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Prevalence of Hepatitis B Virus Infection Among US Adults Aged 20–59 Years With a History of Injection Drug Use: National Health and Nutrition Examination Survey, 2001–2016

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Background. Hepatitis B virus (HBV) can transmit through needle sharing. The national HBV infection prevalence in persons who inject drugs remains ill-defined. We estimated the prevalence of total HBV core antibody (anti-HBc) positivity, indicating a previous or ongoing HBV infection, among adults aged 20–59 years with an injection drug use (IDU) history. We compared select characteristics by anti-HBc status.

Methods. Using 2001–2016 National Health and Nutrition Examination Survey data, we calculated the anti-HBc positivity prevalence among adults with IDU histories and among the general US population. For adults with IDU histories, we compared sex, age group, birth cohort, race/ethnicity, health insurance coverage, and hepatitis A immunity by anti-HBc status. Using marginal structural models, we calculated model-adjusted prevalence rates and ratios to determine the characteristics associated with anti-HBc positivity among adults with IDU histories.

Results. From 2001–2016, the anti-HBc positivity prevalence was 19.7% (95% confidence interval [CI] 16.0–24.0%) among those with IDU histories, compared with 4.6% (95% CI 4.3–5.0%) in the general population. The HBV surface antigen positivity prevalence was 0.4% (95% CI 0.3–0.5%) in the general population. Among adults with IDU histories, 19.8% reported prior-year IDU and 28.5% had a hepatitis A immunity.

Conclusions. One-fifth of adults with IDU histories had a previous or ongoing HBV infection: a rate over 4 times higher than the prevalence in the general population. One-fifth of adults with IDU histories reported prior-year use. Programs promoting safe IDU practices, drug treatment, and hepatitis A and B vaccinations should be key components of viral hepatitis prevention.

Keywords. hepatitis B virus; injection drug use; NHANES; prevalence; United States.

From 2007–2012, approximately 10.8 million persons aged 6 years and older in the noninstitutionalized US population were total hepatitis B core antibody (anti-HBc) positive, indicating a previous or ongoing hepatitis B virus (HBV) infection [1]. Among persons positive for anti-HBc in 2011–2012, approximately 847 000 were positive for an HBV surface antigen (HBsAg), indicating a current HBV infection [1]. After a large national decline in newly reported, acute HBV infection cases from 2000–2010 and some plateauing from 2011–2014, acute HBV infection cases increased by 21% from 2014–2015, then decreased by 5% from 2015–2016 [2]. Regionally, increases have been most marked in rural areas of the United States, especially in the Appalachian states of Kentucky, Tennessee, and West Virginia [3], with a 114% increase in acute HBV infection rates between 2006–2013 and more prominent increases after 2010 for non-Hispanic Whites and adults aged 30–39 years [3].

The Centers for Disease Control and Prevention's (CDC's) viral hepatitis surveillance data indicate that about one-third of people with newly reported, acute HBV infections and with complete risk information, reported injection drug use (IDU) in 2016 [2]. Results from community-based studies in San Francisco, California, and Seattle, Washington, reported characteristics significantly associated with HBV infection among persons who inject drugs (PWID), including older age, a history of male-to-male sex, a history of multiple sexual partners, daily or frequent IDU, and the number of years injecting drugs [4, 5].

National drug use survey data reported increases in the prior-month use of illicit drug prevalences in large, small, and

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nonmetropolitan areas from 2003–2014, while national mortality data reported increases in drug overdose mortality rates in all age groups from 1999–2015 [6]. Despite the 1982 and 1996 Advisory Committee on Immunization Practices (ACIP) recommendations to vaccinate at-risk groups, including PWID, against HBV and hepatitis A virus (HAV) infections, respectively [7, 8], the National Health Interview Survey indicated self-reported vaccination coverage in 2016 was 25% for hepatitis B and 10% for hepatitis A among all US adults, regardless of risk factors [9]. In 2016, the ACIP clarified that persons with HBV infections should also be considered for hepatitis A vaccination [10, 11]. Assessing HAV and HBV immunity among persons with IDU histories, as well as HAV immunity among HBV-infected persons with IDU histories, is pertinent to monitoring ACIP recommendation adherence.

In 1996, self-reported hepatitis B vaccination coverage was 10% in 8 needle exchange sites in San Francisco, California, among PWID aged ≥30 years [5]. In 2010, clinic-based hepatitis B vaccination coverage in local syringe exchange programs in Pierce County, Washington, was 27% [12]. Due to the national increase in illicit drug use, including injectable drugs [6], and regional increases in IDU-related HBV infections [3], HBV infection transmission may continue to rise among susceptible PWID, as HBV infection can be transmitted through contaminated needles and other injection drug paraphernalia [13].

