



Published in final edited form as:

*J Community Health*. 2020 April ; 45(2): 412–418. doi:10.1007/s10900-019-00763-1.

## Healthcare Disparities Identified Between Hmong and Other Asian Origin Groups Living with Chronic Hepatitis B Infection in Sacramento County 2014–2017.

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### Abstract

**Background:** Chronic hepatitis B (CHB) disproportionately affects non-US born Asians. The Hmong have been shown to have the highest rates of CHB and mortality from liver cancer compared to other Asian groups.

**Methods:** From September 2014 - September 2017, testing for CHB within Sacramento County was conducted through community-based testing events and an electronic health record alert that identified Asian patients by surname. Demographic and laboratory data were collected for analysis and patients were followed through the study period to assess linkage to care and treatment to compare differences between Asian origin groups.

**Results:** Of 4,350 patients tested for CHB, 318 (7.3%) were HBsAg positive, including 90 Chinese, 47 Hmong, and 101 Vietnamese. Hmong were more likely to have Medicaid insurance compared to other Asian origin groups (15%,  $p < 0.001$ ). Hmong had significantly lower rates of hepatitis B DNA testing ( $p < 0.001$ ), referral to hepatology ( $p < 0.001$ ), attendance of first ( $p < 0.001$ ) and second medical visit ( $p = 0.0003$ ), and lower rates of antiviral treatment compared to other Asian origin groups. Hmong also had the highest proportion of non-English speakers ( $p < 0.001$ ).

**Conclusions:** Hmong patients in the Sacramento CHB testing and linkage to care program experience socioeconomic disadvantages compared to Vietnamese and Chinese patients. These factors may contribute to decreased linkage of care and decreased anti-viral treatment rates for CHB.

### Keywords

Asian; Hepatitis; Chronic Disease; Community Health; Ethnic Disparities

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**Declaration of Conflicting Interests:** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Introduction

Chronic hepatitis B (CHB) is one of the leading risk factors for hepatocellular carcinoma (HCC) worldwide (1). In 2016 in the United States (US), an estimated 862,000 individuals were infected with CHB, and about 1,700 death certificates had hepatitis B listed as the underlying or contributing cause of death (2–4). Infection rates in the US are < 1%, but Asian and Pacific Islanders (API) who account for < 6% of the US population, comprise about 60% of the burden for CHB-linked HCC (5). Guideline-concordant monitoring and treatment of individuals can prevent the progression of CHB to cirrhosis and may reduce the risk of HCC (6, 7). In addition, surveillance of CHB patients for HCC may improve outcomes (8).

Significant differences in the prevalence and outcomes of CHB exist among different Asian origin groups. Particularly, the Hmong have been shown to have the highest rates of CHB and the highest mortality from HCC compared to other API groups (9). CHB prevalence rates have been reported as high as 16–18% in the Hmong population (10, 11) and Hmong patients with HCC have a median cause-specific survival of 2 months after diagnosis and an all cause survival of 1 month. Compared to other Asian origin groups, cause-specific mortality was significantly higher among the Hmong independent of age of diagnosis, stage at diagnosis, and socio-economic status (12).

The causes for the high burden of CHB in Hmong may include unique social, cultural, and economic barriers to testing and treatment for CHB. Despite current guidelines from the Centers for Disease Control and Prevention and the United States Preventive Services Task Force that recommend testing patients born in countries with intermediate-to-high CHB endemicity ( 2% prevalence), less than one third of API persons in the US have been tested for CHB (13–15). For those who are found to have CHB, proper management and treatment (linkage to care) has been shown to decrease poor outcomes (cirrhosis and HCC) related to the infection (16). Despite the availability of effective anti-viral therapy, treatment rates in the United States remain low (17).

Thus, there remains a need for a better understanding of the barriers as well as the facilitators to testing and linkage to care of high-risk individuals for CHB. The purpose of this analysis was to identify factors associated with linkage to care and anti-viral therapy initiation among Chinese, Vietnamese, and Hmong during a testing and linkage to care program.

