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Incidence and Prevalence of Sexually Transmitted Hepatitis B, United States, 2013 – 2018

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Abstract

Background: Sexual transmission of hepatitis B virus (HBV) is common in the United States. In 2008, an estimated 50% of HBV infections were attributed to sexual transmission. Among 21,600 acute infections that occurred in 2018, the proportion attributable to sexual transmissions is unknown.

Methods: Objectives of this study were to estimate incidence and prevalence of hepatitis B attributable to sexual transmission among the US population aged 15 years and older for 2013–2018. Incidence estimates were calculated for confirmed cases submitted to CDC from 14 states. A hierarchical algorithm defining sexually transmitted acute HBV infections as the absence of injection drug use among persons reporting sexual risk factors, was applied to determine proportion of hepatitis B infections attributable to sexual transmission nationally. NHANES public use data files were analyzed to calculate prevalence estimates of hepatitis B among US households and proportion attributed to sexual transmission was conservatively determined for HBV infected non-US born Americans who migrated from HBV endemic countries.

Results: During 2013–2018, an estimated 47,000 [95% CI (27,000, 116,000)] or 38.2% of acute HBV infections in the United States were attributable to sexual transmission. During 2013–2018, among the US non-institutionalized population, an estimated 817,000 [95% CI (613,000, 1,100,000)] persons aged 15 years and older were living with hepatitis B, with an estimated 103,000 [95% CI (89,000, 118,000)] infections or 12.6% attributable to sexual transmission.

Conclusion: These findings provide evidence sexually transmitted HBV infections remain a public health problem and underscore the importance of interventions to improve vaccination among at-risk populations.

Summary:

During 2013–2018, an estimated 47,000 [95% CI (27,000, 116,000)] or 38.2% of acute HBV infections in the United States were attributable to sexual transmission.

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Competing interest

The authors have declared that no competing interests exist

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Keywords

sexual transmission; hepatitis B virus; incidence; prevalence

INTRODUCTION

Hepatitis B, which is caused by the hepatitis B virus (HBV) is one of the leading causes of chronic liver disease, liver cirrhosis, and a major cause of liver cancer in the United States.¹ Hepatitis B is highly contagious and may be transmitted when an uninfected person comes in contact with the blood or body fluids of someone who is infected with HBV. In the United States common routes of HBV transmission include sexual contact with an infected person and unsafe injection drug use. In 2008, an estimated 50% of acute HBV infections that occurred in the United States were attributed to sexual transmission.² Risk factors associated with sexual transmission of HBV include, but are not limited to, men who have sex with men (MSM); having sexual contact with an HBV-infected person(s); having multiple sex partners; or engaging in unprotected sex with a person at high-risk of HBV infection.^{3, 4} HBV infection disproportionately affects MSM, and it is estimated that 20% of all new HBV infections in the United States are among MSM.⁵

In 2018, the Centers for Disease Control and Prevention (CDC) estimated that 21,600 [95% CI, (12,300, 52,800)] acute HBV infections occurred in the United States.⁴ Largely due to universal infant vaccination implemented in the United States beginning in 1991⁶, persons below the age of 30 have the lowest rate of HBV infection.⁴ Since 2003, adults ages 30–49 have had the highest rate of acute hepatitis B reported, with on average 2.3 infections for every 100,000 adults ages 30–49 in the United States.⁴ About 5–10% of adults infected with HBV will develop chronic HBV infection.⁷ Among the non-institutionalized population in the United States, it is estimated that 862,000 persons were living with chronic HBV infection, during 2011 – 2016.⁸

Sexually transmitted infections (STIs) are the most common infectious diseases in the United States. CDC estimates that 20 million new STIs from all pathogens occur each year in the United States, with acute HBV infections accounting for < 1.0% of all new STIs in the United States.² However, among the >20,000 acute HBV infections, unprotected sexual activity with an infected person may be an important mode of transmission.²⁻⁴ Previous reports have estimated that sexual transmission may be responsible for approximately half of acute HBV cases in the United States.^{2, 3} However, there are scarce studies in the literature over the past 20 years describing sexual transmission of HBV. Because the epidemiology of hepatitis B is changing with the widespread use of hepatitis B vaccine and concurrent increase in injection drug use related to the nation's opioid crisis, understanding those populations most at-risk for HBV infection through sexual exposure is important to inform prevention efforts.

