Texas MD Anderson Cancer Center. All procedures were approved by The University of Texas MD Anderson Cancer Center Institutional Review Board.

Participants

Participants were adults with pathologically confirmed, previously untreated, incident SCCHN, who were evaluated (and later treated) at The University of Texas MD Anderson Cancer Center. Patients with salivary gland, nasopharyngeal, or lip carcinoma, and patients with a prior malignancy were excluded from participation. Data relevant to the current study consisted of the subset of patients from the two most highly represented states (Texas and Louisiana; N=1784). These participants were enrolled between February of 1996 and November 2009.

Procedure

Patients were approached about the study upon initial clinical presentation to The University of Texas MD Anderson Cancer Center with pathologically confirmed, previously untreated, incident SCCHN. Interested persons were screened for eligibility and consented for the study at this initial clinic visit, whereupon they completed a standardized questionnaire that elicited information about sociodemographic variables and medical history. Information about diagnosis and treatment plan, as applicable, was added to the medical record by the treating clinician following the initial visit. This clinical information, as well as survival/recurrence outcomes, was updated by the treating clinician at every subsequent patient visit. Patients' medical records were systematically reviewed for cancer site, cancer stage, cancer treatment, outcomes and dates for the present study. Additional updates were procured annually from institutional cancer registry data.

Participants' residential addresses were gathered at the time of study enrollment and were used to ascertain information on neighborhood deprivation. First, the North American Address Locator geocoding service provided by Environmental Systems Research Institute's ArcGIS Online web site was utilized within ArcGIS Desktop software (version 9.3.1; ESRI, Redlands, CA) to set parameters for batch geocoding of participants' addresses. Geocoding refers to the process of associating an address with a point in geographic space. The majority of the participants' residential addresses were successfully geocoded (n=1334) using the address locator. The remaining 450 addresses required manual geocoding, which was the process of reviewing each of the geocoding address failures and attempting to find their

location through a more intensive search. Overall, 202 of these addresses could be located through manual geocoding. The remaining geocoding failures (n=249) were primarily due to missing addresses and the use of P.O. Box or route addresses. This yielded a sample of 1535 patients for whom neighborhood characteristics could be gathered by associating their locations in space with a Census tract identifier. Census tracts are administratively-created units that have been supported as suitable neighborhood proxies in previous health-related research (Jones, van Sluijs, Ness, Haynes, & Riddoch, 2010; Krieger, Chen, Waterman, Rehkopf, & Subramanian, 2003; Ross, Tremblay, & Graham, 2004; Stafford, Duke-Williams, & Shelton, 2008). The Census tract identifier was then used to link each participant to the associated area-level data from the US Census (2000).

Measures

Patient variables: Patient variables of interest included sociodemographic and clinical factors. Sociodemographic variables collected were: age, sex, race/ethnicity (Non-Hispanic White vs. Others), annual household income (<\$25,000, \$25,000-\$74,900, \$75,000), and smoking status (current/former smoker vs. never smoker). Clinical factors included: cancer site (oropharyngeal versus non-oropharyngeal), cancer stage (I/II versus III/IV), and cancer treatment (single modality versus multiple modality). A total of 384 patients were dropped as a result of unknown primary cancer sites (n=28), insufficient treatment data (n = 303; e.g., no treatment, palliative care only, received treatment elsewhere), and/or because no follow-up data were available (n=291). Dropped patients differed significantly from remaining patients only on cancer sites. Specifically, fewer oropharyngeal than non-oropharyngeal cancer patients were dropped (22.4% versus 28.9%; $p=0.004$). The remaining patients (N=1151) were included in the analyses. Of these patients, 32 declined to provide income data and 17 had missing cancer site data.

