Prevalence of Chronic Hepatitis B Virus (HBV) Infection in U.S. Households: National Health and Nutrition Examination Survey (NHANES), 1988-2012

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The number of persons with chronic hepatitis B virus (HBV) infection in the United States is affected by diminishing numbers of young persons who are susceptible because of universal infant vaccination since 1991, offset by numbers of HBV-infected persons migrating to the United States from endemic countries. The prevalence of HBV infection was determined by serological testing and analysis among noninstitutionalized persons age 6 years and older for: antibody to hepatitis B core antigen (anti-HBc), indicative of previous HBV infection; hepatitis B surface antigen (HBsAg), indicative of chronic (current) infection; and antibody to hepatitis B surface antigen (anti-HBs), indicative of immunity from vaccination. These prevalence estimates were analyzed in three periods of the National Health and Nutrition Examination Survey (NHANES): 1988-1994 (21,260 persons); 1999-2008 (29,828); and 2007-2012 (22,358). In 2011-2012, for the first time, non-Hispanic Asians were oversampled in NHANES. For the most recent period (2007-2012), 3.9% had anti-HBc, indicating approximately 10.8 (95% confidence interval [CI]: 9.4-12.2) million noninstitutionalized U.S. residents having ever been infected with HBV. The overall prevalence of chronic HBV infection has remained constant since 1999: 0.3% (95% CI: 0.2-0.4), and since 1999, prevalence of chronic HBV infection among non-Hispanic blacks has been 2- to 3-fold greater than the general population. An estimated 3.1% (1.8%-5.2%) of non-Hispanic Asians were chronically infected with HBV during 2011-2012, which reflects a 10-fold greater prevalence than the general population. Adjusted prevalence of vaccine-induced immunity increased 16% since 1999, and the number of persons (mainly young) with serological evidence of vaccine protection from HBV infection rose from 57.8 (95% CI: 55.4-60.1) million to 68.5 (95% CI: 65.4-71.2) million. *Conclusion*: Despite increasing immune protection in young persons vaccinated in infancy, an analysis of chronic hepatitis B prevalence in racial and ethnic populations indicates that during 2011-2012, there were 847,000 HBV infections (which included ~400,000 non-Hispanic Asians) in the noninstitutionalized U.S. population. (HEPATOLOGY 2016;63:388-397)

Under-recognized and underdiagnosed, chronic hepatitis B (CHB) affects an estimated 400 million persons worldwide and accounts for 600,000 hepatitis B virus (HBV)-related deaths each year.[1,2] Knowledge of the number of HBV-infected persons living in the United States is essential for public health policy planning. The number of persons chronically infected with HBV has varied in the literature, ranging from 730,000 (95% confidence interval [CI]: 550,000-940,000)[3] to 2.2 million.[3,4] There are several

contributing factors, which may help to explain why the measurement of HBV prevalence in the United States has varied. Subsequent to the implementation of a universal hepatitis B vaccination strategy in the United States in 1991, CHB prevalence in the U.S. non-institutionalized population decreased 79.2% among those ages 6-19 years from 0.24% (95% CI: 0.07-0.56) in 1988-1994 to 0.05% (95% CI: 0.02-0.11) in 1999-2006.[3] Putatively, an estimated 90.0% of children ages 18-35 months, 93.1% of adolescents ages 13-17 years, and 35.3% of adults ages 19-49 years in the United States have completed the hepatitis B vaccine regimen.[5,6] Largely based on the universal hepatitis B vaccination strategy, an estimated 25.2% of the U.S. noninstitutionalized population have vaccine-induced immunity.[3]

Despite the great reductions in acute HBV—and thus chronic HBV—in younger persons from universal infant vaccination for hepatitis B starting in 1991, there has been substantial migration of persons already chronically infected with HBV in the past 40 years, especially from HBV endemic regions: Eastern Asia (e.g., China, Vietnam, and the Philippines) and sub-Saharan Africa (e.g., Nigeria, Ghana, and Ethiopia).[7] An estimated 3.9 million foreign-born persons from these endemic countries currently reside in the United States.[4] Persons living with HBV in the United States are largely foreign born and may account for as many as 70% of HBV infections in the United States.[8] A recent characterization of CHB cases in six U.S. communities concluded that only 6.5% were U.S. born.[9]

The ideal data source to measure prevalence of HBV infections in the United States would balance out accounting for the effect of implementing Centers for Disease Control and Prevention (CDC) vaccination strategy in the 1990s, with the effect that migration from high endemic regions and countries has had on the overall prevalence of HBV in the United States. In the United States, the National Notifiable Disease System, the main component of the CDC's surveillance for infectious agents generally and viral hepatitis specifically, is the main way of "counting cases," but it is a passive system: Not all states and localities report persons with chronic HBV infections, and, of those who do, their ability to identify, verify, and report such cases is widely

variable.[10] Furthermore, the asymptomatic nature of the virus also contributes to under-reporting and underdiagnoses of HBV infections. It is estimated that 44.5% of persons infected with HBV in the United States are reported to their respective state health departments.[11]

