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Toward a More Accurate Estimate of the Prevalence of Hepatitis C in the United States

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Data from the 2003-2010 National Health and Nutrition Examination Survey (NHANES) indicate that about 3.6 million people in the United States have antibodies to the hepatitis C virus, of whom 2.7 million are currently infected. NHANES, however, excludes several high-risk populations from its sampling frame, including people who are incarcerated, homeless, or hospitalized; nursing home residents; active-duty military personnel; and people living on Indian reservations. We undertook a systematic review of peer-reviewed literature and sought out unpublished presentations and data to estimate the prevalence of hepatitis C in these excluded populations and in turn improve the estimate of the number of people with hepatitis C in the United States. The available data do not support a precise result, but we estimated that 1.0 million (range 0.4 million-1.8 million) persons excluded from the NHANES sampling frame have hepatitis C virus antibody, including 500,000 incarcerated people, 220,000 homeless people, 120,000 people living on Indian reservations, and 75,000 people in hospitals. Most are men. An estimated 0.8 million (range 0.3 million-1.5 million) are currently infected. Several additional sources of underestimation, including nonresponse bias and the underrepresentation of other groups at increased risk of hepatitis C that are not excluded from the NHANES sampling frame, were not addressed in this study. *Conclusion*: The number of US residents who have been infected with hepatitis C is unknown but is probably at least 4.6 million (range 3.4 million-6.0 million), and of these, at least 3.5 million (range 2.5 million-4.7 million) are currently infected; additional sources of potential underestimation suggest that the true prevalence could well be higher. (HEPATOLOGY 2015;62:1353-1363)

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Estimates of the number of persons with hepatitis C in the United States are important for assessing the burden of disease caused by the epidemic, designing and targeting public health interventions, allocating resources, and planning for future health care needs. Designed to assess the health and nutritional status of adults and children in the United States, the National Health and Nutrition Examination Survey (NHANES), a probability sample of the US household population, provides extensive information on the prevalence of major diseases and disease risk factors.[1] About 10,000 persons of all ages in about 30 counties are interviewed during each 2-year survey cycle.[2] The data are used to develop public health policy, direct and design health programs and services, expand the health knowledge for the nation, and monitor progress toward Healthy People objectives.[1] Blood specimens are tested for hepatitis C virus (HCV) antibody and RNA to estimate the number of persons with hepatitis C in the United States.[3] The most recent results suggest that during 2003-2010 about 3.6 million persons (95%

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; NHANES, National Health and Nutrition Examination Survey..

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Table 1. Estimated Size of Population Groups Excluded from NHANES

Population	Estimated Size	Source	Years
Incarcerated people	2,186,230	Bureau of Justice Statistics[12]	2005, 2008, 2009, 2010
Homeless people	691,899	US Department of Housing and Urban Development[13]	2005, 2006, 2007, 2008, 2009, 2010
Hospitalized patients	478,054		
Nonfederal hospitals		CDC/NCHS National Hospital Discharge Survey[14]	2005, 2007, 2008, 2009, 2010
Veterans Affairs hospitals		Department of Veterans Affairs[15]	2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010
Nursing home residents	1,446,959	National Nursing Home Survey[16]	2004
		US Census Bureau[17]	2009
Active-duty military	1,404,060	US Census Bureau[18]	2005, 2007, 2008, 2009, 2010
Native Americans living on reservations	1,069,411	US Census Bureau[19]	2010

Abbreviations: CDC/NCHS, Centers for Disease Control and Prevention/National Center for Health Statistics.

confidence interval 3.0 million-4.2 million) had antibody to HCV, indicating past or present infection, of whom about 2.7 million (95% confidence interval 2.2 million-3.2 million) had HCV RNA-positive serum, indicating current infection.[3]

But while NHANES provides a wealth of valuable data on the health of the US population,[1] it was designed to estimate the prevalence of conditions substantially more common than hepatitis C.[4] For estimating hepatitis C prevalence, it suffers from three potential sources of underestimation. First, its sampling frame is the noninstitutionalized, housed, civilian population of the United States. By design it omits several large populations of persons at increased risk of HCV infection, including homeless persons, those in jail or prison, and those living on Indian reservations. Second, several additional groups at increased risk of hepatitis C, while not excluded from the NHANES sampling frame, are poorly represented because of small sample sizes, including Puerto Rican Americans,[5] other ethnic minorities,[6] and people born in high-prevalence countries.[7-9] Third, nonresponse bias[4] could result in underestimation if persons at elevated risk of hepatitis C differentially opt not to participate or do not provide a blood specimen.