## Methods

### CHB Testing

Our analysis was part of a larger multi-center program of community-based services to improve CHB testing and linkage to care (18). From September 2014 – 2017, CHB testing was conducted in Sacramento County through two different methods. A previously described electronic health record (EHR) decision support tool to identify Asian American patients over 18 years of age by self-identified ethnicity, surname, country of origin and language preference who did not have any record of prior hepatitis B surface antigen

(HBsAg) testing was instituted health system-wide starting in January 2016 to the end of the study in September 2017 (19). Using surnames to identify API persons has been validated in prior studies (20, 21).

The second testing effort involved community-based efforts including at a medical student-run free clinic. The clinic operates on a drop-in basis weekly and has appointment-based monthly cancer screening clinics for cervical, colon, and breast cancer. The target demographic for these clinics is uninsured and low-income API patients. Thus, CHB testing was recommended for almost all of these patients. Additional free community testing events for CHB were held at locations or events in the API community including churches, temples, or large community gatherings.

### Linkage to Care

For all patients who tested positive for HBsAg, demographic information including age, gender, year of birth, primary language spoken, ethnicity, body mass index (BMI), smoking status, alcohol use, and health insurance status was collected on a voluntary survey instrument. Basic laboratory testing including alanine aminotransferase (ALT), platelets, international normalized ratio (INR), hepatitis B e-antigen (HBeAg) status, hepatitis B DNA (HBV DNA) level, and alpha fetoprotein (AFP) was also performed. Follow-up was assessed through several linkage to care milestones including measurement of HBV DNA level, referral to a hepatologist, attendance of first and second hepatology appointment, treatment eligibility, and treatment of CHB with antiviral medication.

### Treatment Eligibility

Eligibility for treatment of CHB was assessed retrospectively using American Association for the Study of Liver Diseases guidelines published in 2016 since these were the most current guidelines at the time of this CHB testing program (22). Normal ALT was considered to be <19 U/L for women and <30 U/L for men. Patients were considered treatment eligible if the ALT level was at least 2 times the upper limit of normal and had a HBV DNA of  $\geq 20,000$  IU/ml for HBeAg positive patients and a HBV DNA level  $\geq 2,000$  IU/ml for HBeAg negative patients.

### Statistical Analysis

Patients were grouped by ethnicity into Chinese, Hmong, Vietnamese, and Other. Chinese and Vietnamese were the highest represented Asian subgroups within our patient population, and the Hmong were used as a comparison group given their aforementioned health disparities in CHB and HCC. All other Asian ethnicities were grouped into the 'Other' category, which includes Japanese, Thai, Korean, Pakistani, and Indian patients. The overall distribution of baseline demographics (including insurance status) and laboratory data were compared among all four groups. Multivariable logistic regression analysis was performed to identify factors associated with referral to hepatology, attendance of medical visits, receipt of HBV DNA level, and hepatitis B treatment and demographic variables, including ethnicity, age, gender, type of insurance, HBV DNA, ALT, and language. *A priori*, we decided to analysis on the impact of Medicaid insurance on hepatitis B treatment access because Medicaid insurance has been associated with poorer access to care in other disease

states. Patients with missing values for a given analysis were excluded from that analysis. A *P* value of  $< 0.05$  was considered statistically significant. Statistical analysis was performed using SAS v9.4, (SAS Institute Inc., Cary, NC, USA). Analysis of this CHB testing program evaluation was approved by the Institutional Review Board at the University of California, Davis.