Thus, the CDC has relied on analysis of serum from approximately 5,000 U.S. residents each year from the National Health and Examination Survey (NHANES), a survey representative of the U.S. noninstitutionalized household population, to estimate the prevalence of HBV infection.[3] To assess the current burden and trends in chronic HBV infections in the United States, we analyzed data and serum from NHANES spanning three distinct time periods: 1988-1994, 1999-2006, and 2007-2012. In addition, for the first time in 2011-2012 from this data source, owing to the more extensive sampling of non-Hispanic Asians, we were able to produce estimates for non-Hispanic Asians, who have the highest prevalence of HBV infection in the United States. The CDC estimates that non-Hispanic Asians, who are 5% of the nation's population, account for 50% of all chronic HBV infections in the United States.[12]

Materials and Methods

Data Collection.   Data analyzed here come from the NHANES public use data files, downloaded from the CDC National Center for Health Statistics (NCHS) website (http://www.cdc.gov/nchs/nhanes.htm). The sampling plan for the survey is a stratified, multistage, probability cluster design of the noninstitutionalized civilian U.S. household population. NHANES public use data files contain information about the health, nutritional status, and health behaviors of the sample persons. Because some subgroups of the population are not sufficiently represented in sampling cycles—that is, numbers of certain demographic groups are too small for statistical robustness—certain subgroups were over-sampled to provide more-precise estimates for these groups. In all NHANES cycles analyzed here, non-Hispanic blacks and Mexican Americans were over-sampled. Also, in the period 1999-2006, adolescents ages 12-19 years, the elderly, and low-income persons were sampled at higher frequencies than other persons. Starting in 2007, all Hispanic persons were targeted for

oversampling (rather than just Mexican-American persons). Moreover, non-Hispanic Asians were oversampled during 2011-2012. This was designed to increase the sample of non-Hispanic Asian NHANES participants from < 2% to upward of 13%.

Informed consent for individuals age >=18 years or assent with proxy consent (for those <18 years) was obtained from all sample persons. More-detailed information on NHANES survey design, including approval from the ethics review board for data collection and analysis, is available from the survey documentation.[13-16]

Laboratory Data. NHANES participants who gave informed consent had their serum tested for: antibody to hepatitis B core antigen (anti-HBc), indicative of hepatitis B infection sometime in the past (past or present hepatitis B); hepatitis B surface antigen (HBsAg), indicative of current (active) chronic infection (and, much less commonly, acute infection); and antibody to hepatitis B surface antigen (anti-HBs), indicative of immunity from vaccination or, in the United States less commonly, from previous infection. Among those who tested positive for anti-HBc, persons who also tested positive for HBsAg were considered to be chronically infected. Persons who tested negative for anti-HBc and positive for anti-HBs were considered to have vaccine-induced immunity. Our study sample included those individuals with complete data to all three laboratory measures (anti-HBc, HBsAg, and anti-HBs).

During the first time period, 1988-1994: 30,930 persons age 6 years and over were sampled, of whom 25,733 (83.2%) were interviewed, with 23,527 of 25,733 (91.4%) having completed the medical examination, and 21,260 of the 23,527 examined (90.4%) tested for the presence of total anti-HBc and HBsAg.[3] During the second time period, 1999-2006: 43,029 persons age 6 years and over were sampled, of whom 34,338 (79.8%) were interviewed; 32,534 of 34,338 (94.7%) were examined; and 29,828 of 32,534 (91.7%) were tested for the presence of total anti-HBc, anti-HBs, and HBsAg.[3,15] During the most recent time period, 2007-2012: 33,888 persons age 6 years and over were sampled, of whom 25,410 persons (75.0%) were interviewed, and 24,544 (96.6% of those interviewed) were examined, with 22,358 of 24,544 (91.1%) tested for the presence of total anti-HBc, anti-HBs, and HBsAg. During 2011-2012, a resulting sample of 929 non-Hispanic Asians were interviewed and examined.

Study Variables. NHANES characteristics included in the analysis were recoded as follows: age group (6-19, 20-49, and ≥50+ years); race and His-

panic origin (based on respondents' self-assessment and categorized as non-Hispanic white, non-Hispanic black, non-Hispanic Asian American [years 2011-2012 only], or Mexican American); sex (men, women); country of birth (categorized as born in the United States Vs. not in the United States); insurance status (any insurance, any Medicare, any Medicaid, or no health insurance); heavy alcohol drinker among those age 20 years or more (a male who, on average, drinks at least three alcoholic drinks per day, or a female who on average drinks at least two alcoholic drinks per day); and military veteran status (veteran, nonveteran).[17]

Statistical Analyses. SAS SUDAAN was used to conduct a weighted analysis of the data and incorporated the examination weights and the complex sample design.[18] Unadjusted and adjusted prevalence estimates of past/present and chronic HBV infections were calculated for each of the three time periods of interest: these included reanalysis of the 1988-1994[19] and 1999-2006[3] data sets with the same programming used for 2007-2012. Unadjusted and adjusted prevalence estimates of HBV vaccine-induced immunity were calculated for the 1999-2006 and 2007-2012 time periods only. All estimates for non-Hispanic Asians were calculated using data and examination weights for the 2011-2012 survey cycle only. To estimate the equivalent number of infections in the U.S. noninstitutionalized population, unadjusted prevalence estimates expressed as a percentage were multiplied to population totals provided by NCHS averaged over the time period of interest.[20]

Logistic regression models were used to calculate prevalence estimates, orthogonal polynomial contrasts, and prevalence ratio estimates for select characteristics; overall, race and Hispanic origin, country of birth, sex, insurance status, heavy alcohol drinker, and military veteran status. In each model, past/present HBV infection, chronic HBV infection, or vaccine-induced immunity served as the dependent variable. Each multivariate logistic regression model included a primary independent variable of interest (race and Hispanic origin, country of birth, sex, insurance status, heavy alcohol drinker, and military veteran status), with time period of interest, the interaction term for time period and the primary independent variable, and age group as secondary independent variables. Per NCHS guidelines, prevalence estimates are indicated as unstable when the standard error of the estimate relative to the estimate itself (relative standard error; RSE) was greater than 30% or when the number of positive sample persons was <10.

