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Disparities in stage at diagnosis for hepatocellular carcinoma according to race and ethnicity, neighborhood socioeconomic status, and insurance status; a population-based study in California, 2001-2020

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ABSTRACT

Stage at diagnosis is a key determinant of survival for patients with hepatocellular carcinoma (HCC). No study has concurrently assessed the impact of race, ethnicity, neighborhood socioeconomic status (nSES), and insurance status on stage of HCC diagnosis. We examined stage at diagnosis among 45,695 individuals with primary HCC from 2001-2020 with data from the California Cancer Registry. Multivariable, multinomial logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) of regional and distant stage at diagnosis (compared to localized) according to joint race/ethnicity, nSES, and insurance type; adjusted for age, sex, year of diagnosis, comorbidities, marital status, and clustering by census tract. Race/ethnicity, nSES, and insurance type were independently associated with HCC stage in multivariable models. Compared to the NH White group, the NH Black group had higher odds of later stage compared to local stage diagnosis (OR distant=1.13, 95% CI=1.01, 1.26). Those with public or no insurance compared to private insurance had higher odds of later stage diagnosis (OR public insurance/distant stage=1.37, 95% CI=1.27, 1.49; OR no insurance/distant stage=2.78, 95% CI=2.37, 3.26). Lower nSES was associated with higher odds of late-stage diagnosis (OR lowest compared to highest SES quintile/distant stage=1.46, 95% CI=1.32, 1.61). Stratified analyses highlight racial/ethnic groups for which underinsurance and/or low nSES increased odds of distant stage diagnosis. Targeted, multilevel interventions would facilitate diagnosis of HCC at earlier stages and thus increase HCC survival for vulnerable groups defined by race, ethnicity, nSES, and insurance type.

KEYWORDS: hepatocellular carcinoma, prognosis, race and ethnicity, neighborhood socioeconomic stats, insurance status, sociodemographic, social determinants of health, cancer registry

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Introduction

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related death worldwide.[1] In the USA, HCC incidence and mortality have tripled over the last few decades and mortality rates due to HCC have grown faster than those for nearly every other cancer.[2,3] The overall 5-year survival rate for HCC is only 19.6%.[4] Stage of HCC at diagnosis is a key determinant of low overall survival; the 5-year survival rate among those diagnosed at an early stage is 35% while the 1-year survival rate of late-stage diagnosis is a mere 3%.[2] Thus, early-stage identification and intervention are essential to improve survival.

Disparities in HCC survival have been reported across race, ethnicity, and other sociodemographic measures.[5–9] In a recent meta-analysis, non-Hispanic (NH) Black individuals had worse survival compared to NH White individuals (pooled hazards ratio (HR): 1.08; 95% CI: 1.05, 1.12), while Hispanic (pooled HR: 0.92; 95% CI: 0.87, 0.97) and Asian and Pacific Islander (pooled HR: 0.81; 95% CI: 0.73, 0.88) individuals had better survival.[9] A study of 2011-2015 national Surveillance Epidemiology and End Results (SEER) data indicated that higher county-level poverty was associated with lower overall and HCC-specific survival in multivariable models (HR HCC-specific survival for highest compared to lowest level of poverty: 1.12; 95% CI: 1.03, 1.21).[10] Utilizing a multilevel index measuring socioeconomic status (SES) comprising lower county-level income and education as well as individual-level marital status and insurance type, another study of SEER data from 2012-2016 found that lower multilevel SES index scores were associated with lower HCC-specific survival.[11] Additionally, a study using national SEER data from 2000-2015 to assess intersections of joint race, ethnicity and census tract-level SES reported that the high-SES, NH Asian and Pacific Islander group had the highest survival (5-year survival: 30.0%; 95% CI: 28.2%, 31.9%) and the low-SES, NH Black group had the lowest (11.5%; 95% CI: 10.2%, 12.9%).[12]

Disparities in survival may be partly explained by differences in stage at diagnosis. However, studies of racial/ethnic disparities in HCC stage at diagnosis are limited. Sloane et al. reported racial disparities in HCC stage at diagnosis and subsequent intervention decisions but only compared Black and White individuals in the USA[8]. A study including NH White, NH Black, and Hispanic individuals using Texas state cancer registry data from 2007-2015 showed that the NH Black group was more likely, and the Hispanic group less likely, to be diagnosed with late-stage HCC compared to the NH White group.[13] Wong et al. showed that residents in rural and lower-income counties were at higher risk of late-stage diagnosis and mortality across multiple states in the USA.[14] However, no study to our knowledge has considered insurance type or concurrently assessed race, ethnicity, neighborhood SES (nSES), and insurance type in relation to HCC stage at diagnosis. A better understanding of the sociodemographic factors associated with late-stage diagnosis may identify vulnerable groups that would benefit most from interventions to facilitate earlier stage diagnosis. Thus, we utilize data from the California Cancer Registry (CCR) to examine associations of HCC stage at diagnosis with joint individual level race and ethnicity, insurance type, and census tract-level nSES.

Methods

Study Population

We used data from the California Cancer Registry (CCR), which is part of the National Cancer Institute's SEER program. The study comprised all individuals diagnosed with HCC between 2001-2020. (At the time we conducted analyses for this study (2024), available CCR data reflected

diagnoses through 2020 on account of the time required for data quality control and release.). Cases were defined by site and histology codes in accordance with the International Classification of Diseases for Oncology, 3rd edition site code: C22.0, histology codes: 8170-8175, 8180). Analyses were restricted to individuals with a first primary invasive HCC who were 18 years or older at time of diagnosis with reported sex as male or female. Cases were excluded if their records were solely based on autopsy or death certificate. The final study population consisted of 45,695 individuals diagnosed with HCC.

Predictor and Outcome Classification

Race and ethnicity data from the CCR were jointly classified as NH American Indian and Alaska Native, NH Asian American and Pacific Islander, NH Black, Hispanic, NH White, and another/unknown.

Health insurance type was classified with CCR data on the payer type at last admission for initial diagnosis and/or treatment. Insurance type is conceptualized as a proxy of individual-level SES; thus, categories reflect correlation of insurance type with financial need. Insurance type was classified as (1) private (private insurance managed care, health maintenance organization, or preferred provider organization; private insurance fee-for-service; Veterans Affairs; Tricare; or insurance, not otherwise specified), (2) public (Medicaid; Indian/Public Health Service; or other publicly funded insurance excluding Medicare), (3) Medicare, (4) uninsured, or (5) unknown. The unique structure and policies of Medicare warrant its separate classification from public or private insurance, in line with prior studies.[15,16]

Neighborhood SES was measured using a previously described index that captures SES at the census-tract level.[17,18] It incorporates data from the U.S. Census and American Community Survey (ACS) on education, employment, occupation, household income, poverty rates, rent, and home values. Quintiles of nSES were determined from the distribution of index values for all census tracts in California. Individual addresses in the cancer registry were geocoded, linked to census tracts, and assigned the nSES quintile associated with that tract. nSES was based on Census 2000 data for cases diagnosed 2001-2005 and based on ACS data 2008-2012 for cases diagnosed 2006-2020.

CCR data on stage at diagnosis (SEER Summary Stage) was classified as localized (in-situ, localized), regional (regional by direct extension, regional by lymph nodes, regional by direct extension and lymph nodes, and regional NOS), distant (remote), or unstaged/unknown (not abstracted or unknown or not specified)

Covariates

Additional variables extracted from the CCR were age at diagnosis (<50, 50-59, 60-69, 70-79, 80+ years of age); sex (male, female); marital status (married or domestic partnership, unmarried, unknown); and comorbidity burden.

While marital status is not a main variable of interest in our study of HCC stage at diagnosis, being married is frequently associated with earlier stages of cancer detection, as illustrated in a 2017 systematic review of the topic. Thus, we included marital status as a covariate in our analysis to examine the independent associations of race/ethnicity, nSES, and insurance type with stage at diagnosis.[19]

Comorbidity burden was measured using the Charlson Comorbidity Index. The Charlson Comorbidity Index (CCI) is a weighted index that captures concurrent burden of serious disease from twelve months prior to six months after the date of diagnosis, in which comorbidities are weighted based on disease severity (Charlson et al. 1987, Lichtensztajn et al. 2017).[20,21] Data for the CCI are

available through the annual linkage of CCR data to patient discharge, surgery, and emergency department data from the California Department of Health Care Access and Information Act (HCAI) and include data on myocardial infarction, congestive heart failure, peripheral vascular disease, stroke, dementia, chronic pulmonary disease, peptic ulcer disease, rheumatologic disease, liver disease, diabetes and resultant complications, hemiplegia and paraplegia, kidney disease, and AIDS. The range of values (0-18) was classified as no comorbidity burden (CCI=0), moderate comorbidity burden (CCI=1-2), and high comorbidity burden (CCI≥3).

