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RESEARCH ARTICLE

# Health Disparities in Liver Cancer: An Analysis of the Ohio Cancer Incidence Surveillance System

Robert B. Hood[1]; Rebecca Andridge[2]; Shawnita Sealy-Jefferson[1]; Ashley S. Felix[1]
[1]Division of Epidemiology, College of Public Health, The Ohio State University, Columbus, OH
[2]Division of Biostatistics, College of Public Health, The Ohio State University, Columbus, OH
Corresponding Author: Robert Hood, 1841 Neil Avenue, Columbus, OH 43210, (410) 236-9729, rhood2@emory.edu
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## ABSTRACT

**Background:** We explored associations between neighborhood deprivation and tumor characteristics, treatment, and 5-year survival among primary hepatocellular carcinoma (HCC) patients in Ohio diagnosed between 2008 and 2016.

**Methods:** We used data from the Ohio Cancer Incidence Surveillance System and limited our analysis to adult (>18 years of age) HCC patients with known census tract information based on address at diagnosis. Using principal components analysis, we created a neighborhood deprivation index (NDI) using 9 census tract-level variables. We examined associations between tumor characteristics (stage and tumor size) and NDI quintile using chi-square tests and analysis of variance (ANOVA). Associations between guideline-concordant care and NDI using log-binomial regression adjusted for sex, race, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis were conducted. For 5-year survival, we utilized Cox proportional hazards models with a similar adjustment set.

**Results:** Neighborhood deprivation index was not associated with stage or tumor size. Individuals living in the most deprived neighborhoods were 16% less likely to receive guideline-concordant care as compared to individuals living in the least deprived neighborhoods (adjusted prevalence ratio [PR]: 0.84; 95% confidence interval [CI]: 0.74-0.94). Similarly, individuals living in the most deprived neighborhoods were 15% less likely to survive 5 years compared to individuals living in the least deprived neighborhoods (adjusted Hazard Ratio: 1.15; 95% CI: 1.01-1.29).

**Conclusion:** Our results suggest a negative association between neighborhood deprivation on guideline-concordant care and survival among HCC patients. Interventions targeting disparities of HCC should focus not only on individual-level factors but address larger neighborhood level factors as well.

**Keywords:** Neighborhood deprivation; Hepatocellular carcinoma; Guideline-concordant care; Mortality; Five-year survival

## INTRODUCTION

In the United States (US), liver cancer ranks fifth in cancer mortality and by 2030 is projected to be the third leading cause of cancer mortality.[1] Several epidemiological studies have demonstrated disparities across liver cancer incidence, treatment, and mortality.[2-5] In particular, disparities according to race, ethnicity, and nativity have become apparent. Hispanics and Asian Americans tend to have the highest incidence of liver cancer.[2] Additionally, Black men and women have higher mortality rates from primary liver cancer when compared to non-Hispanic White men and women.[3-5] While these disparities are known, it is less clear how socioeconomic status is related to liver cancer treatment and mortality.[6-9] Most studies of socioeconomic status and liver cancer focus on incidence rather than treatment or mortality.[6,8,9]

One-dimensional socioeconomic status, variously defined according to income (individual or household), employment, educational attainment, and housing, as well as a myriad of other variables,[10] generally demonstrates inverse associations with liver cancer mortality.[7,11,12] The contribution of multidimensional socioeconomic risk factors at the neighborhood-level, while increasingly recognized to be important, is absent from the literature.[6-9] The use of deprivation indexes such as Townsend material deprivation index, Krieger's index, or Messer's index, which combine several census-measured variables, are extensively used in other diseases including low birth weight and infant mortality[10,13,14] but are used less in liver cancer research. These studies demonstrate that multidimensional measures of socioeconomic status provide a more complete picture when trying to understand how socioeconomic status influences health when compared to a one-dimensional measure.

Understanding the contribution of neighborhood deprivation on liver cancer survival would lead to greater clarity regarding the context in which liver cancer occurs. Additionally, a better understanding of neighborhood deprivation would allow for public health and medical providers to target the social determinants of health rather than place the entire burden on the individual patient. To investigate the role of neighborhood deprivation on liver cancer, specifically hepatocellular carcinoma, we obtained data from the Ohio Cancer Incidence Surveillance System (OCISS) from 2008 to 2016. We explored the association between tumor characteristics at diagnosis, treatment course, and 5-year survival of hepatocellular carcinoma and neighborhood deprivation.

