Disparities in Hepatocellular Carcinoma Survival among Californians of Asian Ancestry, 1988 to 2007

Sandy L. Kwong, Susan L. Stewart, Christopher A. Aoki, and Moon S. Chen, Jr.

Abstract

Background: Hepatocellular carcinoma (HCC) represents a significant health disparity affecting Asian Americans, a population comprised of distinct ethnic groups. The purpose of this article is to analyze Californians of Asian ancestry with HCC with respect to socioeconomic status, demographic factors, stage of disease, treatment received, and survival.

Methods: To investigate ethnic differences in survival, we analyzed ethnically disaggregated data from 6,068 Californians of Asian ancestry with HCC diagnosed in 1988 to 2007 and reported to the California Cancer Registry.

Results: Compared with the average of all ethnic groups, cause-specific mortality was significantly higher among Laotian/Hmong (hazard ratio, 2.08; 95% confidence interval [95% CI], 1.78-2.44) and Cambodian patients (hazard ratio, 1.26; 95% CI, 1.06-1.51), groups with higher proportions of their populations at low levels of socioeconomic status; in addition, Laotian/Hmong patients disproportionately presented at later stages of disease, with only 3% receiving local surgical treatment, resection, or liver transplantation. After adjustment for time of diagnosis, age at diagnosis, gender, geographic region, stage at diagnosis, type of surgery, and socioeconomic status, survival disparities remained for both groups (Laotian/Hmong hazard ratio, 1.51; 95% CI, 1.28-1.79; Cambodian hazard ratio, 1.24; 95% CI, 1.03-1.48).

Conclusions: Our hypothesis that survival outcomes would differ by ethnicity was verified.

Impact: Research is needed not only to develop more effective treatments for HCC but also to develop community-based interventions to recruit Asian Americans, particularly Laotian/Hmong and Cambodians, for hepatitis B screening and into medical management to prevent or detect this tumor at an early stage.

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Introduction

Hepatocellular carcinoma (HCC) experienced the highest average annual percent increase in mortality of all cancers for men and women in the United States (1) and is among the lowest in its amenability to medical intervention (2). Although liver cancer is less common in the United States compared with other parts of the world, incidence and mortality rates have been rising, and HCC is a cancer that disproportionately affects all U.S. racial/ethnic minority populations (1, 3-5).

The incidence rate for liver cancer is highest among male Asian Americans and Pacific Islanders, with rates almost 12 times the incidence rates for non-Hispanic White men (6). Based on data from fourteen Surveillance Epidemiology and End Results (SEER) regions for the years 1998 to 2002, liver cancer incidence is ranked among the top five cancers among male Cambodians, Chinese, Filipinos, Koreans, Laotians, and Vietnamese, and female Cambodians, Koreans, Laotians, and Vietnamese (6). Liver cancer incidence among these Asian American ethnic groups is even more prominent in California. Male Californians of Laotian ancestry experienced liver cancer as the most common cause of new cancer cases for the years 2000 to 2004 (7) versus ranking second based on the SEER data (6), and it is the second most common cancer among Vietnamese men (7) versus ranking third based on the SEER data (6). Chronic hepatitis B, acquired through vertical transmission during childbirth or horizontal transmission in early childhood, is the most common cause of liver cancer among Asians (8). Based on the estimated maternal hepatitis B surface antigen prevalence rate of 8.9% among foreign-born Asian Americans compared with 0.13% for non-Hispanic Whites,

Authors' Affiliations: ¹Cancer Surveillance Research Unit, Cancer Surveillance and Research Branch, California Department of Public Health; ²Division of General Internal Medicine, University of California, San Francisco, California; and Divisions of ³Gastroenterology and Hepatology and ⁴Hematology and Oncology, Department of Internal Medicine, University of California, Davis, California

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Corresponding Author: Moon S. Chen, Jr., Suite 2207, 4800 Second Avenue, Sacramento, CA 95817. Phone: 916-734-1191; Fax 916-703-5003. E-mail: moon.chen@ucdmc.ucdavis.edu

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a disparity rate of 68.5:1 was calculated (9). This disparity far exceeds that of any health disparity exemplified in the 10 greatest health disparities based on the Healthy People 2010 Objectives (10) and represents the most significant cancer health disparity affecting Asian Americans (11-14).

However, Asian Americans are not all alike. Asian American ethnic groups differ in terms of their socioeconomic status, age distribution, duration of time since immigration to the United States, and risk factors for the development of liver cancer (15-19). Because of this diversity, we hypothesized that there would be differences in survival outcomes among Asian American ethnic groups with HCC. California is an ideal location to undertake this study because, according to U.S. Census Bureau news releases, California is home to the largest population of Asian Americans in the United States and experienced the largest numerical increase of Asian Americans of any state. There are currently >5 million Asian Americans in California who constitute >14% of the population of the state (20, 21). To monitor the incidence rates, risk factors, treatments, and survival from cancer among the different ethnicities that make up this varied group, we used data from the California Cancer Registry (CCR), which comprises the world’s largest repository of high-quality ethnically specific cancer data for Asian Americans in a geographically contiguous jurisdiction (22). Most recently, ethnically specific HCC survival data from the CCR for the 20-year period of 1988 to 2007 have become available.