The method of orthogonal polynomial contrasts was employed to test for linear trends in the adjusted hepatitis B prevalence estimates for the three time periods of

Table 1. Prevalence of Past/Present HBV Infection (anti-HBc) by Selected Characteristics: NHANES 1988-2012

Characteristic	NHANES (1988-1994)			NHANES (1999-2006)			NHANES (2007-2012)			Trends Analysis	
	Sample Size	No. Positive Tests	Adjusted % (95% CI)	Sample Size	No. Positive Tests	Adjusted % (95% CI)	Sample Size	No. Positive Tests	Adjusted % (95% CI)	P Value$_1$	P Value$_2$
Overall	21,260	1,374	5.5 (4.8, 6.2)	29,828	1,377	4.8 (4.3, 5.3)	22,358	1,185	3.7 (3.3, 4.2)	0.0001	0.5585
Overall unadjusted			5.3 (4.7, 6.0)			4.8 (4.3, 5.3)			3.9 (3.4, 4.4)		
Age, years											
6-19	5,679	77	1.9 (1.3, 2.7)	12,004	81	0.6 (0.4, 0.9)	6,344	23	0.3 (0.2, 0.5)	<0.0001	0.0317
20-49	8,857	624	5.8 (5.0, 6.7)	9,465	501	4.6 (4.0, 5.3)	8,118	363	3.3 (2.8, 3.8)	<0.0001	0.8265
≥50	6,724	673	7.3 (6.3, 8.3)	8,359	795	7.8 (6.8, 8.8)	7,896	799	6.7 (5.8, 7.7)	0.4139	0.1934
Race/ethnicity											
White, NH	7,963	290	3.1 (2.6, 3.6)	12,075	367	2.9 (2.6, 3.2)	8,973	210	1.8 (1.5, 2.2)	0.0001	0.0810
Black, NH	6,133	676	13.8 (12.4, 15.3)	7,302	604	12.2 (11.0, 13.6)	4,865	426	9.3 (8.2, 10.4)	<0.0001	0.3836
Mexican American	6,275	241	4.7 (3.6, 6.1)	8,094	163	2.7 (2.1, 3.4)	4,071	73	1.9 (1.4, 2.6)	0.0001	0.1673
Non-Hispanic Asians*	–	–	–	–	–	–	929	180	20.5 (16.6, 25.1)	–	–
Place of birth											
United States	17,301	967	4.1 (3.6, 4.6)	24,291	893	3.6 (3.2, 4.0)	17,206	568	2.5 (2.2, 2.8)	<0.0001	0.2035
Foreign born	3,901	398	15.6 (12.4, 19.4)	5,528	484	12.2 (10.6, 14.0)	5,138	616	10.4 (9.0, 12.0)	0.0082	0.5353
Sex											
Men	10,088	732	6.5 (5.7, 7.5)	14,523	790	5.8 (5.1, 6.5)	11,132	653	4.1 (3.6, 4.7)	<0.0001	0.3217
Women	11,172	642	4.6 (3.9, 5.5)	15,305	587	3.9 (3.4, 4.5)	11,226	532	3.5 (3.0, 4.0)	0.0151	0.7019
Insurance status											
Insured	16,601	1,069	5.0 (4.3, 5.8)	23,548	1,053	4.2 (3.8, 4.7)	17,526	915	3.5 (3.1, 4.0)	0.0008	0.9779
Medicare, age 50 years and older	3,790	378	7.8 (6.6, 9.1)	4,228	385	7.0 (5.9, 8.3)	3,482	297	5.5 (4.7, 6.5)	0.0040	0.5744
Medicaid	2,862	243	13.7 (9.7, 18.9)	3,974	203	9.5 (7.9, 11.4)	3,268	174	6.9 (5.4, 8.8)	0.0066	0.6283
Not Insured	3,649	238	9.2 (7.5, 11.2)	5,984	303	7.4 (6.2, 8.9)	4,797	268	5.1 (4.3, 6.2)	0.0002	0.7326
Heavy alcohol drinker, age 20 years and older											
Men	2,542	238	7.6 (6.1, 9.4)	2,660	210	7.8 (6.6, 9.3)	2,592	158	4.7 (3.9, 5.5)	0.0017	0.0386
Women	1,818	110	4.0 (2.8, 5.6)	2,685	124	4.2 (3.3, 5.3)	2,469	115	3.3 (2.6, 4.2)	0.4010	0.3738
Military veteran, age 20 years and older											
Yes	2,396	258	6.1 (4.9, 7.5)	2,674	242	6.2 (5.3, 7.2)	1,909	149	4.2 (3.4, 5.2)	0.0190	0.0964

*2011-2012 data only.
P Value 1: Test 1: pair-wise comparison of adjusted prevalence estimates for time period 1 versus time period 3 ($\hat{\pi}_1 = \hat{\pi}_3$).
P Value 2: Test 2: no departure in linearity ($\hat{\pi}_1 + \hat{\pi}_3 = 2\hat{\pi}_2$).
Abbreviation: NH, non-Hispanic.

interest. This assessment was conducted for each characteristic of interests, as indicated above. This assessment was comprised of testing two orthogonal polynomial contrasts: Test 1: pair-wise comparison of adjusted prevalence estimates for time period 1 versus time period 3 ($\hat{\pi}_1 = \hat{\pi}_3$); and Test 2: no departure in linearity ($\hat{\pi}_1 + \hat{\pi}_3 = 2\hat{\pi}_2$).[18,21] Orthogonal polynomial test statistics having P values less than 0.05 were considered statistically significant.

