

BMJ Open Insight into hepatitis B prevalence and risk factors among Vietnamese Americans: a cross-sectional analysis of data from a community-based screening program

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ABSTRACT

Objectives The aims of our study were to describe current hepatitis B prevalence among Vietnamese Americans and to examine predictors of hepatitis B risk in this specific ethnic community.

Design Cross-sectional analysis of data from a community-based screening program.

Setting This analysis was based on hepatitis screening community events in Southern California.

Participants 2508 Vietnamese Americans in Southern California.

Outcome measures Serological tests for hepatitis B surface antigen, hepatitis B surface antibody, and total hepatitis B core antibody were used to classify participants as one of four hepatitis B infection statuses: currently infected, previously infected, susceptible, or immune due to a previous hepatitis B vaccination.

Results Across 2508 participants, 9.0% were currently infected with hepatitis B and 17.7% were at risk for hepatitis B. Females and those reporting a previous hepatitis B vaccination were at significant decreased risk of hepatitis B (OR=0.48, 95% CI 0.33 to 0.69 and OR=0.53, 95% CI 0.31 to 0.93, respectively) whereas those born outside of the USA and with a family history of the disease showed substantial increased risk (OR=13.36, 95% CI 1.62 to 110.05 and OR=4.68, 95% CI 2.66 to 8.22, respectively). Among those who reported a previous hepatitis B vaccination, less than half (42.9%) possessed the protective antibodies that result from a hepatitis B vaccination.

Conclusions Vietnamese Americans remain disproportionately burdened by hepatitis B. Public health efforts that focus on improving hepatitis B awareness and vaccination knowledge and that are tailored to specific high-risk subgroups, such as immigrants and those with infected family members, could help in addressing the disease's burden in this high-prevalence population.

INTRODUCTION

Hepatitis B is an important public health issue affecting ~257 million people worldwide.¹ It is associated with substantial increased risk of severe liver diseases including liver cancer,

Strengths and limitations of this study

- Our analysis is one of the largest evaluations of hepatitis B epidemiology specifically for the Vietnamese American community.
- We used serological tests for hepatitis B surface antigen, hepatitis B surface antibody, and total hepatitis B core antibody to comprehensively and accurately classify each participant's hepatitis B status.
- Questionnaire data were based on self-report, which may result in misclassification of participants.
- We lacked information on other participant characteristics that may be important for hepatitis B risk.
- Some participants were missing information for certain questionnaire questions.

which is the fifth and seventh leading cause of cancer death among males and females, respectively, and the fastest growing cause of cancer death in the USA.^{2,3} Although the USA is considered a low-prevalence region for hepatitis B, the number of infected people is expected to grow due to immigration from endemic regions, particularly in Asia.^{4,5}

Asian Americans were the fastest growing racial group in the USA over the last decade.⁶ They also have the highest rate of hepatitis B, accounting for >50% of all cases in the USA.⁷⁻⁹ However, Asian Americans are often underrepresented in population-based hepatitis B studies and hence aggregated with other racial groups.^{9,10} They also constitute a heterogeneous population, yet most studies evaluate Asian Americans as a single group despite known ethnic-specific variation in hepatitis B's burden.⁸

Vietnamese Americans have one of the highest prevalences of hepatitis B, ranging from 7% to 14%; they also have high incidence and mortality rates of liver cancer.^{8,11,12}

In a recent study by Pham *et al*, incidence of liver cancer among Vietnamese American males was eight times higher than non-Hispanic white males and more than twice that of males of other Asian ancestries.¹³ The study also observed little change in liver cancer incidence among Vietnamese American males and significant increasing rates among Vietnamese American females over the last three decades.¹³ Since hepatitis B is an underlying cause of liver cancer and Vietnamese Americans are the second fastest growing Asian ethnic group in the USA, there is a critical need to better understand hepatitis B and its risk factors in this subpopulation.¹⁴

Our study addresses this important area of research by examining hepatitis B specifically in Vietnamese Americans in Southern California, which is home to >300 000 Vietnamese Americans, the highest number of Vietnamese Americans in the USA.¹⁵ Only one study to our knowledge has examined hepatitis B in Vietnamese Americans in this geographic region; it leveraged data from the Vietnamese American Cancer Foundation (VACF), a non-profit organisation located in Fountain Valley, California, from 10 years ago.¹⁶ Here we provide an updated evaluation of hepatitis B prevalence and risk factors using more recent comprehensive serological and questionnaire data from VACF that includes over 2500 Vietnamese Americans. This constitutes one of the largest analyses of hepatitis B in the Vietnamese American community to date.

