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## Asian American/Pacific Islander and Hispanic ethnic enclaves, neighborhood socioeconomic status, and hepatocellular carcinoma incidence in California: An update

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### Abstract

**Background:** Using more recent cancer registry data, we analyzed disparities in hepatocellular carcinoma (HCC) incidence by ethnic enclave and neighborhood socioeconomic status (nSES) among Asian American/Pacific Islander (AAPI) and Hispanic populations in California.

**Methods:** Primary, invasive HCC cases were identified from the California Cancer Registry during 1988–1992, 1998–2002, and 2008–2012. Age-adjusted incidence rates (per 100,000 population), incidence rate ratios, and corresponding 95% confidence intervals were calculated for AAPI or Hispanic enclave, nSES, and the joint effects of ethnic enclave and nSES by time period (and the combination of the three periods), sex, and race/ethnicity.

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**Conflict of interest:** The authors declare no potential conflicts of interest.

**Results:** In the combined time period, HCC risk increased 25% for highest versus lowest quintile of AAPI enclave among AAPI males. HCC risk increased 22% and 56% for lowest versus highest quintile of nSES among AAPI females and males, respectively. In joint analysis, AAPI males living in low nSES areas irrespective of enclave status were at 17–43% increased HCC risk compared to AAPI males living in areas of non-enclave/high nSES. HCC risk increased by 22% for Hispanic females living in areas of low nSES irrespective of enclave status and by 19% for Hispanic males living in areas of non-enclave/low nSES compared to their counterparts living in areas of non-enclave/high nSES.

**Conclusions:** We found significant variation in HCC incidence by ethnic enclave and nSES among AAPI and Hispanic populations in California by sex and time period.

**Impact:** Future studies should explore how specific attributes of enclaves and nSES impact HCC risk for AAPI and Hispanic populations.

### Keywords

Race/ethnicity; enclave; neighborhood; socioeconomic status; hepatocellular carcinoma; Asian American/Pacific Islander; Hispanic

## Introduction

Hepatocellular carcinoma (HCC) is the dominant histologic type of liver cancer in the United States (U.S.) (1). Nationally, HCC incidence is three times higher in males than females and highest among the American Indian/Alaska Native population, followed by Asian American/Pacific Islander (AAPI) and Hispanic populations (2,3). HCC incidence had been steadily increasing for decades (4,5), until around 2006, when HCC incidence trends began to stabilize and eventually decrease, especially for AAPI and Hispanic populations (3,6).

While individual-level etiologic differences can explain some variation in HCC incidence across different racial/ethnic groups (7), neighborhood contextual factors have emerged as important risk factors for racial/ethnic disparities (8,9). Ethnic enclaves and various measures of neighborhood socioeconomic status (nSES) such as poverty level, household educational attainment, and unemployment rate, have been linked to increased risk of HCC in different regions of the U.S. (10–12). Enclaves are neighborhoods that are more ethnically distinct, often defined by high concentrations of specific racial/ethnic groups, foreign-born residents, and households with limited English proficiency or that are linguistically isolated. Enclaves tend to have businesses and social institutions that reflect the linguistic and cultural values of their residents, allowing greater opportunities to disseminate information that is linguistically and culturally relevant. Moreover, ethnic enclaves offer residents social integration and social support and/or collective efficacy from co-ethnic residents, which are important factors that can positively impact health (8,13). At the same time, ethnic enclaves tend to be underserved and of lower socioeconomic status, therefore lacking resources for education, employment, health care, housing, and lifestyle behaviors such as physical activity and adequate nutrition leading to poorer health (13). Similarly, nSES has been shown to be an independent risk factor for health, beyond individual-level socioeconomic

status, and residence in higher nSES areas may provide better access to resources such as parks and recreational opportunities, healthy food environments, and health care; all factors that can have a cumulative positive impact on health (8).

Two of the fastest-growing racial/ethnic groups in the U.S. are AAPI and Hispanic and California has the largest AAPI and Hispanic populations in the country (14). To our knowledge, only two studies have investigated the associations between ethnic enclaves and/or nSES on the risk of HCC among AAPI and Hispanic populations living in California. These previous studies found that AAPI and Hispanic enclaves and areas of low nSES were at increased risk of HCC (15,16), although patterns differed by sex (15). Given changing patterns of HCC incidence and the ethno demographic and socioeconomic landscape both in California and nationwide, we seek to build upon this work by incorporating the most currently available state cancer registry and decennial census data and provide an update on the disparities in HCC incidence by statewide distributions of ethnic enclave and nSES among AAPI and Hispanic populations in California, separately by race/ethnicity and sex.

## Materials and Methods

### Cancer case and general population data

The fundamentals of the study population, data extraction, and analysis have been reported in detail before (6,15). Briefly, we obtained data for all primary, invasive HCC (International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) site code 22.0, histology codes 8170–8175) from January 1, 1988, through December 31, 2012 from the California Cancer Registry (CCR), which comprises three of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program registries (17).

The analysis included 13,160 HCC cases (1,780 AAPI females, 4,753 AAPI males, 1,744 Hispanic females, and 4,883 Hispanic males) diagnosed within three 5-year intervals around decennial Census years, 1990, 2000 and 2010 yielding diagnoses from 1988–1992, 1998–2002, 2008–2012, respectively. All cases were assigned to census tracts by CCR based on address information at diagnosis. In this analysis, 96% of Hispanic cases and 98% of AAPI cases were assigned to a census tract based on valid street address or zip+4/+2; for the remaining cases, census tracts were assigned based on zip code centroids. AAPI and Hispanic ethnicity were categorized using methods and algorithms described previously (15,18,19). We chose to use “Hispanic” in lieu of terms containing the word “Latin” because the registry defines this racial/ethnic group as origin from any Spanish-speaking country, and therefore includes the European country of Spain, but excludes origin from non-Spanish speaking Latin American countries such as Brazil (20). That being said, the Pew Research Center estimates that 84% of Hispanic Americans in California are of Mexican ancestry (21). We were not able to disaggregate data into specific AAPI ethnic groups for these analyses due to the lack of subgroup-specific population estimates for census tracts; therefore, AAPI populations are presented as an aggregate group. Furthermore, a high proportion of Hispanic cases with unspecified ethnicity precluded our ability to disaggregate Hispanic data into more granular ethnic groups. We used 2000 U.S. Census population estimates by race/ethnicity and sex at the census tract level. Case data was appended to census tract level neighborhood data.

## Ethnic enclave and neighborhood socioeconomic status

Ethnic enclaves are well-established and widely used in cancer surveillance literature (8,12). We operationalized ethnic enclaves as geographic units with higher concentrations of a specific race/ethnicity, foreign-born and/or recent immigrants and non-English language use than other geographic units (22). Principal components analysis, a well-validated statistical method (23), was applied to develop these measures using 1990 and 2000 U.S. Census and 2008–2012 American Community Survey (ACS) variables at the census tract level. For AAPI enclaves, we included data on linguistic isolation, English fluency, AAPI language use, AAPI race, and recent immigration. For Hispanic enclaves, we included data on linguistic isolation, English fluency, Spanish language use, Hispanic ethnicity, recent immigration, and nativity. Each census tract was assigned to a quintile (Q) based on the statewide distribution of each enclave index for each decennial Census year (1990, 2000, 2010). We used enclave quintiles (Q5 = most ethnically distinct neighborhoods versus Q1 = least ethnically distinct neighborhoods) as well as a dichotomous measure of enclave (Q4-Q5 = enclave versus Q1-Q3 = non-enclave) (15).

To measure nSES, we used an established index that incorporates Census and ACS data on education, occupation, employment, household income, poverty, rent, and house values using principal components analysis (24). Each census tract was assigned to an nSES quintile based on the statewide distribution of the index for each decennial Census year (1990, 2000, 2010). We utilized both the full range of nSES quintiles (Q1 = lowest nSES versus Q5 = highest nSES) as well as a dichotomous measure combining Q1-Q3 (low nSES) versus Q4-Q5 (high nSES) (15).

## Statistical Analysis

We used SEER\*Stat software (25) to compute age-adjusted incidence rates (IRs; per 100,000 population; standardized to the 2000 U.S. standard million population) and incidence rate ratios (IRRs) for each strata of ethnic enclave and nSES by sex and race/ethnicity for three time periods: 1988–1992, 1998–2002, 2008–2012, and the combination of the three periods, which will be referred to henceforth as the “combined period.” Confidence intervals (CI) were calculated using Tiwari et al., 2006 modification (26). Population counts for incidence calculations were estimated using 1990, 2000, and 2010 Census counts multiplied by 5. We conducted tests for linear trend of incidence rates across ethnic enclave and nSES quintiles using weighted linear regression where weight was the inverse of the variance of rate. All statistical tests were 2-sided with  $P < 0.05$  indicating statistical significance and CIs set to 95%. Data sets used for this analysis can be made available upon reasonable request.

## Results

HCC cases in our study included approximately three times as many males than females, with little variation in sex distributions by time period or race/ethnicity (Table 1). More AAPI cases were diagnosed at a very young age (<40 years) compared to Hispanic cases. Cases with distant or unknown stage decreased over time, while the number of cases with localized or regional stage increased over time for both AAPI and Hispanic groups.

### AAPI Females

Among AAPI females (Table 2 and Figures 1–3), there was no association between HCC incidence and AAPI enclave. HCC risk increased with decreasing nSES in the combined time period (Q1 vs. Q5: IRR=1.22, 95% CI=1.04–1.44, p-trend=0.03) with stronger associations in the latest time period (2008–2012) (Q1 vs. Q5: IRR=1.50, 95% CI=1.18–1.91, p-trend <0.01). When AAPI enclave and nSES were studied jointly, in the earliest time period (1988–1992), AAPI females in non-enclave/low SES areas had increased risk of HCC (IRR=2.06, 95% CI=1.17–3.80) compared to those in non-enclave/high nSES areas. This association was not observed in later time periods.