The purpose of this paper is to analyze the 6,068 Californians of Asian American ancestry with HCC in this database and determine the differences in survival (or mortality), both HCC cause-specific and overall, among the nine largest Asian American ethnic groups in California and who constitute >93% of all Californians of Asian ancestry. Furthermore, we want to assess the effects of variables such as age at diagnosis, gender, stage at diagnosis, type of surgery, and socioeconomic status that may explain these differences.

**Materials and Methods**

**Data source**

The data source for our study is the CCR, a population-based statewide registry funded in part through the National Cancer Institute SEER Program. The CCR covers the entire state of California and includes three SEER regions: the Greater San Francisco Bay Area, Los Angeles County, and the remainder of the state. The CCR has achieved the highest standards for cancer registry quality established by the North American Association of Central Cancer Registries and the National Program of Cancer Registries for completeness and quality. Reporting of cancer cases to the CCR has been legislatively mandated in California since 1985. Currently, the CCR includes data from all cancer cases (except basal and squamous cell carcinoma of the skin and carcinoma in situ of the cervix) reported from 1988 through 2007. The completeness of the CCR is estimated to be ≥95%.

The CCR follows standardized data collection and quality-control procedures in terms of racial/ethnic categorizations and cancer diagnoses (23). Race/ethnicity information for the HCC cases is primarily based on information contained in the patient’s medical record. This information may be based on self-identification by the patient, on the assumptions by an admissions clerk or other medical personnel, or by inference using race/ethnicity of parents, birthplace, maiden name, or last name. Asian race is further divided into twelve groups, the nine largest in California in rank order according to their 2000 U.S. Census populations as follows: Chinese (including Taiwanese), Filipino, Vietnamese, South Asian (Asian Indian, Pakistani, Bangladeshi, Sri Lankan), Korean, Japanese, Hmong and Laotian, Cambodian, and Thai.

In addition to medical record reports, the CCR uses surname to identify persons of Vietnamese or Hmong ethnicity to compensate for the recognized underreporting of cancer cases for Vietnamese and Hmong ethnicity (24, 25). In our study, Laotian and Hmong have been combined into one group because most foreign-born Hmong were born in Laos (26), and older Hmong individuals may classify themselves as Laotian because they were formerly citizens of Laos (27).

South Asians, whose land of origin is the Indian subcontinent (28, 22), are comprised of Asian Indian, Pakistani, other South Asian, Bangladeshi, Bhutanese, Nepalese, Sikh, and Sri Lankan. Excluded from our analyses were 302 HCC cases from smaller Asian groups or with unspecified ethnicity. Also excluded are Native Hawaiians and other Pacific Islanders because the 2000 Census separated Pacific Islanders from the “Asian or Pacific Islander” category.

The analysis included all invasive HCC cases diagnosed among the nine specified Asian ethnic groups between January 1, 1988, and December 31, 2007, and reported to the CCR as of January 2010. We used the International Classification of Diseases for Oncology, Third Edition, site code (C22.0) and histology code (8170) to identify patients with HCC among all patients with primary liver cancer. Eligibility was restricted to HCC as the first primary cancer to eliminate survival differences due to the effects of other cancers. Only cases with diagnostic confirmation of HCC were included in our study (92.9%). Diagnostic confirmation of HCC was defined as having positive histology (54.4%), positive radiological test (20.5%), cytology (13.7%), laboratory test/marker study (3.6%), or direct visualization (0.6%). A total of 6,068 invasive HCC cases that met the above requirements were analyzed for this study.

Patient vital status was updated using both passive and active follow-up methods. Passive follow-up methods included annual record linkages with the California State death file, National Death Index, Social Security Death Master File, Medicare and Medicaid, California...
Department of Motor Vehicles, Voter Registration, and National Change of Address. Active follow-up methods required contacting physician’s offices, hospitals, patient’s relatives, and patients. Although passive and active follow-up methods were used, most information for follow-up was gathered through the passive follow-up methods. The follow-up period for this study began at HCC diagnosis and ended at the earlier of the date of death or last follow-up and December 31, 2007 (the end of the latest full year of case follow-up).

As a member of SEER, CCR must meet or exceed 95% follow-up on all eligible cases. No difference is seen in the distribution of follow-up dates by Asian ethnic groups. Only 161 cases distributed among the nine Asian ethnic groups had a follow-up date before 2007. With such a high follow-up percentage, survival results should not be affected by loss to follow-up information.

The use of SEER and CCR data on liver transplantation is well established (29-32). However, SEER began coding transplantation as a separate category of surgery in 1998. Therefore, we ran the multivariable analyses with resection and transplantation combined into one category as others have done (33).