METHODS

Study population

This analysis was based on data collected from a series of free hepatitis screening community events from February 2011 to November 2017 in two Southern California counties, Orange and Los Angeles, which are home to the largest population of Vietnamese Americans in California and in the USA.¹⁵ These events were organized by the VACF (<http://www.vacf.org/>), whose mission is to educate and increase awareness of hepatitis and cancers among the Vietnamese community. Their main hepatitis screening events were held twice each year at Orange Coast Memorial Care Medical Center in Fountain Valley, California and advertised in Vietnamese radio and television programs and newspapers as well as through community referral; however, VACF also provided hepatitis screening services at various community health fairs and events.

Because some individuals were likely to have participated in multiple screening events, we only included those who participated in one event. We attempted to avoid duplicate entries by excluding those of the same sex and date of birth since VACF did not keep track of those who received multiple screenings from them. This exclusion resulted in 3264 unique participants. While all who attended the events and desired testing were screened, those who did not report a Southern Californian residence (N=89) or a Vietnamese ethnicity (N=599)

were excluded. In addition, we only included those who had confirmed serological testing results for the hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and total hepatitis B core antibody (anti-HBc), leaving us with a final population of 2508 participants; all three serological tests are needed to properly differentiate those truly at risk of hepatitis B from those previously infected or immune via vaccination.

Data ascertainment

All participants receiving VACF screening services were given a self-administered questionnaire in Vietnamese or English by trained staff. The questionnaire included questions regarding participants' demographics, whether family members have had hepatitis, their hepatitis B vaccination status, and knowledge of their own hepatitis infection status as well as the infection statuses of household members. Written consent was obtained at this time. Participants' blood was then drawn by trained phlebotomists and later tested for HbsAg, anti-HBs, and anti-HBc by various commercial laboratories in the Orange County region that partner with VACF; the majority of testing was done using Advia Centaur chemiluminescence immunoassay for determining hepatitis serology.

For VACF's biannual screening events, participants attended a 30-minute lecture on hepatitis B by a physician specializing in liver diseases only after completion of the questionnaire to minimize any bias in their responses and prior to their blood draw. Because the primary language for most screening participants was Vietnamese, the lecture was delivered in Vietnamese; however, lecture slides were presented in English as well. When the screening results were ready to be disseminated (typically within a month after each biannual screening event), VACF organized follow-up events in which they invited a physician to explain the results to the participants, answer any questions as well as discuss next steps. For those unable to attend (~40%–50%), results were mailed with a detailed letter explaining each serological test. Staff also contacted these individuals to link those who tested positive to insurance and/or medical assistance programs for treatment, navigate those at risk to their primary care physicians, community clinics, and/or local pharmacies for vaccinations, and encourage family members and partners to get tested. VACF was not able to organize follow-up events for those who received screening services at community health fairs and events (ie, not VACF's biannual screening events). However, similar efforts were taken to ensure these individuals received proper follow-up care if needed. Information regarding how many individuals actually received the necessary care was not available due to loss of follow-up.

All data were stored and managed in Community Tech-Knowledge (CTK) Apricot by Social Solutions, a cloud-based client management solution specifically designed for non-profit organizations; CTK Apricot is HIPAA-compliant and data could only be accessed by authorized users via password-protected accounts. The data analyzed

in this report had institutional ethics committee approval from California State University, Fullerton.

Statistical analysis

We considered all participants with positive HBsAg and anti-HBc tests to be currently infected with hepatitis B. In addition, those who had an isolated positive anti-HBs test were considered immune due to having been previously vaccinated. Participants who had an isolated positive anti-HBc test or positive anti-HBs and anti-HBc tests were considered as having a previous hepatitis B infection. Lastly, participants who screened negative for all three tests were considered at risk or susceptible to hepatitis B.