NHANES investigators have emphasized the need to account for its omission of high-prevalence groups.[3,4,10,11] To develop a more accurate estimate of the national burden of hepatitis C, we examined the first of these three potential sources of underestimation. We estimated the HCV prevalence of six populations excluded from NHANES — people who are homeless, incarcerated, or hospitalized; nursing home residents; active-duty military personnel; and Native Americans living on reservations. We used these data to revise the most recent NHANES estimate.

Materials and Methods

Data Sources and Searches. We used publicly available estimates of the size of each of the six population groups excluded from the NHANES sampling frame (Table 1).[12-19] We averaged all available estimates from the years 2003 through 2010 for each group. Hospitalized patient population estimates were obtained by multiplying the number of discharges in each available year by the average length of stay for that year and dividing by the number of days in the year; estimates for nonfederal and Veterans Affairs hospitals were added. All population size estimates reflected the number of people in each population at a single point in time, to ensure that people who move among populations are counted only once. Many more people are homeless during a given year than on a single night,[13] and hepatitis C estimates that use those numbers[20] are therefore severalfold higher than ours.

We then used OVID to systematically search the MEDLINE and Embase databases for articles and conference proceedings reporting the prevalence of HCV antibody in each of the six populations, limiting our search to studies conducted within 10 years of the period of the NHANES estimate (2003-2010) (Table 2). We also searched "related articles" listings, examined the references of retrieved papers, and contacted authors of published data for additional unpublished information.

Study Selection. Studies that reported HCV seroprevalence in representative or unselected samples of one of the excluded population groups in the United States were included; those which sampled subjects at selectively higher risk by virtue of risk factors, symptoms, or requests for testing were excluded.

Data Extraction and Quality Assessment. One investigator extracted the data from each study, and at least one additional investigator verified the accuracy of the data. The dates of testing, number of persons tested, number of persons testing HCV antibody-positive, and HCV seroprevalence were extracted. Authors were contacted to obtain data missing from published reports.

Table 2. Search Terms and Results of Literature Search for Articles with Hepatitis C Prevalence Data in Populations Excluded From NHANES

Population	Search Terms	Medline Articles	Embase Articles	Unique Articles	Full Text Screened	Articles Included
Incarcerated	"hepatitis C" and "prison" or "jail" or "incarceration"	651	766	879	51	16
Homeless	"hepatitis C" and "homeless"	173	223	245	31	9
Hospitalized	"hepatitis C" and "hospitalized" or "emergency room" or "emergency ward" or "inpatient"	559	1252	1340	31	7
Nursing homes	"hepatitis C" and "nursing home," "nursing facility," or "long-term care facility" or "skilled nursing facility"	13	38	38	12	1
Military	"hepatitis C" and "military," "navy," "air force," "army," or "marines"	172	207	228	15	2
Native Americans	"hepatitis C" and "Native American," "Indian, North American" or "Indian reservation"	55	74	98	19	1
Total		1623	2560	2828	159	36

Data Synthesis and Analysis. For the incarcerated population, available seroprevalence estimates for each state were averaged and a national estimate was calculated by weighting the state averages by the size of each state's incarcerated population.[21] Where separate estimates were available for men and women, they were weighted according to the sex ratio of prisoners for the respective state.[22] For each of the other groups, we calculated the mean seroprevalence of the available studies, weighting each study by its sample size. We calculated binomial confidence intervals for the seroprevalence estimate from each study where available data permitted. To conservatively account for interstudy variability within each of the six population groups, we used the range of the point estimates from the separate studies to represent the uncertainty in our estimate. The size of each population group was multiplied by its estimated seroprevalence, and the totals were summed and added to the 2003-2010 NHANES estimate for the number of US residents with HCV antibody. To estimate the number of persons with current HCV infection, we used the NHANES finding that 82% of antibody-positive persons have HCV RNA.[3] The same proportion, 82%, was observed in a high-prevalence sample of people who inject drugs.[23] This analysis updates an earlier one that used the same methods.[24]