## Results

The baseline characteristics of our patient population are summarized in Table 1. During the testing period, a total of 49 CHB testing events were held. Among 4,350 patients tested for CHB from September 2014–2017, 318 (7.3%) were HBsAg positive, which included 90 Chinese, 47 Hmong, 101 Vietnamese, and 80 patients of other Asian ethnicities. Among those with CHB, the mean age of these patients was 49.6 years; 170 (53.6%) were male, and 153 (48.1%) spoke English as their primary language. Twenty-six (8.2%) patients had Medicaid insurance and 29 (9.1%) patients had Medicare insurance, while 131 (41.2%) had private insurance. Twenty-one (6.6%) patients were uninsured and 105 (33%) had unknown insurance status. Compared to Chinese and Vietnamese patients, Hmong patients had the highest mean BMI (29.3) ( $p = 0.0001$ ) and were less likely to speak English as their primary language (17%) compared to Chinese (39%) and Vietnamese patients (45%) ( $p < 0.001$ ). Further, Hmong patients were also most likely to be insured through Medicaid (15%) compared to Chinese (4%) and Vietnamese (10%) ( $p < 0.001$ ).

As shown in Table 2, there were no significant differences in ALT, HBV DNA, and HBeAg positivity across the Asian origin groups. We stratified HBV DNA level multiple ways ( $>20,000$ ; 20,000 to 2,000;  $<2,000$  and 2,000;  $<2000$ ), but still found no differences. However, there were statistically significant differences in AST, platelet count, albumin, alkaline phosphatase, and alpha fetoprotein level, but these differences did not appear to be clinically significant (Table 2). Of the 26 Medicaid patients in our analysis, 7 of 26 (27%) were HBeAg positive compared to 18 of 131 (14%) HBeAg positive among those with private insurance. Of those patients with available HBV DNA data, 6 of 20 (30%) Medicaid patients had HBV DNA  $\geq 20,000$  IU/ml compared to 27 of 126 (21%) among those with private insurance. These data suggest that Medicaid patients had more severe CHB infections.

Of the 318 HBsAg positive patients, 246 patients (77%) had HBV DNA level testing (essential to assess treatment eligibility), 249 patients (78%) were successfully referred to a physician for follow-up care; 223 patients (70%) attended their first follow-up appointment; 138 patients (43%) attended their second follow-up appointment, 66 patients (21%) were treatment eligible, and 51 patients (16%) received anti-viral treatment. The 47 Hmong had the lowest completed linkage to care across the spectrum compared to other API groups, with only 64% receiving HBV DNA level ( $p < 0.001$ ), 57% referral to a hepatologist ( $p < 0.001$ ), 40% attendance of their first appointment ( $p < 0.001$ ), 19% attendance of their second appointment ( $p = 0.0003$ ), 14.9% were treatment eligible ( $p < 0.001$ ), and 8.5% treatment with anti-viral medication ( $p = 0.218$ ) (Figure 1).

Regarding receipt of HBV DNA level and ALT, both of which were required to determine treatment eligibility, Hmong had the lowest proportion receiving both of these labs (28 of 47, 60%) compared to Vietnamese (67 of 101, 66%), Chinese (74 of 90, 82%), and Other (73 of 80, 91%),  $p < 0.001$ . Forty-four of 69 (64%) of all community-based patients were lost to follow up compared to only 25 of 249 (10%) from within our health system.

In total, there were 7 Hmong patients with Medicaid insurance only. Of these, 7 were referred to hepatology, 5 attended their first appointment, 1 attended their second appointment, and 2 were treated with antiviral medication. Of the 8 Hmong patients with private insurance, 8 were referred to hepatology, 4 attended their first appointment, 3 attended their second visit, and none were treated with antiviral medication. There was 1 Hmong patient with Medicaid and Medicare, 2 Hmong patients who were uninsured, and 28 whose insurance status was unknown. 21 of the 28 Hmong patients with unknown insurance status were tested in the community setting, which increased the probability of incomplete data. 62% of Hmong patients less than 40 years of age attended their first medical visit while 32% Hmong patients at least 40 years of age attended their first medical visit suggesting that age may be a factor for Hmong patient's desire to seek medical care. Of the 4 Hmong patients who were treated with antiviral medication, 2 had Medicaid only, 1 had Medicare only, and 1 had unknown insurance status.