Descriptive statistics in percentages were used to characterize the participants with regard to demographics, including age (<40, 40–49, 50–59, 60–69, 70+years), gender (male/female), annual household income (<US\$10 000, US\$10 001–US\$30 000, US\$30 001+), education (less than high school, high school graduate, some college or technical/vocational training, college graduate), marital status (single/married), health insurance status (yes/no) and US birth status (US born/non-US born) as well as relevant hepatitis B information, including family history of hepatitis B (yes/no) and personal history of hepatitis B vaccination (yes/no). A χ^2 test or Fisher's exact test (when one or more cells had an expected frequency of five or less) was used to determine whether factors differed across the four hepatitis B statuses (previous infection, immunity from vaccination, currently infected, susceptible). This analytic approach was also used to identify factors associated with risk of hepatitis B (ie, comparing those currently infected to those susceptible). Characteristics found to be associated with risk of hepatitis B at a p value of ≤ 0.10 were fit into a multivariate logistic regression model to quantify each factor's effect on risk of hepatitis B using an odds ratio (OR) and a 95% confidence interval (CI).¹⁷ Missing categories were created for all variables and modelled where appropriate. To ensure our selection of significant factors in the fully adjusted model was not driven by differences in the missing categories, sensitivity analyses were conducted excluding the missing. Because the overall findings did not change with and without the missing categories, the results with the missing categories are presented.

All tests of statistical significance were two-sided. The analyses were performed using SAS 9.4 Software. Statistical significance was considered at a p value of ≤ 0.05 .

Patient and public involvement

The VACF organized hepatitis screening community events in Orange County, California and Los Angeles County, California every year that were free and open to the public. Participants at these screening events completed a questionnaire and had their blood drawn, which was tested for hepatitis B serology. No specific patient population was included.

RESULTS

Among the 2508 participants, 9.0% were currently infected with hepatitis B (N=225) and 17.7% were at risk or susceptible to hepatitis B (N=443). In addition, close to 46% had been previously infected (N=1151) and ~27% were immune due to having received a hepatitis B vaccination (N=689) (table 1).

The majority of participants were female (55.5%), 50 years of age or older (59.0%) and married (64.2%) with no more than a high school education or equivalent (53.1%) and living in a household with an annual income of <US\$30 000 (64.7%); almost all participants were born outside of the USA (96.2%) (table 2). When characteristics were examined across the four hepatitis B statuses, significant differences in gender (p=0.02), age (p<0.0001), education (p=0.004), marital status (p<0.0001), US birth status (p<0.0001), family history of hepatitis B (p=0.0001), and personal history of hepatitis B vaccination (p<0.0001) were observed (table 2).

Because gender, age, income, family history of hepatitis B, personal history of hepatitis B vaccination and US birth status were statistically significantly associated with hepatitis B risk when comparing only those susceptible to those currently infected (table 2), we jointly modelled those factors with year of screening and found females to be at a 52% reduced risk of hepatitis B relative to males (OR=0.48, 95% CI 0.33 to 0.69; table 3). In addition, those who reported a previous hepatitis B vaccination were at a 47% reduced risk in comparison to those who did not (OR=0.53, 95% CI 0.31 to 0.93; table 3). However, those born outside of the USA as well as those with a family history of hepatitis B were at substantial increased risk

Table 1 Percentage of screening participants by hepatitis B status

Serological results	Interpretation	No. of participants	Percent of participants*
HBsAg–, anti-HBs+/-, anti-HBc+	Previous infection	1151	45.9
HBsAg–, anti-HBs+, anti-HBc–	Immunity from vaccination	689	27.5
HBsAg–, anti-HBs–, anti-HBc–	Susceptible	443	17.7
HBsAg+, anti-HBs+/-, anti-HBc+	Currently infected	225	9.0

*Does not total 100% due to rounding.

HBsAg, hepatitis B surface antigen; anti-HBc, total hepatitis B core antibody; anti-HBs, hepatitis B surface antibody.