Results

The sizes of the six population groups ranged from 478,054 to 2,186,230 (Table 1). The search for seroprevalence data yielded 2828 unique articles, of which 36 met criteria for inclusion (Table 2), with seven additional studies published in abstract form only.[20,25-66] One study of prisoners and two studies of hospitalized patients were excluded because they were conducted >10 years before 2003.

Sixteen published studies and six studies published in abstract form only reported HCV seroprevalence among persons in penal institutions in 23 states (Table 3). The studies differed in sample design and methodology. Most, but not all, sampled persons as they entered these institutions. The weighted mean prevalence of HCV antibody among all persons in all studies combined was 23.1%. The prevalences in the 22 studies ranged from 7.5% through 44.0%.

Nine studies of HCV seroprevalence among homeless persons have been published (Table 4). The study design and selection criteria differed in each study. The weighted mean prevalence of HCV antibody among all persons in all studies combined was 32.1%. The prevalences in the nine studies ranged from 7.5% through 52.5%.

Seven studies of HCV seroprevalence among persons in hospitals have been published, and an additional study was published in abstract form only (Table 4). One studied source patients of needle-stick injuries; two were conducted in emergency departments and two in a psychiatric hospital, with HCV antibody prevalences between 4.0% and 38% in all the studies. The weighted mean prevalence of HCV antibody among persons in all these studies combined was 15.6%.

One small study in nursing home residents demonstrated an HCV seroprevalence of 4.5%. A random sample of 10,000 active-duty military personnel found an HCV antibody prevalence of 0.48%, and a smaller study of military blood donors showed a seroprevalence of 0.84%. A single study of Native Americans served by the Indian Health Service reported an HCV seroprevalence of 11.5% (Table 4).

When we multiplied the estimated seroprevalence for each of the six populations by the population size, we projected that in 2003-2010 505,350 incarcerated people, 222,100 homeless individuals, 74,576 hospitalized patients, 65,113 nursing home residents, 7020 active military personnel, and 123,224 persons living on Indian reservations had HCV antibody. Summing these, we estimated that 997,384 (range 355,466-1,813,661) persons in the United States had HCV antibody in addition to the NHANES estimate (Table 5). Of these, an estimated 817,855 (range 291,482-1,487,202) are currently infected.