Statistical Analysis

All analyses were conducted using SAS version 9.4. Sociodemographic variables of interest were race/ethnicity, nSES, and insurance type. We determined the frequency and percentile distribution of these three variables across stage of diagnosis, for all individuals and by sex. We then examined associations between these three sociodemographic variables and HCC stage at diagnosis using multivariable, multinomial logistic regression with adjustment for clustering by census tract. Results are reported as odds ratios (OR) and 95% confidence intervals. Statistical significance was assessed using the two-sided Wald's z-test with a threshold of $p < 0.05$. ORs represent the odds of being diagnosed with regional or distant disease relative to local disease, comparing categories of each sociodemographic factor to the indicated reference.

Each of the sociodemographic variables of interest were examined separately in models adjusted for age, sex, year of diagnosis, marital status, and CCI. Then they were examined in a similarly adjusted model that included all three sociodemographic variables of interest. To assess heterogeneity by sex, all models were additionally stratified by sex.

To examine the intersection of sociodemographic factors in associations with distant stage at diagnosis, we conducted sub-analyses where we assessed modification of the impact of nSES on distant stage by insurance status and the impact of insurance status on distant stage by nSES for each racial/ethnic group. For these analyses, insurance status was dichotomized to insured (private or Medicare) and underinsured (public or uninsured) and nSES was dichotomized to high (quintiles 3-5) and low (quintiles 1-2).

Results

Table 1 shows frequency distributions of multilevel sociodemographic factors and clinical characteristics according to stage at diagnosis for the total study population (N=45,695). Although the NH Black group was 7.3% of the total study population, it accounted for nearly 9% of those with distant stage at diagnosis. Greater proportions of residents of the lowest two quintiles of nSES were diagnosed with distant disease (16.4% and 15.2%, respectively) compared to higher SES quintiles (from 12.8% in Q5 to 14% in Q3). Those with public insurance or no insurance combined accounted for 21.0% of the total population, but 26.8% of those with distant stage. Table 2 shows analogous distributions among the study population stratified by sex. Among females there were higher proportions of NH Asian American/Pacific Islander (26.2%) and Hispanic (32.5%) and lower proportions of NH White individuals (32.5%), compared to males (23.7% Asian American/Pacific Islander, 30.4% Hispanic, and 37.1% NH White). Females were more frequently older; 44.5% of females were more than 70 years of age, compared to 25.5% of males. Relatedly, more females than males were insured by Medicare (48.1% of females compared to 35.4% of males).

Table 1. Distribution of all covariates according to stage at diagnosis for individuals diagnosed with hepatocellular carcinoma, California Cancer Registry 2001-2020

	Total		Local			Regional			Distant			Unstaged/Unknown		
	N=45,695		N=21,802			N=13,072			N=6,658			N=4,163		
	N	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)
Race/Ethnicity														
NH American Indian/Alaska Native	552	(1.2)	244	(44.2)	(1.1)	165	(29.9)	(1.3)	87	(15.8)	(1.3)	56	(10.1)	(1.3)
NH Asian American/Pacific Islander	11,110	(24.3)	5473	(49.3)	(25.1)	3115	(28.0)	(23.8)	1565	(14.1)	(23.5)	957	(8.6)	(23.0)
NH Black	3343	(7.3)	1459	(43.6)	(6.7)	1010	(30.2)	(7.7)	583	(17.4)	(8.8)	291	(8.7)	(7.0)
Hispanic	14,134	(30.9)	6818	(48.2)	(31.3)	4029	(28.5)	(30.8)	1991	(14.1)	(29.9)	1296	(9.2)	(31.1)
NH White	16,432	(36.0)	7753	(47.2)	(35.6)	4729	(28.8)	(36.2)	2410	(14.7)	(36.2)	1540	(9.4)	(37.0)
Other/Unknown	124	(0.3)	55	(44.4)	(0.3)	24	(19.4)	(0.2)	22	(17.7)	(0.3)	23	(18.5)	(0.6)
Neighborhood socioeconomic status														
Q1	9896	(21.7)	4436	(44.8)	(20.3)	2807	(28.4)	(21.5)	1619	(16.4)	(24.3)	1034	(10.4)	(24.8)
Q2	10,561	(23.1)	4867	(46.1)	(22.3)	3071	(29.1)	(23.5)	1606	(15.2)	(24.1)	1017	(9.6)	(24.4)
Q3	9848	(21.6)	4774	(48.5)	(21.9)	2790	(28.3)	(21.3)	1379	(14.0)	(20.7)	905	(9.2)	(21.7)
Q4	8677	(19.0)	4249	(49.0)	(19.5)	2511	(28.9)	(19.2)	1198	(13.8)	(18.0)	719	(8.3)	(17.3)
Q5	6713	(14.7)	3476	(51.8)	(15.9)	1893	(28.2)	(14.5)	856	(12.8)	(12.9)	488	(7.3)	(11.7)

Insurance type													
Private	17,520	(38.3)	8765	(50.0)	(40.2)	5054	(28.8)	(38.7)	2483	(14.2)	(37.3)	1218	(7.0)	(29.3)
Medicare	17,612	(38.5)	8710	(49.5)	(40.0)	4846	(27.5)	(37.1)	2257	(12.8)	(33.9)	1799	(10.2)	(43.2)
Public	8418	(18.4)	3709	(44.1)	(17.0)	2559	(30.4)	(19.6)	1469	(17.5)	(22.1)	681	(8.1)	(16.4)
Not insured	1183	(2.6)	374	(31.6)	(1.7)	391	(33.1)	(3.0)	313	(26.5)	(4.7)	105	(8.9)	(2.5)
Unknown	962	(2.1)	244	(25.4)	(1.1)	222	(23.1)	(1.7)	136	(14.1)	(2.0)	360	(37.4)	(8.6)
Sex														
Male	34,333	(75.1)	15833	(46.1)	(72.6)	10204	(29.7)	(78.1)	5215	(15.2)	(78.3)	3081	(9.0)	(74.0)
Female	11,362	(24.9)	5969	(52.5)	(27.4)	2868	(25.2)	(21.9)	1443	(12.7)	(21.7)	1082	(9.5)	(26.0)
Age group														
<50	3610	(7.9)	1573	(43.6)	(7.2)	1074	(29.8)	(8.2)	671	(18.6)	(10.1)	292	(8.1)	(7.0)
50-59	12,598	(27.6)	6054	(48.1)	(27.8)	3668	(29.1)	(28.1)	1875	(14.9)	(28.2)	1001	(7.9)	(24.0)
60-69	15,662	(34.3)	7660	(48.9)	(35.1)	4573	(29.2)	(35.0)	2181	(13.9)	(32.8)	1248	(8.0)	(30.0)
70-79	9454	(20.7)	4501	(47.6)	(20.6)	2651	(28.0)	(20.3)	1312	(13.9)	(19.7)	990	(10.5)	(23.8)
>80	4371	(9.6)	2014	(46.1)	(9.2)	1106	(25.3)	(8.5)	619	(14.2)	(9.3)	632	(14.5)	(15.2)
Marital status														
Unmarried	19,951	(43.7)	9282	(46.5)	(42.6)	5583	(28.0)	(42.7)	3113	(15.6)	(46.8)	1973	(9.9)	(47.4)
Married/Domestic partnership	24,410	(53.4)	11936	(48.9)	(54.7)	7153	(29.3)	(54.7)	3342	(13.7)	(50.2)	1979	(8.1)	(47.5)
Unknown	1334	(2.9)	584	(43.8)	(2.7)	336	(25.2)	(2.6)	203	(15.2)	(3.0)	211	(15.8)	(5.1)

Charlson comorbidity burden														
None	5267	(11.5)	2411	(45.8)	(11.1)	1469	(27.9)	(11.2)	1015	(19.3)	(15.2)	372	(7.1)	(8.9)
Moderate	10,514	(23.0)	5264	(50.1)	(24.1)	2887	(27.5)	(22.1)	1659	(15.8)	(24.9)	704	(6.7)	(16.9)
High	20,951	(45.8)	10136	(48.4)	(46.5)	6281	(30.0)	(48.0)	2888	(13.8)	(43.4)	1646	(7.9)	(39.5)
Unknown	8963	(19.6)	3991	(44.5)	(18.3)	2435	(27.2)	(18.6)	1096	(12.2)	(16.5)	1441	(16.1)	(34.6)

a. NH, non-Hispanic

Table 2a. Distribution of all covariates according to stage at diagnosis *among males* diagnosed with hepatocellular carcinoma, California Cancer Registry 2001-2020