### AAPI Males

For AAPI males (Table 2 and Figures 1–3), living in highest versus lowest quintile of AAPI enclave increased risk of HCC during the combined time period (Q5 vs. Q1: IRR=1.25, 95% CI=1.03–1.53) and the latest time period (2008–2012) (Q5 vs. Q1: IRR=1.39, 95% CI=1.05–1.88). In every time period, HCC risk increased 46–64% for lowest versus highest nSES with strong ordinal trends in the later time periods. In the combined time period, compared to AAPI males in non-enclave/high nSES areas, AAPI males in enclave/low nSES areas experienced the greatest risk of HCC (IRR=1.43, 95% CI=1.28–1.60), followed by those living in non-enclave/low nSES areas (IRR=1.17, 95% CI=1.02–1.34). Similar associations were seen in the latest time period (2008–2012) (IRR enclave/low nSES=1.49, 95% CI=1.28–1.75 and IRR non-enclave/low nSES =1.24, 95% CI=1.02–1.51).

### Hispanic Females

Hispanic females (Table 3 and Figures 1–3) living in the highest versus lowest quintile of Hispanic enclave experienced an increased risk of HCC in the combined time period (Q5 vs. Q1: IRR=1.42, 95% CI=1.13–1.82). A stronger, ordinal association existed in the latest time period (2008–2012) (Q5 vs. Q1: IRR=1.72, 95% CI=1.26–2.39, p-trend=0.04). During the latest time period (2008–2012), Hispanic females with lowest versus highest nSES had increased risk of HCC (Q1 vs. Q5: IRR=1.41, 95% CI=1.09–1.86). However, this association was attenuated when the time periods were combined due to non-ordinal inverse associations in the earliest time period (1988–2002). In the combined time period, compared to those in non-enclave/high nSES areas, those in low nSES areas, regardless of enclave status, had a 22% increased risk of HCC. In the latest time period (2008–2012) this risk ranged from 40% to 46%.

### Hispanic Males

There were no ordinal associations with Hispanic enclave nor nSES and HCC incidence among Hispanic males (Table 3 and Figures 1–3). However, when Hispanic enclave and nSES were studied jointly, Hispanic males in non-enclave/low SES areas had a 19% (95% CI=1.07–1.32) increased risk of HCC in the combined period and a 30% (95% CI=1.14–1.47) increased risk in the latest time period (2008–2012), compared to those living in non-enclave/high SES areas. Risk was also elevated 35% (95% CI=1.05–1.70) for those in enclave/high nSES vs. non-enclave/high nSES areas during the latest time period (2008–2012).

## Time Period

In general, ordinal associations for ethnic enclave and nSES were stronger in the latest time period (2008–2012). However, time period patterns varied by race/ethnicity and sex. For AAPI females (Table 2 and Figures 1–3), there were no temporal trends in associations for AAPI enclave but associations of increased HCC incidence with decreasing nSES were limited to the latest time period ( $P_{\text{trend}} < 0.01$ ). For the joint AAPI enclave/nSES variable, a two-fold increased risk of HCC in the earliest time period (1988–1992) for low versus high nSES among those in non-enclave neighborhoods (IRR=2.06, 95% CI=1.17–3.80) became attenuated towards the null in the latest time period. For AAPI males (Table 2 and Figures 1–3), trends for increased HCC incidence with increasing AAPI enclave were not significant in the earliest time period, but were significant in the middle ( $P_{\text{trend}}=0.04$ ) and marginally significant in the latest ( $P_{\text{trend}}=0.08$ ) time periods. Furthermore, positive associations between HCC incidence and nSES and joint AAPI enclave/nSES became stronger in successive time periods. For Hispanic females (Table 3 and Figures 1–3), positive associations for Hispanic enclave, nSES and joint Hispanic enclave/nSES were limited to the latest time period. For Hispanic males (Table 3 and Figures 1–3), associations did not vary by time period for Hispanic enclave or nSES separately, however, positive associations for joint Hispanic enclave/nSES were only evident in the latest time period.

## Discussion

In this population-based study, we found differences in HCC incidence rates by two important neighborhood contextual factors: ethnic enclave and nSES. Among AAPI males, but not AAPI females, living in highest versus lowest quintile of AAPI enclave increased risk of HCC by 25% in the combined time period. For both AAPI females and males, there were ordinal trends of increasing HCC risk with decreasing nSES. Regardless of AAPI enclave status, living in low nSES areas increased risk of HCC in AAPI males by 17–43% compared to those living in a non-enclave/high nSES area in the combined time period. For Hispanic females and males in the combined time period, there were no ordinal trends to the associations found for Hispanic enclave or nSES when analyzed separately, although ordinal patterns were more apparent for Hispanic females in the later time period. When Hispanic enclave and nSES were considered jointly, the influence of lower nSES on HCC risk became evident, especially among Hispanic females for whom risk increased 22% for low versus high nSES, regardless of enclave status in the combined study period. These findings suggest that social, economic, and cultural characteristics of neighborhoods can influence incidence of HCC and differ over time between AAPI and Hispanic females and males in California.

A summary of findings from two prior investigations of ethnic enclave, nSES, and liver cancer/HCC incidence in California, as well from the current study, are presented in Supplemental Table 1. The first analysis, led by Chang et al. (15), looked at liver cancer rates in 1998–2002 (sensitivity analyses restricting to HCC yielded similar results) while the second analysis, led by Yang et al. (16), examined ethnic enclave and HCC-specific incidence during 2008–2012. Our results for AAPI and Hispanic males are similar to Chang et al., however, our findings of increasing HCC risk with decreasing nSES in AAPI females



and no association between nSES and HCC in Hispanic females deviates from previous findings. We found strong positive associations with nSES among AAPI females in the latest time period (2008–2012), which drove findings of significant increased risk of HCC in the combined time period. For Hispanic females, strong inverse associations with nSES in the earliest time period (1988–1992) negated positive associations seen in the latest time period (2008–2012), resulting in no significant associations for the combined time period. Since the years included in our earliest and latest time period are outside the 1998–2002 time frame of the Chang et al. study, some differences are expected. For example, declines in neighborhood and individual economic status due to the 2008 global recession, especially among already marginalized populations, may have had negative effects on personal health, including communicable and non-communicable disease risk (27). Our analysis supports such a pathway as risk of HCC increased with decreasing nSES over time for all groups except Hispanic males, which requires some additional investigation. Furthermore, although Chang et al. reported results for all liver cancers whereas we report on HCC-specific rates, sensitivity analyses restricting to HCC in their analysis yielded similar results. Finally, our finding of higher incidence of HCC for those living in the highest versus lowest quintile of ethnic enclave is in line with results from the HCC incidence analysis conducted by Yang et al. in 2008–2012, although this previous study did not present results by sex, as we did. Sex-specific incidence rates is an important strength of our study as we found that the associations between HCC and ethnic enclave were limited to Hispanic females and AAPI males.

The geographic distribution of characteristics of the neighborhood built environment (such as traffic density, businesses, parks and recreational facilities, and health care services) and high-risk health behaviors that are linked to liver diseases (such as alcohol consumption and tobacco smoking) can provide some rationale for the association between low nSES and high HCC incidence seen in Hispanic and AAPI populations (28). Alcohol consumption has been found to increase the risk of liver cancer by approximately 10% per drink per day (29). A recent nationwide geographic study of alcohol retail density found that greater density of alcohol retailers was associated with higher levels of neighborhood poverty (30). This suggests that our findings could be partially explained by the availability of harmful structural, built, and social attributes of lower nSES areas that can potentially increase the risk of liver disease and HCC. Additionally, HCC risk increases substantially with increasing BMI (31) and individuals living in lower nSES neighborhoods face more constraints to exercise (reduced access to parks and recreational facilities) and nutrition (lower prevalence or absence of retailers that offer whole and nutrient dense food) leading to higher BMI (32). Other factors to consider as pathways for how nSES can influence HCC risk include geographic differences in access to health prevention services, such as hepatitis vaccination and screening (33,34) or high-quality health care (35).

Ethnic enclaves may influence cancer risk differently from nSES. Mortality (overall and cancer-specific) can be lower for Hispanic populations living in Hispanic enclaves, even though these same neighborhoods are also economically disadvantaged, which, as discussed above, is correlated with poorer health (36). Referred to as the Hispanic Paradox, the health benefit of Hispanic enclaves can be explained by a high level of social support and sense of community, consuming traditional and healthier diets, more employment, and more stable

family structures and residential history (37). In our study, we found some evidence of higher risk of HCC incidence in more ethnically Hispanic neighborhoods but there was no linear trend in the combined time period. When paired with nSES, residence in a Hispanic enclave seemed to have a weaker influence over HCC risk than nSES, especially among Hispanic females. It is possible that for cancers that have a strong causal link with infections, ethnic enclaves may not be as influential as they are for cancers that have strong lifestyle risk factors (12). This may partially explain our findings for the weak relation between Hispanic enclaves and HCC risk as HCV infection is the most frequently reported etiologic factor for Hispanic HCC cases (1). Nevertheless, it is important to continue to track the influence of Hispanic enclaves on HCC risk as the increasing prevalence of obesity and NAFLD/MAFLD among Hispanic Americans (38), coupled with highly effective treatments for HCV (39), suggests that lifestyle risk factors will play a larger role in HCC etiology than viral infections in Hispanic populations.