The primary objective of this study is to estimate the incidence of hepatitis B attributable to sexual transmission among the US population aged 15 years and older. The secondary objective is to estimate the prevalence of persons living with chronic HBV in the United States who may have been exposed to HBV through sex with an infected person. Estimates

are generated overall and by selected demographic characteristics: sex, race/ethnicity, and country of birth.

METHODS

Incidence of Hepatitis B attributable to Sexual Transmission

We used two data sources to calculate the incidence of sexually transmitted HBV infections in the United States. First, to calculate the adjusted and the unadjusted incidence of HBV infections in the United States we analyzed hepatitis surveillance data records transmitted to CDC through an electronic platform, National Electronic Disease Surveillance System (NEDSS). Second, using risk factor data from 14 states funded for enhanced viral hepatitis surveillance by the CDC, we determined the proportion of reported cases of hepatitis B that were attributable to sexual transmission. We used a simplified hierarchical algorithm to define sexual transmission as a risk for HBV infection. The distribution is comprised of hierarchical mutually exclusive strata, defined by persons who did not report injection drug use but were likely to have sexually transmitted HBV if one of the following risk factors were reported: (1) sexual contact with an HBV infected person; (2) MSM; (3) multiple sexual partners; and (4) prior history of having been treated for a sexually transmitted disease 6-weeks to 6-months prior to their hepatitis B diagnosis. The number of cases assigned the sexual transmission risk divided by all cases with any risk factor information yielded the proportion that are sexually transmitted denoted as ST_{ACUTE} .

To account for the effects of underreporting, we adopted the adjustment factor developed by Klevens et al., wherein each confirmed case of acute HBV reported to CDC reflected 6.5 [95% bootstrap CI: (3.7, 15.9)] estimated acute hepatitis B infections in the United States.⁹ The estimated number of acute hepatitis B infections attributable to sexual transmission is the product of (adjusted number of acute hepatitis B infections in the United States) * (ST_{ACUTE}). Similarly, the incidence of sexually transmitted HBV infections reported to CDC was calculated by selected demographic and geographic characteristics: sex, age group, race and ethnicity, country of birth, region, and urban/rural status.¹⁰ We also calculated the incidence ratios of sexually transmitted acute HBV infection for each of the selected demographic and geographic characteristics.

Prevalence of Hepatitis B attributable to Sexual Transmission

National Health and Nutrition Examination Survey (NHANES) public use data files were analyzed to estimate the prevalence of chronic hepatitis B among US residents. The sampling plan for the survey is a stratified, multistage, probability cluster design of the noninstitutionalized civilian US household population. NHANES public use data files contain information about the health, nutritional status, and health behaviors of the sample of persons. Some subgroups of the population are not sufficiently represented in sampling cycles, as their numbers are too small for statistical robustness. To provide more stable estimates for subgroups, non-Hispanic Black/African Americans, Mexican Americans, and non-Hispanic Asian Americans were over-sampled.¹¹

NHANES participants were tested for the following HBV infection markers: total hepatitis B core antibody (anti-HBc), indicative of hepatitis B infection currently or sometime in the past (ever HBV infection); and hepatitis B surface antigen (HBsAg), indicative of persons with current HBV infection. Among those who tested positive for anti-HBc, persons who also tested positive for HBsAg were considered to have chronic HBV infection.

A weighted analysis of the respondent's chronic HBV infection status was conducted to estimate the prevalence of hepatitis B among the non-institutionalized population aged 15 and older, by selected characteristics. The overall weighted prevalence estimate expressed as a percentage was multiplied by the US non-institutionalized population total to convert the prevalence estimate to an equivalent number of persons living with chronic HBV infection.¹²

Risk factors for chronic HBV infection cannot be reliably obtained given the indeterminate duration between exposure and diagnosis of chronic infection. For chronic HBV infections among non-US born persons in the United States, the attributable risk factors vary considerably based on the local epidemiology in the country of birth and age at migration to the United States. The proportion of sexually transmitted HBV infections is dependent on the country of birth, but in HBV-endemic countries, most HBV transmission occurs perinatally or during childhood (i.e., not via sexual transmission).