	Total		Local			Regional			Distant			Unstaged/Unknown		
	N=34,333		N=15,833			N=10,204			N=5,215			N=3,081		
	N	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)
Race/Ethnicity														
NH American Indian/Alaska Native	412	(1.2)	177	(43.0)	(1.1)	123	(29.9)	(1.2)	69	(16.7)	(1.3)	43	(10.4)	(1.4)
NH Asian American/Pacific Islander	8137	(23.7)	3829	(47.1)	(24.2)	2415	(29.7)	(23.7)	1223	(15.0)	(23.5)	670	(8.2)	(21.7)
NH Black	2515	(7.3)	1078	(42.9)	(6.8)	767	(30.5)	(7.5)	447	(17.8)	(8.6)	223	(8.9)	(7.2)
Hispanic	10,439	(30.4)	4845	(46.4)	(30.6)	3114	(29.8)	(30.5)	1536	(14.7)	(29.5)	944	(9.0)	(30.6)
NH White	12,735	(37.1)	5861	(46.0)	(37.0)	3768	(29.6)	(36.9)	1924	(15.1)	(36.9)	1182	(9.3)	(38.4)
Other/Unknown	95	(0.3)	43	(45.3)	(0.3)	17	(17.9)	(0.2)	16	(16.8)	(0.3)	19	(20.0)	(0.6)

Neighborhood socioeconomic status														
Q1	7340	(21.4)	3164	(43.1)	(20.0)	2149	(29.3)	(21.1)	1242	(16.9)	(23.8)	785	(10.7)	(25.5)
Q2	7976	(23.2)	3533	(44.3)	(22.3)	2407	(30.2)	(23.6)	1287	(16.1)	(24.7)	749	(9.4)	(24.3)
Q3	7417	(21.6)	3454	(46.6)	(21.8)	2195	(29.6)	(21.5)	1098	(14.8)	(21.1)	670	(9.0)	(21.7)
Q4	6551	(19.1)	3131	(47.8)	(19.8)	1985	(30.3)	(19.5)	922	(14.1)	(17.7)	513	(7.8)	(16.7)
Q5	5049	(14.7)	2551	(50.5)	(16.1)	1468	(29.1)	(14.4)	666	(13.2)	(12.8)	364	(7.2)	(11.8)
Insurance type														
Private	13,930	(40.6)	6819	(49.0)	(43.1)	4116	(29.5)	(40.3)	2039	(14.6)	(39.1)	956	(6.9)	(31.0)
Medicare	12,147	(35.4)	5766	(47.5)	(36.4)	3547	(29.2)	(34.8)	1622	(13.4)	(31.1)	1212	(10.0)	(39.3)
Medicaid/Indian/Public	6485	(18.9)	2754	(42.5)	(17.4)	2028	(31.3)	(19.9)	1179	(18.2)	(22.6)	524	(8.1)	(17.0)
Not insured	961	(2.8)	299	(31.1)	(1.9)	322	(33.5)	(3.2)	255	(26.5)	(4.9)	85	(8.8)	(2.8)
Unknown	810	(2.4)	195	(24.1)	(1.2)	191	(23.6)	(1.9)	120	(14.8)	(2.3)	304	(37.5)	(9.9)
Age group														
<50	2926	(8.5)	1240	(42.4)	(7.8)	887	(30.3)	(8.7)	552	(18.9)	(10.6)	247	(8.4)	(8.0)
50-59	10,508	(30.6)	4924	(46.9)	(31.1)	3124	(29.7)	(30.6)	1611	(15.3)	(30.9)	849	(8.1)	(27.6)
60-69	12,137	(35.4)	5719	(47.1)	(36.1)	3663	(30.2)	(35.9)	1764	(14.5)	(33.8)	991	(8.2)	(32.2)
70-79	6248	(18.2)	2804	(44.9)	(17.7)	1872	(30.0)	(18.3)	907	(14.5)	(17.4)	665	(10.6)	(21.6)
>80	2514	(7.3)	1146	(45.6)	(7.2)	658	(26.2)	(6.4)	381	(15.2)	(7.3)	329	(13.1)	(10.7)

Marital status														
Unmarried	13,597	(39.6)	6024	(44.3)	(38.0)	4009	(29.5)	(39.3)	2277	(16.7)	(43.7)	1287	(9.5)	(41.8)
Married or domestic partnership	19,722	(57.4)	9361	(47.5)	(59.1)	5945	(30.1)	(58.3)	2777	(14.1)	(53.3)	1639	(8.3)	(53.2)
Unknown	1014	(3.0)	448	(44.2)	(2.8)	250	(24.7)	(2.5)	161	(15.9)	(3.1)	155	(15.3)	(5.0)
Charlson comorbidity burden														
None	3820	(11.1)	1694	(44.3)	(10.7)	1107	(29.0)	(10.8)	750	(19.6)	(14.4)	269	(7.0)	(8.7)
Moderate	7840	(22.8)	3797	(48.4)	(24.0)	2230	(28.4)	(21.9)	1325	(16.9)	(25.4)	488	(6.2)	(15.8)
High	15,795	(46.0)	7318	(46.3)	(46.2)	4944	(31.3)	(48.5)	2276	(14.4)	(43.6)	1257	(8.0)	(40.8)
Unknown	6878	(20.0)	3024	(44.0)	(19.1)	1923	(28.0)	(18.8)	864	(12.6)	(16.6)	1067	(15.5)	(34.6)

a. NH, non-Hispanic.

Table 2b. Distribution of all covariates according to stage at diagnosis *among females* diagnosed with hepatocellular carcinoma, California Cancer Registry 2001-2020

	Total		Local			Regional			Distant			Unstaged/Unknown		
	N=11,362		N=5,969			N=2,868			N=1,443			N=1,082		
	N	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)	N	(Row %)	(Col %)
Race/Ethnicity														
NH American Indian/Alaska Native	140	(1.2)	67	(47.9)	(1.1)	42	(30.0)	(1.5)	18	(12.9)	(1.2)	13	(9.3)	(1.2)
NH Asian American/Pacific Islander	2973	(26.2)	1644	(55.3)	(27.5)	700	(23.5)	(24.4)	342	(11.5)	(23.7)	287	(9.7)	(26.5)
NH Black	828	(7.3)	381	(46.0)	(6.4)	243	(29.3)	(8.5)	136	(16.4)	(9.4)	68	(8.2)	(6.3)
Hispanic	3695	(32.5)	1973	(53.4)	(33.1)	915	(24.8)	(31.9)	455	(12.3)	(31.5)	352	(9.5)	(32.5)

NH White	3697	(32.5)	1892	(51.2)	(31.7)	961	(26.0)	(33.5)	486	(13.1)	(33.7)	358	(9.7)	(33.1)
Other/Unknown	29	(0.3)	12	(41.4)	(0.2)	<11	(24.1)	(0.2)	<11	(20.7)	(0.4)	<11	(13.8)	(0.4)
Neighborhood socioeconomic status														
Q1	2556	(22.5)	1272	(49.8)	(21.3)	658	(25.7)	(22.9)	377	(14.7)	(26.1)	249	(9.7)	(23.0)
Q2	2585	(22.8)	1334	(51.6)	(22.3)	664	(25.7)	(23.2)	319	(12.3)	(22.1)	268	(10.4)	(24.8)
Q3	2431	(21.4)	1320	(54.3)	(22.1)	595	(24.5)	(20.7)	281	(11.6)	(19.5)	235	(9.7)	(21.7)
Q4	2126	(18.7)	1118	(52.6)	(18.7)	526	(24.7)	(18.3)	276	(13.0)	(19.1)	206	(9.7)	(19.0)
Q5	1664	(14.6)	925	(55.6)	(15.5)	425	(25.5)	(14.8)	190	(11.4)	(13.2)	124	(7.5)	(11.5)
Insurance type														
Private	3590	(31.6)	1946	(54.2)	(32.6)	938	(26.1)	(32.7)	444	(12.4)	(30.8)	262	(7.3)	(24.2)
Medicare	5465	(48.1)	2944	(53.9)	(49.3)	1299	(23.8)	(45.3)	635	(11.6)	(44.0)	587	(10.7)	(54.3)
Medicaid/Indian/Public	1933	(17.0)	955	(49.4)	(16.0)	531	(27.5)	(18.5)	290	(15.0)	(20.1)	157	(8.1)	(14.5)
Not insured	222	(2.0)	75	(33.8)	(1.3)	69	(31.1)	(2.4)	58	(26.1)	(4.0)	20	(9.0)	(1.8)
Unknown	152	(1.3)	49	(32.2)	(0.8)	31	(20.4)	(1.1)	16	(10.5)	(1.1)	56	(36.8)	(5.2)
Age group														
<50	684	(6.0)	333	(48.7)	(5.6)	187	(27.3)	(6.5)	119	(17.4)	(8.2)	45	(6.6)	(4.2)
50-59	2090	(18.4)	1130	(54.1)	(18.9)	544	(26.0)	(19.0)	264	(12.6)	(18.3)	152	(7.3)	(14.0)
60-69	3525	(31.0)	1941	(55.1)	(32.5)	910	(25.8)	(31.7)	417	(11.8)	(28.9)	257	(7.3)	(23.8)
70-79	3206	(28.2)	1697	(52.9)	(28.4)	779	(24.3)	(27.2)	405	(12.6)	(28.1)	325	(10.1)	(30.0)
>80	1857	(16.3)	868	(46.7)	(14.5)	448	(24.1)	(15.6)	238	(12.8)	(16.5)	303	(16.3)	(28.0)