Among AAPI females in our study, especially in the earlier years, more ethnically AAPI neighborhoods were protective against HCC. Although AAPI enclaves share some similarities with Hispanic enclaves in terms of social support and traditional lifestyle habits (12), AAPI populations, collectively, tend to report higher educational attainment and less poverty than Hispanic populations (40). It is important to note, however, that there is significant educational and income heterogeneity among different AAPI ethnicities (41). In our study, a very high proportion of Hispanic cases who lived in Hispanic enclaves also lived in low nSES areas compared to AAPI cases who lived in AAPI enclaves and this difference persisted over the study period (Supplemental Table 2). Therefore, AAPI enclaves may have characteristics associated with areas that have high individual-level and neighborhood-level socioeconomic status, such as greater access to healthcare resources, awareness about cancer prevention and screening (42), and, as it relates to HCC, adherence to HBV vaccination, screening, and treatment. HBV infection is the most frequently reported HCC risk factor among AAPI cases, especially those who are foreign-born (1). Differences between AAPI and Hispanic enclaves could explain why we saw differential associations for ethnic enclave among these two ethnically aggregate populations, however, a comparison of disaggregated AAPI and Hispanic ethnicities would yield more accurate and valid comparisons.

We detected temporal changes in associations of ethnic enclave and nSES with HCC incidence. Increased risk of HCC with ethnic enclave and low nSES was restricted to or stronger in the latest time period of 2008–2012. Furthermore, between the earliest (1988–1992) and latest (2008–2012) time periods, the proportion of AAPI cases residing in areas of low nSES decreased by 11% while the proportion of Hispanic cases residing in enclaves decreased by 6%. As mentioned earlier, the Great Recession of 2008 had immediate and far-reaching economic impacts on all Americans, but especially for those in marginalized and underserved communities, which may explain these trends. Changes in factors that affect individual-level risk for HCC, such as alcohol abuse and smoking (driven by increased stress and adverse mental health), reduced access to healthcare (driven by lower income and/or unemployment), and changes in factors that have an effect on neighborhood contextual risk factors such as immigration patterns, economic growth and recession, greater wealth gaps, as well as gentrification may have influenced some of these findings and warrants more in-depth analysis in future studies (27,43).



Our study should be viewed in light of some limitations. First, the use of a registry-based population-level dataset limited our ability to control for potential individual-level confounders such as educational attainment, income, lifestyle risk factors, metabolic risk factors, infections, and health care access. Second, we assessed neighborhood characteristics at the time of diagnosis and were unable to assess lifetime residential history. Lifetime exposure to neighborhood contextual factors, and factors affecting duration of residence in a neighborhood and frequency of moves could prove important in predicting cancer risk. For example, long-term exposure to poverty is associated with known risk factors for HCC, such as obesity (44), early smoking initiation (45) and diabetes (46). Third, we were not able to assess associations between enclave and nSES by nativity or disaggregated race/ethnicity (especially for AAPI populations) due to the unavailability of census tract level population data by nativity or disaggregated race/ethnicity. Previous studies in California have found disparities in HCC incidence by specific AAPI groups and/or nativity (6,15,16,47–49). Among AAPI populations, Vietnamese Americans had the highest HCC IRs (6,16,48) and IRs for all groups were generally higher for foreign-born than U.S.-born (6,15). In Hispanic populations, U.S.-born males had higher HCC incidence than foreign-born males, whereas no relative differences by nativity in females were found (6,47). Fourth, we used census tracts based on administrative boundaries to define geographical neighborhoods. Neighborhoods defined by individual-level self-reported measures may be more representative of the lived experience within those areas than geospatial measures (8), however, for population-based health studies such as ours, census tracts offer a useful approximation of neighborhoods (50). Fifth, our findings are specific to the sociodemographic, contextual, and economic environment in California and as such, may not be representative of findings in other geographic locations across the U.S. Sixth, since there is no standard definition of ethnic enclave, our findings are specific to the measurement of enclaves in our study. However, while many prior studies have used a single measure of racial/ethnic percentages (12), our utilization of a multicomponent index measure to capture ethnic enclaves beyond racial/ethnic composition, accounting for immigration and linguistic proficiency and isolation, is a more comprehensive approach. Finally, although we had population data from the 2020 Census, we did not have sufficient years of cancer registry data to create a 5-year assessment of HCC rates around the most recent Census, as we did for previous Census years. Therefore, continued examination of HCC risk in relation to ethnic enclaves and nSES in California is imperative as more data become available.

There are several strengths of our study. Our examination of ethnic enclaves, nSES, and HCC is the largest to date with a long assessment period spanning from 1988 to 2012. We were able to report stratified results highlighting differences by time period, race/ethnicity, and sex. Our cases were ascertained through high quality registry data, which are mandated by the state for reporting, therefore, it is unlikely that a significant number of HCC cases were missed. Furthermore, because separate data were used to operationalize the exposure and the outcome, any misclassification would have been independent and non-differential, typically leading to more conservative estimates toward the null. Finally, because our findings are consistent with previous studies that have examined this same association with earlier waves of data (15,16), it is unlikely that our analysis yielded spurious results.

In summary, we found persistent and significant variation in HCC incidence by ethnic enclave and nSES among AAPI and Hispanic populations living in California, consistent with patterns seen in earlier reports. Associations varied by time period and sex. Analysis of the joint effects of ethnic enclave and nSES demonstrated the interplay of these two important contextual factors and yielded findings that would not have otherwise been detected in separate analysis. Changing patterns in HCC incidence (6,51) and the racial/ethnic milieu in California, a state with dynamic population growth and immigration patterns warrant further surveillance of HCC incidence. Future longitudinal studies are needed to further explore specific attributes of enclaves and nSES that impact HCC risk especially in subpopulations such as recent immigrants.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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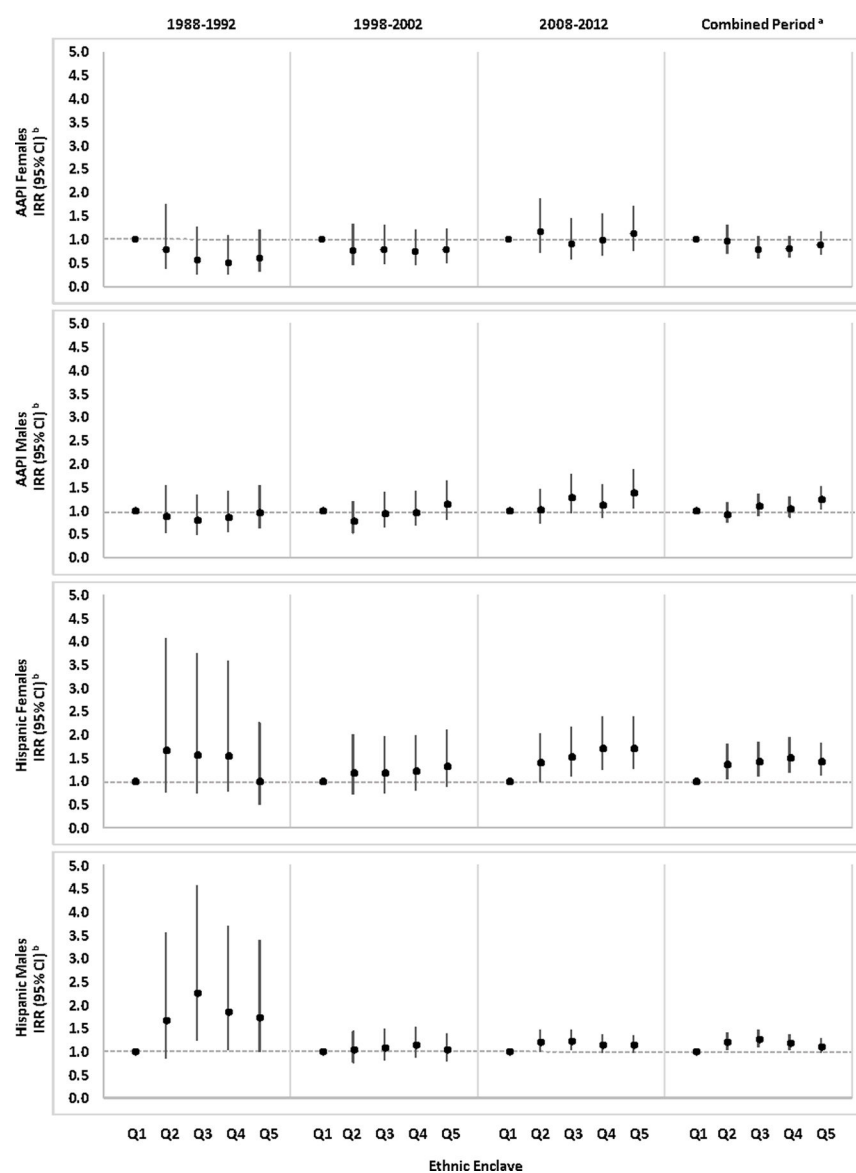
## References