Table 3. Hepatitis C Seroprevalence Studies in Incarcerated Populations*

State	Reference	Study Dates	Total No. Tested	No. HCV Antibody-Positive	HCV Antibody Prevalence	95% Confidence Interval
California	Ruiz et al.[25]	1994	4513	1859	41.2%	39.8%-42.6%
	Ruiz et al.[26]	1999	5595	1850	33.1%	31.8%-34.3%
	Hennessey et al.[27†]	1999-2000	505		10.0%	9.0%-11.0%‡
	Fox et al.[28]	2001	467	160	34.3%	30.0%-38.8%
Colorado	Spaulding et al.[29]	1996	1224		30.0%	27%-33%
Connecticut§	Fennie et al.[30]	1996‖	174	56	32.2%	25.3%-39.7%
Georgia	Spaulding et al.[31†]	2011	4918	371	7.5%	6.8%-8.3%
Illinois	Hennessey et al.[27†]	2000	447		14.0%	13.0%-16.0%‡
Indiana	Varan et al.[20]	2003, 2011	20,506	2198	10.7%	10.3%-11.2%
Iowa	Varan et al.[20]	2001			23.6%	
Maryland	Solomon et al.[32]	2002	3661	1089	29.7%	28.3%-31.3%
Massachusetts	Cocoros et al.[33]	2009-2011	596	122	20.5%	17.3%-23.9%
	Lincoln et al.[34]	1999	463	96	20.7%	17.1%-24.7%
	Eastman et al.[35]	2000	816	290	35.5%	32.3%-38.9%
Michigan	Hennessey et al.[27†]	1999	340		15.0%	14.0%-16.0%‡
	Varan et al.[20]	2004, 2009	4709		10.4%	
Missouri	Wenger et al.[36†]	2012-2013	304	50	16.4%	12.5%-21.1%
Montana	Varan et al.[20]	2012			13.9%	
Nebraska	Varan et al.[20]	2011	4652	448	9.6%	8.8%-10.5%
Nevada	Chen et al.[37]	2001			24.4%	20.5%-28.6%
New Mexico	Varan et al.[20]	2010	3980	1636	41.1%	39.6%-42.7%
	Varan et al.[20]	2011			40.9%	
New York	Alvarez et al.[38]	2009-2013	2788	295	10.6%	9.5%-11.8%
	Wang et al.[39,40]	2000-2009	19,939	2620	13.1%	12.7%-13.6%
North Dakota	Varan et al.[20]	2008-2011			11.2%	
Oregon	Varan et al.[20]	2000, 2005			26.7%	
Pennsylvania	Larney et al.[41]	2004-2012	101,727	18,454	18.1%	17.9%-18.4%
Rhode Island§	Macalino et al.[42]	1996-1997	297	119	40.1%	34.4%-45.9%
	Macalino et al.[43]	1998-2000	4264	983	23.1%	21.8%-24.3%
Texas	Baillargeon et al.[44]	1998-1999	3712	1076	29.0%	27.5%-30.5%
Washington	Varan et al.[20]	2008-2011	25,167	4736	18.8%	18.3%-19.3%
Wisconsin	Pfister et al.[45]	1999	1233		13.5%	11.3%-15.3%
		Weighted prevalence estimate:			**23.1%**	**Range: 7.5%-44.0%**

*All data from state prison systems unless otherwise indicated.
†Data from local jails.
‡Confidence interval reported by authors.
§Data from combined prison and jail.
‖Year of publication.

Adding these numbers to the most recent NHANES estimate suggests that at least 4.6 million people in the United States (range 3.4 million-6.0 million) have HCV antibody (Table 6). Of these, we project that at least 3.5 million (range 2.5 million-4.7 million) are currently infected (Table 6).

Sex-specific prevalence data allowed us to estimate the proportions of men and women among the infected in three of the excluded populations (see Appendix A). Men predominated in the excluded populations overall, as well as among the infected persons in those populations. Men comprised 87.8% of infected prisoners, 74.5% of infected homeless persons, and 90.9% of infected military personnel compared with 64% of infected persons in the NHANES population.[3] Thus, NHANES appears to underestimate the numbers of HCV-infected men more than women.

Discussion

Estimates of disease prevalence are important for establishing disease burdens, identifying health disparities, guiding policy, targeting interventions, and allocating resources. This analysis highlights several challenges to estimating the national prevalence of hepatitis C. First, while household surveys contribute invaluable information about population health, to be accurate their findings must be adjusted to account for populations not sampled or not well represented in the sample. NHANES uses consistent, standardized methodology that allows monitoring of trends over time but yields prevalence estimates that underrepresent the total burden of hepatitis C in the United States. Figures derived from NHANES appear to underestimate the US HCV seroprevalence by at least 1 million persons. Probably at least 4.6 million Americans have HCV antibody and at least 3.5 million are currently infected.

Table 4. Hepatitis C Seroprevalence Studies in Homeless, Hospitalized, Nursing Home, Military, and Native American Populations