To estimate the percentage of chronic HBV infections attributed to a sexual transmission, distinct estimates are calculated for US born vs non-US born persons. Given reports that up to 10% of persons with chronic HBV in HBV-endemic nations are infected during adulthood¹³, and estimates that only 5–10% of persons infected later in life progress to chronic infection¹⁴, we estimated that 1% of chronic HBV infections among non-US born persons in the United States are attributable to sexual transmission. In contrast, vertical transmission of HBV in the United States is rare — of the 4.0 million births reported in the United States during 2015, a small percentage (< 0.5%) were to women living with chronic HBV.¹⁵ Hence, we estimate the number of prevalent sexually transmitted HBV infections among persons aged 15 years as $\{(0.01 * \text{the estimated number of chronic HBV infections among non-US-born persons}) + (\text{ST}_{\text{ACUTE}} * \text{the estimated number of chronic HBV infections among US-born persons})\}$. SAS-callable SUDAAN was used to conduct the analysis of the NEDSS and NHANES data.¹⁶

RESULTS

Incidence of Hepatitis B attributable to Sexual Transmission

Among the 3,516 acute hepatitis B cases that had any risk factor information available from 14 states funded for viral hepatitis surveillance during 2013–2018, 1,342 (38.2%) met the criteria for sexually transmitted acute hepatitis B. The mutually exclusive, hierarchical distribution of sexual risk included 185 (5.3%) cases of sexual contact with an HBV-infected person; 109 (3.1%) who reported MSM; 979 (27.8%) who had multiple sexual partners; and 69 (2.0%) who had a prior history of treatment for a sexually transmitted disease within 6-weeks to 6-months prior to their hepatitis B diagnosis.

During 2013–2018, 19,032 confirmed cases of acute hepatitis B, among persons who were at least 15 years old, were reported to CDC. After adjusting for underreporting, an estimated 124,000 [95% CI (71,000, 303,000)] acute HBV infections occurred among persons ages 15 years and over in the United States, during 2013–2018. Of these, 47,000 [95% CI (27,000, 116,000)] (38.2%) were estimated to be sexually transmitted. The incidence of sexually transmitted HBV infections reported to CDC during 2013–2018, was 1.64 (standard error (s.e.) = 0.04) times greater for males, of which 37.6% (or n=4,420) were attributed to sexual transmission (Table 1), compared to females. When compared to adults who were at least 50 years old, the incidence of sexually transmitted HBV infections reported to CDC during 2013–2018, was 2.14 (s.e. =0.07) times greater for adults aged 30–39 years and 2.67(s.e. =0.08) times greater for adults ages 40–49 years (Table 1). We estimated that 33.1% and 41.5% of acute HBV infections among adults aged 30–39 and adults ages 40–49 years, respectively, were attributed to sexual transmission (Table 1).

Of the four race/ethnicity categories included in the analysis, the African American non-Hispanic population has the largest percentage of acute HBV infections due to sexual transmission; with 68.1% of acute HBV infections being due to sexual transmission. Approximately 34.4% of acute HBV infections among the White non-Hispanic population was attributed to sexual transmission. Among the 7,254 confirmed acute cases of HBV attributed to sexual transmission during 2013–2018, the White and African American non-Hispanic populations accounted for 76.4% (5,540) of the sexually transmitted cases.

Of the four geographic regional categories of interest, the Southern region of the United States has the largest percentage of acute HBV infections due to sexual transmission; with 46.3% of acute HBV infections attributable to sexual transmission. Thirty percent of acute HBV infections among the population residing in the Midwestern region, were due to sexual transmission. Among the estimated 7,254 confirmed acute cases of HBV attributed to sexual transmission, during 2013–2018, populations residing in the Southern and Midwestern regions of the United States accounted for 90.3% (6,551) of cases. The proportion of sexually transmitted HBV infection among persons residing in rural communities was 25.5% (Table 1).