Previous studies have described characteristics of HBV-infected PWID among select US regions and populations [4, 5, 14, 15]; however, the literature regarding both national HBV infection prevalence estimates among PWID and characteristics of nationally representative HBV-infected PWID is lacking. Characterizing this group is further hindered because national viral hepatitis surveillance data do not reliably capture IDU information across jurisdictions. In this study, we determined the anti-HBc positivity prevalence among US adults with IDU histories and among the general adult population, using a nationally representative US sample. Among adults with IDU histories, we compared socio-demographic characteristics, HAV immunity statuses, and HBV infection statuses to determine those characteristics associated with anti-HBc positivity.

METHODS

Data Source

We used data from the National Health and Nutrition Examination Survey (NHANES), retrieved from public-use data files on the CDC's National Center for Health Statistics website [16]. NHANES is a nationally representative survey that uses a complex, stratified, multistage probability cluster sampling design to reach approximately 5000 randomly selected persons annually from the noninstitutionalized US population [16]. In-home computer-assisted personal interviews were used to collect information on socio-demographic variables, health and nutritional statuses, and health behaviors. Physical examinations and biological tests were conducted in the Mobile Examination Center. We acquired data from eight 2-year survey cycles, conducted from 2001–2016.

Study Population/Measures

We limited our study population to persons aged 20–59 years who participated from January 2001–December 2016, since the eligible sample for the NHANES drug use questionnaire for all survey years included this age range. We examined sex, age group, year of birth, race/ethnicity, health insurance, IDU history, and serologic data for HAV immunity and HBV infection status.

Persons with IDU histories were defined as those who responded "yes" to either the question "have you ever used a needle to take street drugs?" in 2001–2004 or "have you ever, even once, used a needle to inject a drug not prescribed by a doctor?" in 2005–2016. Among respondents reporting IDU histories, we assessed the number of years since the last injection, age of the first injection (2005–2016), estimated lifetime number of injections, and injection frequency. Recent IDU was defined as having injected a drug within the prior year.

From 1999–2010, race/ethnicity were categorized as non-Hispanic (NH) White, NH Black, Hispanic, and NH Other (all other non-White/non-Black race/ethnicity categories, including Asians/Pacific Islanders). From 2011–2016, NH Asians were oversampled, allowing this group to be distinguished from the NH Other race/ethnicity group. The year of birth was calculated by subtracting the participant's age at the time of survey participation from the first year of the 2-year survey cycle. We categorized the years of birth into 2 levels—during 1945–1965 and before 1945 or after 1965—because blood-borne infection prevalences, such as of hepatitis C virus (HCV) infections, are disproportionally higher among US persons born between 1945–1965 (the Baby Boomer cohort) [17–19].

Laboratory Testing

Laboratory testing, including hepatitis testing, was performed on participants who provided written, informed consent. Hepatitis A immunity was determined by HAV antibody (anti-HAV) positivity. Participants were classified by the standard hepatitis B serological interpretation profiles defined by the CDC [20]. The presence of a previous or ongoing HBV infection, including an acute, chronic, or resolved HBV infection, was determined by anti-HBc positivity. A finer breakdown of HBV infection status included 4 categories: (1) currently infected (HBsAg positivity); (2) susceptible (negative for all HBV infection markers: anti-HBc, HBsAg, and HBV surface antibody [anti-HBs]); (3) immune from past infection/isolated anti-HBc positive (either negative for HBsAg and positive for anti-HBc and anti-HBs, or positive for anti-HBc and negative for all other HBV laboratory markers); and (4) immune from vaccination (negative for HBsAg and total anti-HBc and

positive for anti-HBs). NHANES data files reported anti-HBs results qualitatively, where anti-HBs levels ≥10 mIU/mL were considered protective or positive and levels <10 mIU/mL were considered negative. Because of changes in the HCV testing protocol in 2013, we were unable to reliably examine HCV antibody and HCV RNA levels in our study using combined data from 2001–2016 [21]. More information about the NHANES survey design, content, and laboratory testing can be found at https://www.cdc.gov/nchs/nhanes/about_nhanes.htm.