Multivariable logistic regression analysis found that private insurance was independently associated with significantly lower odds of anti-viral treatment (OR 0.2; 95% CI, 0.049–0.560;  $p = 0.003$ ) when compared to those with Medicaid insurance (Table 3). Ethnicity (Chinese, Vietnamese, or Hmong), age, gender, HBV DNA, ALT, and English primary language were not found to significantly affect the likelihood of receiving anti-viral treatment. Multivariate logistic regression was also performed to determine factors associated with referral to hepatology, attendance of first and second medical visit, and receipt of HBV DNA level but no significant associations were found.

## Discussion

Our study found that Hmong patients in the Sacramento CHB testing and linkage to care program had risk factors which have been associated with worse CHB outcomes. Hmong patients had the highest BMI, were more likely to have Medicaid insurance, less likely to speak English as their primary language, and were less likely to be linked to CHB care and treatment compared to other Asian origin groups. Hmong patients also had the lowest completion of all CHB linkage to care milestones compared to Chinese and Vietnamese. These factors might partially explain why the Hmong experience the highest mortality rates due to HCC and shorter survival times (9). Another factor that needs to be explored is the role of genetic factors such as *PNPLA3* where a study has documented the very high prevalence of this SNP among Hmong and their potential predisposition to HCC (23).

Prior meta-analyses have shown that higher BMI is associated with an increased risk of HCC in the general population and that this risk was most pronounced among persons with a BMI  $> 32$  kg/m<sup>2</sup> (24). A recent Korean population-based cohort study also showed that BMI is significantly associated with higher risk of HCC among patients with CHB (25). This is

not surprising given that non-alcoholic steatohepatitis (NASH), which is more prevalent in the overweight and obese population, is a known risk factor for development of HCC and is currently the most rapidly growing indication for liver transplantation in the US (26).

Medicaid insurance has been associated with worse health outcomes and decreased access to care across many different disease states (27–29). Prior studies have also shown that Medicaid insurance and lack of insurance are associated with higher rates of CHB infection and lower rates of immunity against CHB (30). This could be attributed to several factors including the poorer socioeconomic status of Medicaid patients and their ability to afford expensive anti-viral medications. This disparity disproportionately affects the Hmong, who were more likely to have Medicaid in our study. Data from the Pew Research Center show that 28% of Hmong live in poverty in the US compared to 12% of all Asians and 15% of all Americans (31). Another study showed that Medicaid patients with chronic liver disease had a 37 times higher risk of developing HCC compared to Medicaid patients without liver disease (32). These data highlight the possibility of worse HCC outcomes for patients with Medicaid insurance compared to those with private insurance.

Our analysis found that private insurance was associated with lower odds of anti-viral treatment compared to Medicaid insurance which conflicts with the aforementioned literature regarding decreased access to treatment for Medicaid patients. This may have been from our finding that Medicaid patients in our program had a more severe hepatitis compared to those who were privately insured, which could have increased the likelihood for anti-viral treatment outside of the typical factors such as ALT, HBe antigen status, and viral load.

Regarding linkage to care, Hmong patients had the lowest rates of referral to a hepatologist, attendance of clinic appointments, and anti-viral treatment. Medicaid insurance has previously been associated with decreased access to care to both primary care and specialist clinics (29, 33). One explanation may be that compared to Chinese and Vietnamese, the Hmong practice a unique combination of traditional, shamanistic medicine, and Western medicine, which may stifle the use of anti-viral treatment (34).