Statistical analyses

We used $\chi^2$ tests to examine bivariate relationships between Asian American ethnic groups and the variables displayed in Table 1. These variables included time of diagnosis divided into four consecutive 5-year intervals; age at diagnosis (≤50, 50-59, 60-69, 70-79, and ≥80 y); gender; geographic region (Los Angeles County, Greater San Francisco Bay Area, Central California, Northern California, and San Diego-Imperial-Orange Counties); stage of diagnosis (remote, regional, local, and unstaged); type of surgery (none, local, and resection or transplantation); and socioeconomic status on the basis of neighborhood income levels in quintiles. The index of socioeconomic status (34) used in this analysis was a composite variable created by principal components analysis using a number of variables from 1990 and 2000 Census data at the block group level. The Census variables used in creating the aggregate socioeconomic status measure included education index, median household income, proportion below 200% of the poverty level, median rent, median house value, proportion with a blue collar job, and proportion older than 16 years in the workforce without a job. The education index weighs the proportion of people in a census block group with a given level of education by the number of years needed to attain that level of education (35). Block group quintiles based on statewide measurement of the socioeconomic status variable were used in the analysis. Cases missing census block group due to incomplete address at time of diagnosis (26.2% of patients) were randomly allocated to census block groups within county of residence because excluding these cases has been shown to bias results (34).

Kaplan-Meier methods were used to estimate cause-specific and overall survival curves for each of the Asian ethnic groups, and the log-rank test was used to assess ethnic differences in survival. Results were very similar, and therefore, cause-specific survival curves are presented in Fig. 1 and all-cause cancer survival curves are presented in Fig. 2. Median survival times with 95% confidence intervals (95% CI) are presented in Table 2. Cox proportional hazards models were used to evaluate the association between ethnicity and survival, before and after adjustment for the effects of time of diagnosis, age, gender, geographic region, socioeconomic status quintile, stage of diagnosis, and type of surgery. Cause-specific and all-cause hazard ratios were calculated.

Using the average of the nine Asian ethnic groups as the reference group for ethnicity, hazard ratios and 95% CIs were calculated for death from HCC. When modeling the variation in survival among the ethnic groups, it seemed most appropriate to assess the difference of each group from the average of the groups rather than to arbitrarily select a particular group as the reference. The use of centered hazard ratios has been recommended for evaluating the performance of institutions (36). We estimated the ethnicity terms of the log hazard rates using the EFFECT parameterization in SAS, which constrains the ethnicity effects to sum to zero over all groups (rather than setting the effect for one of the groups to zero); we then took the antilog of each estimate to obtain the desired hazard ratio.

Analyses were done using PROC LIFETEST and PROC TPHREG in SAS version 9.1 (SAS Institute, Inc.). Survival time was measured in months from the date of diagnosis to death or censoring. Because the outcome of interest was death due to HCC, HCC cases for people who did not die or died of other causes were coded as censored observations.

A competing risk analysis is indicated if the other causes of death produce informative censoring, that is, if they are related to the event of interest (37). Because few of the other causes of death were related to liver cancer (6.1% cases had unknown cause of death, which could be related, but otherwise we could not tell if other causes of death were related), we did not do a competing risk analysis. The assumptions for our models include uninformative censoring and proportional hazards, that is, time invariant effects.

Results

During the 20-year period of our study, 1988 through 2007, there were 6,068 cases diagnosed for the nine largest Asian American ethnic groups in California. Table 1 shows the demographic, disease and treatment characteristics of each of the nine Asian ethnic groups, which differed significantly with respect to all variables tabulated ($P < 0.0001$).

Time of diagnosis

Almost two thirds of HCC cases were diagnosed in 1998 or later. Consistent with immigration patterns, the
proportion diagnosed in this period was highest among South Asians (75%) and lowest among Japanese (59%), Laotian/Hmong (60%), and Chinese (61%).

### Age at diagnosis

Less than 20% of HCC cases were diagnosed before the age of 50 years in all Asian American groups except Laotian/Hmong (29%), Cambodian (34%), and Thai (44%).

### Gender

Most liver cancer diagnoses were among men in all the groups, except Japanese, where women made up 60% of cases. The ratio of male to female HCC cases was highest among Southeast Asians (~4:1). This ratio is particularly pronounced because the ratio of males to females among Vietnamese and among Laotian/Hmong is 1.0; among Cambodians, 0.9; and Thai, 0.8.

### Region

Most of the HCC cases came from the coastal regions of the Greater San Francisco Bay Area, Los Angeles County, and San Diego-Imperial-Orange Counties, reflecting where the respective ethnic populations predominantly reside. At the same time, among the Laotian/Hmong, Cambodian, and Thai, the ratio of males to females is much lower than in other groups.