1. El-Serag HB. Epidemiology of viral hepatitis and hepatocellular carcinoma. *Gastroenterology* 2012;142(6):1264–73 e1 doi 10.1053/j.gastro.2011.12.061. [PubMed: 22537432]
2. Altekruse SF, Henley SJ, Cucinelli JE, McGlynn KA. Changing hepatocellular carcinoma incidence and liver cancer mortality rates in the United States. *Am J Gastroenterol* 2014;109(4):542–53 doi 10.1038/ajg.2014.11. [PubMed: 24513805]
3. Shiels MS, O'Brien TR. Declining U.S. Hepatocellular Carcinoma Rates, 2014–2017. *Clin Gastroenterol Hepatol* 2021 doi 10.1016/j.cgh.2021.02.011.
4. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. *J Clin Oncol* 2009;27(9):1485–91 doi 10.1200/JCO.2008.20.7753. [PubMed: 19224838]
5. Njei B, Rotman Y, Ditah I, Lim JK. Emerging trends in hepatocellular carcinoma incidence and mortality. *Hepatology* 2015;61(1):191–9 doi 10.1002/hep.27388. [PubMed: 25142309]
6. Sangaramoorthy M, Yang J, DeRouen MC, Ho C, Somsouk M, Tana MM, et al. Disparities in Hepatocellular Carcinoma Incidence in California: An Update. *Cancer Epidemiol Biomarkers Prev* 2020;29(1):79–87 doi 10.1158/1055-9965.EPI-19-0560. [PubMed: 31719066]
7. Song TJ, Fong Y, Cho SJ, Gonen M, Hezel M, Tuorto S, et al. Comparison of hepatocellular carcinoma in American and Asian patients by tissue array analysis. *J Surg Oncol* 2012;106(1):84–8 doi 10.1002/jso.23036. [PubMed: 22234941]
8. Gomez SL, Shariff-Marco S, DeRouen M, Keegan TH, Yen IH, Mujahid M, et al. The impact of neighborhood social and built environment factors across the cancer continuum: Current research, methodological considerations, and future directions. *Cancer* 2015;121(14):2314–30 doi 10.1002/cncr.29345. [PubMed: 25847484]

9. Schootman M, Gomez SL, Henry KA, Paskett ED, Ellison GL, Oh A, et al. Geospatial Approaches to Cancer Control and Population Sciences. *Cancer Epidemiol Biomarkers Prev* 2017;26(4):472–5 doi 10.1158/1055-9965.EPI-17-0104. [PubMed: 28325736]
10. Shebl FM, Capo-Ramos DE, Graubard BI, McGlynn KA, Altekruse SF. Socioeconomic status and hepatocellular carcinoma in the United States. *Cancer Epidemiol Biomarkers Prev* 2012;21(8):1330–5 doi 10.1158/1055-9965.EPI-12-0124. [PubMed: 22669949]
11. Ford MM, Ivanina E, Desai P, Highfield L, Qiao B, Schymura MJ, et al. Geographic epidemiology of hepatocellular carcinoma, viral hepatitis, and socioeconomic position in New York City. *Cancer Causes Control* 2017;28(7):779–89 doi 10.1007/s10552-017-0897-8. [PubMed: 28573469]
12. Fang CY, Tseng M. Ethnic density and cancer: A review of the evidence. *Cancer* 2018;124(9):1877–903 doi 10.1002/cncr.31177. [PubMed: 29411868]
13. Becares L, Shaw R, Nazroo J, Stafford M, Albor C, Atkin K, et al. Ethnic density effects on physical morbidity, mortality, and health behaviors: a systematic review of the literature. *Am J Public Health* 2012;102(12):e33–66 doi 10.2105/AJPH.2012.300832.
14. Pew Research Center. U.S. Hispanic and Asian populations growing, but for different reasons. Washington, D.C. 2014.
15. Chang ET, Yang J, Alfaro-Velcamp T, So SK, Glaser SL, Gomez SL. Disparities in liver cancer incidence by nativity, acculturation, and socioeconomic status in California Hispanics and Asians. *Cancer Epidemiol Biomarkers Prev* 2010;19(12):3106–18 doi 10.1158/1055-9965.epi-10-0863. [PubMed: 20940276]
16. Yang B, Liu JB, So SK, Han SS, Wang SS, Hertz A, et al. Disparities in hepatocellular carcinoma incidence by race/ethnicity and geographic area in California: Implications for prevention. *Cancer* 2018;124(17):3551–9 doi 10.1002/cncr.31598. [PubMed: 30113700]
17. Surveillance Epidemiology and End Results Program. February 20, 2018. Overview of the SEER Program. National Cancer Institute <<http://seer.cancer.gov/about>>. February 20, 2018.
18. NAPIIA NAACCR Race and Ethnicity Work Group. NAACCR Asian Pacific Islander Identification Algorithm [NAPIIA v1.2.1]. Springfield, IL: North American Association of Central Cancer Registries; 2010.
19. NAACCR Race and Ethnicity Work Group. NAACCR guideline for enhancing Hispanic/Latino identification: revised NAACCR Hispanic/Latino Identification Algorithm [NHIA v2.2.1]. Springfield, IL: North American Association of Central Cancer Registries; 2011.
20. Flanagan A, Frey T, Christiansen SL, Bauchner H. The Reporting of Race and Ethnicity in Medical and Science Journals: Comments Invited. *JAMA* 2021;325(11):1049–52 doi 10.1001/jama.2021.2104. [PubMed: 33616604]
21. Pew Research Center. Demographic profile of Hispanics in California, 2014. Washington, D.C.2014.
22. Gomez SL, Glaser SL, McClure LA, Shema SJ, Kealey M, Keegan TH, et al. The California Neighborhoods Data System: a new resource for examining the impact of neighborhood characteristics on cancer incidence and outcomes in populations. *Cancer Causes Control* 2011;22(4):631–47 doi 10.1007/s10552-011-9736-5. [PubMed: 21318584]
23. Jolliffe IT, Cadima J. Principal component analysis: a review and recent developments. *Philos Trans A Math Phys Eng Sci* 2016;374(2065):20150202 doi 10.1098/rsta.2015.0202. [PubMed: 26953178]
24. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control* 2001;12(8):703–11. [PubMed: 11562110]
25. National Cancer Institute. Surveillance Research Program, SEER\*Stat software (seer.cancer.gov/seerstat) version 8.3.4. 2017. 2017.
26. Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. *Stat Methods Med Res* 2006;15(6):547–69 doi 10.1177/0962280206070621. [PubMed: 17260923]
27. Karanikolos M, Heino P, McKee M, Stuckler D, Legido-Quigley H. Effects of the Global Financial Crisis on Health in High-Income Oecd Countries: A Narrative Review. *Int J Health Serv* 2016;46(2):208–40 doi 10.1177/0020731416637160. [PubMed: 27076651]

28. Major JM, Sargent JD, Graubard BI, Carlos HA, Hollenbeck AR, Altekruse SF, et al. Local geographic variation in chronic liver disease and hepatocellular carcinoma: contributions of socioeconomic deprivation, alcohol retail outlets, and lifestyle. *Ann Epidemiol* 2014;24(2):104–10 doi 10.1016/j.annepidem.2013.11.006. [PubMed: 24332863]
29. Chuang SC, Lee YC, Wu GJ, Straif K, Hashibe M. Alcohol consumption and liver cancer risk: a meta-analysis. *Cancer Causes Control* 2015;26(9):1205–31 doi 10.1007/s10552-015-0615-3. [PubMed: 26134046]
30. Berke EM, Tanski SE, Demidenko E, Alford-Teaster J, Shi X, Sargent JD. Alcohol retail density and demographic predictors of health disparities: a geographic analysis. *Am J Public Health* 2010;100(10):1967–71 doi 10.2105/AJPH.2009.170464. [PubMed: 20724696]
31. Campbell PT, Newton CC, Freedman ND, Koshiol J, Alavanja MC, Freeman LEB, et al. Body Mass Index, Waist Circumference, Diabetes, and Risk of Liver Cancer for US Adults. *Cancer Res* 2016;76(20):6076–83 doi 10.1158/0008-5472.Can-16-0787. [PubMed: 27742674]
32. Do DP, Dubowitz T, Bird CE, Lurie N, Escarce JJ, Finch BK. Neighborhood context and ethnicity differences in body mass index: a multilevel analysis using the NHANES III survey (1988–1994). *Econ Hum Biol* 2007;5(2):179–203 doi 10.1016/j.ehb.2007.03.006. [PubMed: 17507298]
33. Hsu CE, Liu LC, Juon HS, Chiu YW, Bawa J, Tillman U, et al. Reducing liver cancer disparities: a community-based hepatitis-B prevention program for Asian-American communities. *J Natl Med Assoc* 2007;99(8):900–7. [PubMed: 17722668]
34. Hu KQ, Pan CQ, Goodwin D. Barriers to screening for hepatitis B virus infection in Asian Americans. *Dig Dis Sci* 2011;56(11):3163–71 doi 10.1007/s10620-011-1840-6. [PubMed: 21861105]
35. Li J, Hansen BE, Peppelenbosch MP, De Man RA, Pan QW, Sprengers D. Factors associated with ethnic disparity in overall survival for patients with hepatocellular carcinoma. *Oncotarget* 2017;8(9):15193–204 doi 10.18632/oncotarget.14771. [PubMed: 28122352]
36. Pruitt SL, Tiro JA, Xuan L, Lee SJ. Hispanic and Immigrant Paradoxes in U.S. Breast Cancer Mortality: Impact of Neighborhood Poverty and Hispanic Density. *Int J Environ Res Public Health* 2016;13(12) doi 10.3390/ijerph13121238.
37. Eschbach K, Ostir GV, Patel KV, Markides KS, Goodwin JS. Neighborhood context and mortality among older Mexican Americans: is there a barrio advantage? *Am J Public Health* 2004;94(10):1807–12 doi 10.2105/ajph.94.10.1807. [PubMed: 15451754]
38. Ha J, Chaudhri A, Avirineni A, Pan JJ. Burden of hepatocellular carcinoma among hispanics in South Texas: a systematic review. *Biomark Res* 2017;5:15 doi 10.1186/s40364-017-0096-5. [PubMed: 28439416]
39. Panel A-IHG. Hepatitis C Guidance 2018 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Clin Infect Dis* 2018;67(10):1477–92 doi 10.1093/cid/ciy585. [PubMed: 30215672]
40. Glaser SL, Chang ET, Clarke CA, Keegan TH, Yang J, Gomez SL. Hodgkin lymphoma incidence in ethnic enclaves in California. *Leuk Lymphoma* 2015;56(12):3270–80 doi 10.3109/10428194.2015.1026815. [PubMed: 25899402]
41. Pew Research Center. Key facts about Asian Americans, a diverse and growing population. Washington, DC2021.
42. Baker DP, Leon J, Smith Greenaway EG, Collins J, Movit M. The education effect on population health: a reassessment. *Popul Dev Rev* 2011;37(2):307–32 doi 10.1111/j.1728-4457.2011.00412.x. [PubMed: 21984851]
43. Smith GS, Breakstone H, Dean LT, Thorpe RJ Jr. Impacts of Gentrification on Health in the US: a Systematic Review of the Literature. *J Urban Health* 2020;97(6):845–56 doi 10.1007/s11524-020-00448-4. [PubMed: 32829469]
44. Sheehan CM, Cantu PA, Powers DA, Margerison-Zilko CE, Cubbin C. Long-term neighborhood poverty trajectories and obesity in a sample of california mothers. *Health Place* 2017;46:49–57 doi 10.1016/j.healthplace.2017.04.010. [PubMed: 28499148]
45. Kravitz-Wirtz N A discrete-time analysis of the effects of more prolonged exposure to neighborhood poverty on the risk of smoking initiation by age 25. *Soc Sci Med* 2016;148:79–92 doi 10.1016/j.socscimed.2015.11.027. [PubMed: 26685707]