Neighborhood SES: Five widely-used tract-level Census variables were selected to represent different aspects of patients' neighborhood SES (e.g., education, employment status, poverty): the percentage of the total population 25 years or older with less than high school/GED degree, the percentage of residents 16 years old who were unemployed, the percentages of households with income below the poverty level in 1999, the percentage of single parent households, and the percentage of households with no vehicle available for use. The internal reliability of these area-level variables was good ($\alpha=.86$). An index of neighborhood economic deprivation (hereafter referred to as neighborhood deprivation) was created for each patient by summing the z-scores of these area-level variables and dividing by five. Higher scores indicated greater neighborhood disadvantage (i.e., deprivation). Next, the resulting neighborhood deprivation scores were rank-ordered and quartiled. Because we were interested in the effects of the most deprived neighborhoods on survival, a bivariate predictor variable was created from these data that was comprised of the top 25% (High Neighborhood Deprivation) versus the remaining 75% (Low to Moderate Neighborhood Deprivation).

Survival/Recurrence/Second Primary Malignancy outcomes: There were four clinical outcomes of interest in the present study: overall survival, disease-specific survival, disease-free survival, and second primary malignancy development. Analyses were completed for time from first appointment, using death, recurrence, or second primary malignancy development as censoring variables. Death in overall survival analyses was defined as death from any cause. Death in disease-specific survival analyses was defined as death from incident disease only. Disease-free survival was defined as the absence of disease recurrence (relapse). Finally, second primary malignancy development was defined as the development of a second malignant cancer following the SCCHN index cancer diagnosis. Second lesions were considered second primary malignancies if they were of different histopathologic type,

occurred >5 years after treatment for the index tumor, and/or were clearly separated by normal epithelium based on clinical and radiographic assessment. Pulmonary lesions were considered second primary malignancies if they had a non-squamous histology, or if they were isolated squamous lesions appearing >5 years after the initial SCCHN and designated as second primary malignancies by the thoracic oncologist or surgeon. Any discrepancies in opinions regarding the origin of the tumor as recurrence versus second primary malignancies were handled by classifying the second lesion as a local recurrence. If none of the four events of interest occurred over the period of analysis, participants were automatically censored at the end of the study.

Data Analyses—Because participants were clustered within Census tracts (neighborhoods), we used a robust sandwich estimate approach in all survival analyses to account for any location-based correlation in outcomes (Ying & Liu, 2006). Our main analyses examined the effect of neighborhood SES on overall survival, disease-specific survival, disease-free survival, and second primary malignancy development for the total sample of SCCHN patients. Unadjusted and adjusted analyses were performed using the Statistical Analysis Software PROC PHREG command, which is a semi-parametric procedure to fit the Cox proportional hazard regression models. Adjusted analyses included the following covariates: age, sex, race/ethnicity, income, smoking status, cancer site, cancer stage, and treatment approach. Adjusted survival curves were calculated using the corrected group prognosis method (Ghali et al., 2001). Next, cancer site (oropharyngeal versus non-oropharyngeal) was examined in each of the adjusted models as a potential moderator of the effect of neighborhood deprivation on survival. This was accomplished by including an interaction term (neighborhood deprivation x cancer site) in each adjusted model. Significant interaction results were followed up with unadjusted and adjusted survival analyses (using procedures described above) for each cancer site, respectively. All analyses were performed using Statistical Analysis Software (version 9.2; SAS Institute Inc., Cary, NC). Proportional hazard assumptions were examined for each model with no resulting violations.

Results

Patient Population

Patients (N=1151) were largely Non-Hispanic White (82%) and male (77%). Patients resided within 735 Census tracts within Texas and 82 Census tracts within Louisiana. The number of patients residing within tracts ranged from 1 to 6, with 239 tracts being home to two or more participants. Chi-square and t-tests indicated a statistically significant difference between the oropharyngeal (n=555) and non-oropharyngeal (n=579) cancer patients on several variables, including age, sex, race/ethnicity, household income, smoking status, cancer stage, cancer treatment, and neighborhood deprivation (Table 1). See Table 1 for detailed information on patient characteristics for the total sample and by cancer site.