### Table 1. Demographic and tumor characteristics by Asian American ethnic groups among patients with HCC from 1988 to 2007 in California ($N = 6,068$)

|              | Chinese ($n = 1,924$) | Vietnamese ($n = 1,367$) | Filipino ($n = 1,016$) | Korean ($n = 807$) |
|--------------|-----------------------|---------------------------|-------------------------|-------------------|
| **Time of diagnosis** |                       |                           |                         |                   |
| 1988-1992 ($n = 881$) | 332 (17.3%)          | 127 (9.3%)                | 158 (15.6%)             | 112 (13.9%)       |
| 1993-1997 ($n = 1,263$) | 426 (22.1%)          | 269 (19.7%)               | 192 (18.9%)             | 173 (21.4%)       |
| 1998-2002 ($n = 1,760$) | 521 (27.1%)          | 421 (30.8%)               | 296 (29.1%)             | 262 (32.5%)       |
| 2003-2007 ($n = 2,144$) | 645 (33.5%)          | 550 (40.2%)               | 370 (36.4%)             | 260 (32.2%)       |
| **Age at diagnosis (y)** |                       |                           |                         |                   |
| <50          | 334 (17.4%)          | 247 (18.1%)               | 171 (16.8%)             | 135 (16.7%)       |
| 50-59        | 387 (20.1%)          | 346 (25.3%)               | 212 (20.9%)             | 203 (25.2%)       |
| 60-69        | 539 (28.0%)          | 398 (29.1%)               | 230 (22.6%)             | 260 (32.2%)       |
| 70-79        | 488 (25.4%)          | 296 (21.7%)               | 273 (26.9%)             | 170 (21.1%)       |
| ≥80          | 176 (9.1%)           | 80 (5.8%)                 | 130 (12.8%)             | 39 (4.8%)         |
| **Gender**   |                       |                           |                         |                   |
| Male         | 1,479 (76.9%)        | 1,089 (79.7%)             | 769 (75.7%)             | 550 (68.2%)       |
| Female       | 445 (23.1%)          | 278 (20.3%)               | 247 (24.3%)             | 257 (31.8%)       |
| **Region**   |                       |                           |                         |                   |
| San Francisco-Oakland | 1,039 (54.0%)  | 440 (32.2%)               | 356 (35.0%)             | 139 (17.2%)       |
| Central California | 53 (2.8%)        | 71 (5.2%)                 | 72 (7.1%)               | 49 (6.1%)         |
| Northern California | 107 (5.6%)      | 68 (5.0%)                 | 81 (8.0%)               | 22 (2.7%)         |
| San Diego-Imperial-Orange | 101 (5.3%)   | 523 (38.2%)               | 183 (18.0%)             | 135 (16.7%)       |
| Los Angeles   | 624 (32.4%)          | 265 (19.4%)               | 324 (31.9%)             | 462 (57.3%)       |
| **Stage at diagnosis** |                       |                           |                         |                   |
| Local        | 740 (38.5%)          | 547 (40.0%)               | 373 (36.7%)             | 314 (39.8%)       |
| Regional     | 407 (21.2%)          | 322 (23.6%)               | 233 (22.9%)             | 174 (21.6%)       |
| Remote       | 536 (27.9%)          | 353 (25.8%)               | 285 (28.1%)             | 197 (24.4%)       |
| Unstaged     | 241 (12.5%)          | 145 (10.6%)               | 125 (12.3%)             | 122 (15.1%)       |
| **Type of surgery** |                       |                           |                         |                   |
| None         | 1,467 (76.3%)        | 1,050 (76.8%)             | 845 (83.2%)             | 604 (74.8%)       |
| Local        | 93 (4.8%)            | 120 (8.8%)                | 38 (3.7%)               | 54 (6.7%)         |
| Resection or transplantation | 364 (18.9%)| 197 (14.4%)               | 133 (13.1%)             | 149 (18.5%)       |
| **SES**      |                       |                           |                         |                   |
| 1 - low SES  | 259 (13.5%)          | 214 (15.7%)               | 152 (15.0%)             | 148 (18.3%)       |
| 2            | 307 (16.0%)          | 366 (26.8%)               | 182 (17.9%)             | 142 (17.6%)       |
| 3            | 327 (17.0%)          | 296 (21.6%)               | 256 (22.5%)             | 118 (14.6%)       |
| 4            | 489 (25.4%)          | 269 (19.7%)               | 273 (26.9%)             | 172 (21.3%)       |
| 5 - high SES | 542 (28.2%)          | 222 (16.2%)               | 153 (15.1%)             | 227 (28.1%)       |

(Continued on the following page)
Hmong a higher proportion of HCC cases were from the primarily inland Central California and Northern California regions, where the greater proportion of Laotians and Hmong reside.

**Stage at diagnosis and treatment**

On average, the groups had 27% of tumors staged in remote locations, but among Laotian/Hmong, 43% had disease spread to remote sites. Overall, 22% of Asian Americans with HCC, but only 3% of Laotian/Hmong patients, underwent local surgical treatment, resection, or liver transplantation.

**Socioeconomic status**

About two thirds of Asian Americans with HCC lived in neighborhoods with socioeconomic status in the ≥3rd quintile, except in the Laotian/Hmong and Cambodian groups, in which more than half were in the lowest quintile.