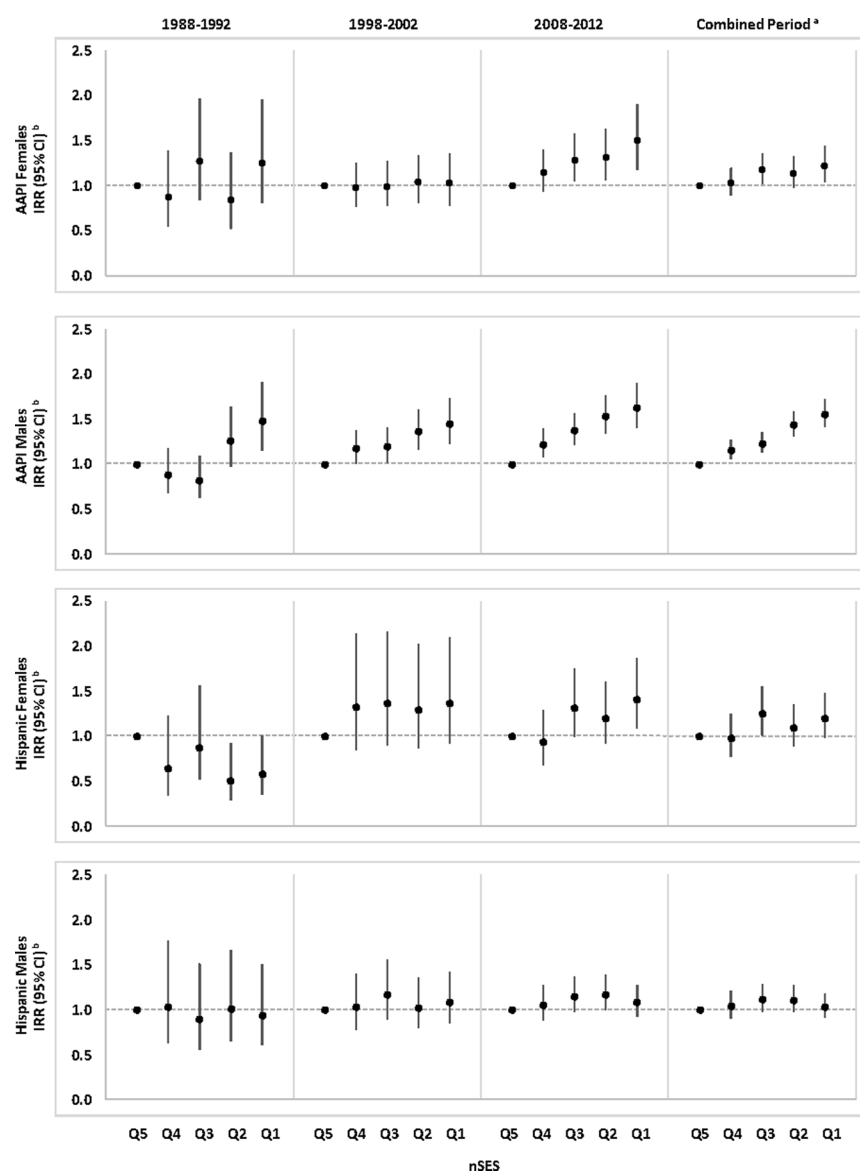
46. Christine PJ, Auchincloss AH, Bertoni AG, Carnethon MR, Sanchez BN, Moore K, et al. Longitudinal Associations Between Neighborhood Physical and Social Environments and Incident Type 2 Diabetes Mellitus The Multi-Ethnic Study of Atherosclerosis (MESA). *Jama Intern Med* 2015;175(8):1311–20 doi 10.1001/jamainternmed.2015.2691. [PubMed: 26121402]
47. Setiawan VW, Wei PC, Hernandez BY, Lu SC, Monroe KR, Le Marchand L, et al. Disparity in liver cancer incidence and chronic liver disease mortality by nativity in Hispanics: The Multiethnic Cohort. *Cancer* 2016;122(9):1444–52 doi 10.1002/cncr.29922. [PubMed: 26916271]
48. Pham C, Fong TL, Zhang J, Liu L. Striking Racial/Ethnic Disparities in Liver Cancer Incidence Rates and Temporal Trends in California, 1988–2012. *J Natl Cancer Inst* 2018;110(11):1259–69 doi 10.1093/jnci/djy051. [PubMed: 29617913]
49. Chang ET, Keegan TH, Gomez SL, Le GM, Clarke CA, So SK, et al. The burden of liver cancer in Asians and Pacific Islanders in the Greater San Francisco Bay Area, 1990 through 2004. *Cancer* 2007;109(10):2100–8 doi 10.1002/cncr.22642. [PubMed: 17385214]
50. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, Carson R. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. *Am J Epidemiol* 2002;156(5):471–82 doi 10.1093/aje/kwf068. [PubMed: 12196317]
51. Han SS, Kelly SP, Li Y, Yang B, Nguyen M, So S, et al. Changing Landscape of Liver Cancer in California: A Glimpse Into the Future of Liver Cancer in the United States. *J Natl Cancer Inst* 2018 doi 10.1093/jnci/djy180.



**Figure 1.**

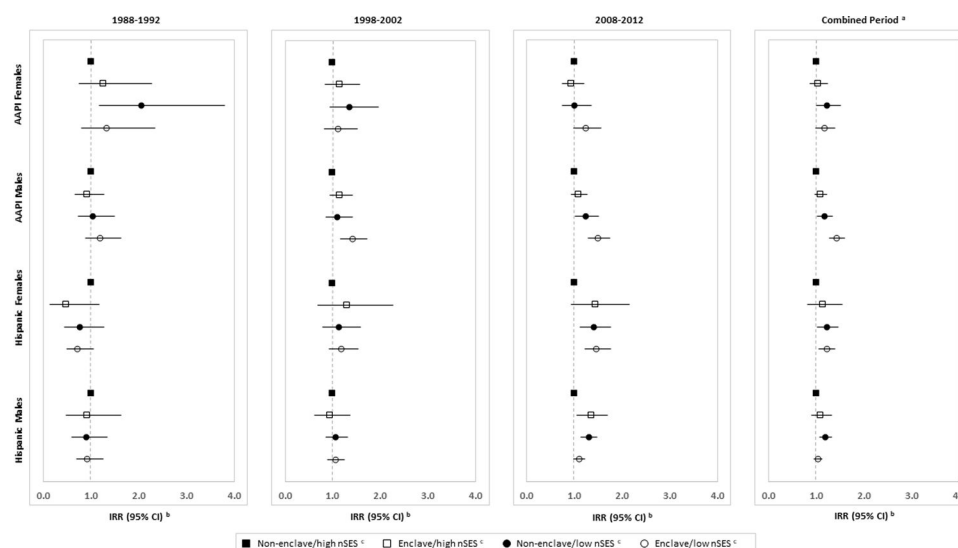
Incidence Rate Ratios of Hepatocellular Carcinoma for Ethnic Enclave in the Asian American/Pacific Islander and Hispanic Population, by Sex, California, 1988–1992, 1998–2002, 2008–2012. Abbreviations are as follows: AAPI, Asian American/Pacific Islander; CI, confidence interval; IRR, incidence rate ratio; Q, quintile. <sup>a</sup> Combination of the three 5-year pericentennial windows: 1988–1992, 1998–2002, 2008–2012. <sup>b</sup> Age adjusted.





**Figure 2.**

Incidence Rate Ratios of Hepatocellular Carcinoma for Neighborhood Socioeconomic Status in the Asian American/Pacific Islander and Hispanic Population, by Sex, California, 1988–1992, 1998–2002, 2008–2012. Abbreviations are as follows: AAPI, Asian American/Pacific Islander; CI, confidence interval; IRR, incidence rate ratio; nSES, neighborhood socioeconomic status; Q, quintile. <sup>a</sup> Combination of the three 5-year pericentral windows: 1988–1992, 1998–2002, 2008–2012. <sup>b</sup> Age adjusted.