## METHODS

### Setting, Design, and Participants

We obtained data on primary hepatocellular carcinoma patients diagnosed from 2008 to 2016 from across the state of Ohio (n = 5984). We excluded 22 cases of hepatocellular carcinoma in patients less than 18 years of age since we sought to generalize to adult liver cancer patients rather than pediatric cases. Hepatocellular carcinomas were identified based on the following ICO-3 histology codes: 8170/3, 8171/3, 8172/3, 8173/3, 8174/3, and 8175/3.

Liver cancer includes several different subtypes, which may not progress at the same rate and require different treatments as well. Therefore, to reduce confounding by liver cancer subtype, we restricted the sample to hepatocellular carcinoma. In addition, hepatocellular carcinoma is the most common liver cancer type and provides the largest homogenous sample among all types of incident liver cancers. Data collected from OCISS include some individual patient demographic characteristics and clinical information such as age at diagnosis and tumor characteristics. According to the North American Association of Central Cancer Registries, Ohio was considered a certified gold standard for cancer registries in 2013, 2014, and 2016.[15] Additionally, Ohio was a silver certified registry in 2008, 2009, 2011, and 2012.[15] Ohio was not ranked in 2010, and data on 2016 certifications are not available.[15]

### Measures—Outcomes

We examined 2 hepatocellular carcinoma characteristics, specifically, stage and tumor size. Stage was categorized as 1) localized, 2) regional (including various degrees of lymph node involvement), 3) distant, and 4) unstaged. Tumor size was measured in millimeters and examined as a continuous variable. Tumor size was missing among 39.5% of the study population (n = 2353).

We examined whether patients received guideline-concordant care based on recommendations published on UpToDate. Briefly, UpToDate provides evidence-based clinical information for health care providers. Based on published recommendations, specifically the Barcelona Clinic Liver Cancer (BCLC) system,[16] we assumed that patients with lower stage cancers would receive surgery while patients with regional tumors would require a mix of surgery and chemotherapy or radiation while individuals with advanced tumors should receive chemotherapy or radiation. Guideline-concordant treatment was classified as missing for 1180 (19.8%) patients with unstaged disease. We examined 5-year overall survival among patients diagnosed between 2008 and 2013; we used 2013 as the last date because 2018 was the last year of follow-up available. Patients' vital status was recorded as alive or dead and survival time was recorded in months.

### Measures—Exposure

We obtained census data at the tract level from the 2010 Census and the American Community Survey (ACS). Census tracts are large geographic areas but tend to be more stable estimates over time when compared to census blocks.[10] We obtained the following 9 variables from the US Census Bureau: percent of the tract with less than high school diploma, percent of the tract with less than a college degree, percent of the tract living below the federal poverty line, percent of individuals 16 years and older who are unemployed in the tract, median household income, percent of housing units vacant, percent of housing units not owned, median value of mortgage, and percent of individuals self-identifying as African American or Black. We selected these variables based on previous studies exploring associations of these variables or similar measures at the individual level with liver cancer.[6-9,11,12,17-20] We then created a neighborhood deprivation index using similar methods described in detail elsewhere.[10] Briefly, we utilized principal component analysis to create weights for each of the nine variables. We then combined these weights to create a single index and created quintiles of deprivation with higher quintiles indicating greater deprivation.

### Measures—Covariates

We selected covariates by identifying the minimal adjustment set of variables using a direct acyclic graph (DAG).[21,22] Our covariates included sex assigned at birth (male vs female), race (White, Black, Other), age at diagnosis in years (continuous), metropolitan status (urban vs rural), stage, and year of diagnosis. Metropolitan status was defined using the 2003 Beale codes to create a dichotomous categorization where nonmetropolitan areas were those with a Beale code between 4 and 9 and metropolitan areas were those with a Beale code between 1 and 3.

### Statistical Analysis

Tumor Characteristics by Neighborhood Deprivation

We compared the distribution of hepatocellular carcinoma stage and mean tumor size by quintile of neighborhood deprivation using chi-square and ANOVA tests, respectively.

Treatment by Neighborhood Deprivation

We used unadjusted and adjusted log-binomial models with receipt of guideline-concordant treatment as the outcome and quintile of neighborhood deprivation index as the exposure. We used the least deprived neighborhoods (ie, quintile 1) as the reference category. In our adjusted model, we included sex, race (as a proxy for racism), age at diagnosis, metropolitan status, cancer stage, and year of diagnosis. In addition to utilizing a model with all patients, we stratified the models by race to examine potential racial disparities in treatment because racial disparities are known to exist for liver cancer. However, we could not fit the full model for individuals who did not report their race as either White or Black because the sample size was too small.