Main Analyses

The median follow-up time for patients alive at last contact was 30.7 months. There were 281 incidents of death in overall survival analyses, 167 incidents of death in disease-specific analyses, 218 incidents of recurrence in disease-free survival analyses, and 97 incidents of second primary malignancy development. Unadjusted Cox proportional hazards models indicated significant differences between two neighborhood deprivation groups for each outcome examined (p s=0.001, 0.009, 0.088, and 0.002, respectively). However, this pattern of results changed in adjusted Cox proportional hazard models, which failed to reveal any significant differences by neighborhood deprivation on the outcomes of interest (p s=0.899, 0.970, 0.524, and 0.159, respectively).

Moderator Analyses

Because we were interested in the influence of cancer site on the association between neighborhood deprivation and survival/recurrence, an interaction term between neighborhood deprivation and cancer site was added to the adjusted Cox proportional hazards models. Results indicated a significant interaction term for all outcomes (p s=0.001, 0.011, 0.034, and 0.006, respectively). With the reference groups of low/moderate deprivation and oropharyngeal cancer, hazard ratios (HRs) and 95% confidence intervals for the interaction terms were as follows: overall survival = 2.91 (1.63-5.17), disease specific survival = 2.55 (1.24-5.27), disease-free survival = 1.95 (1.05-3.62), and second primary malignancy development = 3.62 (1.44-9.09). The median follow-up time for oropharyngeal patients alive at last contact was 32.8 months, and the median follow-up time for non-oropharyngeal patients alive at last contact was 27.9 months. The number of overall deaths, disease-specific deaths, recurrences, and second primary malignancy events were higher among non-oropharyngeal than oropharyngeal cancer patients, with the largest difference emerging for overall deaths (28.3% non-oropharyngeal group versus 19.5% oropharyngeal group). Therefore, follow-up analyses were conducted for each site separately. Result of unadjusted analyses indicated significant effects of neighborhood deprivation on all outcomes among oropharyngeal cancer patients (p s=0.001, 0.005, 0.040, and 0.003), but not the non-oropharyngeal group (p s=0.885, 0.706, 0.995, and 0.860). Results of adjusted analyses, however, indicated significant effects of neighborhood deprivation on overall survival and second primary malignancy among oropharyngeal cancer patients (Table 2), but not the non-oropharyngeal group (p s = 0.413 and 0.504; results not shown). Figure 1 displays the unadjusted and adjusted survival curves for overall survival, and Figure 2 displays the unadjusted and adjusted survival curves for second primary malignancy among oropharyngeal cancer patients. Results indicated that oropharyngeal cancer patients from the most deprived neighborhoods had a significantly greater risk of overall death and second primary malignancy development than oropharyngeal cancer patients from less deprived neighborhoods.

Discussion

To our knowledge, this was the first study to examine the unique effect of neighborhood deprivation on SCCHN recurrence and survival among patients evaluated and treated at a single, large multidisciplinary cancer center. Although results failed to support a main effect of neighborhood deprivation on SCCHN outcomes among the sample as a whole, a significant interaction effect was observed. Specifically, stratified results indicated that among oropharyngeal cancer patients, a high level of neighborhood deprivation was associated with poorer overall survival and the development of second primary malignancies, even after controlling for a number of patient-level sociodemographic and clinical variables, including individual-level annual household income. Thus, results suggest that oropharyngeal cancer patients residing in deprived neighborhoods, marked by low levels of education and income and high levels of unemployment, single-parent households, and vehicle non-availability, may be at increased risk of some negative SCCHN outcomes relative to oropharyngeal cancer patients from neighborhoods with more socioeconomic capital, even when treated at the same hospital for their incident cancer. These findings add to a growing literature supporting relations between area-level SES and survival from other cancers [e.g., colon cancer (Gorey et al., 2011), colorectal cancer (Le, Ziogas, Lipkin, & Zell, 2008)]. It also contributes to the literature linking low SES with lower survival among head and neck cancer patients in the US [e.g., (Arbes et al., 1999; Chu et al., 2011; Molina et al., 2008)]. However, the current study significantly adds to that literature by highlighting the unique role of neighborhood deprivation on clinical outcomes independent of individual-level SES. Clinicians treating oropharyngeal cancer patients may want to understand more

about the places their patients live, as those living in deprived areas may be at increased risk for worse clinical outcomes regardless of personal income.