Statistical Analysis

We calculated weighted prevalence estimates of selected characteristics among adults aged 20–59 years with IDU histories and among the general US population from 2001–2016. A sub-analysis was conducted among adults who reported no IDU history. Weighted prevalence estimates for characteristics were calculated among adults with an IDU history, stratified by anti-HBc status (anti-HBc positive vs anti-HBc negative). We extrapolated population estimates by multiplying weighted prevalence estimates by the NHANES current population survey totals from 2001–2010 and the American Community Survey totals from 2011–2016 (n = 163 425 850), determined by synthetic estimations of current population survey and American Community Survey counts using weighted NHANES prevalence estimates [22]; 95% confidence intervals (CIs) were calculated using Clopper-Pearson CIs. Rao-Scott Chi-square tests were used to determine statistical comparability between characteristics, by anti-HBc status, among adults with IDU histories.

We used marginal structural models to calculate HBV infection prevalence rates and model-adjusted prevalence ratios to determine those characteristics associated with anti-HBc positivity among adults with IDU histories. Multicollinearity was assessed using Pearson correlation coefficients and variance inflation factors (VIFs). A commonly used VIF cutoff is 5.0; however, 1 study found that VIFs less than 5.0 could impact epidemiologic results [23]. We selected a conservative VIF cutoff value of 2.0. Therefore, the model for year of birth (VIF 2.33) excluded an adjustment by age group (VIF 2.36). Independent models were generated for all variables, adjusting for sex, age group, race/ethnicity, and health insurance coverage, as appropriate. P values <.05 were considered statistically significant. Prevalence estimates were not displayed if the numerator count was less than 15, due to the instability of those rates. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC) and SAS-Callable SUDAAN, Release 10.0 (Research Triangle Institute, Research Triangle Park, NC).

RESULTS

Characteristics of US Adults Aged 20–59 Years

From 2001–2016, 29 529 adults aged 20–59 years were sampled, interviewed, and medically examined in NHANES (Table 1). Of these, 26 785 (90.7%) were tested for anti-HBc and 20 431 (69.2%) responded to the question assessing IDU history. Approximately one-half were female (50.8%), aged 20–39 years (49.4%), and born before 1945 or after 1965 (57.9%). Overall, 12 183 (65.1%) were NH White and 21 027 (77.6%) had health insurance. The estimated IDU prevalence was 3.0% (95% CI 2.6%–3.4%), representing 4.9 million (range 4.3–5.6 million) adults with IDU histories.

Characteristics of US Adults With an Injection Drug Use History

Among adults with an IDU history, 321 (53.3%) were born during 1945–1965, 351 (78.8%) were NH White, and 338 (62.4%) had health insurance. Additionally, 94 (19.8%) reported recent or current IDU, 378 (85.1%) reported first injecting drugs before the age of 30 years (from NHANES 2005–2016), 126 (25.0%) reported ≥100 lifetime injections, and 293 (73.3%) reported injecting drugs ≥1 times a week, with 194 (44.5%) injecting drugs ≥1 times a day.

Hepatitis B Virus Infection Prevalences Among US Adults With an Injection Drug Use History and the General Population

From 2001–2016, the anti-HBc positivity prevalence among adults aged 20–59 years was 4.6% (95% CI 4.3–5.0%) in the general population, representing 7.6 million (range 7.0–8.2 million) persons, compared to 19.7% (95% CI 16.0–24.0%) for those with an IDU history, representing 970 000 (range 789 000–1.2 million) persons (Table 1). The current HBV infection (HBsAg+) prevalence in the general population was 0.4% (95% CI 0.3–0.5%), representing 686 000 (range 557 000–856 000) persons. The current HBV infection prevalence among persons with an IDU history was considered unstable, due to the small sample size of HBsAg+ persons with IDU histories.

The estimated prevalence of immunity from past infection/isolated core anti-HBc positivity was 4.8% (95% CI 4.4–5.3%) for adults in the general US population, versus 22.0% (95% CI 18.1–26.4%) among those with an IDU history. The prevalence of vaccine-induced immunity was 21.7% (95% CI 20.8–22.5%) for adults in the general US population, versus 14.7% (95% CI 11.0–19.4%) for those with an IDU history. The prevalence of HBV susceptibility was 73.1% (95% CI 72.2–74.0%) for adults in the general US population, versus 62.3% (95% CI 56.9–67.3%) for those with an IDU history. The anti-HAV prevalence was 31.3% (95% CI 29.9–32.6%) for adults in the general US population, versus 28.5% (95% CI 23.7–33.9%) for those with an IDU history.