Prevalence of Hepatitis B attributable to Sexual Transmission

During 2013–2018, among the US non-institutionalized population aged 15 years, an estimated 817,000 [95% CI (613,000, 1,100,000)] or 0.3% [95% CI (0.2, 0.4)] persons were living with chronic hepatitis B (Table 2). Among the 817,000 Americans with chronic hepatitis B, an estimated 437,000 [95% CI (332,000, 538,000)] (or 53.5%) were men. Non-US born persons accounted for 563,000 [95% CI (445,000, 657,000)] (or 68.9%) of the population with chronic hepatitis B, of whom 69.4% were Asian American, and 13.8% were African American.

Among the 817,000 persons aged 15 years with chronic hepatitis B during 2013–2018, an estimated 103,000 [95% CI (89,000, 118,000)] or about 12.6% of the chronic HBV infections were attributed to sexual transmission. Among the 103,000 Americans with chronic hepatitis B attributed to sexual transmission, we estimate that: 5.4% were non-US

born Americans. Overall, the African American non-Hispanic population constituted 49.3% of the population with chronic hepatitis B attributed to sexual transmission, (Table 2).

DISCUSSION

The findings in this study suggest that sexual transmission of HBV is common in the United States and remains a public health problem despite availability of safe and highly effective vaccines to prevent HBV infection. Among the estimated 124,000 incident HBV infections that occurred in the United States during 2013–2018, we estimate that 38.2% were attributable to sexual transmission. Although most HBV infections acquired in adolescence and adulthood do not progress to chronicity, the burden of sexually transmitted chronic HBV infection remains a concern due to the associated morbidity of disease and potential for ongoing transmission.

The Advisory Committee on Immunization Practices (ACIP) recommends administration of hepatitis B vaccine for all persons at risk for HBV infection by sexual exposure, including sex partners of hepatitis B surface antigen-positive persons, sexually active persons who are not in a long-term, mutually monogamous relationship, persons seeking evaluation or treatment for a sexually transmitted infection, and men who have sex with men.⁶ Understanding the epidemiology of sexually transmitted HBV infections is important for public health officials to assess the burden of disease, develop strategic plans, and assess the effects of ongoing prevention campaigns. This study suggests that a higher proportion of incident HBV infections are sexually transmitted in urban areas and in the South, and that sexual transmission was the primary route of HBV transmission for incident infections among the African American non-Hispanic and Hispanic populations. These findings should be used to guide vaccination efforts in disproportionately affected populations.

Estimating the incidence and prevalence of sexually transmitted HBV infection can be challenging because the clinical manifestations of HBV infection become apparent long after exposure, most infections do not progress to chronicity, and the delayed diagnosis of chronic HBV infection makes ascertainment of risk factors for chronic HBV infection unreliable. We used risk factor data from hepatitis B case reports to determine the proportion of sexually transmitted acute HBV infection in the United States. Although HBV can be transmitted in many ways, the mode of transmission is dependent on the prevailing epidemiology and other factors, such as timing of introduction of hepatitis B vaccine and programs to stop transmission of sexually transmitted infections.

In countries with intermediate and high HBV endemicity, HBV transmission mainly occurs during infancy and early childhood through vertical or horizontal transmission. In one estimate, approximately 90% of infections occur before 10 years of age, leaving many adults immune from infection later in life.¹³ Of adolescents and adults who acquire acute HBV infection, only 5–10% will develop chronic infection.¹⁴ In the United States, the majority of chronic HBV infections are identified among non-US born persons. We believe most (up to 90%) of the non-US born persons with chronic HBV infection may have been infected during infancy and early childhood. Hence, we make a conservative assumption that among

non-US born chronic HBV infections in the United States, only 1% are attributable to sexual transmission.