Among this sample of oropharyngeal cancer patients, who were all treated at a single cancer center using a multidisciplinary team approach, the effects of neighborhood deprivation on outcomes were limited to overall survival and second primary malignancy development. These outcomes were less related to their incident SCCHN than were disease-free or disease-specific survival outcomes. This pattern of results suggests that oropharyngeal cancer patients from economically deprived areas may be more likely to have significant comorbidities, exposures, or other risk factors that affected non-SCCHN-related overall survival or second primary malignancy development relative to oropharyngeal cancer patients from the less deprived areas. A number of previous studies have linked neighborhood deprivation to increased morbidity, mortality, and engagement in health risk behaviors among residents [e.g., (Cubbin & Winkleby, 2005; Diez-Roux et al., 1997; Diez Roux & Mair, 2010; Macintyre, Ellaway, & Cummins, 2002; Sampson, Raudenbush, & Earls, 1997)], with negative health outcomes persisting after accounting for the influence of individual-level SES (Chaix, Rosvall, & Merlo, 2007; Davidson, Bastani, Nakazono, & Carreon, 2005; Pickett & Pearl, 2001; van Lenthe et al., 2005; Wight et al., 2008). We controlled for one of these health risk behaviors in our analyses (i.e., smoking), and post-hoc analyses indicated no differences in gross alcohol use patterns (current/former weekly drinker versus never weekly drinker) among oropharyngeal cancer patients in low to moderate versus high deprivation neighborhoods in this sample. However, data on other behavioral risk factors (e.g., overweight/obesity status, dietary habits, sedentary behavior) were unknown. Recent schematic models of neighborhood effects on health and health-related behaviors highlight the importance of psychosocial and ecologic mechanisms (Diez Roux & Mair, 2010). Supporting such models are a host of theoretical and empirical studies citing associations between economically deprived neighborhoods and mechanisms that underlie health-related behaviors and health outcomes, including less social support (Black, Cook, Murry, & Cutrona, 2005; Young, Russell, & Powers, 2004), greater negative affect/depression (Cutrona et al., 2005; Cutrona, Wallace, & Wesner, 2006; Echeverria, Diez-Roux, Shea, Borrell, & Jackson, 2008; Hill & Angel, 2005; Mair et al., 2009; Wen, Hawkey, & Cacioppo, 2006), more stress (Burdette & Hill, 2008; Cutrona et al., 2006; Hill & Angel, 2005; Wen et al., 2006; Young et al., 2004), and less social capital and collective efficacy (Kawachi & Berkman, 2003; Kawachi & Berkman, 2000; Kawachi, Kennedy, & Glass, 1999). Of course, systematic differences between oropharyngeal and non-oropharyngeal cancer patients on some of these mechanisms (engagement in health risk behaviors, for example) might have contributed to null results for the non-oropharyngeal group and led to a lack of main effects for the sample as a whole. More studies are needed to better understand the mechanisms that underlie the associations between neighborhood deprivation and SCCHN outcomes among oropharyngeal cancer patients.