The following characteristics were more frequent among adults with IDU histories who were anti-HBc positive versus anti-HBc negative: being 50–59 years old (56.7% vs 25.5%, respectively), being born during 1945–1965 (79.5% vs. 46.8%, respectively), being of NH Black race/ethnicity (16.6% vs. 5.0%, respectively), having health insurance (73.1% vs. 59.6%, respectively), being anti-HAV positive (40.6% vs. 25.7%, respectively),

Table 1. Prevalence Estimates of Select Characteristics Among Adults in the General US Population and Adults With an Injection Drug Use History

	Overall		Reported IDU History	
Characteristic	n	Weighted % (95% CI)[a]	n	Weighted % (95% CI)[a]
Overall[b]	29 529	…	561	3.0 (2.6–3.4)
Sex				
Sex known	29 529 (100.0%)	…	561 (100.0%)	…
Male	14 132	49.2 (48.7–49.7)	369	67.3 (63.0–71.4)
Female	15 397	50.8 (50.3–51.3)	192	32.7 (28.6–37.0)
Age group, years				
Age known	29 529 (100.0%)	…	561 (100.0%)	…
20–39	15 447	49.4 (48.4–50.5)	194	38.1 (33.1–43.3)
40–49	7486	26.6 (25.827.4)	170	30.1 (25.0–35.7)
50–59	6596	24.0 (23.1–24.8)	197	31.9 (26.6–37.7)
Year of birth				
Year of birth known	29 529 (100.0%)	…	561 (100.0%)	…
During 1945–1965	11 410	42.1 (41.1–43.2)	321	53.3 (47.7–58.9)
Before 1945 or after 1965	18 119	57.9 (56.8–58.9)	240	46.7 (41.1–52.3)
Race/ethnicity				
Race/ethnicity known	29 529 (100.0%)	…	558 (99.4%)	…
Non-Hispanic White	12 183	65.1 (62.6–67.5)	351	78.8 (74.8–82.3)
Non-Hispanic Black	6379	12.1 (10.8–13.5)	90	8.1 (6.0–10.8)
Hispanic	7984	15.5 (13.7–17.3)	88	7.9 (6.1–10.1)
Non-Hispanic Asian[b]	1648	2.3 (1.9–2.7)	DI	…
Non-Hispanic other	1335	5.1 (4.6–5.7)	29	5.1 (3.3–7.8)
Health insurance status				
Health insurance status known	29 400 (99.6%)	…	557 (99.3%)	…
Covered	21 027	77.6 (76.5–78.6)	338	62.4 (56.7–67.8)
Not covered	8373	22.4 (21.4–23.5)	219	37.6 (32.2–43.3)
Hepatitis A immunity				
Anti-HAV result known	26 600 (90.1%)	…	492 (87.7%)	…
Anti-HAV positive	10 898	31.3 (29.9–32.6)	170	28.5 (23.7–33.9)
Anti-HAV negative	15 673	68.6 (67.3–70.0)	322	71.5 (66.1–76.3)
Anti-HAV indeterminate	29	0.1 (0.1–0.2)	0	…
Anti-HBc result				
Result known	26 785 (90.7%)	…	522 (93.0%)	…
Positive	1652	4.6 (4.3–5.0)	127	19.7 (16.0–24.0)
Negative	25 133	95.4 (95.0–95.7)	395	80.3 (76.0–84.0)
HBV infection status[c]				
HBV infection status known	23 646 (80.1%)	…	470 (83.8%)	…
Current infection	156	0.4 (0.3–0.5)	DI	…
Susceptible	17 139	73.1 (72.2–74.0)	279	62.3 (56.9–67.3)
Immune from past infection/isolated anti-HBc positive	1493	4.8 (4.4–5.3)	121	22.0 (18.1–26.4)
Immune from vaccination	4858	21.7 (20.8–22.5)	64	14.7 (11.0–19.4)
IDU history				
IDU history known	20 431 (69.2%)	…	561 (100.0%)	…
Yes	561	3.0 (2.6–3.4)	561	…
No	19 870	97.0 (96.6–97.4)	0	…
Number of years since last injection				
Number of years since last injection known	446 (79.5%)	…	446 (79.5%)	…
0–1 year	94	19.8 (15.4–25.1)	94	19.8 (15.4–25.1)
2–10 years	147	33.1 (27.6–39.1)	147	33.1 (27.6–39.1)
11+ years	205	47.1 (40.1–54.3)	205	47.1 (40.1–54.3)
Age of first injection[d]				
Age of first injection known	453 (80.7%)	…	453 (80.7%)	…
<20 years	145	33.3 (27.6–39.5)	145	33.3 (27.6–39.5)
20–29 years	233	51.8 (45.9–57.7)	233	51.8 (45.9–57.7)
30+ years	75	14.9 (11.0–19.9)	75	14.9 (11.0–19.9)
Lifetime number of injections				
Lifetime number of injections known	454 (80.9%)	…	454 (80.9%)	…