Table 2 Characteristics of screening participants by hepatitis B status

Characteristic	Previous Infection N (% previous infection)§	Immunity from vaccination N (% vaccinated)§	Susceptible N (% susceptible)§	Currently infected N (% infected)§	Total*	P value†	P value‡
Gender						0.02	0.006
Male	540 (46.9)	276 (40.1)	176 (39.7)	116 (51.6)	1108		
Female	609 (52.9)	408 (59.2)	265 (59.8)	108 (48.4)	1390		
Missing	2 (0.2)	5 (0.7)	2 (0.5)	0 (0.0)	9		
Age (years)						<0.0001	0.09
<40	103 (8.9)	208 (30.2)	125 (28.2)	45 (20.0)	481		
40–49	232 (20.2)	143 (20.8)	108 (24.4)	62 (27.6)	545		
50–59	384 (33.4)	167 (24.2)	114 (25.7)	68 (30.2)	733		
60–69	304 (26.4)	120 (17.4)	63 (14.2)	39 (17.3)	526		
70+	126 (11.0)	50 (7.3)	33 (7.5)	11 (4.9)	220		
Missing	2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	3		
Annual household income						0.066	0.021
≤US\$10 000	363 (31.5)	208 (30.2)	137 (20.9)	65 (28.9)	773		
US\$10 001 to US\$30 000	405 (35.2)	223 (32.4)	130 (29.4)	91 (40.4)	849		
US\$30 001+	185 (16.1)	115 (16.7)	92 (20.8)	32 (14.2)	424		
Missing	198 (17.2)	143 (20.8)	84 (19.0)	37 (16.4)	462		
Education						0.004	0.24
Less than high school	260 (22.6)	104 (15.1)	87 (19.6)	39 (17.3)	490		
High school graduate	394 (34.2)	225 (32.7)	136 (30.7)	87 (38.7)	842		
Some college or technical/vocational training	190 (16.5)	128 (18.6)	77 (17.4)	40 (17.8)	435		
College graduate	223 (19.4)	178 (25.8)	113 (25.5)	44 (19.6)	558		
Missing	84 (7.3)	54 (7.8)	30 (6.8)	15 (6.7)	181		
Marital status						<0.0001	0.31
Single	290 (25.2)	264 (38.3)	147 (33.2)	63 (28.0)	764		
Married	794 (69.0)	387 (56.2)	279 (63.0)	150 (66.7)	1610		
Missing	67 (5.8)	38 (5.5)	17 (3.8)	12 (5.3)	134		
Health insurance						0.075	0.20
No	331 (28.8)	190 (27.6)	137 (30.9)	85 (37.8)	743		
Yes	718 (62.4)	428 (62.1)	260 (58.7)	118 (52.4)	1524		
Missing	102 (8.9)	71 (10.3)	46 (10.4)	22 (9.8)	241		
Born outside of the USA						<0.0001	0.006
No	7 (0.6)	31 (4.5)	19 (4.3)	1 (0.4)	58		
Yes	1130 (98.2)	644 (93.5)	415 (93.7)	223 (99.1)	2412		
Missing	14 (1.2)	14 (0.6)	9 (2.0)	1 (0.4)	38		
Family history of hepatitis B						0.0001	<0.0001
No	707 (61.4)	395 (57.3)	281 (63.4)	118 (52.4)	1501		
Yes	116 (10.1)	69 (10.0)	37 (8.4)	44 (19.6)	266		
Missing	328 (28.5)	225 (32.7)	125 (28.2)	63 (28.0)	741		

Continued

Table 2 Continued

Characteristic	Previous Infection N (% previous infection)§	Immunity from vaccination N (% vaccinated)§	Susceptible N (% susceptible)§	Currently infected N (% infected)§	Total*	P value†	P value‡
Previous hepatitis B vaccination						<0.0001	0.017
No	662 (57.5)	263 (38.2)	245 (55.4)	150 (66.7)	1320		
Yes	203 (17.6)	225 (32.7)	71 (16.0)	25 (11.1)	524		
Missing	286 (24.9)	201 (29.2)	127 (28.7)	50 (22.2)	664		
Total	1151	689	443	225	2508		

*Number of participants by each characteristic.

† χ^2 p value comparing all four hepatitis B statuses.

‡ χ^2 p value comparing only those susceptible to hepatitis B to those currently infected with hepatitis B.

§May not total 100% due to rounding.