The nine ethnic groups differed significantly with respect to cause-specific and all-cause survival ($P < 0.0001$).

### Table 1. Demographic and tumor characteristics by Asian American ethnic groups among patients with HCC from 1988 to 2007 in California ($N = 6,068$) (Cont’d)

|            | Japanese | Laotian/Hmong | Cambodian | South Asian | Thai | Total | $P$  |
|------------|----------|---------------|-----------|-------------|------|-------|------|
|            | ($n = 459$) | ($n = 171$) | ($n = 158$) | ($n = 114$) | ($n = 52$) |       |      |
| No.        | %        | No.           | %         | No.         | %    | No.   | %    |
| 82         | 17.9     | 29            | 17.0      | 22          | 13.9 | 12    | 10.5 |
| 106        | 23.1     | 39            | 22.8      | 30          | 19.0 | 17    | 14.9 |
| 130        | 28.3     | 55            | 32.2      | 45          | 28.5 | 30    | 26.3 |
| 141        | 30.7     | 48            | 28.1      | 61          | 38.6 | 55    | 48.3 |
| 25         | 5.5      | 50            | 29.2      | 54          | 34.2 | 8     | 7.0  |
| 80         | 17.4     | 42            | 24.6      | 49          | 31.0 | 30    | 26.3 |
| 169        | 36.8     | 45            | 26.3      | 36          | 22.8 | 37    | 32.5 |
| 145        | 31.6     | 20            | 11.7      | 13          | 8.2  | 26    | 22.8 |
| 40         | 8.7      | 14            | 8.2       | 6           | 3.8  | 13    | 11.4 |
| 184        | 40.1     | 136           | 79.5      | 126         | 79.8 | 79    | 69.3 |
| 275        | 59.9     | 35            | 20.5      | 32          | 20.2 | 35    | 30.7 |
| 114        | 24.8     | 19            | 11.1      | 21          | 13.3 | 34    | 29.8 |
| 37         | 8.1      | 51            | 29.8      | 19          | 12.0 | 15    | 31.2 |
| 59         | 12.9     | 56            | 32.8      | 19          | 12.0 | 25    | 21.9 |
| 86         | 18.7     | 39            | 22.8      | 13          | 8.2  | 21    | 18.4 |
| 163        | 35.5     | 6             | 3.5       | 86          | 54.4 | 19    | 16.7 |
| 175        | 38.1     | 41            | 24.0      | 65          | 41.1 | 50    | 43.9 |
| 94         | 20.5     | 27            | 15.8      | 34          | 21.5 | 25    | 21.9 |
| 125        | 27.2     | 73            | 42.7      | 44          | 27.9 | 27    | 23.7 |
| 65         | 14.2     | 30            | 17.5      | 15          | 9.5  | 12    | 10.5 |
| 342        | 74.5     | 166           | 97.1      | 133         | 84.2 | 90    | 78.9 |
| 33         | 7.2      | *             | *         | 8           | 5.1  | 9     | 7.9  |
| 84         | 18.3     | *             | *         | 17          | 10.7 | 15    | 13.2 |
| 31         | 6.8      | 91            | 53.2      | 85          | 53.8 | 11    | 9.6  |
| 79         | 17.2     | 44            | 25.7      | 25          | 15.8 | 14    | 12.3 |
| 109        | 23.7     | 20            | 11.7      | 21          | 13.3 | 22    | 19.3 |
| 119        | 25.9     | 15            | 8.8       | 14          | 8.9  | 33    | 29.0 |
| 121        | 26.4     | *             | *         | 13          | 8.2  | 34    | 29.8 |

Abbreviation: SES, socioeconomic status.

*Less than 5 cases.
The Kaplan-Meier curves (Fig. 1) and estimates of median survival (Table 2) show Laotian/Hmong patients having the worst survival, with a median of 2 months cause-specific and 1 month all cause, followed closely by Cambodians (6 and 3 months, respectively) and Thais (both 4 months). Koreans and South Asians had the longest all-cause survival, with a median of 7 months.