Marital status														
Unmarried	6354	(55.9)	3258	(51.3)	(54.6)	1574	(24.8)	(54.9)	836	(13.2)	(57.9)	686	(10.8)	(63.4)
Married or domestic partnership	4688	(41.3)	2575	(54.9)	(43.1)	1208	(25.8)	(42.1)	565	(12.1)	(39.2)	340	(7.3)	(31.4)
Unknown	320	(2.8)	136	(42.5)	(2.3)	86	(26.9)	(3.0)	42	(13.1)	(2.9)	56	(17.5)	(5.2)
Charlson comorbidity burden														
None	1447	(12.7)	717	(49.6)	(12.0)	362	(25.0)	(12.6)	265	(18.3)	(18.4)	103	(7.1)	(9.5)
Moderate	2674	(23.5)	1467	(54.9)	(24.6)	657	(24.6)	(22.9)	334	(12.5)	(23.1)	216	(8.1)	(20.0)
High	5156	(45.4)	2818	(54.7)	(47.2)	1337	(25.9)	(46.6)	612	(11.9)	(42.4)	389	(7.5)	(36.0)
Unknown	2085	(18.4)	967	(46.4)	(16.2)	512	(24.6)	(17.9)	232	(11.1)	(16.1)	374	(17.9)	(34.6)

a. NH, non-Hispanic.

Associations between each sociodemographic factor and stage at diagnosis did not differ substantially in models including each variable separately or all three simultaneously (Supplemental Tables S1-S3), so the fully adjusted models are discussed.

Figure 1 and Supplemental Table 1 show associations between race/ethnicity and stage at diagnosis. The NH Black group had higher odds of diagnosis with regional or distant stage compared to the NH White group, (OR Regional=1.11, 95% CI=1.01, 1.21; OR Distant=1.13, 95% CI=1.01, 1.26) (Figure 1). Compared to the NH White group, the NH Asian American/Pacific Islander and Hispanic groups had lower odds of later stage disease (distant: Asian American/Pacific Islander OR=0.88, 95% CI=0.82, 0.95; Hispanic OR =0.86, 95% CI=0.80, 0.92). Sex-specific models (Figure 1b and 1c and Supplemental Table 1) suggested a stronger protective association for NH Asian American/Pacific Islander females compared to males; effect estimates of regional and distant compared to local stage were significant among females but not males.

Figure 2 and Supplemental Table 2 show associations between insurance type and stage at diagnosis. Individuals with public insurance or no insurance had substantially higher odds of later-stage diagnosis compared to those with private insurance (distant stage: public OR=1.37, 95% CI=1.27, 1.49; uninsured OR=2.78, 95% CI=2.37, 3.26). Those with Medicare, on the other hand, had lower odds of later-stage diagnosis compared to those with private insurance (distant stage: OR=0.87; 95% CI=0.81, 0.93). Sex-specific models showed similar patterns although fully adjusted model results for Medicare among females were not statistically significant (Supplemental Table 2).

Figure 3 and Supplemental Table 3 show associations between nSES and stage at diagnosis. Individuals residing in lower SES neighborhoods had higher odds of later-stage diagnosis compared to local stage (p-trend for regional and distant stage=0.001 and <0.001, respectively). This pattern appears stronger for distant compared to local stage at diagnosis: among those residing in the lowest compared to the highest SES neighborhoods, there was 13% higher odds of regional versus local stage and 46% higher odds of distant versus local stage. Sex-specific models showed that the impact of nSES on stage was stronger among males than females (p-trend males=0.002; females=0.154; Figure 3b and 3c and Supplemental Table 3).

Table 3 shows results of analyses stratified jointly by race/ethnicity, insurance status, and nSES. Across all racial/ethnic groups, underinsurance was associated with distant stage among residents of both higher and lower SES neighborhoods, although these results were not statistically significant among the relatively small NH American Indian/Alaska Native group. Among the NH Black group, nSES was not associated with distant stage among groups stratified by insurance. Among the NH Asian American/Pacific Islander group, lower nSES was associated with distant stage only among those with private or Medicare insurance. Among the Hispanic and NH White groups however, both insurance status and nSES impacted stage at diagnosis across stratified groups.

Figure 1. Odds ratios and 95% confidence intervals of regional or distant stage compared to local stage at diagnosis for hepatocellular carcinoma (HCC) across groups defined by race/ethnicity among (A) all, (B) males, and (C) females; California Cancer Registry 2001-2020, N=45,695. Models include sociodemographic variables of interest (race/ethnicity, insurance type, and neighborhood socioeconomic status) as well as age at diagnosis, sex (Figure 1A only), year of diagnosis, marital status, and Charlston Comorbidity Index.