**Figure 3.**

Incidence Rate Ratios of Hepatocellular Carcinoma for Ethnic Enclave and Neighborhood Socioeconomic Status in the Asian American/Pacific Islander and Hispanic Population, by Sex, California, 1988–1992, 1998–2002, 2008–2012. Abbreviations are as follows: AAPI, Asian American/Pacific Islander; CI, confidence interval; IRR, incidence rate ratio; nSES, neighborhood socioeconomic status; Q, quintile. <sup>a</sup> Combination of the three 5-year pericensal windows: 1988–1992, 1998–2002, 2008–2012. <sup>b</sup> Age adjusted. <sup>c</sup> Non-enclave are ethnic enclave quintiles 1–3 and enclave are quintiles 4–5. High nSES are quintiles 4–5 and low nSES are quintiles 1–3.

Table 1:

Characteristics of Hepatocellular Carcinoma Cases by Race/Ethnicity, California, 1988–1992, 1998–2002, 2008–2012

	Asian American/Pacific Islander						Hispanic					
	1988–1992		1998–2002		2008–2012		Combined period <sup>d</sup>		1988–1992		1998–2002	
	N	%	N	%	N	%	N	%	N	%	N	%
Cases <sup>b</sup>	1,065		2,266		3,278		6,609		674		1,817	
Sex												
Females	259	24%	640	28%	919	28%	1,818	28%	208	31%	516	28%
Males	806	76%	1,626	72%	2,359	72%	4,791	72%	466	69%	1,301	72%
Age at diagnosis												
<40	90	8%	102	5%	90	3%	282	4%	38	6%	32	2%
40–49	124	12%	260	11%	244	7%	628	10%	56	8%	261	14%
50–59	260	24%	467	21%	784	24%	1,511	23%	135	20%	428	24%
60–69	304	29%	690	30%	862	26%	1,856	28%	218	32%	529	29%
70–79	203	19%	545	24%	837	26%	1,585	24%	153	23%	432	24%
80+	84	8%	202	9%	461	14%	747	11%	74	11%	135	7%
SEER summary stage												
Localized	232	22%	820	36%	1,689	52%	2,741	41%	153	23%	621	34%
Regional	153	14%	370	16%	849	26%	1,372	21%	76	11%	247	14%
Distant	338	32%	654	29%	429	13%	1,421	22%	185	27%	494	27%
Unknown	342	32%	422	19%	311	9%	1,075	16%	260	39%	455	25%
Ethnic enclave												
Quintile 1 (Least ethnically distinct)	38	4%	63	3%	83	3%	184	3%	25	4%	101	6%
Quintile 2	84	8%	124	5%	204	6%	412	6%	65	10%	177	10%
Quintile 3	114	11%	234	10%	368	11%	716	11%	108	16%	276	15%
Quintile 4	198	19%	432	19%	617	19%	1,247	19%	173	26%	527	29%
Quintile 5 (Most ethnically distinct)	630	59%	1,412	62%	2,006	61%	4,048	61%	303	45%	736	41%
Unassigned <sup>c</sup>	1	0%	1	0%	0	0%	2	0%	0	0%	0	0%
nSES												
Quintile 5 (Highest nSES)	192	18%	499	22%	679	21%	1,370	21%	54	8%	114	6%
Quintile 4	199	19%	499	22%	762	23%	1,460	22%	83	12%	224	12%

	Asian American/Pacific Islander						Hispanic					
	1988–1992		1998–2002		2008–2012		1988–1992		1998–2002		2008–2012	
	N	%	N	%	N	%	N	%	N	%	N	%
Quintile 3	204	19%	463	20%	770	23%	132	20%	362	20%	840	20%
Quintile 2	223	21%	466	21%	643	20%	161	24%	467	26%	1,158	28%
Quintile 1 (Lowest nSES)	247	23%	339	15%	424	13%	244	36%	650	36%	1,409	34%
Unassigned <sup>c</sup>	0	0%	0	0%	0	0%	0	0%	0	0%	1	0%
Combined period <sup>a</sup>												
	N		N		N		N		N		N	
	1,437		1,332		1,010		244		650		2,303	
	22%		20%		15%		0%		0%		0%	

Abbreviations: SEER, Surveillance Epidemiology and End Results; nSES, neighborhood socioeconomic status.

<sup>a</sup>Combination of the three 5-year pericensal windows: 1988–1992, 1998–2002, 2008–2012.

<sup>b</sup>Hepatocellular carcinoma cases were restricted to liver cancer cases with morphology codes 8170 – 8175.

<sup>c</sup>Two Asian American/Pacific Islander cases resided in census tracts with assigned values for nSES but no values for ethnic enclave and one Hispanic case resided in a census tract with an assigned value for ethnic enclave but not nSES.

Table 2:

Incidence Rates (per 100,000) and Incidence Rate Ratios of Hepatocellular Carcinoma in the Asian American/Pacific Islander Population, by Sex, Ethnic Enclave, and Neighborhood Socioeconomic Status, California, 1988–1992, 1998–2002, 2008–2012

	1988–1992			1998–2002			2008–2012			Combined Period <sup>a</sup>		
	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>
Females	259	5.55 (4.85 – 6.32)	Reference	639	7.41 (6.83 – 8.01)	Reference	919	6.73 (6.29 – 7.18)	Reference	1817	6.74 (6.43 – 7.06)	Reference
Ethnic enclave												
Quintile 1 (Least ethnically distinct)	14	9.07 (4.6 – 15.97)	Reference	25	9.53 (6.12 – 14.25)	Reference	29	6.28 (4.17 – 9.14)	Reference	68	7.71 (5.95 – 9.83)	Reference
Quintile 2	29	7.15 (4.59 – 10.62)	0.79 (0.38 – 1.75)	44	7.4 (5.33 – 10.00)	0.78 (0.46 – 1.34)	71	7.29 (5.68 – 9.23)	1.16 (0.73 – 1.87)	144	7.45 (6.25 – 8.80)	0.97 (0.71 – 1.32)
Quintile 3	29	5.18 (3.31 – 7.66)	0.57 (0.27 – 1.26)	70	7.52 (5.81 – 9.55)	0.79 (0.49 – 1.31)	96	5.73 (4.63 – 7.03)	0.91 (0.59 – 1.45)	195	6.14 (5.29 – 7.09)	0.80 (0.60 – 1.07)
Quintile 4	47	4.66 (3.32 – 6.33)	0.51 (0.26 – 1.09)	124	7.10 (5.88 – 8.49)	0.74 (0.48 – 1.20)	178	6.26 (5.36 – 7.26)	1.00 (0.66 – 1.54)	349	6.26 (5.61 – 6.97)	0.81 (0.62 – 1.08)
Quintile 5 (Most ethnically distinct)	140	5.46 (4.54 – 6.49)	0.60 (0.33 – 1.22)	376	7.42 (6.68 – 8.22)	0.78 (0.51 – 1.23)	545	7.09 (6.50 – 7.71)	1.13 (0.77 – 1.72)	1061	6.90 (6.49 – 7.33)	0.90 (0.70 – 1.17)
P-trend			0.50			0.51			0.35			0.95
nSES												
Quintile 5 (Highest nSES)	47	5.26 (3.73 – 7.17)	Reference	151	7.4 (6.23 – 8.72)	Reference	193	5.64 (4.85 – 6.51)	Reference	391	6.18 (5.56 – 6.84)	Reference
Quintile 4	48	4.6 (3.30 – 6.22)	0.87 (0.55 – 1.39)	140	7.27 (6.09 – 8.61)	0.98 (0.77 – 1.25)	215	6.45 (5.61 – 7.39)	1.14 (0.93 – 1.40)	403	6.40 (5.78 – 7.07)	1.04 (0.90 – 1.20)
Quintile 3	70	6.7 (5.09 – 8.64)	1.27 (0.84 – 1.97)	135	7.35 (6.14 – 8.73)	0.99 (0.78 – 1.27)	219	7.27* (6.33 – 8.31)	<b>1.29 (1.05 – 1.58)</b>	424	7.28* (6.59 – 8.02)	<b>1.18 (1.02 – 1.36)</b>
Quintile 2	41	4.45 (3.10 – 6.15)	0.85 (0.52 – 1.37)	126	7.74 (6.44 – 9.24)	1.05 (0.82 – 1.34)	172	7.41* (6.34 – 8.63)	<b>1.32 (1.06 – 1.63)</b>	339	7.03 (6.29 – 7.82)	1.14 (0.98 – 1.32)
Quintile 1 (Lowest nSES)	53	6.62 (4.92 – 8.68)	1.26 (0.82 – 1.96)	88	7.63 (6.12 – 9.41)	1.03 (0.78 – 1.36)	120	8.46* (6.99 – 10.16)	<b>1.50 (1.18 – 1.91)</b>	261	7.56* (6.67 – 8.54)	<b>1.22 (1.04 – 1.44)</b>
P-trend			0.64			0.18			<0.01			<b>0.03</b>
Joint ethnic enclave/nSES <sup>c</sup>												