Table 3 presents multivariable models of survival from HCC among the nine specified Asian groups in California. Compared with the average of all ethnic groups, cause-specific mortality was significantly higher among Laotian/Hmong (hazard ratio, 2.08; 95% CI, 1.78-2.44) and Cambodian patients (hazard ratio, 1.26; 95% CI, 1.06-1.51). After adjusting for time of diagnosis, age at diagnosis, gender, geographic region, stage at diagnosis, type of surgery, and socioeconomic status, survival disparities remained for both groups (Laotian/Hmong hazard ratio, 1.51; 95% CI, 1.28-1.79; Cambodian hazard ratio, 1.24; 95% CI, 1.03-1.48). Cause-specific mortality was lower for more recent time of diagnosis versus 1988 to 1992 (1993-1997 hazard ratio, 0.79; 95% CI, 0.72-0.87; 1998-2002 hazard ratio, 0.66; 95% CI, 0.60-0.73;
2003-2007 hazard ratio, 0.57; 95% CI, 0.51-0.64); ages 50 to 69 years versus <50 years (50-59 y hazard ratio, 0.87; 95% CI, 0.79-0.96; 60-69 y hazard ratio, 0.85; 95% CI, 0.77-0.94); higher socioeconomic status versus the lowest quintile (quintile 3 hazard ratio, 0.88; 95% CI, 0.79-0.99; quintile 4 hazard ratio, 0.89; 95% CI, 0.80-0.98; quintile 5 hazard ratio, 0.73; 95% CI, 0.66-0.82); earlier-versus remote-stage disease (regional hazard ratio, 0.58; 95% CI, 0.49-0.69; local hazard ratio, 0.37; 95% CI, 0.31-0.44; unstaged hazard ratio, 0.65; 95% CI, 0.55-0.78); and surgery versus no curative treatment (local hazard ratio, 0.40; 95% CI, 0.33-0.47; resection or transplantation hazard ratio, 0.31; 95% CI, 0.27-0.35). Results were similar for all-cause mortality, except that patients with the age of ≥80 years had higher mortality and those with the age of 50 to 69 years had no survival advantage compared with patients <50 years.

Discussion

This article focuses on 6,068 HCC cases among Californians of Asian ancestry who were diagnosed from 1988 through 2007. To our knowledge, these data represent the largest number of HCC cases focused solely on Asian Americans collected in a population-based Gold Certification (highest award) North American Association of Central Cancer Registries. Previously published reports focusing on HCC survival among Asian Americans in California were more limited in number, geographic scope, and period covered, and included fewer ethnic groups such as by Barazani et al. (38). Thus, the value of our study is the quality and size of the database and the vantage point of examining the data disaggregated by ethnic group.

This large database with detailed demographic data and other selected variables along with survival outcomes allowed us to verify that the HCC patterns differ among the nine Asian American ethnic groups. Substantial differences in HCC survival outcomes exist among the nine largest Asian American populations in California. Cancer survival for Asian American groups is markedly different when their data are disaggregated than when viewed in the aggregate. In our study, among the most striking differences were the percentages younger than the age of 50 years at diagnosis among the Laotian/Hmong (29%), Cambodian (34%), and Thai (44%). We acknowledge there were <100 deaths in two of the groups. Therefore, our power may have been inadequate to detect survival disparities for the smallest groups, South Asian, and Thai. The ethnic-specific sample sizes were not large enough to assess whether the effects of sociodemographic, disease, and treatment-related variables on survival differed by ethnicity. However, our sample sizes were sufficient to detect substantial survival disadvantages among Laotian/Hmong and Cambodians. Although Laotian/Hmong patients disproportionately presented at later stages and were therefore at a survival disadvantage for that reason, very few at any stage of diagnosis received curative treatment. If patients diagnosed at remote stage are excluded, 28% of the entire sample, but only 5% of Laotian/Hmong, underwent local treatment, resection, or transplantation. Laotian/Hmong and Cambodian patients came from the lowest socioeconomic groups, and Laotian/Hmong presented at a much later stage compared with all other Asian American ethnic groups. The reasons for this disparity and why so few Laotian/Hmong received any type of treatment strongly suggests the presence of barriers to detection and treatment such as cultural, linguistic, or socioeconomic factors (27, 39, 40). However, even after controlling for age, gender, socioeconomic status, stage, and treatment, Laotian/Hmong and Cambodians did poorly compared with the average. Unfortunately, these data are unable to completely explain this finding. Unlike many other tumors, the treatment of liver cancer is strongly influenced by the underlying condition of the patient in regards to their liver disease, as well as specific size, number, and location of tumors, which play a major role in overall survival and candidacy for the various treatments. It is likely that the underlying patient condition played a role in explaining the lack of treatment for all Asian Americans.

### Table 2. Median survival for patients with HCC by Asian American ethnic groups; California, 1988 to 2007

| Ethnic Group       | Median survival months | 95% CI | Cause-specific survival | Median survival months | 95% CI | All-cause survival |
|--------------------|------------------------|--------|-------------------------|------------------------|--------|-------------------|
| Chinese            | 10                     | 9-11   |                         | 6                      | 6-7    |                   |
| Japanese           | 12                     | 8-14   |                         | 6                      | 5-9    |                   |
| Filipino           | 7                      | 6-9    |                         | 4                      | 3-5    |                   |
| Korean             | 11                     | 9-13   |                         | 7                      | 6-9    |                   |
| South Asian        | 12                     | 7-43   |                         | 7                      | 3-10   |                   |
| Vietnamese         | 12                     | 9-14   |                         | 6                      | 6-8    |                   |
| Laotian/Hmong      | 2                      | 1-2    |                         | 1                      | 1-2    |                   |
| Cambodian          | 6                      | 3-8    |                         | 3                      | 2-5    |                   |
| Thai               | 4                      | 2-9    |                         | 4                      | 1-5    |                   |
## Table 3. Multivariable model of survival from HCC; California, 1988 to 2007 (N = 6,068)

