

Data Supporting Updating Estimates of the Prevalence of Chronic Hepatitis B and C in the United States

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The current estimates of chronic hepatitis B (CHB) and chronic hepatitis C (CHC) prevalence that are widely used by the press and cited in many publications and presentations are 805,000-1,405,000 persons with CHB (prevalence 0.8%-1.2%)¹ and 2.7 million (confidence interval 2.2 million-3.2 million) with CHC (prevalence 0.3%-0.5%).² Although these figures accurately represent findings from national prevalence studies, we believe that because of underrepresented or excluded populations they should be revised upward to increase public awareness about viral hepatitis and to support increasing funding for both the National Institutes of Health's viral hepatitis research and the Centers for Disease Control and Prevention's (CDC's) Division of Viral Hepatitis, which has by far the smallest budget in the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. The CHC estimate is based entirely and the CHB estimate in large part (with some adjustments) on data from the National Health and Nutrition Examination Survey

Abbreviation: CDC, Centers for Disease Control and Prevention; CHB, chronic hepatitis B; CHC, chronic hepatitis C; HBV, hepatitis B virus; HCV, hepatitis C virus; NHANES, National Health and Nutrition Examination Survey.

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(NHANES), which the CDC is careful to point out excludes some populations with increased infection risk, including the incarcerated, the homeless, and institutionalized persons, and does not adequately represent multiple racial/ethnic groups with higher infection rates, including Native Americans, Alaskan Natives, and Asians and Pacific Islanders.

Using the same approach the CDC uses to estimate CHB prevalence in the foreign-born, a meta-analysis of hepatitis B surface antigen seroprevalence rates in 102 countries multiplied country-specific CHB prevalence rates by the number of foreign-born in the United States by country of birth. This study estimated 1.32 million foreign-born persons with CHB and, adding the current prevalence estimates for the general population and institutionalized persons, a total CHB population of up to 2.2 million.³ A similar estimate of 2.09 million was calculated by Hepatitis B Foundation researchers, using NHANES and 2005 census data, with an estimated additional 100,000 CHB persons among undocumented Asians and Pacific Islanders.⁴

The current CHB estimate for institutionalized persons, which includes residents both of correctional settings (2.0% estimated prevalence) and of other group living quarters, and the homeless (0.5%) may be too low. US incarcerated population prevalence estimates range from 0.9% in Tennessee⁵ to 8.7% in Maryland.⁶ The current 2.0% estimate considered only five peer-reviewed studies reporting 0.9%-3.1% prevalence rates.⁷ Because 20% of state and 13% of federal inmates are injection drug users,⁸ CHB prevalence is likely much higher. Similarly, prevalence in the homeless may be much higher than 0.5%. An estimated 24.2% of those in homeless shelters are current or former injection drug users.⁹ One study found that 32.5% of homeless persons with mental illness and substance use disorders were positive for antibody to hepatitis B core antigen and 29.8% were anti-hepatitis C virus-positive (HCV⁺).¹⁰ Taking all of this into consideration, we believe that the 2012 estimate of 2.2 million US CHB persons³ may be the most accurate.

In the NHANES-based study that provides the CHC prevalence estimate that is currently most often used by the press and cited in many journal publications and conference presentations, the CDC researchers state, "A major limitation of NHANES is that it does not include

homeless and incarcerated persons, who are probably at higher risk for HCV infection. Accordingly, considerations of the prevalence and effect of chronic HCV infection in the United States should supplement data from NHANES with those from populations with a higher risk for and prevalence of HCV infection, such as institutionalized (incarcerated) and homeless persons.² We would like future publications to note this and present the study's prevalence figure with adjustments and an emphasis on the probability that the true prevalence is higher.