	1988–1992			1998–2002			2008–2012			Combined Period <sup>a</sup>		
	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>
Non-enclave/ high nSES	21	4.07 (2.40 – 6.42)	Reference	56	6.58 (4.91 – 8.62)	Reference	96	6.35 (5.12 – 7.79)	Reference	173	6.12 (5.21 – 7.13)	Reference
Enclave/high nSES	74	5.15 (3.95 – 6.57)	1.26 (0.74 – 2.27)	234	7.51 (6.56 – 8.56)	1.14 (0.84 – 1.58)	312	5.95 (5.29 – 6.65)	0.94 (0.74 – 1.19)	620	6.33 (5.83 – 6.86)	1.03 (0.87 – 1.24)
Non- enclave/low nSES	51	8.39* (6.07 – 11.27)	<b>2.06 (1.17 – 3.80)</b>	83	8.87 (7.03 – 11.05)	1.35 (0.94 – 1.95)	100	6.39 (5.19 – 7.79)	1.01 (0.75 – 1.35)	234	7.51 (6.57 – 8.56)	1.23 (1.00 – 1.51)
Enclave/low nSES	113	5.42 (4.42 – 6.57)	1.33 (0.80 – 2.34)	266	7.28 (6.43 – 8.22)	1.11 (0.82 – 1.52)	411	7.83 (7.09 – 8.64)	1.23 (0.98 – 1.56)	790	7.17 (6.67 – 7.69)	1.17 (0.99 – 1.40)
Males	805	18.93 (17.56 – 20.38)		1626	22.38 (21.28 – 23.53)		2359	20.84 (19.99 – 21.73)		4790	21.05 (20.44 – 21.67)	
Ethnic enclave												
Quintile 1 (Least ethnically distinct)	24	20.68 (12.97 – 31.07)	Reference	38	21.18 (14.84 – 29.25)	Reference	54	16.17 (12.02 – 21.31)	Reference	116	18.08 (14.85 – 21.79)	Reference
Quintile 2	55	18.34 (13.44 – 24.31)	0.89 (0.53 – 1.54)	80	16.58 (13.06 – 20.74)	0.78 (0.52 – 1.20)	133	16.60 (13.81 – 19.80)	1.03 (0.73 – 1.45)	268	16.89 (14.86 – 19.11)	0.93 (0.74 – 1.18)
Quintile 3	85	16.51 (12.98 – 20.66)	0.80 (0.49 – 1.35)	164	19.90 (16.84 – 23.33)	0.94 (0.65 – 1.39)	272	20.94 (18.44 – 23.68)	1.29 (0.95 – 1.79)	521	19.82 (18.08 – 21.66)	1.10 (0.89 – 1.36)
Quintile 4	151	17.74 (14.82 – 21.03)	0.86 (0.55 – 1.41)	308	20.65 (18.32 – 23.18)	0.97 (0.69 – 1.42)	439	18.37 (16.64 – 20.23)	1.14 (0.85 – 1.55)	898	19.05 (17.78 – 20.38)	1.05 (0.86 – 1.30)
Quintile 5 (Most ethnically distinct)	490	19.77 (17.95 – 21.71)	0.96 (0.63 – 1.54)	1036	24.07 (22.59 – 25.62)	1.14 (0.82 – 1.63)	1461	22.49* (21.33 – 23.70)	<b>1.39 (1.05 – 1.88)</b>	2987	22.62* (21.80 – 23.47)	<b>1.25 (1.03 – 1.53)</b>
P-trend nSES			0.32			<b>0.04</b>			0.08			0.05
Quintile 5 (Highest nSES)	145	18.09 (14.61 – 22.06)	Reference	348	18.76 (16.70 – 21.00)	Reference	486	16.27 (14.79 – 17.86)	Reference	979	17.24 (16.11 – 18.42)	Reference
Quintile 4	151	16.07 (13.37 – 19.12)	0.89 (0.68 – 1.17)	359	22.06* (19.74 – 24.57)	1.18 (1.00 – 1.38)	547	19.91* (18.23 – 21.70)	<b>1.22 (1.08 – 1.39)</b>	1057	19.96* (18.73 – 21.24)	<b>1.16 (1.06 – 1.27)</b>
Quintile 3	134	14.95 (12.34 – 17.91)	0.83 (0.63 – 1.10)	328	22.47* (20.03 – 25.12)	<b>1.20 (1.02 – 1.41)</b>	551	22.44* (20.56 – 24.45)	<b>1.38 (1.21 – 1.57)</b>	1013	21.33* (20.00 – 22.73)	<b>1.24 (1.13 – 1.36)</b>
Quintile 2	182	22.79 (19.4 – 26.57)	1.26 (0.97 – 1.64)	340	25.64* (22.94 – 28.57)	<b>1.37 (1.17 – 1.60)</b>	471	25.05* (22.80 – 27.47)	<b>1.54 (1.35 – 1.76)</b>	993	24.89* (23.34 – 26.52)	<b>1.44 (1.32 – 1.59)</b>



	1988–1992			1998–2002			2008–2012			Combined Period <sup>a</sup>		
	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>
Quintile 1 (Lowest nSES)	194	26.77* (23.07 – 30.86)	<b>1.48 (1.15 – 1.92)</b>	251	27.32* (24.04 – 30.92)	<b>1.46 (1.23 – 1.73)</b>	304	26.63* (23.69 – 29.84)	<b>1.64 (1.41 – 1.90)</b>	749	26.91* (23.69 – 28.91)	<b>1.56 (1.41 – 1.72)</b>
P-trend			0.20			<b>0.01</b>			<b>&lt;0.01</b>			<b>&lt;0.01</b>
Joint ethnic enclave/nSES <sup>c</sup>												
Non-enclave/ high nSES	71	18.15 (13.41 – 23.83)	Reference	132	18.18 (15.05 – 21.76)	Reference	206	16.82 (14.52 – 19.38)	Reference	409	17.27 (15.55 – 19.13)	Reference
Enclave/high nSES	225	16.52 (14.16 – 19.14)	0.91 (0.66 – 1.28)	575	20.93 (19.15 – 22.81)	1.15 (0.94 – 1.42)	827	18.23 (16.96 – 19.56)	1.08 (0.92 – 1.28)	1627	18.86 (17.91 – 19.85)	1.09 (0.97 – 1.23)
Non- enclave/low nSES	93	18.81 (15.08 – 23.14)	1.04 (0.73 – 1.50)	150	20.03 (16.89 – 23.57)	1.10 (0.86 – 1.42)	253	20.89* (18.32 – 23.72)	<b>1.24 (1.02 – 1.51)</b>	496	20.15* (18.38 – 22.04)	<b>1.17 (1.02 – 1.34)</b>
Enclave/low nSES	416	21.53 (19.43 – 23.78)	1.19 (0.89 – 1.63)	769	25.64* (23.84 – 27.54)	<b>1.41 (1.16 – 1.73)</b>	1073	25.11* (23.61 – 26.69)	<b>1.49 (1.28 – 1.75)</b>	2258	24.71* (23.69 – 25.77)	<b>1.43 (1.28 – 1.60)</b>

Abbreviations: CI, confidence interval; IR, incidence rate; IRR, incidence rate ratio; nSES, neighborhood socioeconomic status.

<sup>a</sup>Combination of the three 5-year pericenters windows: 1988–1992, 1998–2002, 2008–2012.

<sup>b</sup>Age adjusted.

<sup>c</sup>Non-enclave are ethnic enclave quintiles 1–3 and enclave are quintiles 4–5. High nSES are quintiles 4–5 and low nSES are quintiles 1–3.

\*  $P < 0.05$ ; significantly different from reference group.

Table 3:

Incidence Rates (per 100,000) and Incidence Rate Ratios of Hepatocellular Carcinoma in the Hispanic Population, by Sex, Ethnic Enclave, and Neighborhood Socioeconomic Status, California, 1988–1992, 1998–2002, 2008–2012