Table 1. Continued

Characteristic	Overall		Reported IDU History	
	n	Weighted % (95% CI)[a]	n	Weighted % (95% CI)[a]
<20 times	214	49.5 (43.1–55.9)	214	49.5 (43.1–55.9)
20–99 times	114	25.5 (20.7–31.0)	114	25.5 (20.7–31.0)
100+ times	126	25.0 (20.4–30.3)	126	25.0 (20.4–30.3)
Injection frequency				
IDU frequency known	392 (69.9%)	…	392 (69.9%)	…
≥Once a day	194	44.7 (38.7–50.8)	194	44.7 (38.7–50.8)
Once a week	99	28.6 (24.3–33.4)	99	28.6 (24.3–33.4)
Once a month	99	26.7 (21.4–32.8)	99	26.7 (21.4–32.8)

Data are among adults aged 20–59 years, United States, NHANES 2001–2016.

Abbreviations: anti-HBc, total HBV core antibody; anti-HBs, hepatitis B surface antibody; CI, confidence interval; DI, data insufficient (sample size between 1 to 14); HAV, hepatitis A virus; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IDU, injection drug use; NHANES, National Health and Nutrition Examination Survey.

[a]Denominator excluded "don't know," "refused," "unknown," and "missing" responses.

[b]Non-Hispanic Asian data available only from 2011–2016.

[c]HBV infection statuses are defined as: current infection, meaning positive for HBsAg; susceptible, meaning negative for HBsAg, anti-HBc, and anti-HBs; immune from past infection/isolated anti-HBc positive, meaning either negative for HBsAg and positive for anti-HBs and total anti-HBc, or positive for anti-HBc and negative for all other HBV laboratory markers; and immune from vaccination, meaning positive for anti-HBs and negative for anti-HBc and HBsAg.

[d]Age of first injection data only available from 2005–2016.

and injecting ≥100 times over a lifetime (33.0% vs. 21.9%, respectively; Table 2; $P < .05$).

Adjusted Prevalence Ratios of Hepatitis B Virus Core Antibody Positivity Among Adults With an Injection Drug Use History

Among adults with IDU histories, crude and adjusted anti-HBc positivity prevalence rates were higher for those aged 40–59 years versus those aged 20–39 years; for those born during 1945–1965 versus born before 1945 or after 1965; and for those who were NH Black versus NH White (Table 3; $P < .05$).

Characteristics Among US Adults With No Injection Drug Use History

From 2001–2016, 991 (3.7%) adults aged 20–59 years who reported no IDU history were anti-HBc positive. Adults with no IDU history who were anti-HBc positive, versus anti-HBc negative, were more frequently male (57.2% vs 49.7%, respectively), aged 50–59 years (40.0% vs 23.7%, respectively), born during 1945–1965 (60.8% vs 39.4%, respectively), NH Black (29.0% vs 10.7%, respectively), NH Asians (10.8% vs 2.0%, respectively), NH Other (13.4% vs 4.2%, respectively), without health insurance (28.4% vs 22.0%, respectively), and anti-HAV positive (55.0% vs 28.6%, respectively; see Supplementary Table 1; $P < .05$).

DISCUSSION

This is the first study to establish a baseline anti-HBc positivity prevalence, indicating a previous or ongoing HBV infection, among adults with a history of IDU in a representative, noninstitutionalized, US population. Among adults aged 20–59 years, 19.7% of those with an IDU history were anti-HBc positive, compared with 4.6% in the general US population.

In 1982 and in subsequent years, the ACIP and CDC recommended a comprehensive strategy to eliminate HBV infection transmission in the United States through various interventions, including hepatitis B vaccination of at-risk adults, such as PWID [7, 24], and universal childhood vaccination [24, 25]. As recommended by the ACIP, CDC, and other federal agencies, PWID should also receive a hepatitis A vaccination [10, 26, 27]. Our analyses indicated that many adults, regardless of their IDU history, were susceptible to HBV infection, while only a small proportion were seropositive for anti-HBs and anti-HAV.