| Asian American ethnic groups | Cause-specific survival | All-cause survival |
|-----------------------------|-------------------------|-------------------|
|                             | Unadjusted HR (95% CI)  | Multivariate HR (95% CI) | Unadjusted HR (95% CI) | Multivariate HR (95% CI) |
| Chinese                     | 0.83 (0.77-0.90)         | 0.89 (0.82-0.96)      | 0.80 (0.75-0.85)       | 0.85 (0.79-0.91)         |
| Vietnamese                  | 0.83 (0.76-0.90)         | 0.86 (0.79-0.94)      | 0.81 (0.75-0.87)       | 0.84 (0.78-0.91)         |
| Filipino                    | 0.91 (0.83-0.99)         | 0.89 (0.81-0.98)      | 0.97 (0.90-1.05)       | 0.94 (0.87-1.02)         |
| Korean                      | 0.80 (0.73-0.89)         | 0.90 (0.82-1.00)      | 0.77 (0.71-0.84)       | 0.86 (0.79-0.94)         |
| Japanese                    | 0.89 (0.80-1.00)         | 0.99 (0.87-1.11)      | 0.85 (0.77-0.95)       | 0.93 (0.83-1.03)         |
| Laotian/Hmong               | 2.08 (1.78-2.44)         | 1.51 (1.28-1.79)      | 1.90 (1.64-2.19)       | 1.43 (1.23-1.66)         |
| Cambodian                   | 1.26 (1.06-1.51)         | 1.24 (1.03-1.48)      | 1.25 (1.07-1.46)       | 1.23 (1.05-1.44)         |
| South Asian                 | 0.72 (0.57-0.92)         | 0.81 (0.64-1.03)      | 0.84 (0.69-1.02)       | 0.92 (0.76-1.11)         |
| Thai                        | 1.17 (0.87-1.57)         | 1.09 (0.81-1.50)      | 1.21 (0.94-1.56)       | 1.15 (0.89-1.48)         |
| Time of diagnosis           |                         |                   |                   |                   |
| 1988-1992                   | 1.00                     |                   |                   | 1.00                     |
| 1993-1997                   | 0.79 (0.72-0.87)         | 0.83 (0.76-0.91)     |                   |                   |
| 1998-2002                   | 0.66 (0.60-0.73)         | 0.71 (0.65-0.77)     |                   |                   |
| 2003-2007                   | 0.57 (0.51-0.64)         | 0.61 (0.55-0.67)     |                   |                   |
| Age at diagnosis (y)        |                         |                   |                   |                   |
| <50                         | 1.00                     |                   |                   | 1.00                     |
| 50-59                       | 0.87 (0.79-0.96)         | 0.95 (0.87-1.04)     |                   |                   |
| 60-69                       | 0.85 (0.77-0.94)         | 0.93 (0.85-1.02)     |                   |                   |
| 70-79                       | 0.93 (0.84-1.03)         | 1.03 (0.94-1.13)     |                   |                   |
| ≥80                         | 0.97 (0.85-1.12)         | 1.17 (1.04-1.32)     |                   |                   |
| Gender                      |                         |                   |                   |                   |
| Male                        | 1.00                     |                   |                   | 1.00                     |
| Female                      | 1.03 (0.96-1.11)         | 1.05 (0.98-1.12)     |                   |                   |
| Region                      |                         |                   |                   |                   |
| Los Angeles                 | 1.00                     |                   |                   | 1.00                     |
| San Francisco-Oakland       | 1.05 (0.97-1.15)         | 1.01 (0.94-1.09)     |                   |                   |
| Central California          | 1.11 (0.96-1.28)         | 1.08 (0.96-1.23)     |                   |                   |
| Northern California         | 1.05 (0.92-1.20)         | 1.03 (0.92-1.16)     |                   |                   |
| San Diego-Imperial-Orange   | 1.12 (1.01-1.24)         | 1.10 (1.01-1.20)     |                   |                   |
| Stage at diagnosis          |                         |                   |                   |                   |
| Remote                      | 1.00                     |                   |                   | 1.00                     |
| Regional                    | 0.58 (0.49-0.69)         | 0.55 (0.48-0.64)     |                   |                   |
| Local                       | 0.37 (0.31-0.44)         | 0.37 (0.32-0.43)     |                   |                   |
| Unstaged                    | 0.65 (0.55-0.78)         | 0.62 (0.53-0.72)     |                   |                   |
| Type of surgery             |                         |                   |                   |                   |
| None                        | 1.00                     |                   |                   | 1.00                     |
| Local                       | 0.40 (0.33-0.47)         | 0.42 (0.36-0.49)     |                   |                   |
| Resection or transplantation | 0.31 (0.27-0.35)         | 0.34 (0.31-0.38)     |                   |                   |
| SES                         |                         |                   |                   |                   |
| 1 - low SES                 | 1.00                     |                   |                   | 1.00                     |
| 2                           | 0.99 (0.89-1.10)         | 1.00 (0.91-1.10)     |                   |                   |
| 3                           | 0.88 (0.79-0.99)         | 0.93 (0.85-1.03)     |                   |                   |
| 4                           | 0.89 (0.80-0.98)         | 0.88 (0.80-0.97)     |                   |                   |
| 5 - high SES                | 0.73 (0.66-0.82)         | 0.76 (0.69-0.84)     |                   |                   |