Hmong patients in our program had the lowest rate of English language proficiency, which may be a risk factor for decreased health care access as lack of access to a physician that speaks a patient's primary language has been identified as a barrier for patients to seek medical care (35). This could be due to several factors such as patient comfort and patient experience. Patient experience assesses whether something that should happen in a health care setting, actually happens and how often. APIs with limited English proficiency have been shown to have worse patient experiences compared to non-Hispanic Whites based on standardized consumer surveys (36, 37). Specifically, APIs reported worse access to care, worse promptness of care, and worse communication with providers compared to Whites.

Our study had four main limitations. The first is incomplete data. This was more pronounced in our community-based patients who were tested during health fairs and similar events and therefore were not integrated into our EHR. These patients were more likely to be lost to follow-up and we had both incomplete laboratory data and information regarding referral to

hepatology, attendance of clinic visits, and anti-viral treatment. In reality, these patients who were deemed lost to follow up could have already been linked to care to their respective community physicians, but this information was considered missing if it was not communicated to us during the study period. Patients with missing values for a given analysis were excluded from that analysis. Second, our sample size is relatively small and larger cohort studies would be required to confirm our findings. To ensure data quality, modeling diagnostics were conducted using SAS and no error messages or numerical problem warnings were found. Third, we did not illicit possible reasons why Hmong patients in our study had less access to care. For example, preferred use of Hmong traditional healers in place of western physicians or assessment of median income of Hmong compared to Chinese and Vietnamese patients could be assessed in future studies. Lastly, the Asian ethnic composition of Sacramento County is unique and the results of our testing program may not be generalizable to other geographic areas.

In conclusion, our analysis identified significant disparities among Hmong program patients living with CHB that may have been associated with decreased access to care and treatment. Disparities we identified among Hmong included a higher BMI, higher proportion with Medicaid, and higher proportion of non-English speakers. These disparities may have led to decreased rates of referral to specialty care, attendance of medical visit, and antiviral treatment prescriptions. Future studies should confirm these results in a larger cohort and explore determinants of CHB, HCC, and related outcomes among the Hmong.

## Funding:

This work was supported in part by the Centers for Disease Control and Prevention (1U51PS004633); the National Cancer Institute (P30CA093373), and the Bristol-Meyers Squibb Foundation.

**Disclaimer:** The views expressed are those of the authors and not necessarily of the funding agencies.

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### Summary Box

**1. What is the current understanding of this subject?**

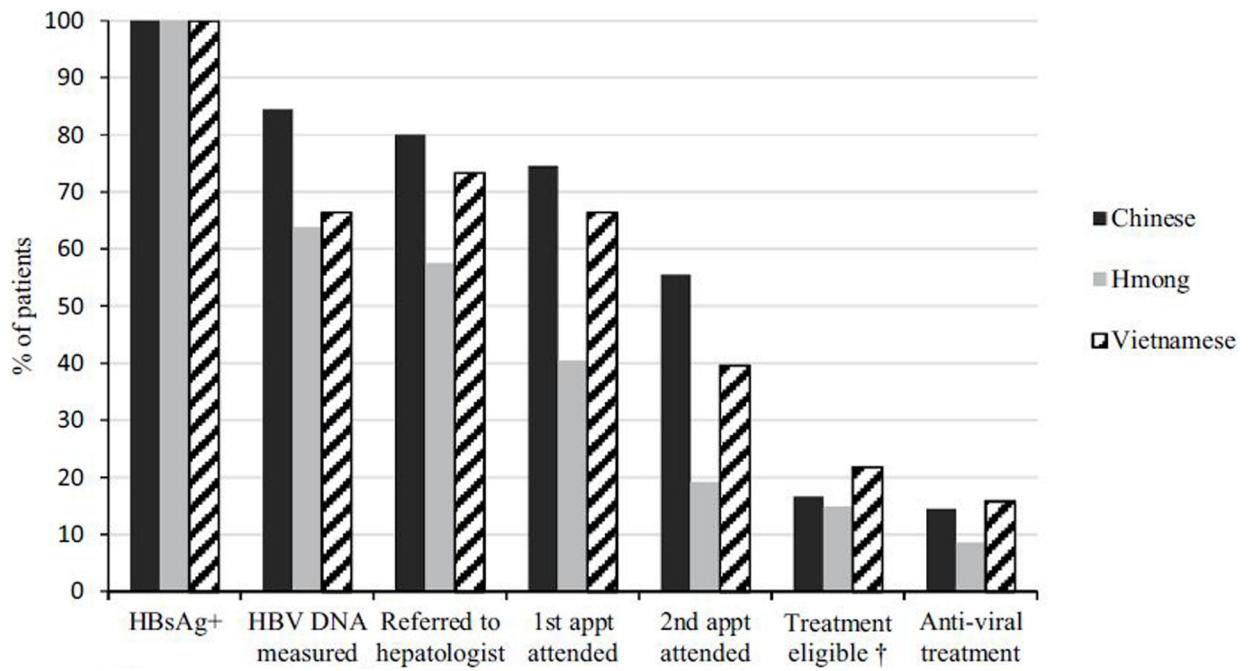
Persons of Hmong descent have high rates of chronic hepatitis B (CHB) and have the highest liver cancer-related mortality when compared to other Asian origin groups.