Five-Year Survival by Neighborhood Deprivation

Finally, we examined 5-year survival by quintile of neighborhood deprivation index using Cox proportional hazards models for liver cancer patients diagnosed from 2008 to 2013. Individuals diagnosed after 2013 were excluded from this analysis. We used the least deprived neighborhoods (ie, quintile 1) as our reference for our models, and a DAG to identify the minimally sufficient adjustment set identified[21,22] sex, race (as a proxy for racism), age at diagnosis, metropolitan status, cancer stage, and year of diagnosis as relevant covariates for which we adjusted. Similarly, we stratified the model by race, in addition to utilizing a model with all subjects, to examine potential racial disparities in 5-year survival. Again, we were unable to fit the full model for individuals who did not report their race as either White or Black due to sample size constraints.

Missing Data Analysis

To assess the impact of missing data on the results of the guideline-concordant treatment models and the 5-year survival models, we utilized multiple imputation using fully conditional specification (FCS) to impute missing data for neighborhood deprivation quintiles, outcomes, and covariates. We specified 100 imputations with 20 burn-in iterations. Results were combined across imputed datasets using the standard multiple imputation combining rules. Stata version 15 (StataCorp LLC, College Station, TX USA) was utilized to create the neighborhood deprivation index. All other analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC USA). All results presented are from the available case analysis unless otherwise stated.

### Ethical Statement

This study was approved by the institutional review boards at The Ohio State University and the Ohio Department of Health.

## RESULTS

### Neighborhood Deprivation

From 2008 to 2016, a total of 5962 adult hepatocellular carcinoma cases were diagnosed. Among these patients, 2364 Ohio census tracts were identified. Approximately 2.9% of patients (n = 173) lacked census tract information and could not be assigned a neighborhood deprivation index quintile. Means and standard deviations for each of the 9 component variables followed expected patterns across the neighborhood deprivation quintiles (Supplemental Table 1). The neighborhood deprivation index was slightly skewed and ranged from -4.18 to 1.36. The mean value for the least deprived quintile (quintile 1) was -1.68 (standard deviation [SD]: 0.72) while the mean value for the most deprived quintile (quintile 5) was 0.98 (SD: 0.13).

### Patient and Tumor Characteristics

Similar to national trends,[23] a majority of the patients with hepatocellular carcinoma were male (n = 4577; 76.8%) and had an average age at diagnosis around 65 years. However, unlike national trends which find that liver cancer is more common among non-Hispanic Asian/Pacific Islanders and non-Hispanic American Indian/Alaskan Native,[23] the sample was predominately White (n = 4503; 75.5%) (Table 1). Approximately 41% of the patients had a localized tumor while almost 20% of cancers were unstaged. Among all hepatocellular carcinoma patients, 76.7% (n = 4574) were deceased in 2018. Neither cancer stage (*P* value = 0.19) nor tumor size (*P* value = 0.80) differed by quintile of neighborhood deprivation.

### Guideline-Concordant Treatment by Neighborhood Deprivation

In the unadjusted model, the prevalence of patients living in the most deprived neighborhoods receiving guideline-concordant care was 12% lower (PR: 0.88; 95% CI: 0.78, 1.00) than the prevalence of patients living in the least deprived neighborhoods receiving guideline-concordant care (Table 2). Similarly, when comparing patients in lower quintiles of deprivation (ie, quintiles 2, 3, and 4) to patients in the least deprived neighborhoods (quintile 1), these patients were less likely to receive guideline-concordant care although these associations were not significant. After adjustment, the prevalence of patients living in the most deprived neighborhoods receiving guideline-concordant care was 16% lower (PR: 0.84; 95% CI: 0.74, 0.94) when compared to patients living in the least deprived neighborhoods.

When the model was stratified by race, in the adjusted model, the prevalence of White patients living in the most deprived neighborhoods receiving guideline-concordant care was 14% lower (PR: 0.86; 95% CI: 0.75, 0.99) than the prevalence of White patients living in the least deprived neighborhoods receiving guideline concordant care (Table 3). The prevalence ratios for the other quintiles of deprivation were similar for White patients when compared to the full model. In the adjusted model, the prevalence of Black patients living in the most deprived neighborhoods re-