In April 2017, the National Academies of Sciences, Engineering, and Medicine published their Phase II report on a national strategy for the elimination of hepatitis B and C by 2030 [28]. Among their recommendations was the expansion of access to adult hepatitis B vaccination and the removal of barriers to vaccination in all states, including through offering free immunizations in pharmacies and other easily accessible settings [24, 28]. Our finding of low serologic evidence of immunity in the general US adult population corroborates findings from the 2016 National Health Interview Survey, which indicated the self-reported hepatitis B vaccination coverage among all US adults was 24.8%, regardless of risk factors [9], supporting the need to expand hepatitis B vaccination efforts to reach more adults.

This study has important targeted public health implications, by identifying those socio-demographic populations among adults with IDU histories who had disproportionately higher anti-HBc positivity prevalences, including persons aged 40–59 years versus 20–39 years, those born during 1945–1965 versus born before 1945 or after 1965, and those who were NH Black versus NH White. A lower prevalence of adults aged 20–39 years with IDU histories who were anti-HBc positive may be the result of childhood immunization practices benefiting the youngest of the US adult population.

Our finding of a higher anti-HBc positivity prevalence among adults with IDU histories who were born during 1945–1965 (the Baby Boomer cohort) compared to those born before

Table 2. Prevalence Estimates of Select Characteristics Among Adults With Injection Drug Use History

	Anti-HBc Positive		Anti-HBc Negative		
Characteristic	n	Weighted % (95% CI)	n	Weighted % (95% CI)	*P* Value[a]
Overall[b]	127	19.7 (16.0–24.0)	395	80.3 (76.0–84.0)	…
Sex	…	…	…	…	.700
Male	85	70.1 (59.2–79.1)	263	67.7 (62.2–72.7)	…
Female	42	29.9 (20.9–40.8)	132	32.3 (27.3–37.8)	…
Age group, years	…	…	…	…	<.001*
20–39	15	13.7 (7.3–24.3)	168	44.0 (37.6–50.7)	…
40–49	36	29.6 (21.3–39.5)	122	30.5 (24.5–37.2)	…
50–59	76	56.7 (45.7–67.1)	105	25.5 (19.5–32.7)	…
Year of birth	…	…	…	…	<.001*
During 1945–1965	102	79.5 (70.1–86.5)	194	46.8 (39.8–54.0)	…
Before 1945 or after 1965	25	20.5 (13.5–29.9)	201	53.2 (46.0–60.2)	…
Race/ethnicity	…	…	…	…	.002*
Non-Hispanic White	64	71.3 (62.2–79.0)	266	81.6 (77.5–85.0)	…
Non-Hispanic Black	36	16.6 (11.2–23.9)	42	5.0 (3.5–7.2)	…
Hispanic	19	7.1 (4.2–11.7)	63	7.8 (5.8–10.3)	…
Non-Hispanic Asian[c]	DI	…	DI	…	…
Non-Hispanic other	DI	…	23	5.5 (3.4–8.9)	…
Health insurance status	…	…	…	…	.020*
Covered	87	73.1 (62.6–81.6)	224	59.6 (53.3–65.6)	…
Not covered	39	26.9 (18.4–37.4)	168	40.4 (34.4–46.7)	…
HBV infection status[d]	…	…	…	…	<.001*
Current infection	DI	…	0	…	…
Susceptible	0	…	279	80.9 (75.2–85.6)	…
Immune from past infection/isolatedanti-HBc positive	121	95.2 (88.2–98.2)	0	-	…
Immune from vaccination	0	-	64	19.1 (14.4–24.8)	…
Hepatitis A immunity	…	…	…	…	.008*
Anti-HAV positive	59	40.6 (31.0–50.9)	111	25.7 (20.5–31.6)	…
Anti-HAV negative	58	59.4 (49.1–69.0)	264	74.3 (68.4–79.5)	…
Number of years since last injection	…	…	…	…	.064
0–1 year	17	14.3 (7.9–24.6)	71	20.4 (15.3–26.7)	…
2–10 years	18	19.6 (11.0–32.4)	116	35.3 (28.8–42.3)	…
11+ years	49	66.1 (52.0–77.8)	144	44.3 (35.9–53.1)	…
Age of first injection[e]	…	…	…	…	.230
<20 years	33	44.2 (30.7–58.6)	99	31.2 (25.1–38.0)	…
20–29 years	41	41.5 (28.7–55.6)	176	53.1 (46.5–59.7)	…
30+ years	15	14.3 (7.6–25.2)	59	15.7 (11.0–21.9)	…
Lifetime number of injections	…	…	…	…	.027*
<20 times	25	34.0 (22.4–47.9)	183	54.4 (46.9–61.7)	…
20–99 times	29	33.0 (21.7–46.8)	77	23.7 (18.7–29.5)	…
100+ times	36	33.0 (22.3–45.8)	73	21.9 (16.8–28.1)	…
Injection frequency	…	…	…	…	.790
≥Once a day	49	47.5 (33.8–61.7)	122	42.1 (34.6–49.9)	…
Once a week	20	26.5 (16.8–39.2)	74	29.8 (24.9–35.3)	…
Once a month	16	25.9 (14.9–41.2)	80	28.1 (21.3–36.2)	…