	1988–1992			1998–2002			2008–2012			Combined Period <sup>a</sup>		
	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>
Females	208	2.65 (2.29 – 3.05)		516	4.26 (3.88 – 4.65)		1051	5.26 (4.94 – 5.59)		1775	4.42 (4.21 – 4.46)	
Ethnic enclave												
Quintile 1 (Least ethnically distinct)	10	2.11 (0.96 – 3.92)	Reference	26	3.42 (2.20 – 5.04)	Reference	48	3.31 (2.41 – 4.41)	Reference	84	3.14 (2.49 – 3.91)	Reference
Quintile 2	26	3.52 (2.24 – 5.19)	1.67 (0.76 – 4.07)	49	4.03 (2.96 – 5.33)	1.18 (0.71 – 2.00)	105	4.62 (3.76 – 5.61)	1.40 (0.98 – 2.03)	180	4.28* (3.66 – 4.96)	<b>1.36 (1.04 – 1.80)</b>
Quintile 3	34	3.31 (2.26 – 4.64)	1.57 (0.75 – 3.74)	73	4.07 (3.17 – 5.12)	1.19 (0.75 – 1.97)	177	5.05* (4.32 – 5.87)	<b>1.53 (1.10 – 2.17)</b>	284	4.45* (3.93 – 5.01)	<b>1.42 (1.10 – 1.84)</b>
Quintile 4	58	3.26 (2.44 – 4.25)	1.55 (0.77 – 3.57)	142	4.20 (3.52 – 4.97)	1.23 (0.80 – 1.98)	297	5.63* (4.98 – 6.32)	<b>1.70 (1.24 – 2.38)</b>	497	4.73* (4.31 – 5.17)	<b>1.50 (1.19 – 1.94)</b>
Quintile 5 (Most ethnically distinct)	80	2.08 (1.63 – 2.61)	0.99 (0.50 – 2.25)	226	4.54 (3.95 – 5.19)	1.33 (0.88 – 2.11)	424	5.67* (5.13 – 6.26)	<b>1.72 (1.26 – 2.39)</b>	730	4.46* (4.13 – 4.8)	<b>1.42 (1.13 – 1.82)</b>
P-trend nSES			0.37			0.02			<b>0.04</b>			0.19
Quintile 5 (Highest nSES)	21	4.08 (2.47 – 6.24)	Reference	30	3.24 (2.16 – 4.63)	Reference	70	4.26 (3.30 – 5.40)	Reference	121	3.90 (3.22 – 4.67)	Reference
Quintile 4	25	2.62 (1.66 – 3.88)	0.64 (0.34 – 1.23)	65	4.3 (3.30 – 5.48)	1.33 (0.84 – 2.14)	109	3.97 (3.25 – 4.80)	0.93 (0.68 – 1.29)	199	3.81 (3.28 – 4.38)	0.98 (0.77 – 1.24)
Quintile 3	54	3.57 (2.64 – 4.70)	0.87 (0.52 – 1.56)	101	4.43 (3.59 – 5.40)	1.37 (0.90 – 2.16)	218	5.59 (4.85 – 6.39)	1.31 (0.99 – 1.75)	373	4.85* (4.36 – 5.38)	<b>1.25 (1.01 – 1.55)</b>
Quintile 2	41	2.05* (1.44 – 2.81)	<b>0.50 (0.29 – 0.91)</b>	133	4.19 (3.49 – 4.99)	1.29 (0.86 – 2.02)	271	5.12 (4.51 – 5.79)	1.20 (0.92 – 1.60)	445	4.24 (3.84 – 4.66)	1.09 (0.88 – 1.35)
Quintile 1 (Lowest nSES)	67	2.35 (1.80 – 2.99)	0.57 (0.35 – 1.01)	187	4.41 (3.78 – 5.10)	1.36 (0.92 – 2.10)	383	6.01* (5.40 – 6.66)	<b>1.41 (1.09 – 1.86)</b>	637	4.68 (4.31 – 5.07)	1.20 (0.98 – 1.48)
P-trend Joint ethnic enclave/nSES <sup>c</sup>			0.27			0.22			0.07			0.22

	1988–1992			1998–2002			2008–2012			Combined Period <sup>a</sup>		
	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>
Non-enclave/ high nSES	41	3.54 (2.49 – 4.82)	Reference	80	3.72 (2.93 – 4.64)	Reference	149	3.87 (3.26 – 4.56)	Reference	270	3.76 (3.32 – 4.25)	Reference
Enclave/high nSES	5	1.70 (0.53 – 3.81)	0.48 (0.14 – 1.17)	15	4.86 (2.68 – 7.94)	1.30 (0.69 – 2.27)	30	5.59 (3.73 – 7.99)	1.44 (0.93 – 2.15)	50	4.27 (3.14 – 5.63)	1.13 (0.81 – 1.54)
Non- enclave/low nSES	29	2.69 (1.76 – 3.89)	0.76 (0.45 – 1.27)	68	4.18 (3.22 – 5.31)	1.12 (0.80 – 1.58)	181	5.42* (4.64 – 6.29)	<b>1.40 (1.12 – 1.76)</b>	278	4.60* (4.06 – 5.19)	<b>1.22 (1.03 – 1.46)</b>
Enclave/low nSES	133	2.51 (2.08 – 2.99)	0.71 (0.49 – 1.05)	353	4.38 (3.92 – 4.88)	1.18 (0.92 – 1.53)	691	5.65* (5.23 – 6.10)	<b>1.46 (1.22 – 1.76)</b>	1177	4.58* (4.31 – 4.85)	<b>1.22 (1.06 – 1.40)</b>
Males	466	6.66 (6.00 – 7.36)		1301	11.80 (11.11 – 12.52)		3135	16.73 (16.10 – 17.37)		4902	13.39 (12.99 – 13.81)	
Ethnic enclave												
Quintile 1 (Least ethnically distinct)	15	3.73 (1.95 – 6.37)	Reference	75	11.02 (8.48 – 14.03)	Reference	199	14.51 (12.46 – 16.79)	Reference	289	11.62 (10.24 – 13.12)	Reference
Quintile 2	39	6.27 (4.17 – 8.96)	1.68 (0.85 – 3.54)	128	11.43 (9.41 – 13.72)	1.04 (0.76 – 1.43)	345	17.55* (15.62 – 19.63)	1.21 (1.00 – 1.46)	512	13.96* (12.68 – 15.32)	<b>1.20 (1.03 – 1.41)</b>
Quintile 3	74	8.47* (6.45 – 10.85)	<b>2.27 (1.24 – 4.55)</b>	203	12.03 (10.30 – 13.94)	1.09 (0.82 – 1.48)	584	17.84* (16.32 – 19.46)	<b>1.23 (1.04 – 1.47)</b>	861	14.65* (13.62 – 15.74)	<b>1.26 (1.09 – 1.46)</b>
Quintile 4	115	6.95* (5.58 – 8.54)	<b>1.86 (1.04 – 3.68)</b>	385	12.64 (11.31 – 14.07)	1.15 (0.88 – 1.52)	826	16.56 (15.36 – 17.82)	1.14 (0.97 – 1.35)	1326	13.71* (12.92 – 14.53)	<b>1.18 (1.03 – 1.36)</b>
Quintile 5 (Most ethnically distinct)	223	6.49 (5.59 – 7.48)	1.74 (1.00 – 3.38)	510	11.45 (10.39 – 12.59)	1.04 (0.80 – 1.37)	1182	16.56 (15.55 – 17.62)	1.14 (0.97 – 1.35)	1915	12.88 (12.26 – 13.52)	1.11 (0.97 – 1.27)
P-trend nSES			0.33			0.88			0.77			0.94
Quintile 5 (Highest nSES)	33	6.92 (4.43 – 10.18)	Reference	84	11.00 (8.60 – 13.83)	Reference	214	15.06 (12.98 – 17.36)	Reference	331	12.56 (11.13 – 14.11)	Reference
Quintile 4	58	7.16 (5.23 – 9.51)	1.04 (0.63 – 1.76)	159	11.40 (9.58 – 13.46)	1.04 (0.78 – 1.40)	386	15.91 (14.25 – 17.77)	1.06 (0.88 – 1.27)	603	13.06 (11.95 – 14.23)	1.04 (0.90 – 1.21)
Quintile 3	78	6.24 (4.74 – 8.01)	0.90 (0.56 – 1.51)	261	12.89 (11.24 – 14.69)	1.17 (0.90 – 1.55)	622	17.34 (15.90 – 18.85)	1.15 (0.97 – 1.37)	961	13.99 (13.05 – 14.97)	1.11 (0.97 – 1.28)
Quintile 2	120	7.03 (5.72 – 8.54)	1.02 (0.65 – 1.66)	334	11.30 (10.02 – 12.69)	1.03 (0.79 – 1.35)	887	17.69* (16.45 – 19.00)	1.18 (1.00 – 1.39)	1341	13.91 (13.12 – 14.74)	1.11 (0.97 – 1.27)
Quintile 1 (Lowest nSES)	177	6.47 (5.46 – 7.59)	0.93 (0.61 – 1.50)	463	11.95 (10.79 – 13.18)	1.09 (0.84 – 1.42)	1026	16.29 (15.22 – 17.42)	1.08 (0.92 – 1.27)	1666	12.98 (12.31 – 13.68)	1.03 (0.91 – 1.18)

	1988–1992			1998–2002			2008–2012			Combined Period <sup>d</sup>		
	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>	Case N	IR (95% CI) <sup>b</sup>	IRR (95% CI) <sup>b</sup>
P-trend												
Joint ethnic enclave/nSES <sup>c</sup>			0.54			0.73			0.55			0.95
Non-enclave/ high nSES	72	7.19 (5.42 – 9.30)	Reference	208	11.35 (9.74 – 13.13)	Reference	504	14.97 (13.6 – 16.43)	Reference	784	12.70 (11.75 – 13.69)	Reference
Enclave/high nSES	19	6.58 (3.57 – 10.86)	0.91 (0.47 – 1.64)	35	10.64 (7.27 – 15.03)	0.94 (0.62 – 1.37)	96	20.15* (16.04 – 24.92)	<b>1.35 (1.05 – 1.70)</b>	150	13.92 (11.58 – 16.56)	1.10 (0.90 – 1.33)
Non- enclave/low nSES	56	6.46 (4.68 – 8.61)	0.90 (0.59 – 1.35)	198	12.00 (10.27 – 13.92)	1.06 (0.85 – 1.31)	623	19.41* (17.81 – 21.1)	<b>1.30 (1.14 – 1.47)</b>	877	15.14* (14.08 – 16.24)	<b>1.19 (1.07 – 1.32)</b>
Enclave/low nSES	319	6.63 (5.85 – 7.48)	0.92 (0.69 – 1.25)	860	11.95 (11.09 – 12.85)	1.05 (0.89 – 1.25)	1912	16.41 (15.62 – 17.23)	1.10 (0.99 – 1.22)	3091	13.16 (12.66 – 13.67)	1.04 (0.95 – 1.13)

Abbreviations: CI, confidence interval; IR, incidence rate; IRR, incidence rate ratio; nSES, neighborhood socioeconomic status.

<sup>a</sup>Combination of the three 5-year pericentennial windows: 1988–1992, 1998–2002, 2008–2012.

<sup>b</sup>Age adjusted.

<sup>c</sup>Non-enclave are ethnic enclave quintiles 1–3 and enclave are quintiles 4–5. High nSES are quintiles 4–5 and low nSES are quintiles 1–3.

\*  $P < 0.05$ ; significantly different from reference group.