**Table 1. Sample Characteristics Adult Ohioans Diagnosed with Primary Hepatocellular Carcinoma 2008 to 2016 (n=5962)**

| Characteristic | N | % |
|---|---|---|
| **Sex** | | |
| Male | 4577 | 76.8 |
| Female | 1385 | 23.2 |
| **Race** | | |
| White | 4503 | 75.5 |
| Black | 1261 | 21.2 |
| Other | 181 | 3.0 |
| Missing | 17 | 0.3 |
| **Metropolitan status** | | |
| Metropolitan | 5063 | 84.9 |
| Nonmetropolitan | 899 | 15.1 |
| **Stage** | | |
| Localized | 2458 | 41.2 |
| Regional | 1533 | 25.7 |
| Distant | 803 | 13.5 |
| Unstaged | 1168 | 19.6 |
| **Guideline-concordant treatment** | | |
| Nonconcordant | 3216 | 53.9 |
| Concordant | 1566 | 26.3 |
| Missing | 1180 | 19.8 |
| **Vital status** | | |
| Alive | 1388 | 23.3 |
| Deceased | 4574 | 76.7 |
| | **Average** | **SD** |
| **Age (years)** | 64.6 | 11.1 |
| **Tumor size** | 62.8 | 70.3 |
| Missing (n, %) | 2353 | 39.5% |
| **Survival time (months)** | 9.5 | 12.7 |
| Missing (n, %) | 497 | 8.3% |
| **Neighborhood deprivation index** | | |
| Quintile 1 (Least deprived) | -1.68 | 0.72 |
| Quintile 2 | -0.25 | 0.23 |
| Quintile 3 | 0.31 | 0.12 |
| Quintile 4 | 0.65 | 0.09 |
| Quintile 5 (Most deprived) | 0.98 | 0.02 |

**Table 2. Prevalence Ratio Patients Receiving Guideline-Concordant Care by Neighborhood Deprivation Index among Ohioans with Primary Liver Cancer Diagnosed 2008-2016 using log-binomial regression**

| | **Unadjusted** | | **Adjusted** [a] | |
|---|---|---|---|---|
| | PR [b] | 95% CI [c] | PR [b] | 95% CI [c] |
| **Neighborhood deprivation index** [d] | | | | |
| Quintile 1 [e] | --- | --- | --- | --- |
| Quintile 2 | 0.90 | 0.79, 1.02 | 0.90 | 0.81, 1.01 |
| Quintile 3 | 0.95 | 0.84, 1.08 | 0.91 | 0.81, 1.02 |
| Quintile 4 | 0.90 | 0.79, 1.03 | 0.89 | 0.79, 1.01 |
| Quintile 5 | 0.88 | 0.78, 1.00 | 0.84 | 0.74, 0.94 |

[a]Adjusted for sex, race, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis.
[b]PR: prevalence ratio
[c]95% CI: 95% confidence interval
[d]Higher quintiles indicate higher areas of deprivation.
[e] Quintile 1 is the lowest deprivation and the reference category.

**Table 3. Prevalence Ratio Patients Receiving Guideline-Concordant Care by Neighborhood Deprivation Index among Ohioans with Primary Liver Cancer Diagnosed from 2008-2016 using log-binomial regression stratified by race**

| | **White** | | **Black** | |
|---|---|---|---|---|
| | Unadjusted | Adjusted [a] | Unadjusted | Adjusted [a] |
| **Neighborhood deprivation index** [d] | PR [b] (95% CI [c]) | PR [b] (95% CI [c]) | PR [b] (95% CI [c]) | PR [b] (95% CI [c]) |
| Quintile 1 [e] | --- | --- | --- | --- |
| Quintile 2 | 0.95 (0.82, 1.10) | 0.98 (0.86, 1.11) | 0.77 (0.52, 1.13) | 0.71 (0.50, 1.00) |
| Quintile 3 | 0.97 (0.84, 1.11) | 0.93 (0.82, 1.06) | 1.05 (0.74, 1.50) | 0.95 (0.70, 1.31) |
| Quintile 4 | 0.92 (0.80, 1.07) | 0.93 (0.81, 1.06) | 0.98 (0.70, 1.38) | 0.94 (0.70, 1.27) |
| Quintile 5 | 0.87 (0.74, 1.01) | 0.86 (0.75, 0.99) | 1.11 (0.82, 1.50) | 0.97 (0.74, 1.27) |

[a]Adjusted for sex, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis.
[b]PR: prevalence ratio
[c]95% CI: 95% confidence interval
[d]Higher quintiles indicate higher areas of deprivation.
[e]Quintile 1 is the lowest deprivation and the reference category.

ceiving guideline-concordant care was 3% lower (PR: 0.97; 95% CI: 0.74, 1.27) than the prevalence of Black patients living in the least deprived neighborhoods receiving guideline concordant care (Table 3). However, this association was not statistically significant. The prevalence ratios for the other quintiles of deprivation were closer to null for Black patients when compared to the full model.