**2. What does this report add to the literature?**

We found that Hmong patients were more likely to have Medicaid insurance compared to other Asian origin groups and poorer access to hepatitis B-directed care.

**3. What are the implications for public health practice?**

Culturally and linguistically appropriate outreach efforts may be needed to decrease Hmong CHB disparities in access to hepatitis B-directed care.



**Fig. 1.**

Linkage to care cascade of HBsAg positive patients enrolled in Sacramento County hepatitis B program, September 2014–2017. HBsAg, hepatitis B surface antigen., HBV DNA, hepatitis B DNA level. †Based on 2016 American Association for the Study of Liver Diseases guidelines

Baseline demographic data of HBsAg positive API patients enrolled in the Sacramento County hepatitis B program, September 2014–2017

Table 1

Characteristic	Chinese (N= 90)	Hmong (N= 47)	Vietnamese (N= 101)	Other (N = 80)	p value	Overall (N= 318)
Age (mean ± SE) N=318	49.0 ±1.34	52.1 ±2.3	51.3± 1.5	46.9 ±1.8	0.102	49.6±0.8
Male gender (%) N=317	52 (57.8)	20 (43.5)	58 (57.4)	40 (50)	0.316	170 (53.6)
Primary language N=317					<0.0001	
Non-english (%)	55(61)	39 (83)	55 (55)	15(19)		164(52)
English (%)	35 (39)	8(17)	45 (45)	65 (81)		153 (48)
BMI (kg/m <sup>2</sup> ) N= 67	23.3 ±0.62	29.3 ±1.2	24.3 ±0.6	27.7 ±3.6	0.0001	25.7 ±0.6
Smoker (%) N = 66	9(10)	3 (6.4)	6 (5.9)	2 (2.5)	0.197	20 (6.3)
Alcohol use (%) N = 65	5 (5.6)	5 (7.7)	3 (3.0)	1 (1.3)	0.812	14(4.4)
Health insurance N= 318					<0.0001	
Medicaid (%)	4(4)	7(15)	10(9.9)	5(6)		26 (8)
Medicare (%)	7(8)	1 (2)	9 (8.9)	12(15)		29 (9)
Both medicaid/medicare (%)	1 (1)	1 (2)	4 (4.0)	0(0)		6(2)
Private (%)	36 (40)	8(17)	39 (38.6)	48(60)		131 (41)
Uninsured (%)	11(12)	2(4)	4 (4.0)	4(5)		21 (7)
Unknown (%)	31 (34)	28 (60)	35 (34.7)	11 (14)		105 (33)

HBsAg hepatitis B surface antigen, API Asian-Pacific Islander, SE standard error, BMI body mass index

Baseline Laboratory data of HBsAg positive API patients enrolled in the Sacramento County hepatitis B program, September 2014–2017