Data are among adults aged 20–59 years (n = 561), stratified by anti-HBc status, United States, NHANES 2001–2016. Having an IDU history was defined as having ever used a needle to inject street or other illegal drugs. * $P < .05$.

Abbreviations: anti-HBc, total HBV core antibody; anti-HBs, hepatitis B surface antibody; CI, confidence interval; DI, data insufficient (sample size between 1 to 14); HAV, hepatitis A virus; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IDU, injection drug use; NHANES, National Health and Nutrition Examination Survey.

[a]Statistical testing of differences in characteristics between persons who ever injected drugs and who were anti-HBc positive, versus those who were anti-HBc negative.

[b]There were 39 adults who reported an IDU history and had a missing anti-HBc result.

[c]Non-Hispanic Asian data only available from 2011–2016.

[d]HBV infection statuses are defined as: current infection, meaning positive for HBsAg; susceptible, meaning negative for HBsAg, anti-HBc, and anti-HBs; immune from past infection/isolated anti-HBc positive, meaning either negative for HBsAg and positive for anti-HBs and anti-HBc, or positive for anti-HBc and negative for all other HBV laboratory markers; and immune from vaccination, meaning positive for anti-HBs and negative for anti-HBc and HBsAg.

[e]Age of first injection data only available from 2005–2016.

Table 3. Prevalence Ratios of Total Hepatitis B Virus Core Antibody Positivity

	Crude Prevalence Weighted % (95% CI)	Adjusted Prevalence[a] Weighted % (95% CI)	Adjusted Prevalence Ratio (95% CI)	Adjusted Prevalence Ratio *P* Value
Overall	19.7 (16.0–24.0)	...	...	...
Sex				
Men	20.3 (15.4–26.2)	20.4 (15.6–26.4)	1.13 (.72–1.79)	.577
Women	18.5 (12.9–25.9)	18.0 (12.7–24.9)	Ref	...
Age group, years				
20–39	7.1 (3.6–13.4)	7.1 (3.5–13.7)	Ref	...
40–49	19.3 (13.2–27.1)	18.4 (12.5–26.3)	2.60 (1.16–5.79)	.012*
50–59	35.3 (26.3–45.4)	34.7 (25.5–45.2)	4.89 (2.20–10.83)	<.001*
Year of birth				
During 1945–1965	29.4 (22.9–36.9)	28.1 (21.4–36.0)	3.15 (1.66–6.00)	<.001*
Before 1945 or after 1965	8.6 (5.5–13.3)	8.9 (5.2–14.9)	Ref	...
Race/ethnicity[b]				
Non-Hispanic White	17.7 (13.5–22.8)	18.1 (13.9–23.2)	Ref	...
Non-Hispanic Black	44.8 (34.9–55.2)	35.3 (25.3–46.9)	1.95 (1.28–2.99)	.007*
Hispanic	18.3 (10.8–29.4)	17.1 (10.0–27.7)	0.95 (.55–1.63)	.835
Health insurance coverage				
Covered	23.1 (18.1–28.9)	22.1 (17.2–27.9)	Ref	...
Not covered	14.0 (9.6–19.9)	15.2 (10.2–21.9)	0.69 (.43–1.09)	.092
Hepatitis A immunity				
Anti-HAV positive	27.4 (20.7–35.3)	22.8 (16.9–30.0)	1.30 (.89–1.88)	.180
Anti-HAV negative	16.0 (11.9–21.1)	17.5 (13.4–22.7)	Ref	...

Data are among adults aged 20–59 years with IDU histories and known anti-HBc results (n = 522), United States, NHANES 2001–2016. Having an IDU history was defined as having ever used a needle to inject street or other illegal drugs. *$P < .05$.