Prevalence ratio estimates of hepatitis B vaccine-induced immunity were obtained from the logistic regression models: $PR_{3/2} = \frac{P_3}{P_2}$, where the subscripts 3 and 2 represent time periods 2007-2012 and 1999-2006, respectively. Prevalence ratio estimates having 95% CIs that excluded the value 1.0 were considered to be statistically significant.

Results

Previous (Past or Present) HBV Infection. During 1988-2012, among the U.S. noninstitutionalized population, of at least 6 years of age, the overall adjusted prevalence of past/present hepatitis B steadily declined ($P = 0.0001$): 5.5% (1988-1994), 4.8% (1999-2006), and 3.7% (2007-2012; Table 1). Based on the unadjusted prevalence estimates of 5.3%, 4.8%, and 3.9%, respectively (Table 1), an estimated 12.1 (95% CI: 10.7-13.7) million persons in 1988-1994, 12.5 (95% CI: 11.2-13.8) million persons in 1999-2006, and 10.8 (95% CI: 9.4-12.2) million persons in 2007-2012 had ever been infected with HBV. However, throughout 1988-2012, the decreasing trend in the prevalence of previous HBV infection was not significant among

adults age 50 years or older (P-value$_1$ test for linear trend = 0.4139; P-value$_2$ test for departure from linearity = 0.1934; Table 1). During 2011-2012, 20.5%, of non-Hispanic Asians had anti-HBc, indicating approximately 2.8 (95% CI: 2.3-3.5) million noninstitutionalized non-Hispanic Asians having ever been infected with HBV (Table 1).

Chronic (Current) HBV Infection. The overall adjusted prevalence of chronic HBV infection has remained fairly constant since 1988. When considering the three time periods of interest, decreases in the overall prevalence of chronic HBV infection were statistically not significant: 0.4% (1988-1994), 0.3% (1999-2006), and 0.3% (2007-2012). However, among persons less than 20 years, the prevalence of chronic HBV infection decreased significantly from 0.2% (95% CI: 0.1-0.6) during 1988-1994 to 0.03% (95% CI: 0.01-0.08) during 2007-2012 (prevalence ratio [PR] =9.4; 95% CI: 2.1- 41.8). As expected, chronic HBV infection among those of age less than 20 years is rare, and, as a result, the estimate for 2007-2012 is based on only 3 positive sample persons and should be interpreted with caution.

During 2007-2012, the overall prevalence of chronic (current) HBV infection was 0.3% (95% CI: 0.2-0.4; Table 2). These chronic infections were almost entirely in the 20- to 49-year-old (0.4%) and 50 and older (0.3%) age groups (Table 2). Higher rates of chronic HBV infection were noted in foreign-born persons and non-Hispanic blacks. An estimated 1.1% (95% CI: 0.7- 1.6) of foreign-born Americans and 0.6% (95% CI: 0.4-1.0) of non-Hispanic blacks were chronically infected during 2007-2012. Prevalence of chronic HBV infection among non-Hispanic blacks has been 2- to 3-fold greater than the general population. Among the estimated 199,000 (95% CI: 119,000-308,000) non-Hispanic blacks with chronic HBV infection, prevalence of chronic HBV infection was 2.5% (95% CI: 0.9-5.6) among foreign-born non-Hispanic blacks as compared to 0.4% (95% CI: 0.2-0.7) among U.S.-born non-Hispanic blacks.

Similarly, among the estimated 427,000 (95% CI: 248,000-688,000) non-Hispanic Asians with chronic HBV infection during 2011-2012, 93.1% (95% CI: 67.4-99.8) were foreign born. Prevalence of chronic HBV infection among non-Hispanic Asians was 10-fold greater than the general population. Estimating numbers of chronically HBV-infected U.S. residents from the prevalence in each racial and ethnic group indicated 847,000 {range, 565,000-1,130,000) HBV-infected persons in 2011-2012. This suggests that non-Hispanic Asians account for 50% of the HBV disease burden in the noninstitutionalized United States in 2011-2012.

Prevalence of Vaccine-Induced Protection: (1999-2006) Versus (2007-2012). Since 1999, the overall adjusted prevalence of hepatitis B vaccine-induced immunity increased 16% (PR = 1.16; 95% CI: 1.09-1.23), from 21.7% (95% CI: 20.8-22.7) during 1999-2006 to 25.1% (95% CI: 24.1-26.1) during 2007-2012 (Table 3). Based on unadjusted estimates of 22.2% in 1999-2006 and 24.7% in 2007-2012 (Table 3), this equates to an increase from 57.8 (95% CI: 55.4-60.1) million persons with serological evidence of vaccine-induced immunity in 1999-2006 to 68.5 (95% CI: 65.4-71.2) million with vaccine-induced immunity during 2007-2012. The increase in hepatitis B vaccine-induced immunity is primarily owing to the 69% increase in hepatitis B vaccine-induced immunity observed among persons ages 20-49 years (Table 3), which equates to an increase from 20.9 (95% CI: 19.6-22.3) million persons in 1999-2006 to 35.6 (95% CI: 33.6-37.6) million persons in 2007-2012. However, among children and young adults (ages 6-19), the adjusted prevalence of hepatitis B vaccine-induced immunity somewhat decreased from 56.8% in 1999-2006 to 44.4% during 2007-2012 (PR = 0.78; 95% CI: 0.73-0.84).