Figure 1A. Males and Females

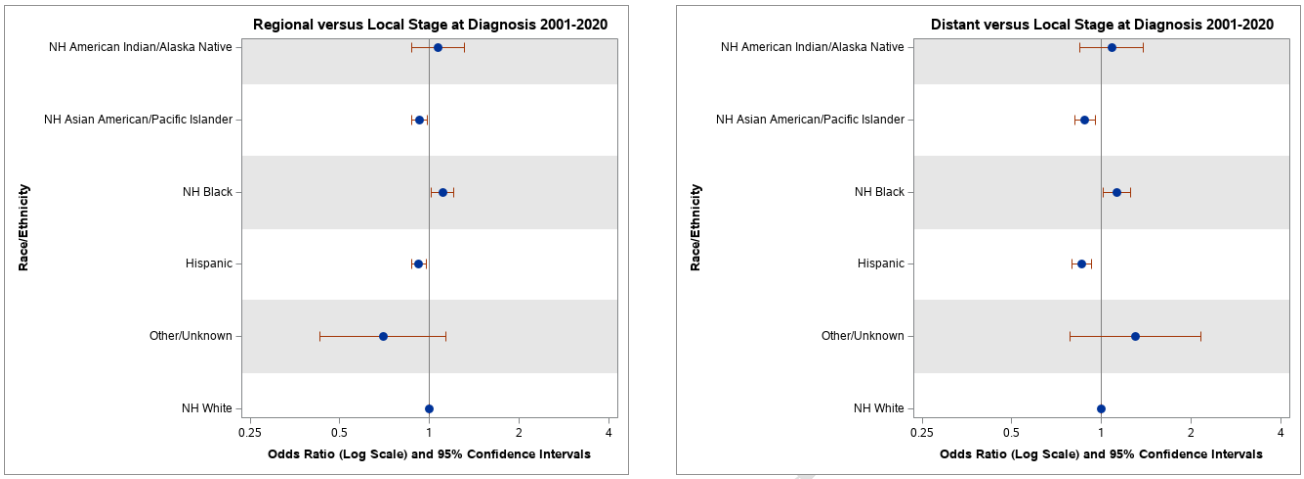


Figure 1B. Males

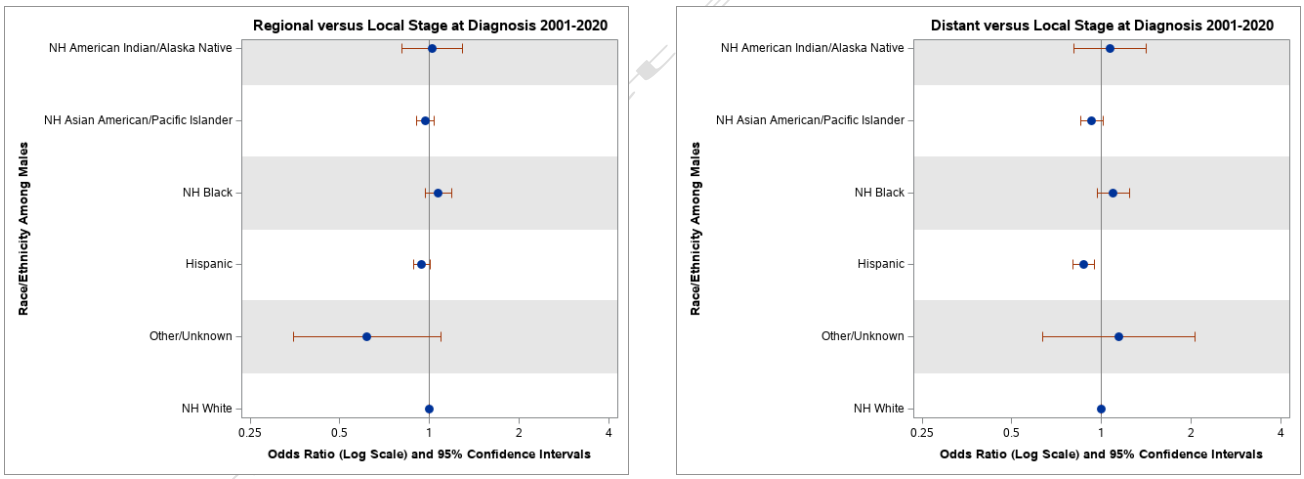


Figure 1C. Females

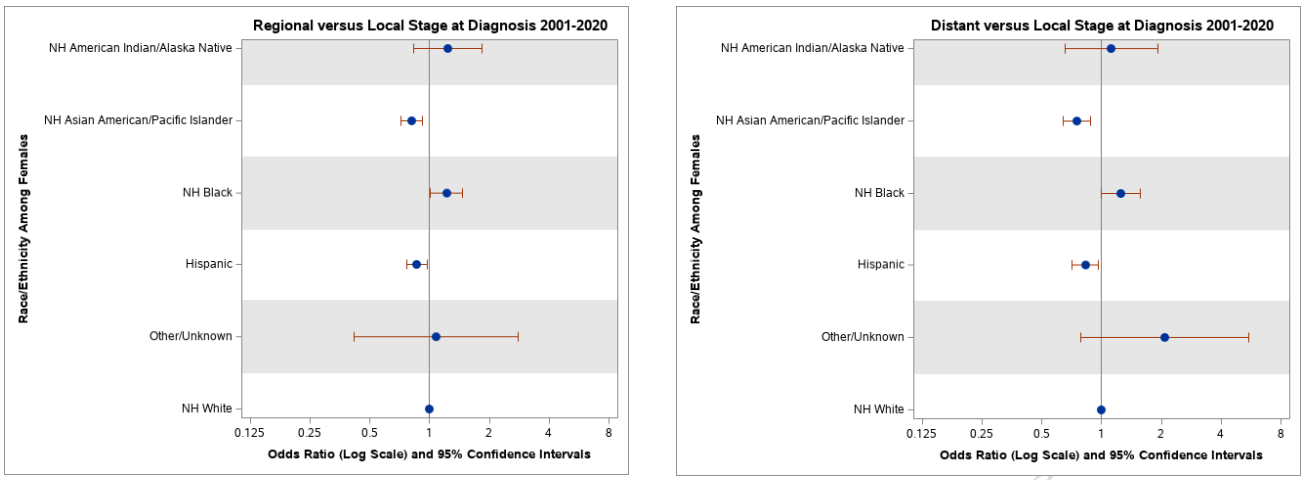


Figure 2. Odds ratios and 95% confidence intervals of regional or distant stage compared to local stage at diagnosis for hepatocellular carcinoma (HCC) across groups defined by insurance type among (A) all, (B) males, and (C) females; California Cancer Registry 2001-2020, N=45,695. Models include sociodemographic variables of interest (race/ethnicity, insurance type, and neighborhood socioeconomic status) as well as age at diagnosis, sex (Figure 2A only), year of diagnosis, marital status, and Charlston Comorbidity Index.