Abbreviations: anti-HBc, total HBV core antibody; HAV, hepatitis A virus; HBV, hepatitis B virus; IDU, injection drug use; NHANES, National Health and Nutrition Examination Survey; Ref, reference.

[a]Model-adjusted prevalence estimates for all variables were adjusted for sex, age group, race/ethnicity, and health insurance status, as appropriate. Independent models for each variable were not adjusted for the variable for which the model was generated.

[b]The sample sizes were insufficient (n < 15) for the non-Hispanic Asian and non-Hispanic Other race/ethnicity groups, so the results for these categories were not reported.

1945 or after 1965 was expected, since Baby Boomers have been found to have a higher prevalence of HCV infection [19], which carries a similar mode of transmission as HBV infection. During the 1960s-1980s, some Baby Boomers may have been infected through medical interventions, since infection control was not as thorough as it is today [19]. The hepatitis B vaccine was not licensed and approved for use in the United States until 1982, and universal infection control measures for blood-borne infections were not adopted until 1992 [24].

The finding of a higher prevalence of NH Blacks with IDU histories who were anti-HBc positive versus anti-HBc negative may be explained by a sub-analysis among NH Blacks, indicating that Baby Boomers and those who had ≥20 lifetime injections were more frequently anti-HBc positive versus anti-HBc negative ($P < .05$; results not shown). In our main analysis, after controlling for sex, age group, and health insurance, the anti-HBc positivity prevalence was still higher among NH Blacks than NH Whites with IDU histories. These racial disparities may be due, in part, to factors such as education, sexual behaviors, and immigration from high-prevalence countries. Among adults who reported no IDU history, we found a higher prevalence of NH Blacks were anti-HBc positive, versus anti-HBc negative. These results suggest our main findings may not entirely be attributable to IDU effects.

This study had limitations. The NHANES drug use questionnaire was self-reported, potentially resulting in underestimated prevalence estimates and ratios that were biased toward the null due to a social desirability bias (eg, participants falsely reporting never injecting drugs) and a nonresponse bias (eg, PWID more likely skipping IDU questions). We conducted a sensitivity analysis assessing selection bias, and found that, compared to persons who responded to the IDU question, nonresponders were more frequently female, born during 1945–1965, of NH Other race/ethnicity, anti-HAV positive, anti-HBc positive, and susceptible to HBV infection or immune from a past infection (see Supplementary Table 2). Thus, selection bias cannot be ruled out. Further, the IDU question asked in NHANES cycles 2001–2002 and 2003–2004 only assessed injectable street drugs, which excluded injectable drugs that were pharmaceutically manufactured and may or may not have been prescribed by a health-care provider. The IDU question asked in subsequent cycles was expanded to include diverted, injectable prescription drugs. Because of the differences in wording for the IDU history question from 2001–2004 to 2005–2016, respondents who injected prescription drugs in 2001–2004 were likely not represented in our prevalence estimates of IDU history. Additionally, as mentioned here and in other studies [1, 29], NHANES does not include homeless or institutionalized individuals (eg,

incarcerated persons), who may have higher likelihoods of IDU and viral hepatitis infections [7, 27, 30]. Because this study used cross-sectional data, temporality between exposure and anti-HBc positivity cannot be assessed. Further, we limited our study population to participants aged 20–59 years, since the eligible samples for the NHANES drug use questionnaires for all survey cycles from 2001–2016 mutually included this age range. In doing so, approximately 2500 participants were excluded from 2001–2016, in the category representing persons born during 1945–1965. Finally, levels of anti-HBs typically wane after response to a complete vaccine series and may fall below 10 mIU/mL, despite the persistence of immunity [31–33]. Thus, some persons classified as susceptible may have been vaccinated and remained immune to infection. Despite unavoidable limitations, this study is the first to establish baseline prevalence estimates and describe characteristics of anti-HBc positive adults with IDU histories.

In summary, these data indicate that from 2001–2016, 1 in 5 US adults aged 20–59 years with an IDU history had a previous or ongoing HBV infection: a rate over 4 times higher than the anti-HBc positivity prevalence in the general population. Similarly, 1 in 5 US adults aged 20–59 years with an IDU history had injected drugs within the prior year. Programs promoting safe IDU practices, drug treatment, and hepatitis A and B vaccination should be key components of viral hepatitis prevention programs to minimize the risk of transmission to susceptible PWID.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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