The adjusted prevalence of hepatitis B vaccine-induced immunity increased at least 40% among the following demographics: 67% among female heavy alcohol drinkers (PR = 1.7; 95% CI: 1.4- 2.0); 77% among male heavy alcohol drinkers (PR = 1.8; 95% CI: 1.5-2.1); 42% among military veterans (PR = 1.4; 95% CI: 1.2- 1.8); 41% among the uninsured (PR = 1.4; 95% CI: 1.3- 1.6); and 41% among foreign-born Americans (PR = 1.4; 95% CI: 1.3-1.6).

Discussion

Prevalence measures are utilized by public health officials to assess the burden of the disease, develop strategic plans, and assess the effects of ongoing prevention campaigns. Implementation of the universal hepatitis B vaccination strategy in 1991 had an immediate impact on reducing HBV infection rates among children and adolescents in the United States. The findings in this study provide further evidence that migration of HBV-infected persons from HBV endemic countries has largely contributed to prevalence rates remaining constant since 1999. Recommendations, released by the Institute of Medicine in 2010, advised the CDC and other federal agencies to expand screening and vaccination hepatitis programs that target foreign-born populations.[22] The Department of Health and Human Services (HHS), comprised of the CDC and other

Table 2. Prevalence of Chronic (Active) HBV Infection (HBsAg), by Selected Characteristics, 1988-2012

Characteristic	NHANES (1988-1994)			NHANES (1999-2006)			NHANES (2007-2012)			Trends Analysis		
	Sample Size	No. Positive Tests	Adjusted % (95% CI)	Sample Size	No. Positive Tests	Adjusted % (95% CI)	Sample Size	No. Positive Tests	Adjusted % (95% CI)	P Value₁	P Value₂	PR
Overall	21,260	82	0.4 (0.3, 0.5)	29,828	80	0.3 (0.2, 0.4)	22,358	88	0.3 (0.2, 0.4)	0.1753	0.2390	1.3 (0.9, 2.0)
Age, years												
6-19	5,679	11	0.2 (0.1, 0.6)‡	12,004	8	0.05 (0.02, 0.12)‡††	6,344	3	0.03 (0.01, 0.08)§††	0.0565	0.1582	9.4 (2.1, 41.8)
20-49	8,857	49	0.4 (0.3, 0.6)	9,465	36	0.3 (0.2, 0.4)	8,118	43	0.4 (0.2, 0.6)	0.7942	0.2372	1.1 (0.6, 2.0)
≥50	6,724	22	0.4 (0.2, 0.8)†	8,359	36	0.4 (0.3, 0.6)	7,896	42	0.3 (0.2, 0.5)	0.4862	0.9564	1.3 (0.6, 2.8)
Race/ethnicity												
White, NH	7,963	13	0.2 (0.1, 0.4)†	12,075	13	0.09 (0.06, 0.15)	8,973	10	0.10 (0.05, 0.20)†	0.1821	0.1808	2.0 (0.8, 5.2)
Black, NH	6,133	43	1.0 (0.7, 1.3)	7,302	43	0.9 (0.6, 1.4)	4,865	28	0.6 (0.4, 1.0)	0.1017	0.6299	1.6 (0.9, 2.7)
Mexican American	6,275	8	0.14 (0.05, 0.40)§††	8,094	3	0.05 (0.01, 0.18)§††	4,071	3	0.06 (0.01, 0.24)§††	0.3143	0.2950	2.5 (0.4, 14.1)
Non-Hispanic Asians*							929	25	3.1 (1.8, 5.2)			
Place of birth												
United States	17,301	48	0.2 (0.1, 0.3)	24,291	41	0.17 (0.12, 0.24)	17,206	33	0.14 (0.09, 0.21)	0.2045	0.9628	1.5 (0.8, 2.9)
Foreign born	3,901	34	1.6 (1.1, 2.2)	5,528	39	0.9 (0.6, 1.4)	5,138	55	1.1 (0.7, 1.6)	0.1243	0.1287	1.5 (0.9, 2.6)
Sex												
Men	10,088	54	0.5 (0.4, 0.8)	14,523	49	0.4 (0.3, 0.5)	11,132	50	0.4 (0.2, 0.6)	0.2081	0.3089	1.4 (0.8, 2.5)
Women	11,172	28	0.3 (0.2, 0.4)	15,305	31	0.2 (0.1, 0.3)	11,226	38	0.21 (0.15, 0.28)	0.5631	0.5310	1.2 (0.7, 2.1)
Insurance status												
Insured	16,601	57	0.3 (0.2, 0.5)	23,548	59	0.3 (0.2, 0.4)	17,526	63	0.3 (0.2, 0.4)	0.2757	0.5852	1.3 (0.8, 2.2)
Medicare, age 50 years and older	3,790	10	0.2 (0.1, 0.6)‡	4,228	13	0.3 (0.2, 0.5)†	3,482	13	0.3 (0.1, 0.5)†	0.9561	0.6725	1.0 (0.3, 3.0)
Medicaid	2,862	15	0.9 (0.4, 1.8)†	3,974	14	0.7 (0.3, 1.4)†	3,268	12	0.4 (0.2, 0.6)†	0.1361	0.8931	2.4 (0.9, 6.1)
Not insured	3,649	21	0.8 (0.3, 1.7)‡	5,984	21	0.4 (0.2, 0.6)	4,797	25	0.4 (0.3, 0.8)	0.3545	0.1764	1.7 (0.6, 4.6)
Heavy alcohol drinker, age 20 years and older												
Men	2,542	17	0.4 (0.2, 0.7)†	2,660	13	0.4 (0.2, 0.8)†	2,592	12	0.4 (0.2, 0.8)†	0.7662	0.9504	0.9 (0.3, 2.3)
Women	1,818	5	0.2 (0.1, 0.5)§††	2,685	5	0.11 (0.04, 0.28)‡††	2,469	11	0.3 (0.1, 0.6)†	0.3666	0.1836	0.6 (0.1, 2.3)
Military veteran, age 20 years and older												
Yes	2,396	11	0.3 (0.1, 0.8)‡	2,674	7	0.2 (0.1, 0.6)‡††	1,909	6	0.2 (0.1, 0.8)§††	0.6475	0.8040	1.4 (0.3, 5.9)