**Five-Year Survival by Neighborhood Deprivation**

Prior to adjustment, individuals living in the most deprived neighborhoods had a 16% decrease in survival (Hazard ratio [HR]: 1.16; 95% CI: 1.03, 1.30) compared to individuals living in the least deprived neighborhoods (Table 4). A similar trend emerged in the other quintiles of deprivation, with greater deprivation associated with decreasing survival; the trend was almost linear apart from quintile 4. After adjustment, individuals living in deprived neighborhoods still had approximately a 15% decrease (HR: 1.15; 95% CI: 1.01, 1.29) in survival when compared to individuals in the least deprived neighborhoods.

When the model was stratified by race, in the adjusted model, White patients living in the most deprived neighborhoods had a 16% decrease in survival (HR: 1.16; 95% CI: 1.00, 1.34) compared to White patients living in the least deprived neighborhoods (Table 5). The hazard ratios for the other quintiles of deprivation were similar for White patients when compared to the full model. In the adjusted model, Black patients living in the most deprived neighborhoods had a 9% decrease in survival (HR: 1.09; 95% CI: 0.84, 1.41) compared to Black patients living in the least deprived neighborhoods (Table 5). The hazard ratio for the other quintiles of deprivation were wider for Black patients when compared to the full model.

**Missing Data Analysis**

Generally, the characteristics between the available (n = 4711) and incomplete cases (n = 1251) were similar for the guideline-concordant care analysis (Supplemental Table 1). Among the incomplete cases, the characteristics with the highest percent of missingness were guideline-concordant treatment (n = 1180, 94.3%) and neighborhood deprivation quintile (n = 173, 13.8%). Incomplete cases were likely missing guideline-concordant care because their cancer was unstaged or they were missing information on the treatment they received.

After imputing missing values, we observed associations that were closer to the null value when compared to the results from our available case analysis (Supplemental Table 2). Additionally, none of the prevalence ratios were statistically significant after multiple imputation.

For the 5-year survival analysis, there were a few key differences in characteristics of the available (n=3271) and incomplete cases (n = 486) (Supplemental Table 3). Generally, a higher proportion of the cancers in the incomplete cases were unstaged compared to the available cases (87.4% vs 12.1%). Additionally, incomplete cases on average were about 2 years older (66.0 vs 64.1 years) and a higher percent were dead (97.7% vs 84.4%). Survival time was also slightly shorter in the incomplete cases compared to the available cases (10.0 vs 11.7 months). The characteristics with the

**Table 4. Hazard Ratios Five-year Survival Liver Cancer by Neighborhood Deprivation Index among Ohioans with Primary Liver Cancer Diagnosed 2008-2013 using Cox proportional hazards regression.**

| | Unadjusted | | Adjusted [a] | |
|---|---|---|---|---|
| | HR [b] | 95% CI [c] | HR [b] | 95% CI [c] |
| **Neighborhood deprivation index [d]** | | | | |
| Quintile 1 [e] | --- | --- | --- | --- |
| Quintile 2 | 1.11 | 0.98, 1.25 | 1.11 | 0.98, 1.25 |
| Quintile 3 | 1.13 | 1.00, 1.25 | 1.12 | 0.99, 1.28 |
| Quintile 4 | 1.04 | 0.92, 1.17 | 1.05 | 0.92, 1.19 |
| Quintile 5 | 1.16 | 1.03, 1.30 | 1.15 | 1.01, 1.29 |

[a]Adjusted for sex, race, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis.
[b]HR: hazard ratio
[c]95% CI: 95% confidence interval
[d]Higher quintiles indicate higher areas of deprivation.
[e]Quintile 1 is the lowest deprivation and the reference category.

**Table 5. Hazard Ratios Five-year Survival Liver Cancer by Neighborhood Deprivation Index among Ohioans with Primary Liver Cancer Diagnosed 2008-2013 using Cox proportional hazards regression stratified by race.**

| | White | | Black | |
|---|---|---|---|---|
| **Neighborhood deprivation index [d]** | Unadjusted PR [b] (95% CI [c]) | Adjusted [a] PR [b] (95% CI [c]) | Unadjusted PR [b] (95% CI [c]) | Adjusted [a] PR [b] (95% CI [c]) |
| Quintile 1 [e] | --- | --- | --- | --- |
| Quintile 2 | 1.15 (1.00, 1.32) | 1.16 (1.01, 1.33) | 0.95 (0.71, 1.29) | 0.94 (0.69, 1.27) |
| Quintile 3 | 1.14 (0.99, 1.30) | 1.13 (0.99, 1.30) | 1.13 (0.83, 1.54) | 1.14 (0.84, 1.56) |
| Quintile 4 | 1.01 (0.88, 1.17) | 1.02 (0.88, 1.17) | 1.18 (0.89, 1.56) | 1.19 (0.89, 1.59) |
| Quintile 5 | 1.17 (1.01, 1.35) | 1.16 (1.00, 1.34) | 1.15 (0.90, 1.49) | 1.09 (0.84, 1.41) |