Reference	Location	Study Dates	Total No. Tested	No. HCV Antibody-Positive	HCV Antibody Prevalence	95% Confidence Interval
Homeless people						
Desai et al.[46]	Bedford, MA	1993-1998	418	184	44%	39.2%-48.9%
Nyamathi et al.[47]	Los Angeles, CA	1995-1999	884	197	22%	19.6%-25.2%
Cheung et al.[48]	Palo Alto, CA	1995-2000	787	314	39.9%	36.5%-43.4%
Rosenblum et al.[49]	New York, NY	1997-1998	139	45	32%	24.7%-40.8%
Schwarz et al.[50]	Baltimore, MD	2001-2004	168	32	19%	13.4%-25.8%
Stein and Nyamathi[51]	Los Angeles, CA	2002-2003	198	104	52.5%	45.3%-59.6%
Gelberg et al.[52]	Los Angeles, CA	2003-2004	534		26.7%	23.1%-30.8%*
Strehlow et al.[53]	8 cities	2003-2004	387	120	31.0%	26.4%-35.9%
Boyce et al.[54]	Hawaii	2006	40	3	7.5%	1.6%-20.4%
		Weighted mean prevalence:			**32.1%**	**Range: 7.5%-52.55**
Hospitalized patients						
Austin et al.[55]	Atlanta, GA *VA hospital*	1993-1994	530	56	10.6%	8.1%-13.5%
Pham et al.[56]	Washington, DC *VA hospital*	1994	839	173	20.6%	17.9%, 23.5%
Cheung[57]	Palo Alto, CA *VA hospital*	1994-1997	72	13	18%	10.0%-28.9%
Brillman et al.[58]	Albuquerque, NM *Emergency department*	1996	223	38	17%	12.3%-22.6%
Meyer[59]	Salem, OR *Psychiatric hospital*	1999-2001	507	103	20.3%	16.9%-24.1%
Tabibian et al.[60]	Los Angeles, CA *Psychiatric VA hospital*	2002-2003	129	49	38%	29.6%-46.9%
Hall et al.[61]	Grand Rapids, MI *Emergency department*	2005	404	16	4.0%	2.3%-6.4%
Calore et al.[62]	Palo Alto, CA *VA hospital*	2007-2009	381	32	8.4%	5.8%-11.6%
		Weighted mean prevalence:			**15.6%**	**Range: 4.0%-38.0%**
Nursing home residents						
Chien et al.[63]	St. Louis, MO	1996-1997	199	9	4.5%	2.1%-8.4%
		Weighted mean prevalence:			**4.5%**	**Range: 2.1%-8.4%**
Active-duty military						
Hyams et al.[64]	United States	1997	10,000	48	0.48%	0.35%-0.64%
Hakre et al.[65]	US Service members in Iraq or Afghanistan	2002-2007	475	4	0.84%	0.23%-2.14%
		Weighted mean prevalence:			**0.50%**	**Range: 0.48%-0.84%**
Native Americans living on reservations						
Neumeister et al.[66]	Omaha, NE	2007†	243	28	11.5%	7.8%-16.2%
		Weighted mean prevalence:			**11.5%**	**Range: 7.8%-16.2%**

*Confidence interval reported by authors.
†Year of publication.
Abbreviation: VA, Veterans Affairs.

Second, household surveys underestimate the prevalence of conditions concentrated in disenfranchised populations and, therefore, underestimate the extent of health disparities. The largest contributions to the hepatitis C underestimate are from prisoners, homeless persons, and residents of Indian reservations—marginalized groups facing social stigma, economic disadvantage, elevated rates of comorbidities, severe health disparities, and reduced access to high-quality health care. These groups also include a disproportionately high representation of ethnic minorities affected by health disparities and ethnic bias. It is particularly important that these vulnerable populations are not overlooked when allocating resources, designing interventions, and planning for health care needs.

Third, this analysis reveals the paucity of reliable data on the prevalence of hepatitis C in populations known to be at increased risk of the disease. A number of

Table 5. Estimated Numbers of HCV Infections in Population Groups Excluded From NHANES

Population	Estimated Size	HCV Prevalence		Number of Infected Persons	
		Estimate	Range	Estimate	Range
Incarcerated	2,186,230	23.1%	7.5%-44.0%	505,350	163,967-961,941
Homeless	691,899	32.1%	7.5%-52.5%	222,100	51,892-363,246
Hospitalized	478,054	15.6%	4.0%-38.0%	74,576	19,122-181,660
Nursing homes	1,446,959	4.5%	2.1%-8.4%	65,113	30,386-121,545
Military	1,404,060	0.5%	0.48%-0.84%	7020	6,739-11,794
Indian reservations	1,069,411	11.5%	7.8%-16.2%	123,224	83,358-173,474
Total				**997,384**	**355,466-1,813,661**