*2011-2012 data only.
†Estimate may be unstable RSE >= 30% and < 40%.
‡Estimate may be unstable RSE >= 40% and < 50%.
§Estimate may be unstable RSE >= 50%.
††Estimate may be unstable based on <10 positive.
Abbreviation: NH, non-Hispanic.

Table 3. Age Specific Prevalence of HBV Vaccine Immunity (anti-HBs) by Selected Characteristics: NHANES 1999-2012

Characteristic	NHANES 1999-2006		NHANES 2007-2012		
	Sample Size	Prevalence, % (95% CI)	Sample Size	Prevalence, % (95% CI)	PR
Overall adjusted	29,828	21.7 (20.8, 22.7)	22,358	25.1 (24.1, 26.1)	1.16 (1.09, 1.23)
Overall unadjusted		22.2 (21.3, 23.1)		24.7 (23.6, 25.7)	
Age, years					
6-19	12,004	56.8 (54.2, 59.4)	6,344	44.4 (42.0, 46.9)	0.78 (0.73, 0.84)
20-49	9,465	17.0 (15.9, 18.1)	8,118	28.6 (27.0, 30.2)	1.69 (1.54, 1.84)
≥50	8,359	7.6 (6.9, 8.5)	7,896	8.7 (7.6, 10.1)	1.15 (0.96, 1.37)
Race and ethnicity					
White, NH	12,075	22.0 (20.9, 23.1)	8,973	25.2 (23.9, 26.6)	1.15 (1.07, 1.23)
6-19	3,058	57.0 (53.8, 60.1)	1,785	42.5 (38.8, 46.3)	0.75 (0.67, 0.83)
20-49	4,176	17.7 (16.3, 19.1)	3,330	29.7 (27.5, 32.0)	1.68 (1.50, 1.88)
≥50	4,841	7.7 (6.8, 8.7)	3,858	8.3 (7.0, 9.8)	1.08 (0.87, 1.33)
Black, NH	7,302	20.7 (19.3, 22.2)	4,865	25.0 (23.7, 26.4)	1.21 (1.11, 1.32)
6-19	3,830	53.6 (49.7, 57.5)	1,600	46.4 (43.5, 49.3)	0.86 (0.79, 0.95)
20-49	2,018	15.7 (13.9, 17.8)	1,619	28.2 (25.8, 30.7)	1.79 (1.54, 2.09)
≥50	1,454	7.3 (5.9, 9.0)	1,646	8.8 (7.3, 10.7)	1.21 (0.91 1.61)
Mexican American	8,094	19.7 (18.3, 21.1)	4,071	20.2 (18.9, 21.5)	1.03 (0.93, 1.13)
6-19	4,148	56.9 (53.2, 60.6)	1,585	46.9 (43.6, 50.3)	0.82 (0.75, 0.91)
20-49	2,398	12.2 (10.5, 14.1)	1,455	18.5 (16.1, 21.1)	1.52 (1.24, 1.85)
≥50	1,548	6.2 (4.6, 8.2)	1,031	6.4 (5.0, 8.0)	1.03 (0.71, 1.50)
Asian non-Hispanic*			929	35.6 (31.2, 40.2)	
6-19			237	42.8 (35.7, 50.2)	
20-49			421	40.3 (34.0, 47.0)	
≥50			271	22.6 (18.4, 27.4)	
Overall adjusted	29,828	21.7 (20.8, 22.7)	22,358	25.1 (24.1, 26.1)	1.16 (1.09, 1.23)
Overall unadjusted		22.2 (21.3, 23.1)		24.7 (23.6, 25.7)	
Age, years					
6-19	12,004	56.8 (54.2, 59.4)	6,344	44.4 (42.0, 46.9)	0.78 (0.73, 0.84)
20-49	9,465	17.0 (15.9, 18.1)	8,118	28.6 (27.0, 30.2)	1.69 (1.54, 1.84)
≥50	8,359	7.6 (6.9, 8.5)	7,896	8.7 (7.6, 10.1)	1.15 (0.96, 1.37)
Race and ethnicity					
White, NH	12,075	22.0 (20.9, 23.1)	8,973	25.2 (23.9, 26.6)	1.15 (1.07, 1.23)
6-19	3,058	57.0 (53.8, 60.1)	1,785	42.5 (38.8, 46.3)	0.75 (0.67, 0.83)
20-49	4,176	17.7 (16.3, 19.1)	3,330	29.7 (27.5, 32.0)	1.68 (1.50, 1.88)
≥50	4,841	7.7 (6.8, 8.7)	3,858	8.3 (7.0, 9.8)	1.08 (0.87, 1.33)
Black, NH	7,302	20.7 (19.3, 22.2)	4,865	25.0 (23.7, 26.4)	1.21 (1.11, 1.32)
6-19	3,830	53.6 (49.7, 57.5)	1,600	46.4 (43.5, 49.3)	0.86 (0.79, 0.95)