[a]Adjusted for sex, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis.
[b]HR: hazard ratio
[c]95% CI: 95% confidence interval
[d]Higher quintiles indicate higher areas of deprivation.
[e]Quintile 1 is the lowest deprivation and the reference category.

highest missingness included survival time (n = 340, 70.0%) and neighborhood deprivation quintile (n = 159, 32.7%).

The association between neighborhood deprivation and survival were similar after using multiple imputation (Supplemental Table 4).

## DISCUSSION

Among Ohioan adults diagnosed with hepatocellular carcinoma between 2008 and 2016, we observed lower likelihood of receiving guideline-concordant treatment among those living in the most deprived areas compared to those living in the least deprived neighborhoods. Furthermore, individuals living in more deprived areas had lower 5-year survival than patients living in the least deprived neighborhoods. However, in this analysis, neighborhood deprivation was not associated with worse tumor characteristics (ie, later stage at diagnosis or larger tumor size), indicating that neighborhood deprivation influences survival through mechanisms unrelated to tumor characteristics. We also observed limited evidence for racial disparities in receiving guideline-concordant care as well as 5-year survival. However, this may be the result of small sample size.

To our knowledge, this is the first study examining associations between neighborhood deprivation, hepatocellular carcinoma treatment, and survival. However, studies of other cancers such as breast and prostate provide some context. In one study of patients with an abnormal screening for breast cancer in Ohio, patients residing in areas of higher deprivation had a longer time to resolution for their abnormal test, potentially indicating less access to treatment.[24] Other components of the deprivation measure, including lower educational attainment, lower household income, and greater unemployment, may indicate that a lack of health literacy and income prevent people from seeking care in a health care system that is prohibitively expensive. In addition, it is reasonable to hypothesize that lower odds of receiving guideline-concordant care may be linked to more advanced disease because of nonoptimal treatment options or delay in treatment that may

**Supplemental Table 1.**

Comparison of characteristics between available [a] and incomplete cases for adult Ohioans diagnosed with primary hepatocellular carcinoma from 2008-2016 (n = 5962).

| Characteristic | Available Cases [a] (n = 4711) n | % | Incomplete Cases (n = 1251) n | % |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | 3614 | 76.7 | 963 | 77.0 |
| Female | 1097 | 23.3 | 288 | 23.0 |
| **Race** | | | | |
| White | 3558 | 75.5 | 945 | 75.5 |
| Black | 997 | 21.2 | 264 | 21.0 |
| Other | 156 | 3.3 | 25 | 2.0 |
| Missing | 0 | 0 | 17 | 1.4 |
| **Metropolitan status** | | | | |
| Metropolitan | 4006 | 85.0 | 1057 | 84.5 |
| Nonmetropolitan | 705 | 15.0 | 194 | 15.5 |
| **Stage** | | | | |
| Localized | 2410 | 51.2 | 48 | 3.8 |
| Regional | 1508 | 32.0 | 25 | 2.0 |
| Distant | 793 | 16.8 | 10 | 0.8 |
| Unstaged | 0 | 0 | 1168 | 93.4 |
| **Age (Years) – Average, SD** | 64.1 | 10.9 | 66.5 | 11.5 |
| **Guideline-concordant treatment** | | | | |
| Nonconcordant | 3171 | 67.3 | 45 | 3.6 |
| Concordant | 1540 | 32.7 | 26 | 2.1 |
| Missing | 0 | 0 | 1180 | 94.3 |
| **Neighborhood deprivation index** | | | | |
| Quintile 1 (Least deprived) | 883 | 18.7 | 164 | 13.1 |
| Quintile 2 | 936 | 19.9 | 212 | 17.0 |
| Quintile 3 | 938 | 19.9 | 223 | 17.8 |
| Quintile 4 | 937 | 19.9 | 228 | 18.2 |
| Quintile 5 (Most deprived) | 1017 | 21.6 | 251 | 20.1 |
| Missing | 0 | 0 | 173 | 13.8 |

[a]Available cases had complete data for the log-binomial models examining the association between quintiles of neighborhood deprivation and receiving guideline concordant care.