The estimated proportion of sexually transmitted acute HBV infections assumed by Satterwhite et al was 50.0% and based on a study conducted by Goldstein et al (2002) of acute hepatitis B cases in the United States. Specifically, the findings of Goldstein et al were based on surveillance data collected among cases reported in four US counties: Jefferson (Birmingham), Alabama; Denver, Colorado; Pinellas (St. Petersburg), Florida; and Pierce (Tacoma), Washington, between 1982 and 1998. In contrast, the current study estimates the proportion of acute HBV infections attributable to sexual transmission is 38.2%. There may be several possible explanations for the differences in these two estimates. First, Goldstein et al. used data from four sentinel counties which may not be representative of the 14 states used in the current study. Second, although we applied a similar hierarchical algorithm as Goldstein et al., differences in methodology could account for differences in estimates of sexual transmission. Lastly, the current study may reflect a true change in the epidemiology of acute HBV since the study conducted by Goldstein et al occurred in the 1980-1990s. In recent years, the United States has observed an increase in injection drug use concurrent with the nation's opioid crisis, which has been attributed to increases in hepatitis C. A higher proportion of acute HBV may also be attributed to injection drug use in recent years, but additional analysis is needed to further explore this potential association.

There are a few limitations with this analysis. The timing of acquisition of infection relative to immigration to the United States is difficult to determine. It is also possible that non-US born persons may not have equal likelihood to participate in NHANES, thus resulting in underestimating of prevalence in this population. Finally, all surveys, including NHANES, suffer from nonresponse bias, but nonresponse and poststratification adjustments performed by the National Center for Health Statistics adjust for, and largely remove, bias due to non-responders. Lastly, the underrepresentation of individuals at high risk for HBV infection (e.g., incarcerated persons) from the NHANES sample, may result in an underestimation of chronic HBV prevalence.

In conclusion, the findings in this study provide further evidence that sexual transmission of HBV infection remains an important public health problem in the United States and that disparities in sexual transmission of HBV infection remain. Targeted public health strategies are needed to improve hepatitis B vaccine coverage among at-risk adults and prevent sexual transmission of HBV among disproportionately affected populations.

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ACRONYMS AND ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
anti-HBc	Hepatitis B core

CDC	Centers for Disease Control and Prevention
CI	Confidence interval
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
IR	Incidence ratio
MSM	Men who have sex with men
NHANES	National Health and Nutrition Examination Survey
NEDSS	National Electronic Disease Surveillance System
SE	Standard error
ST_{ACUTE}	Proportion of acute HBV infections attributed to sexual transmission
ST_{CHRONIC}	Proportion of chronic HBV infections attributed to sexual transmission
US	United States of America

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Unadjusted Number and Rate of Acute Hepatitis B Cases, among persons ages 15 years and older, United States, 2013 – 2018

Table 1.

Characteristic	Acute Cases ^a	Rate per 100,000	IR, (SE)	ST _{ACUTE}	Acute Cases ^b	Rate per 100,000	IR, (SE)
Overall	19,032	1.2	N/A	38.2%	7,270	0.5	N/A
Sex							
Male	11,754	1.5	1.71 (0.03)	37.6%	4,420	0.6	1.64 (0.04)
Female	7,211	0.9	Ref	39.3%	2,834	0.4	Ref
Age Group (years)							
15-29	1,866	0.5	0.55 (0.02)	31.2%	582	0.1	0.41 (0.02)
30-39	5,831	2.3	2.70 (0.05)	33.1%	1,930	0.8	2.14 (0.07)
40-49	5,646	2.3	2.69 (0.05)	41.5%	2,343	1.0	2.67 (0.08)
50+	5,689	0.9	Ref	41.9%	2,384	0.4	Ref
Race/Ethnicity							
Asian/Pacific Islander	344	0.4	0.80 (0.05)	36.1%	124	0.1	0.54 (0.05)
Non-Hispanic, Black	2,296	1.2	2.58 (0.09)	68.1%	1,419	0.7	2.97 (0.14)
Non-Hispanic, White	11,981	1.2	2.59 (0.08)	34.4%	4,121	0.4	1.67 (0.07)
Hispanic	1,143	0.5	Ref	53.5%	612	0.2	Ref
Region^c							
Southern	11,682	2.0	3.18 (0.08)	46.3%	5,409	0.9	4.23 (0.18)
Western	1,827	0.5	0.79 (0.03)	11.6%	212	0.1	0.27 (0.02)
Midwestern	3,807	1.2	1.84 (0.05)	30.0%	1,142	0.3	1.58 (0.08)
Northeastern	1,716	0.6	Ref	34.8%	597	0.2	Ref
Rural/Urban							
Rural geographic area	3,342	2.3	2.18 (0.04)	25.5%	852	0.6	1.39 (0.05)
Urban geographic area	13,605	1.1	Ref	40.0%	5,442	0.4	Ref

Abbreviations: IR, incident rate; SE, standard error; ST_{ACUTE}, proportion of acute HBV infections attributed to sexual transmission.