(OR=13.36, 95% CI 1.62 to 110.05 and OR=4.68, 95% CI 2.66 to 8.22, respectively; table 3). We conducted a subset analysis among those born outside of the USA to examine

Table 3 ORs and 95% CIs for the association between screening participant characteristics and risk of hepatitis B

Characteristic	OR*	95% CI	P value
Gender			
Male	1.00	–	–
Female	0.48	0.33 to 0.69	<0.0001
Age (years)			
<40	1.00	–	–
40–49	1.40	0.83 to 2.36	0.20
50–59	1.58	0.95 to 2.62	0.078
60–69	1.54	0.85 to 2.79	0.15
70+	0.76	0.32 to 1.77	0.52
Annual household income			
≤US\$10 000	1.00	–	–
US\$10 001 to US\$30 000	1.32	0.86 to 2.03	0.35
US\$30 001+	0.56	0.32 to 0.99	0.046
Born outside of the USA			
No	1.00	–	–
Yes	13.36	1.62 to 110.05	0.016
Family history of hepatitis B			
No	1.00	–	–
Yes	4.68	2.66 to 8.22	<0.0001
Previous hepatitis B vaccination			
No	1.00	–	–
Yes	0.53	0.31 to 0.93	0.023

*Adjusted for all other characteristics as well as year of screening.

whether year of entry into the USA would differentially affect risk; however, no significant association was found (data not shown). Lastly, there appeared to be increased risk after age 40 (ORs=1.40, 1.58, 1.54 for 40–49, 50–59, 60–69 years, respectively) until age 70 (OR=0.76) although none of the effect estimates were statistically significant (table 3).

DISCUSSION

Although the literature recognizes Asian Americans as having the highest rate of hepatitis B in the USA, the overall Asian population is diverse with variations in disease burden by ethnicity.^{7,8} For this reason, our report focuses specifically on Vietnamese Americans who have one of the highest prevalences of hepatitis B.⁸ Using data from community screening events from 2011 to 2017, 9.0% of participants were currently infected with hepatitis B; this is similar to the 8.8% prevalence determined by Nguyen *et al*'s study of VACF data spanning 2008–2010, indicating little change in disease prevalence for this community.¹⁶ Nguyen *et al* also observed 15.4% of their participants were at risk of hepatitis B, 53.8% had a previous infection, and 21.9% were immune from vaccination; this is in comparison to our percentages of 17.7%, 45.9%, and 27.5%, respectively.¹⁶ Given efforts to improve understanding of hepatitis B among the Vietnamese American community, it is not surprising that our updated evaluation shows a greater proportion with immunity from vaccination and a lower proportion with natural immunity via a previous infection. However, we did observe a higher percentage of susceptible participants, which may be a result of increased awareness prompting those still at risk to undergo screening. This higher percentage could also reflect a growth in the number of at-risk Vietnamese Americans in the Southern California region, highlighting the need for continued hepatitis B public health efforts.

Not surprisingly, most participants whose serology indicated immunity from vaccination were those who reported having been previously vaccinated. However, among those who reported a previous vaccination, only 42.9% possessed protective antibodies with 13.6% still susceptible to hepatitis B and 4.8% currently infected with hepatitis B. This discrepancy between self-reported vaccination status and confirmed serology is an important issue and could be due to several reasons. First, participants may have inaccurately reported their vaccination status because they confused a vaccine for another disease with a vaccine for hepatitis B. The contrary may also be true; our data showed close to 20% of those who reported not having been previously vaccinated possessing protective antibodies that indicate previous immunization. Second, because the hepatitis B vaccine is given as a series of shots over a 6-month time period, some participants may not have received all necessary shots and hence were not immunized, but thought they were. These reasons highlight the need for improved health education and hepatitis B vaccination knowledge in the Vietnamese American community. Another explanation for why some participants who reported being vaccinated were currently infected may be due to the fact that they were already infected at the time of their vaccination. It is currently not standard clinical practice to test for hepatitis B prior to administering the vaccine, but this may be worthwhile to do particularly for high-risk individuals.¹⁸

Our study found those born outside of the USA to be over 13 times as likely to be infected with hepatitis B compared with those born in the USA, a finding supported by another screening study by Kallman *et al.*¹⁹ Given that these individuals are likely immigrants from Vietnam, they may lack knowledge regarding hepatitis B and hence are unaware of their infection status. Unlike the USA where there is a multipronged strategy for hepatitis B prevention (eg, antenatal screenings, hepatitis B immune globulin at birth for babies born to mothers who are HBsAg-positive, two-dose hepatitis B vaccine for adults, education and awareness of accessible resources for reducing transmission), migrants from Vietnam where there is a heavy reliance on infant vaccination as the main prevention strategy could be at higher risk due to lack of awareness of disease transmission and prevention strategies.²⁰ There could also be a lack of health literacy or access to care due to financial, linguistic, and cultural barriers (eg, stigma, feelings of shame and guilt), which have been documented as contributing factors to health disparities among Vietnamese Americans and Asian American immigrants generally.^{21–24} More culturally tailored public health programs and interventions that aim to increase hepatitis B awareness and knowledge, particularly among Vietnamese Americans born outside of the USA, are needed.