Previous research has suggested that the survival disparity experienced by cancer patients of lower SES is largely attributable to diagnosis at later stages of cancer and lower access to quality treatment (Byers et al., 2008; Woods, Rachet, & Coleman, 2006). However, the current study controlled for disease stage and included patients with known access to a quality treatment resource, and still found significant relations between neighborhood-level SES and clinical outcomes (albeit only among the oropharyngeal patents). Therefore, these usual suspects (i.e., later detection and lower access) may only partially explain relations between socioeconomic indicators and cancer survival outcomes for oropharyngeal SCCHN patients. In fact, at least one prior study suggested that SES was not associated with treatment stage at presentation among head and neck cancer patients (S. Johnson, Corsten, McDonald, & Chun, 2010). Therefore, it behooves clinicians and stakeholders concerned with survival disparities to better understand the role that neighborhood deprivation plays in

the health status of oropharyngeal patients. However, it is important to acknowledge that the strength of relations between neighborhood deprivation and clinical outcomes may vary based on geographic area. For example, previous research has cited a Canadian advantage in cancer survival outcomes for patients from economically deprived neighborhoods relative to some US cities and states, even when controlling for cancer stage (Gorey et al., 2000a, 2000b; Gorey et al., 2011). In those cases, the geographic advantage may have to do with differences in insurance coverage, provider availability, and preventive care between the countries, but it is certainly also possible to find these variations within a single country or region of the country for reasons other than those cited. For example, distance to quality treatment resources may also affect health services utilization and cancer survival outcomes (Lamont et al., 2003). To address this possibility in our data, we conducted post-hoc analyses in which we additionally controlled for distance in miles along the road network from the patient's residence to The University of Texas MD Anderson Cancer Center, and our pattern of results was unchanged. Nevertheless, issues such as delay in diagnosis, access to care, and geographically-varying relationships continue to be important considerations for future research linking area-level characteristics to cancer outcomes.

Our results suggest that different strategies may be necessary to improve outcomes among oropharyngeal versus non-oropharyngeal cancer patients, and that attention to interventions directed at the neighborhood-level would be most relevant among the former group. The current study is an important preliminary step to better understanding the role of neighborhood SES on SCCHN outcomes, but additional research in this area is needed to inform such interventions. However, results may have some immediate relevance for clinical practice. For example, clinicians treating oropharyngeal SCCHN patients should be aware that neighborhood deprivation has the potential to affect clinical outcomes independent of patients' personal income levels, and patients from deprived areas may face additional challenges to their health following the SCCHN treatment protocol. Thus, clinicians might want to identify comorbidities that are likely to contribute to mortality and secondary primary malignancy development, and facilitate appropriate referrals for these conditions in conjunction with and following incident oropharyngeal SCCHN cancer treatment. Clinicians might also stress the importance of regular cancer screenings and work with institutional social workers or other personnel to identify free or low cost and accessible screening and treatment resources in the patient's local community. Information on neighborhood deprivation can be accessed with a patient's address via publically available national and local resources (e.g., American FactFinder), and these data might be used to identify at-risk patients.

The inability to account for the influence of oncogenic HPV status is a major limitation of this study, as HPV status was assessed in only a minority of patients in this sample. Oncogenic HPV is most strongly associated with the development and prognosis of oropharyngeal cancers, and it has been suggested that HPV-positive oropharyngeal cancer is a "clinically, biologically, and epidemiologically distinct disease" from other SCCHN types (Schrunk et al., 2011; Sturgis & Ang, 2011). Specifically, patients with HPV-positive oropharyngeal cancers tend to present at a later stage of the disease, are less likely to be smokers, and have a better treatment response to and survival than HPV-negative oropharyngeal cancer patients (Schrunk et al., 2011; Sturgis & Ang, 2011). Estimates suggest that approximately 50-70% of oropharyngeal cancers are HPV-positive (Sturgis & Ang, 2011). Of the oropharyngeal cancer patients in our analyses with known HPV status ($n=190$), 76% had HPV-positive tumors. However, there were no significant differences in the proportion of HPV-positive patients in the high versus the low to moderate neighborhood deprivation groups [$\chi^2=728$ (1), $p=.399$]. Also, although we were unable to control for the HPV-status in the current study, smoking status (a covariate in our analyses) is known to be a strong proxy for HPV-related cancers.