^aUnadjusted number and rate of Hepatitis B infections in the United States, all means of transmission.

^bUnadjusted number and rate of Hepatitis B infections in the United States, attributed to sexual transmission.

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The 4 regions of residence used in this report are defined by the US Census Bureau as follows:

- Northeastern: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont
- Midwestern: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin
- Western: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming
- Southern: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia

Estimated Prevalence of Chronic Hepatitis B Virus Infection (Ages 15 or older), by Selected Characteristics: NHANES 2013 - 2018

Table 2.

Characteristic	Sample Size	Weighted Prevalence % (95% CI)	Weighted Column ^b % (95% CI)	Chronic HBV n (95% CI)	ST _{CHRONIC}	Chronic HBV (STI) n (95% CI)
Overall	17,411	0.32% (0.24%, 0.41%)	0.32% (0.24%, 0.41%)	817,000 (613,000, 1,100,000)	n/a	103,000 (89,000, 118,000)
Place of Birth						
Non-US Born						
Non-US Born	5,071	1.24% (0.92%, 1.66%)	68.9% (54.44%, 80.44%)	563,000 (525,000, 598,000)	1.0%	5,600 (5,300, 6,000)
United States	12,340	0.12% (0.07%, 0.20%)	31.1% (19.56%, 45.56%)	254,000 (219,000, 292,000)	38.2%	97,000 (84,000, 112,000)
Place of Birth, Gender						
Non-US Born						
Men	2,407	1.40% (0.89%, 2.18%)	54.9% (40.7%, 68.4%)	309,000 (229,000, 385,000)	1.0%	3,100 (2,300, 3,900)
Women	2,664	1.09% (0.76%, 1.56%)	45.1% (31.6%, 59.3%)	254,000 (178,000, 334,000)	1.0%	2,500 (1,800, 3,300)
United States						
Men	5,989	0.12% (0.07%, 0.22%)	50.3% (23.0%, 77.3%)	128,000 (58,000, 196,000)	37.6%	48,000 (22,000, 74,000)
Women	6,351	0.11% (0.04%, 0.30%)	49.7% (22.7%, 77.0%)	126,000 (58,000, 196,000)	39.3%	49,000 (23,000, 77,000)
Place of Birth, Race/Ethnicity ^a						
Non-US Born						
African American, NH	376	2.57% (1.33%, 4.91%)	13.81% (7.23%, 24.78%)	78,000 (41,000, 140,000)	1.0%	780 (410, 1,400)
Asian American, NH	1,753	3.30% (2.61%, 4.18%)	69.40% (55.67%, 80.38%)	391,000 (313,000, 453,000)	1.0%	250 (180, 330)
United States						
African American, NH	3,283	0.32% (0.18%, 0.57%)	31.75% (14.85%, 55.38%)	81,000 (38,000, 141,000)	61.8%	50,000 (24,000, 87,000)
Asian American, NH	360	n/a	n/a	n/a	n/a	n/a

Abbreviations: NHANES, National Health and Nutrition Examination Survey; CI, confidence interval; STI, sexually transmitted infection; NH, non-Hispanic; ST_{CHRONIC}, proportion of chronic HBV infections attributed to sexual transmission.

^aChronic HBV prevalence estimates were unreliable due to the small sample of positive anti-HBc results, and not reported for the following populations defined by (race/ethnicity) (U.S. Born status): American Indian/Alaskan Native, non-Hispanic White, and Hispanic.

^bThe NHANES examination sampling weights were used to estimate the prevalence of chronic HBV among the US non-institutionalized population, ages 15 and older, and the column proportion of the chronic HBV infected population, for each characteristic of interest.

^cThis column contains the estimated number of chronic HBV infections attributable to sexual transmission.