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allow the tumor to progress. Indeed, in a study of prostate cancer, Zeigler-Johnson et al (2011) observed that neighborhood deprivation was associated with higher Gleason score.[25] However, in this analysis we did not observe an association between neighborhood deprivation and worse tumor characteristics.

This analysis also demonstrated a decrease in survival when neighborhood deprivation increased, and these results are consistent with previous findings. In one study of chronic liver disease and hepatocellular carcinoma, higher area deprivation was associated with lower survival from chronic liver disease when compared to less deprived areas.[6] However, this study did not observe an association between area deprivation and hepatocellular carcinoma survival.[6] Our study differs slightly by examining all-cause mortality rather than cause-specific mortality and we do not adjust for other area-level factors such as alcohol retail outlets. In other cancer sites such as lung cancer, others have observed that greater neighborhood deprivation is associated with lower survival.[26] The results from our analysis may differ from previous liver specific research due to the underlying population,

**Supplemental Table 2.**

Prevalence ratio for patients receiving guideline-concordant care by neighborhood deprivation index among Ohioans with primary liver cancer diagnosed from 2008-2016 using log-binomial regression and multiple imputation.

| | Unadjusted | | Adjusted [a] | |
|---|---|---|---|---|
| | PR [b] | 95% CI [c] | PR [b] | 95% CI [c] |
| **Neighborhood deprivation index [d]** | | | | |
| Quintile 1 [e] | --- | --- | --- | --- |
| Quintile 2 | 0.98 | 0.89, 1.07 | 0.99 | 0.95, 1.02 |
| Quintile 3 | 1.01 | 0.92, 1.11 | 0.99 | 0.95, 1.02 |
| Quintile 4 | 0.99 | 0.90, 1.09 | 0.98 | 0.95, 1.02 |
| Quintile 5 | 0.99 | 0.90, 1.08 | 0.98 | 0.94, 1.01 |

[a]Adjusted for sex, race, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis.
[b]PR: prevalence ratio
[c]95% CI: 95% confidence interval
[d]Higher quintiles indicate higher areas of deprivation.
[e]Quintile 1 is the lowest deprivation and the reference category.

**Supplemental Table 3.**

Comparison of characteristics between available [a] and incomplete cases for adult Ohioans diagnosed with primary hepatocellular carcinoma from 2008-2016 (n = 3757).

| | Available Cases [a] (n = 3271) | | Incomplete Cases (n = 486) | |
|---|---|---|---|---|
| **Characteristic** | **n** | **%** | **n** | **%** |
| **Sex** | | | | |
| Male | 2504 | 76.5 | 387 | 79.6 |
| Female | 767 | 23.5 | 99 | 20.4 |
| **Race** | | | | |
| White | 2457 | 75.1 | 354 | 72.8 |
| Black | 708 | 21.6 | 110 | 22.6 |
| Other | 106 | 3.3 | 9 | 1.9 |
| Missing | 0 | 0 | 13 | 2.7 |
| **Metropolitan status** | | | | |
| Metropolitan | 2766 | 84.6 | 419 | 86.2 |
| Nonmetropolitan | 505 | 15.4 | 67 | 13.8 |
| **Stage** | | | | |
| Localized | 1441 | 44.0 | 33 | 6.8 |
| Regional | 926 | 28.3 | 19 | 4.0 |
| Distant | 510 | 15.6 | 9 | 1.8 |
| Unstaged | 394 | 12.1 | 425 | 87.4 |
| **Age (years) – Average, SD** | 64.1 | 11.5 | 66.0 | 11.9 |
| **Vital status** | | | | |
| Alive | 509 | 15.6 | 11 | 2.3 |
| Dead | 2762 | 84.4 | 475 | 97.7 |
| Missing | 0 | 0 | | |
| **Survival time (months)** | 11.7 | 14.9 | 10.0 | 15.9 |
| Missing | 0 | 0 | 340 | 70.0 |
| **Neighborhood deprivation index** | | | | |
| Quintile 1 (Least deprived) | 509 | 18.0 | 57 | 11.7 |
| Quintile 2 | 673 | 20.6 | 65 | 13.4 |
| Quintile 3 | 663 | 20.3 | 69 | 14.2 |
| Quintile 4 | 635 | 19.4 | 66 | 13.6 |
| Quintile 5 (Most deprived) | 710 | 21.7 | 70 | 14.4 |
| Missing | 0 | 0 | 159 | 32.7 |

[a]Available cases had complete data for the Cox proportional hazards models examining the association between quintiles of neighborhood deprivation and 5-year mortality.