We identified family history as a significant predictor of hepatitis B risk, which is in line with other screening studies conducted in Vietnamese Americans and Asian Americans.^{12 18 19} The substantial increased risk among

those with a family history is not surprising given that hepatitis B is often transmitted from an infected mother to her baby during birth or through direct contact with blood, semen, or other bodily fluids from an infected person. We also identified gender as a significant predictor with females having a lower risk of hepatitis B than males, which may be a result of biological factors and gender-specific health behaviours and perceptions. Biologically, the observed sex disparity could be due to differences in immune responses which are shaped by sex steroid hormones (eg, androgens, estrogens) that have been shown to influence the function of immune cells and interact with the complex clinical course of hepatitis B.^{25 26} Behaviorally, females are generally more health conscious and hence may have higher levels of hepatitis B awareness and knowledge as well as greater use of hepatitis B-related prevention services.^{27 28} Males also tend to possess certain lifestyle factors that promote the adoption of more traditional masculine perspectives that underplay the importance of health-protective behaviours.^{29 30} For example, a Vietnamese American male who constructs masculinity as self-reliance or putting work ahead of all other responsibilities may not make time for self-care or seek routine health services, indicating a need to improve health education and outreach for males.

The strengths of our analysis include its large sample size as well as our primary focus on Vietnamese Americans, a community disproportionately burdened by hepatitis B. With the growing literature highlighting the need to disaggregate Asian Americans in research due to the diverse cultures, languages, and sociodemographic factors that characterize each Asian subgroup, it is important that ethnic-specific data are used so more effective public health strategies can be developed.³¹ Our study also used serological tests for HBsAg, anti-HBc, and anti-HBs to accurately classify each participant's hepatitis B status. Many screening fairs have relied solely on HBsAg testing despite the need for anti-HBs and anti-HBc tests to properly identify those truly at risk. We recognize that our findings may not necessarily be generalizable to the entire Vietnamese American population given that attendees of health fairs that offer free services are often foreign-born and from low-income backgrounds. This is indeed true in our analysis since the majority of participants were foreign-born with an annual household income of <US\$30 000 in comparison to only 64% of Vietnamese in the USA who are foreign-born with a median annual household income of US\$58 700 according to data from the 2013–2015 American Community Survey (ACS).¹⁵ However, there is some comparability with regard to education and marital status when the ACS data are restricted to only those foreign-born (eg, percent who have a high school education or less: 53% in our data vs 52% in the ACS, percent who are married: 61% in our data vs 64% in the ACS).¹⁵ In addition, Southern California has the highest concentration of Vietnamese Americans in the USA, making it the ideal region to study hepatitis B for this ethnicity.

Other limitations of our analysis include the lack of information on other factors that may affect hepatitis B risk as well as missing participant data for certain characteristics. These are often issues with questionnaires administered at screening fairs due to time constraints. We did conduct sensitivity analyses with and without the missing data and the overall results did not change. Lastly, our questionnaire data were based on self-report, which may result in misclassification as we noted for participants' hepatitis B vaccination status. However, there is little reason to believe that the misclassification would occur more or less often for those of a certain hepatitis B status, hence any bias would only be towards the null.

Overall, our study provides an updated evaluation on hepatitis B prevalence in the Vietnamese American community and identifies certain subgroups within it, particularly those born outside of the USA and those with a hepatitis B family history, who may be at increased risk and require targeted interventions. In addition, we observed important discrepancies between self-reported hepatitis B vaccination status and confirmed serological results, which highlight the need to improve hepatitis B vaccination knowledge among Vietnamese Americans and their health providers. Our comprehensive serological testing makes this a unique effort with findings that can inform strategies to address hepatitis B's burden in the Vietnamese American community.

Contributors AWL, WJ, BN, and TVN contributed to the conception and design of the study. BN, DNH, JNH, and TVN contributed to the study's data collection. AL, WJ, EC, and PY contributed to statistical analysis and interpretation of the data. AL, WJ, and EC drafted the manuscript. All authors reviewed and approved the final version of the manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

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