Figure 2A. Males and Females

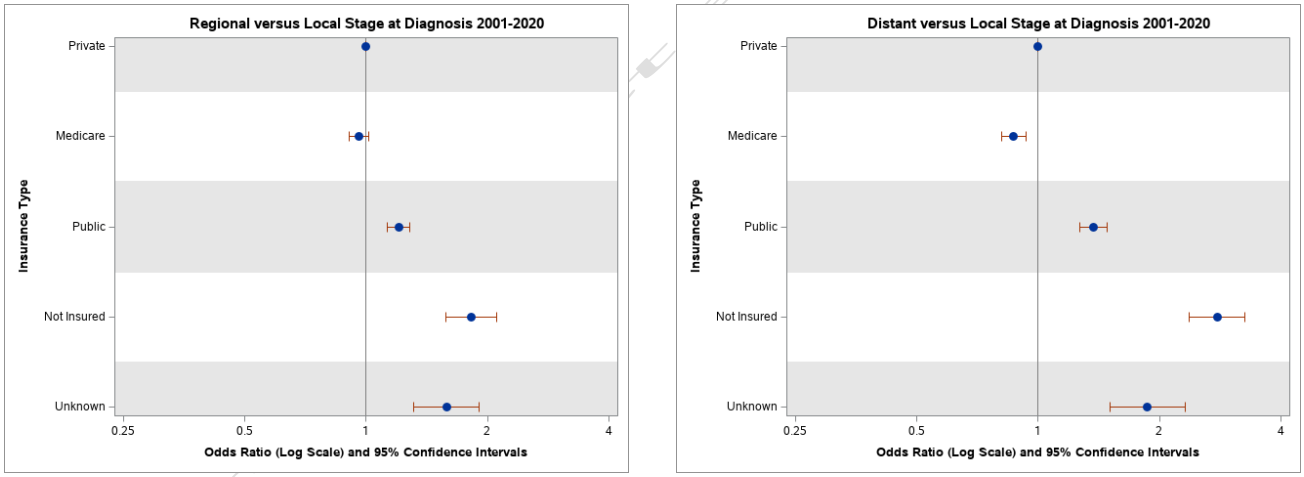


Figure 2B. Males

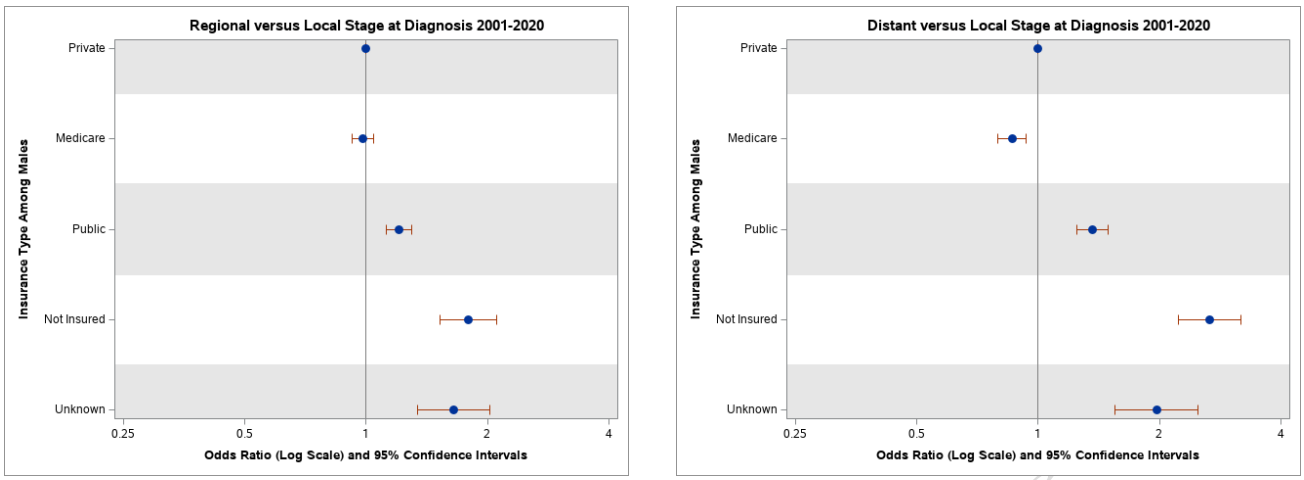


Figure 2C. Females

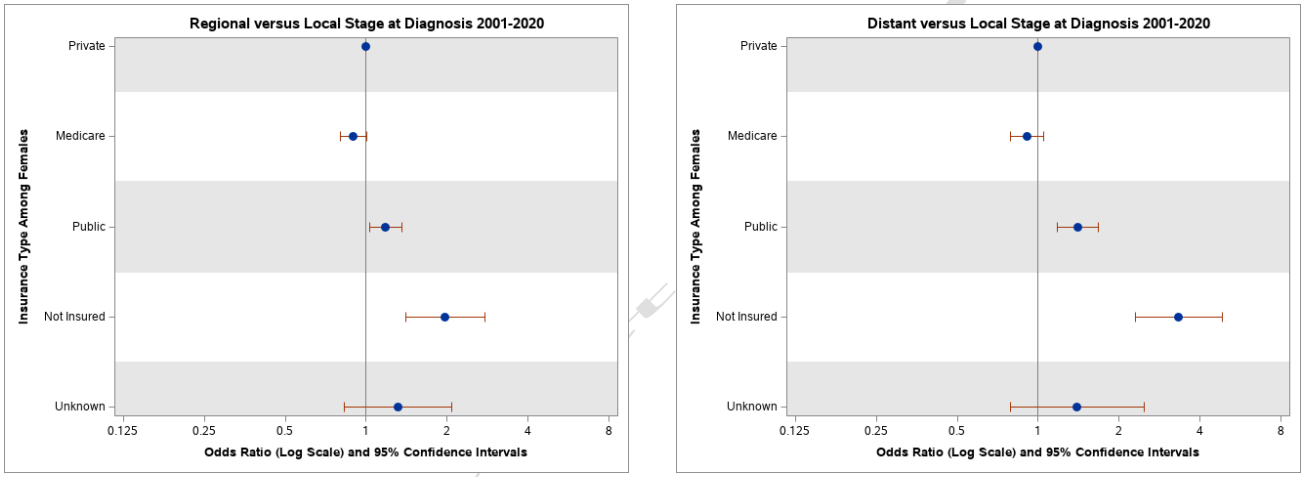
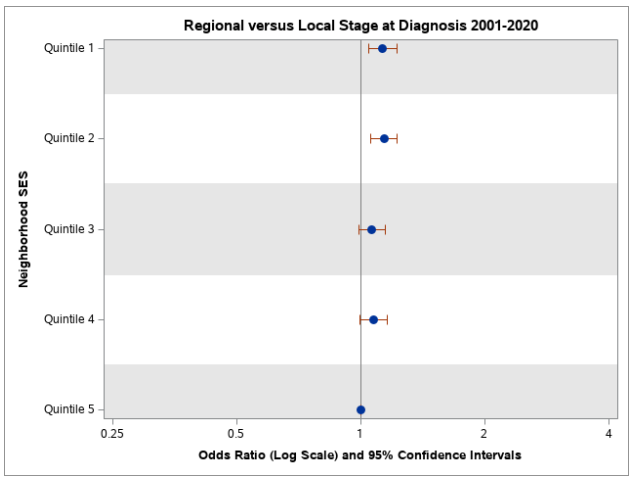


Figure 3. Odds ratios and 95% confidence intervals of regional or distant stage compared to local stage at diagnosis for hepatocellular carcinoma (HCC) across groups defined by neighborhood socioeconomic status among (A) all, (B) males, and (C) females; California Cancer Registry 2001-2020, N=45,695. Models include sociodemographic variables of interest (race/ethnicity, insurance type, and neighborhood socioeconomic status) as well as age at diagnosis, sex (Figure 3A only), year of diagnosis, marital status, and Charlston Comorbidity Index.

Figure 3A. Males and Females



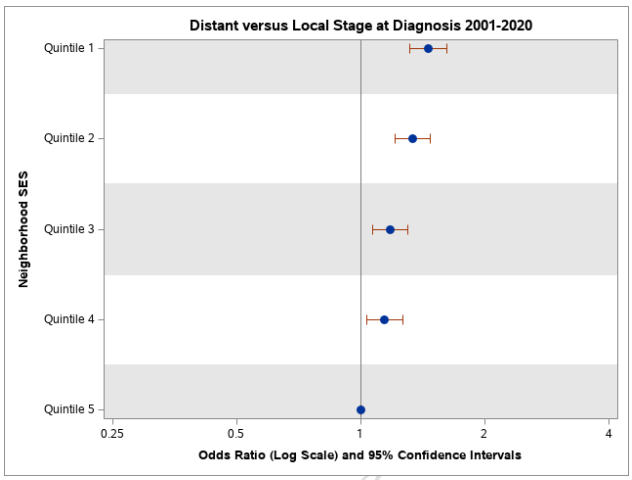
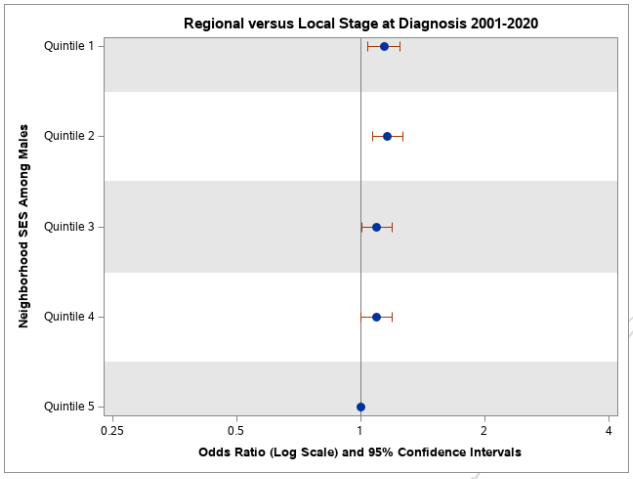


Figure 3B. Males



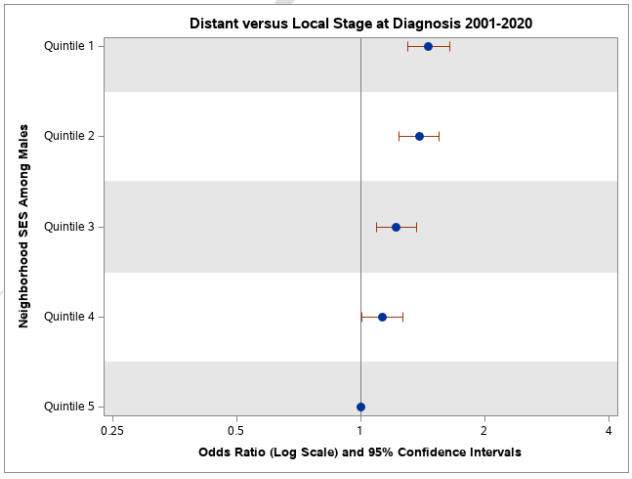
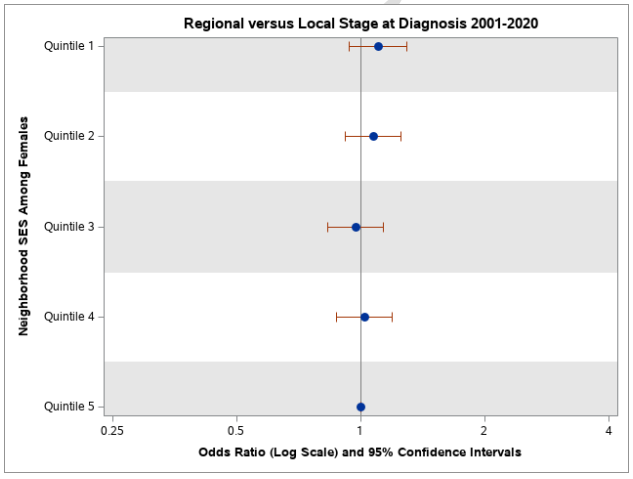


Figure 3C. Females



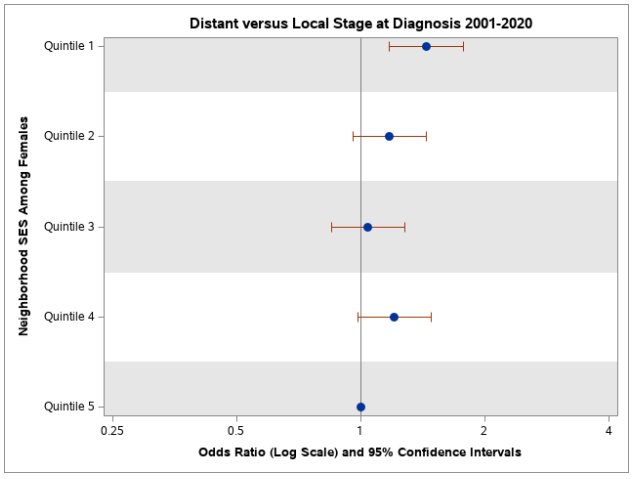


Table 3. Odds ratios and 95% confidence intervals of distant stage at diagnosis, compared to local stage, for hepatocellular carcinoma across groups defined by jointly by race/ethnicity, neighborhood socioeconomic stats (nSES), and insurance status; California Cancer Registry 2001-2020				
NH American Indian / Alaska Native				
	Higher nSES (N=231)		Lower nSES (N=305)	
	Odds ratio	95% CI	Odds ratio	95% CI
Underinsured vs. Insured	2.05	(0.71, 5.96)	2.36	(0.96, 5.77)
	Insured (N=399)		Underinsured (N=137)	
	Odds ratio	95% CI	Odds ratio	95% CI
Lower vs. Higher nSES	1.51	(0.74, 3.05)	1.25	(0.38, 4.14)
NH Asian American/Pacific Islander				
	Higher nSES (N=7305)		Lower nSES (N=3682)	
	Odds ratio	95% CI	Odds ratio	95% CI
Underinsured vs. Insured	2.04	(1.70, 2.45)	1.63	(1.30, 2.06)
	Insured (N=8684)		Underinsured (N=2303)	
	Odds ratio	95% CI	Odds ratio	95% CI
Lower vs. Higher nSES	1.34	(1.16, 1.55)	1.04	(0.82, 1.31)
NH Black				
	Higher nSES (N=1285)		Lower nSES (N=2020)	
	Odds ratio	95% CI	Odds ratio	95% CI
Underinsured vs. Insured	1.92	(1.30, 2.83)	1.45	(1.08, 1.95)
	Insured (N=2426)		Underinsured (N=879)	
	Odds ratio	95% CI	Odds ratio	95% CI
Lower vs. Higher nSES	1.04	(0.82, 1.33)	0.80	(0.54, 1.19)
Hispanic				
	Higher nSES (N=5255)		Lower nSES (N=8678)	
	Odds ratio	95% CI	Odds ratio	95% CI
Underinsured vs. Insured	1.33	(1.08, 1.64)	1.49	(1.29, 1.72)
	Insured (N=10078)		Underinsured (N=3855)	
	Odds ratio	95% CI	Odds ratio	95% CI
Lower vs. Higher nSES	1.20	(1.06, 1.36)	1.32	(1.08, 1.62)