**Supplemental Table 4.**

Hazard ratios for 5-year survival of liver cancer by neighborhood deprivation index among Ohioans with primary liver cancer diagnosed from 2008-2013 using Cox proportional hazards regression and multiple imputation.

| | Unadjusted | | Adjusted [a] | |
|---|---|---|---|---|
| | HR [b] | 95% CI [c] | HR [b] | 95% CI [c] |
| **Neighborhood deprivation index [d]** | | | | |
| Quintile 1 [e] | --- | --- | --- | --- |
| Quintile 2 | 1.12 | 1.00, 1.26 | 1.12 | 0.99, 1.26 |
| Quintile 3 | 1.13 | 1.01, 1.27 | 1.14 | 1.00, 1.28 |
| Quintile 4 | 1.05 | 0.50, 1.18 | 1.06 | 0.93, 1.20 |
| Quintile 5 | 1.15 | 1.03, 1.29 | 1.16 | 1.02, 1.31 |

[a]Adjusted for sex, race, age at diagnosis, metropolitan status, cancer stage, and year of diagnosis.
[b]HR: hazard ratio
[c]95% CI: 95% confidence interval
[d]Higher quintiles indicate higher areas of deprivation.
[e]Quintile 1 is the lowest deprivation and the reference category.

different adjustment sets, and differing neighborhood deprivation scales.

Based on these results, clinicians and other health care providers should be made aware of potential disparities that may exist by neighborhoods with regard to hepatocellular carcinoma treatment and mortality. Health care providers should be aware that several other cancers such as breast, prostate and lung cancer, in addition to hepatocellular carcinoma, have been associated with neighborhood deprivation.[24-26] Taken together this evidence suggests neighborhood-level factors play an important role in human health. Understanding these disparities by neighborhood may help to explain why individual-level factors cannot solely predict cancer risk. Neighborhoods can be both helpful and harmful to health depending on the conditions (ie, stress, physical conditions, environmental exposures, safety, etc). People spend a significant amount of time in their neighborhoods, and if the neighborhood is not optimized for people's health it can be detrimental. If health care providers are made aware of potential disparities, clinicians could provide additional resources to help lessen these disparities by, for example, connecting patients with social workers to assist them in accessing food, income, and housing assistance. At the same time, disparities in neighborhood resources and access need to be made more equitable to protect human health which should be the goal of sound public policy and advocacy.

Our study is not without limitations. Our main limitation was missing data for tumor characteristics, specifically stage and tumor size. We addressed this by using multiple imputation to assess the impact of missing data on our results and found that our results were robust to the missing information. Additionally, we lacked some clinical information about the patient's tumor such as the Child-Pugh score and the operability of a patient's tumor. Without this information we may have oversimplified the guideline-concordant variable, potentially introducing nondifferential misclassification. However, as this would bias our results toward the null, our findings may be viewed as conservative. Additionally, we utilized a simplified version of the BCLC guidelines, but the most commonly used guidelines come from the National Comprehensive Cancer Network (NCCN). However, the BCLC guidelines have been validated extensively[16] and may not differ from NCCN guidelines in clinically meaningful ways. Next, our measure of neighborhood deprivation has not been extensively validated but similar methods have been used in other contexts. However, we built the deprivation index using variables that have been previously linked with cancer outcomes, and we were able to tailor the index to our specific population and outcome. The NDI also has the advantage of partially incorporating the racial composition of a neighborhood which is linked to redlining and structural racism; something that is absent from many other indices. Additionally, we utilized census tracts rather than smaller units such as a census block group or block, which means there could be heterogeneity in the variables used to build the NDI. However, we selected the census tracts because they are generally more stable over time and heterogeneity within a census tract would likely lead to nondifferential bias, which means our findings would be conservative. Due to sample size constraints, we were unable to fully explore potential racial disparities that exist for hepatocellular carcinoma treatment and mortality in Ohio. Lastly, our results may not be generalizable to other states or cancer types, warranting a cautious interpretation.

## PUBLIC HEALTH IMPLICATIONS

In summary, we observed greater deprivation associated with worse treatment and survival outcomes. Clinicians and other health care professionals should be aware of the context in which people live and how it may impact one's health. Future analyses are needed to confirm these results and understand potential mechanisms between neighborhood deprivation and liver cancer outcomes.

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### DISCLAIMER

This study includes data provided by the Ohio Department of Health which should not be considered an endorsement of this study or conclusion.

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