Other limitations of the current study include the use of Census data gathered at a single point in time, despite a rolling enrollment period for patients. Future studies in this area can make use of American Community Survey data, which would allow for a better temporal matching of area-level to patient-level data. Participants in the present study were residing in Texas and Louisiana at the time they were assessed and treated at a large, multidisciplinary cancer center in the southwest. Thus, our results may not be generalized to untreated patients, patients from other areas of the country, or patients treated at other facilities. Also, selection and referral biases may exist. We estimate that approximately 90% of incident SCCHN patients at MD Anderson Cancer Center were recruited and agreed to participate in this study; unfortunately, information about those who refused to participate was not collected. Thus, systematic differences between participants and non-participants are unknown.

Future studies in this area should include more information about patients' engagement in health risk behaviors (e.g., detailed alcohol use patterns, overweight/obesity status, dietary habits, and sedentary behavior) in order to better understand their association with neighborhood effects on clinical outcomes. Our independent variable was comprised of five Census variables that were selected based on a priori ideas about important and complementary components of neighborhood deprivation (e.g., education, employment status, poverty) rather than in response to empirical estimation [i.e., principal components analysis (Messer et al., 2006)]. In addition, our neighborhood deprivation index was based only on Census data from the tracts in which our patients resided. A comparison of these tracts to all tracts in Texas and Louisiana suggests that, on average, our patients resided in areas with a larger population size and less deprivation across all five Census variables included in the index. Thus, our methodology for developing the neighborhood deprivation index has some limitations that might affect the generalizability of results. Relatedly, the extent to which other area-level variables, such as racial/ethnic segregation, might contribute to our results was not assessed. Finally, although our analyses had adjusted for several potential confounders, the presence of unknown and unmeasured confounders might have influenced the results.

In conclusion, this study was the first to link neighborhood SES to overall survival and second primary malignancy development among oropharyngeal cancer patients treated at a multidisciplinary cancer center, independent of individual-level SES and other sociodemographic and clinical variables. Results are in need of replication, but the unique influence of the neighborhood context in survival outcomes among oropharyngeal cancer patients suggests directions for future research, which can better inform clinical practice and intervention development.

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Highlights

- Neighborhood economic deprivation may have a unique effect on cancer outcomes.
- We examine this among head and neck cancer patients from a large treatment center.
- Neighborhood deprivation predicted poorer survival among oropharyngeal patients.
- It also predicted more secondary malignancies among oropharyngeal patients.
- Oropharynx cancer patients from deprived areas may need additional interventions.

Figure 1.

Survival curves for overall survival by neighborhood deprivation among oropharyngeal cancer patients (High ND = High Neighborhood Deprivation, Low ND = Low to Moderate Neighborhood Deprivation).

Note: Adjusted analyses controlled for the following: age, sex, race/ethnicity, income, smoking status, cancer site, cancer stage, and treatment approach. Age was treated as a binary variable (< 55 years and >55 years) in adjusted curve calculation due to macro specifications.

Figure 2.

Survival curves for second primary malignancy development by neighborhood deprivation among oropharyngeal cancer patients (High ND = High Neighborhood Deprivation, Low ND = Low to Moderate Neighborhood Deprivation)

Note: Adjusted analyses controlled for the following: age, sex, race/ethnicity, income, smoking status, cancer site, cancer stage, and treatment approach. Age was treated as a binary variable (< 55 years and >55 years) in adjusted curve calculation due to macro specifications.