NH White				
	Higher nSES (N=10816)		Lower nSES (N=5355)	
	Odds ratio	95% CI	Odds ratio	95% CI
Underinsured vs. Insured	1.45	(1.21, 1.73)	1.83	(1.50, 2.23)
	Insured (N=13693)		Underinsured (N=2478)	
	Odds ratio	95% CI	Odds ratio	95% CI
Lower vs. Higher nSES	1.19	(1.06, 1.33)	1.56	(1.24, 1.96)

a. NH, Non-Hispanic; USA, United States of America; nSES, neighborhood socioeconomic status; OR, odds ratio; CI, 95% confidence interval)

b. nSES was dichotomized to higher nSES (quintiles 3-5) and lower nSES (quintiles 1 and 2).

c. Insurance status was dichotomies to insured (private or Medicare insurance) and underinsured (public insurance or uninsured).

Discussion

Our study highlights multilevel sociodemographic disparities in HCC stage at diagnosis. Odds of later stage were higher for the NH Black compared to the NH White group. Those who resided in lower SES neighborhoods had higher odds of later stage compared to those who resided in higher SES neighborhoods. Individuals who were uninsured or had public insurance at diagnosis had higher odds of later stage, compared to the privately insured. Importantly, these observations persisted in fully adjusted models that included all three social factors, indicating that each is independently associated with stage at diagnosis. Stratified analyses identified groups defined jointly by race/ethnicity, nSES, and insurance status that were most likely to experience the most advanced stage at diagnosis. Below, we discuss each sociodemographic factor in the context of HCC stage at diagnosis; however, we stress that our results highlight the importance of multilevel interventions to adequately address disparities in delayed HCC diagnosis.[22]

Similar to a prior SEER study,[8] we observed higher odds of late stage diagnosis among the NH Black group compared to other racial/ethnic groups that persisted after adjustment for nSES and insurance type, which is consistent with a recent study reporting that an area deprivation index only partially mediated racial/ethnic disparities in HCC stage at diagnosis.[13] Although a second, institutional study reported lower HCC surveillance among Black, compared to White, cirrhotic patients, racial and ethnic disparities in stage at diagnosis may be impacted by surveillance guidelines that inadequately account for variations in risk across racial and ethnic groups, racial disparities in the quality of surveillance received, or delays in diagnostic evaluations leading up to cancer diagnoses.[23]

It is well known that underinsurance is associated with delayed diagnosis and lower survival of HCC and other cancers.[24,25] Our results additionally demonstrate that the increased odds of later stage HCC diagnosis among the uninsured or those with public insurance is independent of race/ethnicity as well as nSES. Insurance status is a key determinant of healthcare accessibility and frequency of visits. As observed in prior studies of associations between insurance type and stage at diagnosis across multiple cancer sites, we observe equivocal outcomes across Medicare and private insurance.[26]

That non-Medicare public insurance programs and uninsurance, but not publicly-administered Medicare, are associated with delayed diagnosis of HCC, highlights insurance type as a proxy of individual-level SES. For those with Medicaid and other need-based public insurance programs and those who are uninsured, a lack of healthcare accessibility and financial strain coincides with lack of timely receipt of regular healthcare, which likely leads to delayed identification of HCC.[23,27,28] Therefore, efforts to facilitate earlier HCC diagnosis should also consider barriers to risk assessment and reduction as well as appropriate surveillance among those with public insurance and, in particular, no insurance.

Few studies have considered area-level sociodemographic factors and HCC stage at diagnosis. Moreover, our study shows that the association between lower nSES and later-stage diagnosis is independent of race/ethnicity and individual-level insurance status.[29] However, the association between nSES and later stage HCC diagnosis is stronger among males than females. Specific attributes of lower SES neighborhoods may contribute to later-stage diagnosis of HCC in many ways, including sociocultural healthcare norms, accessibility to healthcare resources, social capital, or social support.

Analyses stratified jointly by race/ethnicity, insurance status, and nSES show that complete independence of underinsurance and nSES in associations with distant stage was only present among the NH White and Hispanic groups. While the NH Asian American/Pacific Islander group was less likely to be diagnosed with HCC at distant stages compared to the NH White group in the overall analysis, stratified analyses indicate that underinsurance and nSES are important factors that contribute to later stage diagnosis *within* this group; namely, among the underinsured, lower nSES did not have an additional impact. For the NH Black group, which had greater odds of distant stage at diagnoses compared to the NH White group in the overall analysis, stratified analyses suggest that underinsurance has a greater impact on distant stage than nSES *within* the NH Black group. A report from Flores et al. assessed the interaction between race/ethnicity and nSES with SEER data and reported that, within each racial/ethnic group examined, lower nSES was associated with later stage; an observation that may have been driven by high levels of underinsurance among those residing in lower SES neighborhoods.[12] Our stratified analysis, thus, allows for the distinction of the impact between of these two sociodemographic factors (insurance status and nSES).

Given this is a population-based study leveraging the California Cancer Registry, our results are generalizable to the entire state and capture large-scale patterns in the impact of multilevel sociodemographic factors on the stage of HCC diagnosis. However, there may be observable differences in the patterns we observe in CCR data compared to the USA. Our selection of social factors was limited by information collected in the CCR. Accordingly, we were unable to consider other aspects of socioeconomic status (e.g., personal income, education level), etiology of liver diseases (e.g., metabolic dysfunction-associated steatotic liver disease), specific comorbidities (e.g., Hepatitis infection), or health behaviors (e.g., alcohol consumption). Furthermore, payer type was collected only at the last admission for initial diagnosis or treatment. Therefore, this variable did not account for individuals who may have had different forms of insurance prior to diagnosis. Finally, this analysis aggregated Asian American and Pacific Islander individuals into a single racial/ethnic group. Further study of disaggregated Asian American and Pacific Islander ethnic groups would be warranted given that prior studies have

highlighted important differences in cancer diagnosis across disaggregated groups.

Conclusion

Our study highlights multilevel disparities in stage of HCC diagnosis. Certain groups defined by joint race/ethnicity, neighborhood SES, and insurance type are particularly vulnerable to delayed HCC diagnosis. Public health and medical interventions that target the needs of groups who are at heightened risk of delayed diagnosis are needed.

Acknowledgement

None to add

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Conflicts of interest

None to declare.

Authors' contributions

PG and MCD conceived of the study. SL and AJC curated data. PG, SL, AJC, and MSan conducted formal analyses. PG, CAT, JC, MT, MSom, HES, SSM, and MCD conducted investigation. PG, SL, AJC, MSan, and MCD developed methodology, PG and SL created visualizations, PG and MCD wrote the original draft. MCD provided study supervision. All authors reviewed and edited the manuscript.

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Supplemental Table 1. Odds ratios and 95% confidence intervals of regional or distant stage compared to local stage at diagnosis for hepatocellular carcinoma across groups defined by race/ethnicity; California Cancer Registry 2001-2020, N=45,695.