**NOTE:** Each value provides independent risk for death after adjusting for all other factors presented in the table.

**Abbreviation:** HR, hazard ratio.
Americans, as well as among the Laotian/Hmong and Cambodian patient population. In the future, these data should be collected in addition to model for end-stage liver disease (MELD) score, the Cancer of the Liver Italian Program Investigators (CLIP) scores (the CLIP score includes Child-Pugh stage, tumor morphology and extension, serum alpha-fetoprotein (AFP) levels, and portal vein thrombosis), and Okuda classification data, which are important predictors of survival (41). The model for end-stage liver disease score has been shown to be an important predictor of survival from end-stage liver disease (41) and would provide accurate information about the patient's overall long-term prognosis from their liver disease. Although there is an overall lack of consensus upon the most accurate way to stage patients with HCC, the one most accepted by experts and takes into account the patient's clinical status, tumor characteristics, and treatment rendered is the Barcelona-Clinic-Liver-Cancer staging system (42). The Barcelona-Clinic-Liver-Cancer stage should also be included in the registry because it is a more accurate predictor of survival than the current TNM staging (43, 44).

As expected and consistent with others (33), we found survival to be positively associated with more recent diagnosis, as well as earlier stage of disease and receipt of curative treatment; however, we did not find a survival advantage for females. In smaller, clinically based studies on HCC survival in Asian Americans, one (45) found higher mortality in males, but another (46) did not. The latter study did not find differences in survival among Asian American ethnic groups but was not population based and only included Chinese, Vietnamese, Japanese, and Koreans. Our findings about a survival advantage among persons with higher socioeconomic status are consistent with those of Artinyan et al. (29), who also found that racial and ethnic differences in survival remained after accounting for socioeconomic status, tumor characteristics, and treatment.

Consistent with others (47), we found that, although HCC is a disease that is more commonly found in men, this finding was not apparent among Japanese Americans, wherein there was an observed preponderance of female HCC cases. The reasons for this are unknown but are presumed to be related to the etiology of HCC among Japanese patients. In contrast to other Asian groups who develop HCC because of hepatitis B, patients of Japanese ancestry are at higher risk for HCC because of infection with hepatitis C virus (HCV) related to “unsterilized medical practices” in the 1920s to 1940s (48). Japanese with HCC who migrated to California would be expected to fall into this category of those who were infected with HCV during this period. It is unclear why this group had a predominance of women. One possible explanation is that because HCC in Japanese Americans is found in patients who were infected with HCV in the 1920s to 1940s, the men may be more likely to die at an earlier age from other causes such as cardiovascular disease or other forms of cancers.

Despite having access to the largest known cancer registry in a geographically contiguous jurisdiction with a large number of diverse Asian ethnic groups, we recognize several methodologic challenges. Racial misclassification has been documented to exist in the CCR database (49), although this limitation exists in most population-based registry research (24). Gomez et al. (50) reported differential completeness rates of birthplace information across race/ethnicity, hospital type, and language, and therefore, birthplace was not used as a proxy for acculturation. Lastly, the aggregate socioeconomic status variable is not a measure of the individual’s socioeconomic status level but rather that of his or her block group or neighborhood (34).

Nevertheless, the patterns that emerge from these data seem clear. In conclusion, our data and analyses support the finding that not all Asian Americans are the same; disaggregating the HCC data by ethnicity has elucidated Laotian/Hmong as the ethnic group with the worst survival outcomes. However, as our data indicate, none of the Asian Americans with HCC have favorable survival outcomes, and HCC by comparison with other cancers is almost invariably fatal (19, 33, 51). Viral hepatitis, especially hepatitis B among Asian Americans, was likely a major contributor to the development of liver cancer in this population (19), and unless one’s hepatitis status is known, proper medical management cannot occur. Unfortunately, a large proportion of Asian Americans, as well as others from HBV-endemic areas, are unaware of their HBV status and have never been screened (13, 52, 53). Less than one third of HCC patients were screened before their diagnosis (54). Therefore, research is needed not only to better develop more effective treatments but also to develop community-based interventions to recruit Asian Americans, particularly Laotian/Hmong and Cambodians, for hepatitis B screening (14) and into medical management to prevent or detect this tumor at an early stage. In ongoing community-based research (54-56), we are learning that awareness of liver cancer is not sufficient to assure screening. Much more research is needed in overcoming cultural barriers to screening and earlier medical management among Asian Americans.

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No potential conflicts of interest were disclosed.

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