20-49	2,018	15.7 (13.9, 17.8)	1,619	28.2 (25.8, 30.7)	1.79 (1.54, 2.09)
≥50	1,454	7.3 (5.9, 9.0)	1,646	8.8 (7.3, 10.7)	1.21 (0.91 1.61)
Mexican American	8,094	19.7 (18.3, 21.1)	4,071	20.2 (18.9, 21.5)	1.03 (0.93, 1.13)
6-19	4,148	56.9 (53.2, 60.6)	1,585	46.9 (43.6, 50.3)	0.82 (0.75, 0.91)
20-49	2,398	12.2 (10.5, 14.1)	1,455	18.5 (16.1, 21.1)	1.52 (1.24, 1.85)
≥ 50	1,548	6.2 (4.6, 8.2)	1,031	6.4 (5.0, 8.0)	1.03 (0.71, 1.50)
Asian non-Hispanic*			929	35.6 (31.2, 40.2)	
6-19			237	42.8 (35.7, 50.2)	
20-49			421	40.3 (34.0, 47.0)	
≥50			271	22.6 (18.4, 27.4)	
Insurance status					
Insured	23,548	22.9 (21.9, 23.9)	17,526	25.5 (24.4, 26.5)	1.11 (1.05, 1.18)
6-19	9,439	57.7 (55.0, 60.3)	5,435	43.3 (40.8, 45.9)	0.75 (0.70, 0.81)
20-49	6,628	18.7 (17.4, 20.1)	5,324	30.6 (28.8, 32.4)	1.63 (1.49, 1.79)
≥50	7,481	7.6 (6.8, 8.5)	6,767	8.9 (7.7, 10.3)	1.18 (0.98, 1.41)
Medicare					
6-19					
20-49					
≥50	4,228	4.0 (3.2, 4.9)	3,482	4.4 (3.5, 5.5)	1.12 (0.82, 1.53)
Medicaid	3,974	20.5 (18.8, 22.3)	3,268	19.2 (17.7, 20.9)	0.94 (0.83, 1.05)
6-19	2,614	53.8 (49.6, 57.9)	1,879	39.4 (36.3, 42.5)	0.73 (0.66, 0.82)
20-49	756	11.5 (8.4, 15.5)	716	26.7 (23.2, 30.5)	2.33 (1.66, 3.26)
≥50	604	3.4 (2.1, 5.5)	673	3.8 (2.7, 5.3)	1.10 (0.61, 1.97)
Not insured	5,984	16.7 (15.2, 18.3)	4,797	23.5 (21.7, 25.5)	1.41 (1.25, 1.59)
6-19	2,422	51.9 (47.0, 56.8)	885	52.3 (47.2, 57.3)	1.01 (0.88, 1.15)

Table 3. *Continued*

Characteristic	NHANES 1999-2006		NHANES 2007-2012		
	Sample Size	Prevalence, % (95% CI)	Sample Size	Prevalence, % (95% CI)	PR
20-49	2,750	11.7 (10.1, 13.5)	2,789	23.1 (20.7, 25.8)	1.98 (1.64, 2.38)
≥50	812	7.8 (5.5, 11.0)	1,123	7.2 (5.2, 9.9)	0.92 (0.58, 1.48)
Heavy alcohol drinker					
Men	2,660	9.6 (8.5, 10.9)	2,592	17.0 (15.0, 19.3)	1.77 (1.49,2.10)
20-49	1,913	13.4 (11.7, 15.2)	1,764	23.8 (21.1, 26.6)	1.78 (1.49, 2.12)
≥50	747	4.5 (3.2, 6.4)	828	7.1 (4.6, 10.7)	1.57 (0.90, 2.72)
Women	2,685	16.0 (14.2, 18.0)	2,469	26.7 (24.0, 29.6)	1.67 (1.43, 1.96)
20-49	1,981	21.9 (19.4, 24.6)	1,775	37.0 (33.4, 40.7)	1.69 (1.45, 1.97)
≥50	704	7.3 (5.1, 10.4)	694	10.1 (7.2, 14.0)	1.38 (0.85, 2.25)
Military veteran					
Veterans	2,674	12.8 (10.9, 14.9)	1,909	18.2 (15.6, 21.0)	1.42 (1.15,1.75)
20-49	592	17.6 (13.7, 22.4)	379	32.4 (26.5, 39.0)	1.84 (1.35, 2.52)
≥50	2,082	6.0 (4.7, 7.6)	1,530	6.0 (4.2, 8.5)	1.01 (0.66, 1.54)

*2011-2012 data only
Abbreviation: NH, non-Hispanic.

federal agencies, released a strategic plan in 2014 that, in part, describes a comprehensive plan for achieving universal vaccination among vulnerable adults in the United States.[23] To achieve universal vaccination coverage among adults in the United States, the HHS strategic plan must be widely implemented.