A 2011-2012 survey in 12 state prison systems reported anti-HCV⁺ prevalence of 9.6%-41.1%, with national state prisoner prevalence estimated as 17.4%.¹¹ Based on the total US correctional population, 1,857,629 people were projected to be anti-HCV⁺; if 75%-85% develop CHC,¹² this could add 1.4 million to 1.6 million CHC persons to the national estimate. One of the most recent and likely most accurate estimates of HCV prevalence in the homeless comes from a multisite study that investigated HCV seroprevalence in a broad national cross section of the homeless population; 31% were anti-HCV⁺.¹³ With an estimated 2,150,000 US adults experiencing homelessness in 2014, if 31% are anti-HCV⁺ (666,500), this could add 500,000-567,000 persons to the overall CHC estimate. Following the suggestion to supplement NHANES data (2.7 million CHC persons)² with data from populations with higher CHC prevalence, including the incarcerated (1.4-1.6 million) and homeless (500,000-567,000), would yield 4.6 million to 4.9 million CHC persons. This estimate could be further increased with accurate estimates from the other groups with known higher infection rates not adequately represented by NHANES (Asians and Pacific Islanders) and not included at all (residents of American Indian reservations and Alaska Native village statistical areas). In their review in this issue of HEPATOLOGY, Edlin et al.¹⁴ estimate that 123,000 anti-HCV⁺ people living on Indian reservations were excluded from NHANES, with at least 0.8 million CHC people excluded overall and, thus, an estimated national CHC prevalence of at least 3.5 million. In their conclusion, they note that, for multiple reasons, including additional sources of potential underestimation not accounted for in their study, their findings may still very substantially underestimate CHC prevalence, with the possibility that the true seroprevalence might be 5 million to 7 million.¹⁴ In light of a possible 2.5-fold to 5.75-fold underestimate of CHC in Massachusetts found through a recent survey, the researchers note that to address HCV prevention, testing, and treatment needs it is crucial to provide more accurate national estimates of prevalence and conclude, "Without knowing the true scope and scale of the epidemic, we can't appropriately plan or argue for necessary resources."¹⁵ We agree.

The 2014 estimate of 2.7 million CHC persons is a decrease from the previously estimated 3.2 million.¹⁶ Although it is clear to us that this is a substantial underestimate, we are concerned that any actual decrease is explained by a high death rate resulting from failure to diagnose and treat this population. The Chronic Hepatitis Cohort Study has shown steadily increasing mortality rates in CHC patients, rising from 1.4 per 100 person-years in 2006 to 4.4 in 2010.¹⁷ Fourteen percent of the cohort patients had died (any cause) by the end of 2010, with most deaths occurring in the 1945-1964 birth cohort. Disturbingly, despite the fact that prior to death 63% had medical record evidence of chronic liver disease, 76% had elevated Fibrosis-4 scores, and of those biopsied 70% had moderate or worse liver fibrosis, only 19% of all Chronic Hepatitis Cohort Study decedents and 30% of those with recorded liver disease had HCV noted on their death certificates.¹⁸ This could mean a five-fold underreporting of HCV-associated deaths. In addition, HCV-infected persons died on average 15 years younger than comparison groups,¹⁷ a serious cost to society. These high rates of premature death underscore the importance of improving CHC detection and treatment, especially in the current era of highly effective oral antiviral therapy that leads to a sustained viral response in most people. Holmberg et al. recently estimated that only about half of HCV-infected people have been tested and know their status, only about one-third have been referred for care, and only 7%-11% have been treated, only 5%-6% successfully.¹⁹ Thus, it seems very possible that there are at least 3.4 million and possibly 5 million or more people chronically infected with hepatitis C in the United States, 94%-95% of whom have not yet been successfully treated, a population of at least 3.2 million and possibly up to 4.8 million or more people in need of treatment.

Clearly, accurate national prevalence estimates are essential in order to address hepatitis B virus (HBV) and HCV prevention, testing, and treatment needs, as well as to accurately project future HBV-associated and HCV-associated costs, which may currently be significantly underestimated. Showing broader ranges of prevalence data could expand opportunities for advocacy and awareness, as well as provide a solid basis for advocating for increased funding for research, education, prevention efforts, screening, and treatment. We would very much like to see funding which is proportional to the US health care costs and death and cancer rates associated with CHB and CHC. We believe that in the United States the attention a disease receives from the general public, health care workers and researchers, and the members of Congress who approve budgets is tied in many ways to the total number of people estimated

to be affected. We hope that in consideration of the benefits we believe would accrue, current CHB and CHC estimates will be reconsidered and the need for adjustments noted in future publications and presentations.

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