Table 2

Laboratory test	Chinese (N = 90)	Hmong (N = 47)	Vietnamese (N = 101)	Other (N = 80)	p-value	Overall (N = 318)
HBsAg+ (%) N = 102	21 (23.3)	7 (14.9)	14 (13.9)	10 (12.5)	0.079	52 (16.4)
HBV DNA (%) N = 246					0.186	
<2000	48 (53.3)	15 (31.9)	47 (46.5)	41 (51.3)		151 (47.5)
2000	28 (31.1)	15 (31.9)	20 (19.8)	32 (40)		95 (29.9)
ALT (mean ± SE) N = 260	31.1 ± 2.0	38.6 ± 7.5	42.6 ± 5.8	33.8 ± 3.1	0.341	35.9 ± 2.1
AST (Mean ± SE) N = 262	27.6 ± 1.1	30.9 ± 2.5	33.5 ± 2.1	34.8 ± 5.6	0.039	31.7 ± 1.78
Bilirubin (mean ± SE) N = 255	0.74 ± 0.03	0.75 ± 0.05	0.72 ± 0.03	0.70 ± 0.05	0.225	0.73 ± 0.02
Albumin (mean ± SE) N = 256	4.77 ± 0.55	3.89 ± 0.07	4.10 ± 0.06	3.88 ± 0.05	<0.0001	4.22 ± 0.17
Aik Phos (mean ± SE) N = 254	60.6 ± 1.8	82.0 ± 6.3	74.1 ± 8.4	64.9 ± 3.0	0.006	68.1 ± 2.7
Platelets (mean ± SE) N = 251	215.7 ± 5.8	203.3 ± 15.8	203.2 ± 6.8	240.3 ± 10.2	0.008	217.9 ± 4.4
INR (mean ± SE) N = 131	0.99 ± 0.02	1.02 ± 0.01	1.00 ± 0.01	1.08 ± 0.04	0.069	1.03 ± 0.01
AFP (mean ± SE) N = 160	5.37 ± 1.58	4.87 ± 1.57	7.40 ± 3.98	5.31 ± 1.37	0.048	5.77 ± 1.18

HBsAg hepatitis B surface antigen, API Asian-Pacific Islander, HBsAg hepatitis B envelope antigen, HBV DNA hepatitis B virus DNA, ALT alanine aminotransferase, AST aspartate aminotransferase, Aik Phos alkaline phosphatase, INR international normalized ratio, AFP alpha fetoprotein, SE standard error

**Table 3**  
Multivariable logistic regression analysis for characteristics associated with receiving anti-viral therapy for CHB

Analysis of maximum likelihood estimates					
Characteristic	Estimate	Standard error	OR (95% CI)	Pr>	ChiSq
Ethnicity					
Chinese versus Hmong	0.580	0.879	1.787 (0.319, 10.007)	0.608	
Vietnamese versus Hmong	0.323	0.872	1.381 (0.250,7.626)		
Other versus Hmong	-0.054	0.888	0.948 (0.166,5.399)		
Age	0.016	0.015	1.016(0.986, 1.047)	0.299	
Gender					
Male versus female	0.489	0.410	1.630(0.730,3.638)	0.233	
Type of insurance					
Medicare versus medicaid	-0.203	0.726	0.816(0.197,3.387)	0.003	
Private versus medicaid	-1.797	0.621	0.166 (0.049,0.560)		
HBV DNA viral load ALT					
2000 versus < 2000	-0.375	0.401	0.687 (0.313, 1.509)	0.350	
Language	0.002	0.005	1.001 (0.992, 1.011)	0.753	
English versus non-English	1.054	0.567	2.869 (0.944, 8.717)	0.063	

CHB chronic hepatitis B, OR odds ratio, CI confidence interval, HBV DNA hepatitis B virus DNA, ALT alanine aminotransferase