	Males and Females				Males				Females			
	Race/ethnicity only		Including insurance type and nSES		Race/ethnicity only		Including insurance type and nSES		Race/ethnicity only		Including insurance type and nSES	
Regional versus local stage												
Race/Ethnicity	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
NH American Indian/ Alaska Native	1.10	(0.90, 1.35)	1.07	(0.87, 1.31)	1.06	(0.84, 1.33)	1.02	(0.81, 1.29)	1.25	(0.85, 1.86)	1.23	(0.83, 1.83)
NH Asian American/ Pacific Islander	0.95	(0.89, 1.01)	0.93	(0.87, 0.98)	0.99	(0.93, 1.06)	0.97	(0.91, 1.04)	0.83	(0.73, 0.93)	0.81	(0.72, 0.92)
NH Black	1.15	(1.05, 1.25)	1.11	(1.01, 1.21)	1.11	(1.00, 1.23)	1.07	(0.97, 1.19)	1.27	(1.06, 1.53)	1.22	(1.01, 1.46)
Hispanic	0.97	(0.92, 1.02)	0.92	(0.87, 0.98)	0.99	(0.93, 1.05)	0.94	(0.88, 1.00)	0.91	(0.82, 1.02)	0.86	(0.77, 0.97)
Another/Unknown	0.71	(0.44, 1.16)	0.70	(0.43, 1.14)	0.63	(0.36, 1.11)	0.62	(0.35, 1.09)	1.10	(0.43, 2.83)	1.08	(0.42, 2.81)
NH White	1.00		1.00		1.00		1.00		1.00		1.00	
Distant versus local stage												
Race/Ethnicity	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
NH American Indian/ Alaska Native	1.17	(0.91, 1.50)	1.08	(0.84, 1.38)	1.17	(0.88, 1.54)	1.07	(0.81, 1.42)	1.17	(0.68, 1.99)	1.12	(0.65, 1.91)
NH Asian American/ Pacific Islander	0.92	(0.86, 1.00)	0.88	(0.82, 0.95)	0.98	(0.90, 1.07)	0.93	(0.85, 1.01)	0.78	(0.67, 0.91)	0.75	(0.64, 0.88)
NH Black	1.25	(1.12, 1.39)	1.13	(1.01, 1.26)	1.21	(1.07, 1.36)	1.09	(0.97, 1.24)	1.40	(1.12, 1.75)	1.25	(0.99, 1.57)

Hispanic	0.98	(0.91, 1.05)	0.86	(0.80, 0.92)	0.99	(0.91, 1.07)	0.87	(0.80, 0.94)	0.95	(0.82, 1.10)	0.83	(0.71, 0.96)
Another/Unknown	1.34	(0.81, 2.23)	1.30	(0.78, 2.15)	1.18	(0.65, 2.12)	1.14	(0.63, 2.06)	2.14	(0.80, 5.73)	2.08	(0.79, 5.51)
NH White	1.00		1.00		1.00		1.00		1.00		1.00	

a. NH, non-Hispanic

b. Local stage (in situ, localized), regional stage (regional by direct extension, regional by lymph nodes, regional by direct extension and lymph nodes, regional not otherwise specified), distant stage (remote).

c. Model adjusted for year of diagnosis, age at diagnosis, sex, Charlson Comorbidity Index, and marital status.

d. Additionally adjusted for insurance type and neighborhood socioeconomic status.

Supplemental Table 2. Odds ratios and 95% confidence intervals of regional or distant stage compared to local stage at diagnosis for hepatocellular carcinoma across groups defined by insurance type; California Cancer Registry 2001-2020, N=46,026.

	Males and Females				Males				Females			
	Insurance type only		Including race/ ethnicity and nSES		Insurance type only		Including race/ ethnicity and nSES		Insurance type only		Including race/ ethnicity and nSES	
Regional versus local stage												
Insurace type	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Private	1.00		1.00		1.00		1.00		1.00		1.00	
Medicare	0.96	(0.91, 1.02)	0.96	(0.91, 1.01)	0.99	(0.93, 1.05)	0.98	(0.92, 1.05)	0.90	(0.80, 1.00)	0.90	(0.80, 1.00)
Public	1.21	(1.13, 1.28)	1.20	(1.13, 1.28)	1.21	(1.13, 1.30)	1.21	(1.12, 1.30)	1.17	(1.02, 1.34)	1.18	(1.03, 1.35)
Not insured	1.82	(1.58, 2.11)	1.83	(1.58, 2.11)	1.80	(1.53, 2.11)	1.79	(1.52, 2.10)	1.93	(1.37, 2.70)	1.97	(1.40, 2.77)
Unknown	1.59	(1.32, 1.92)	1.58	(1.31, 1.91)	1.66	(1.35, 2.04)	1.65	(1.34, 2.03)	1.33	(0.84, 2.10)	1.31	(0.83, 2.09)

Distant versus local stage												
Insurace type	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Private	1.00		1.00		1.00		1		1.00		1	
Medicare	0.89	(0.83, 0.95)	0.87	(0.81, 0.93)	0.88	(0.81, 0.96)	0.862	(0.80, 0.93)	0.91	(0.79, 1.06)	0.91	(0.79, 1.05)
Public	1.41	(1.31, 1.53)	1.37	(1.27, 1.49)	1.41	(1.29, 1.54)	1.36	(1.25, 1.49)	1.42	(1.20, 1.69)	1.41	(1.18, 1.68)
Not insured	2.83	(2.41, 3.31)	2.78	(2.37, 3.26)	2.72	(2.28, 3.24)	2.66	(2.23, 3.18)	3.31	(2.29, 4.77)	3.34	(2.29, 4.85)
Unknown	1.92	(1.55, 2.39)	1.87	(1.51, 2.32)	2.03	(1.60, 2.56)	1.97	(1.55, 2.49)	1.44	(0.81, 2.55)	1.40	(0.79, 2.47)

a. NH, non-Hispanic; nSES, neighborhood socioeconomic status

b. Local stage (in situ, localized), regional stage (regional by direct extension, regional by lymph nodes, regional by direct extension and lymph nodes, regional not otherwise specified), distant stage (remote).

c. Model adjusted for year of diagnosis, age at diagnosis, sex, Charlson Comorbidity Index, and marital status.

d. Additionally adjusted for insurance type and neighborhood socioeconomic status.

Supplemental Table 3. Odds ratios and 95% confidence intervals of regional or distant stage compared to local stage at diagnosis for hepatocellular carcinoma across groups defined by insurance type; California Cancer Registry 2001-2020, N=46,026.

	Males and Females				Males				Females			
	nSES only		Including race/ethnicity and insurance type		nSES only		Including race/ethnicity and insurance type		nSES only		Including race/ethnicity and insurance type	
Regional versus local stage												
Neighborhood SES	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Q1 (lowest)	1.16	(1.07, 1.25)	1.13	(1.04, 1.22)	1.16	(1.07, 1.27)	1.14	(1.04, 1.25)	1.13	(0.97, 1.32)	1.10	(0.94, 1.30)
Q2	1.15	(1.07, 1.24)	1.14	(1.06, 1.23)	1.17	(1.08, 1.28)	1.16	(1.07, 1.26)	1.09	(0.93, 1.26)	1.07	(0.92, 1.25)

Q3	1.07	(0.99, 1.15)	1.06	(0.99, 1.14)	1.10	(1.01, 1.20)	1.09	(1.00, 1.19)	0.98	(0.84, 1.15)	0.97	(0.83, 1.14)
Q4	1.08	(1.00, 1.17)	1.08	(1.00, 1.16)	1.10	(1.01, 1.20)	1.09	(1.00, 1.19)	1.02	(0.88, 1.20)	1.02	(0.87, 1.19)
Q5 (highest)	1.00		1.00		1.00		1.00		1.00		1.00	
				p trend=0.001				p trend=0.002				p trend=0.154
Distant versus local stage												
Neighborhood SES	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Q1 (lowest)	1.50	(1.36, 1.66)	1.46	(1.32, 1.61)	1.50	(1.34, 1.67)	1.46	(1.30, 1.64)	1.53	(1.26, 1.87)	1.44	(1.17, 1.78)
Q2	1.36	(1.23, 1.49)	1.34	(1.21, 1.48)	1.40	(1.25, 1.56)	1.39	(1.24, 1.55)	1.22	(1.00, 1.49)	1.18	(0.96, 1.44)
Q3	1.19	(1.08, 1.31)	1.18	(1.07, 1.30)	1.23	(1.10, 1.37)	1.22	(1.09, 1.37)	1.08	(0.88, 1.32)	1.04	(0.85, 1.28)
Q4	1.15	(1.04, 1.27)	1.14	(1.03, 1.26)	1.13	(1.01, 1.27)	1.13	(1.00, 1.26)	1.22	(0.99, 1.50)	1.21	(0.98, 1.49)
Q5 (highest)	1.00		1.00		1.00		1.00		1.00		1.00	
				p trend<0.001				p trend<0.001				p trend<0.001

a. NH, non-Hispanic; nSES, neighborhood socioeconomic status.

b. Local stage (in situ, localized), regional stage (regional by direct extension, regional by lymph nodes, regional by direct extension and lymph nodes, regional not otherwise specified), distant stage (remote).

c. Model adjusted for year of diagnosis, age at diagnosis, sex, Charlson Comorbidity Index, and marital status.

d. Additionally adjusted for insurance type and neighborhood socioeconomic status.