The success of the HHS strategic plan is largely dependent on strengthening state and local viral hepatitis surveillance programs' capacity to identify and report viral hepatitis infections. Continued enhancements to surveillance methods will reduce under-reporting of viral hepatitis infections, which will result in readily reporting county and state-level prevalence estimates of HBV infections. NHANES is not an appropriate data source for estimating county- and state-specific prevalence of HBV infection owing to the small sample of persons, who tested positive for anti-HBc and HBsAg.

NHANES has been the primary source for measuring HBV prevalence among the US population.[3,19] The NHANES 2011-2012 over-sampling of non-Hispanic Asians has provided the first opportunity to estimate the prevalence of chronic HBV infection among non-Hispanic Asians. Prior to the release of these data, prevalence estimates of chronic HBV infection among non-Hispanic Asians were largely attributed to data collected in select US cities, or in highly endemic countries.[4,24-27] Given these better, more robust NHANES data, we can now directly estimate that 3.1%, or 427,000 Asians, both immigrants and citizens, were living with hepatitis B in the United States during 2011–2012. Compared to the 12.3% HBV prevalence imputed to Asian immigrants in other studies 4, direct measurements in the United States indicate much lower prevalence: 3.8% of Asian immigrants in Northern California; 5.6% of Chinese-Americans born in China in 2006-2008; 7.2% of

3,187 Chinese-Americans born in China and living in New York City, Minneapolis-St. Paul, and San Diego in 2012-2014; and 7.4% of 12,210 Asian and Pacific Islanders living in Hawaii in 2006-2008.[24-27] Future NHANES data, that over-sample Non-Hispanic Asians, should instill more statistical confidence that the true prevalence of chronic HBV infections among Non-Hispanic Asians, both immigrants and natural citizens, is closer to 3.1%.

In addition, the 16% increase in HBV vaccine-induced immunity among the U.S. noninstitutionalized population during 2007-2012 is the result of implementing universal HBV vaccination of infants—with "catch-up" vaccination of children and adolescents—starting in 1991.[28] The increase in HBV vaccine-induced immunity were largely adults of at least 20 years of age, primarily in those ages 20-49 years. The decrease in vaccine coverage among persons ages 6-19 years may be attributed to the natural decline in anti-HBs observed especially in those vaccinated in infancy compared with the slower decrease in anti-HBs in those vaccinated in adolescence and adulthood. In fact, almost all vaccinated persons, even those vaccinated in infancy and early childhood, seem to retain immune protection.[29] NHANES data cannot explain the contradictory trend of decreasing immunity in children ages 6-12 years and increasing immunity in adults ages 20-49 years. However, this might occur because of major efforts to vaccinate all infants and catch-up vaccination of children in the 1990s, whereas adults were vaccinated at more or less steady rates over the past 20 years[6] and thus nearer in time to, and less likely to have, substantial declines in anti-HBs at the time of NHANES 2007-2012 sampling.

These NHANES data are important from a public health perspective in providing insight into the large

percentages of chronically HBV-infected persons who remain undiagnosed (untested), not reported to health authorities, not referred for care for their hepatitis B infection, and not receiving therapy.[30] Examination of persons in the Chronic Hepatitis Cohort Study indicated that 21% of persons with chronic HBV infection in the community were never diagnosed with a HBV infection.[31] In terms of reasons that people are not tested, there is little known regarding why immigrants and refugees are not screened for hepatitis B, or why HBV-infected persons generally first need to have symptoms referable to the liver before they are tested.[32-34]

There are several limitations inherent in analyzing NHANES data. Some of the problems in estimating U.S.-resident persons of Asian and Pacific Island (API) descent as described in previous NHANES analyses[5] are now being addressed by specific sampling (and weighting) of APIs in recent surveys. Still, the sample size from 2011 and 2012 surveys is only 929 API in these analyses—and so the weighted estimate has relatively wide confidence intervals. Nonetheless, the percentage of foreign-born API with HBV infection is still in line with other recent direct measurements of HBV in resident Asian persons who are foreign born.[24-27] The estimate for foreign-born non-Hispanic blacks is based on a 9-person sample with a RSE >40%, so results should be interpreted with caution. Another limitation of any NHANES analysis is that it reflects sampling of the noninstitutionalized population of the United States and does not include homeless or incarcerated persons. For this latter group, there are approximately 2.2 million persons in U.S. jails and prisons, of which an estimated 2.0% (44,000) are HBV infected; the estimate from NHANES can be adjusted upward by at least another 44,000 persons.[35]

Finally, all surveys, including NHANES, suffer from a nonresponse bias, but nonresponse and poststratification adjustments performed by the NCHS adjust for, and largely remove, these as sources of bias.[36]

In summary, the recent NHANES with oversampling of non-Hispanic Asians indicates that during 2011-2012, there were approximately 850,000 Americans with chronic HBV infection (~400,000 non-Hispanic Asians). There has been decreasing prevalence of persons with serological evidence of past HBV infection (anti-HBc) and increasing immune protection (anti-HBs) in young persons vaccinated in infancy, given that they now age.

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