Table 1
Patient Characteristics for Total Sample and by Cancer Site

Variables	Oropharyngeal (n=555)	Non-Oropharyngeal (n=579)	Total Sample (N=1151)
	n (%) / M (SD)	n (%) / M (SD)	N (%) / M (SD)
Neighborhood deprivation **			
Low to Moderate	451 (81.3)	406 (70.1)	863 (75.0%)
High	104 (18.7)	173 (29.9)	288 (25.0%)
Cancer stage **			
Stage I/II	47 (8.5)	232 (40.1)	283 (24.6%)
Stage III/IV	508 (91.5)	347 (59.9)	868 (75.4%)
Cancer Treatment **			
Single Modality	188 (33.9)	256 (44.2)	447 (38.8%)
Multiple Modalities	367 (66.1)	323 (55.8)	704 (61.2%)
Sex **			
Female	82 (14.8)	174 (30.1)	260 (22.6%)
Male	473 (85.2)	405 (69.9)	891 (77.4%)
Race/Ethnicity **			
Other	65 (11.7)	141 (24.4)	211 (18.3%)
Non-Hispanic White	490 (88.3)	438 (75.6)	940 (81.7%)
Smoking status **			
Current/Former	342 (61.6)	464 (80.1)	821 (71.3%)
Never	213 (38.4)	115 (19.9)	330 (28.7%)
Annual household income **			
<\$25,000	75 (14.0)	185 (32.6)	265 (23.7%)
\$25,000-74,900	182 (34.0)	250 (44.1)	439 (39.2%)
\$75,000	278 (52.0)	132 (23.3)	415 (37.1%)
Age **	55.7 (9.1)	59.5 (12.0)	57.7 (10.8)
Overall Death Event **			
No	447 (80.5)	415 (71.7)	870 (75.6%)
Yes	108 (19.5)	164 (28.3)	281 (24.4%)
Disease-specific Death Event *			
No	489 (88.1)	484 (83.6)	984 (85.5%)
Yes	66 (11.9)	95 (16.4)	167 (14.5%)
Cancer Recurrence Event			
No	463 (83.4)	457 (78.9)	933 (81.1%)
Yes	92 (16.6)	122 (21.1)	218 (18.9%)
Second Primary Malignancy Event			
No	517 (93.2)	534 (92.2)	1054 (91.6%)
Yes	38 (6.8)	45 (7.8)	97 (8.4%)

*
Note: $p < 0.05$

**
 $p < 0.001$: M=mean, SD=standard deviation.

Table 2

Effect of Neighborhood Deprivation on Survival and Second Primary Malignancy Outcomes among Oropharyngeal Cancer Patients in Adjusted Analyses

Variables Included in Each Model	Overall Survival	Disease-specific Survival	Disease-free Survival	Second Primary Malignancy
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)
Neighborhood Deprivation				
(Ref=Low/Moderate)	1.59 (1.00-2.53) *	1.38 (0.78-2.46)	1.04 (0.63-1.74)	2.99 (1.46-6.11) *
Cancer Stage				
(Ref=III/IV)	0.55 (0.22-1.37)	0.77 (0.22-2.74)	1.18 (0.49-2.80)	1.49 (0.51-4.38)
Cancer Treatment				
(Ref=Multiple Modalities)	0.53 (0.34-0.85) *	0.29 (0.14-0.62) **	0.44 (0.26-0.77) *	0.74 (0.36-1.50)
Sex				
(Ref=Male)	0.95 (0.51-1.75)	0.88 (0.42-1.87)	0.94 (0.50-1.78)	1.36 (0.52-3.56)
Race/Ethnicity				
(Ref=Non-Hispanic White)	2.36 (1.47-3.79) **	2.82 (1.62-4.90) **	2.90 (1.73-4.87) **	0.99 (0.33-3.01)
Smoking Status				
(Ref=Never Smoker)	2.61 (1.53-4.43) **	1.89 (1.03-3.48) *	1.58 (0.96-2.59)	1.78 (0.78-4.06)
Annual household income				
<\$25,000	2.08 (1.19-3.64) *	1.73 (0.85-3.53)	1.22 (0.65-2.32)	0.60 (0.19-1.86)
\$25,000-74,900	1.06 (0.65-1.73)	0.91 (0.50-1.67)	0.90 (0.54-1.48)	1.31 (0.64-2.69)
(Ref= \$75,000)				
Age	1.04 (1.02-1.06) **	1.04 (1.01-1.07) *	1.05 (1.02-1.08) **	1.05 (1.01-1.08) *

Note: "Ref" is reference group.

*
 $p < 0.05$

**
 $p < 0.001$; HR=hazard ratio.