Table 6. New Estimate of Number of Individuals in the United States With Hepatitis C Antibody

Estimate	HCV Antibody-Positive Number (Range)	HCV RNA-Positive Number (Range)
NHANES (2003-2010)	3.6 million (3.0 million-4.2 million)	2.7 million (2.2 million-3.2 million)
Added populations	1.0 million (0.4 million-1.8 million)	0.8 million (0.3 million-1.5 million)
Total	**4.6 million (3.4 million-6.0 million)**	**3.5 million (2.5 million-4.7 million)**

limitations of the available data impair the accuracy of the estimates presented here. First, there are no representative samples of five of the six populations examined. The seroprevalence studies we used, with the exception of a single study of active-duty military personnel, were not designed to recruit nationally representative samples. Second, the size of two of the populations is not known with accuracy. There is no precise estimate of the number of homeless persons in the United States,[67,68] and the US census faces substantial challenges in enumerating the Native American population on reservations.[69,70] Third, HCV seroprevalence studies were available from jails and prisons in only 23 states and no federal prisons. While these states cannot be considered representative of the United States as a whole, it is worth noting that taken together they account for 55% of the nation's prisoners. Fourth, HCV seroprevalence estimates were available for only nine homeless samples and eight hospitals, including several Veterans Affairs and psychiatric hospitals, which may have higher rates of HCV seroprevalence than other hospitals. Fifth, only a single clinic-based study of Native Americans was available, which might have overestimated the hepatitis C prevalence in that population. Surveillance data suggest, however, that the prevalence of hepatitis C on Indian reservations is elevated.[71,72] It should also be noted that we did not examine the ethnic composition of the undercounted persons we report and that our methods cannot be used to monitor trends over time. Finally, studies showing higher prevalence rates may have been more likely to be published, which would have biased our estimates upward.

But balanced against these possible sources of overestimation are several reasons the current study may still underestimate the number of infected persons. First, persons in temporary or unstable housing outnumber those who are literally homeless on any given night by severalfold.[67,68,73] For example, an estimated 6.8 million people were "doubled-up"—i.e., living with others—in 2010.[74] Persons not in their "usual place of residence" were not included in NHANES. While the HCV seroprevalence of this precariously housed population is not known, these persons could conservatively account for another half-million to 1 million or more additional persons with HCV antibody.

Second, nearly all of the prison studies cited in our study sampled new entrants to prison, who are on average younger than the overall prison population and include fewer members of the higher-prevalence birth cohorts. HCV seroprevalence in the United States peaked among persons born during 1945-1965.[10,75] Adjusting seroprevalence of prisoners for this difference, an average of about 3 years, would add 2.45% to the seroprevalence estimate, or about 50,000 additional infected persons (see Appendix B).

Third, nearly one-third of persons sampled by NHANES were not interviewed or did not provide a blood specimen. The NHANES HCV seroprevalence estimate is based on only 381 positive antibody tests, while 13,824 sampled persons were not interviewed or did not provide a blood sample.[3] If even 1%-2% of these unsampled persons had injected illicit drugs unsafely and did not want to be asked questions about their health behavior, reveal needle tracks, undergo what may have been a painful or embarrassing phlebotomy experience, or participate in government research at all, the true prevalence could be one-third to two-thirds higher than the NHANES estimate. In addition, NHANES phlebotomists reported that at times they were unable to obtain a blood sample because prior illicit injection drug use made venipuncture too difficult.[4] A study of nonresponse bias in a household survey of human immunodeficiency virus (HIV) seroprevalence illustrates the potential magnitude of this effect. Persons who declined to participate in the seroprevalence survey (but consented to be interviewed in a subsequent study) were more than twice as likely as survey responders to report a history of injection drug use.[76] (Of note, adjustment for nonresponse of this magnitude still resulted in an underestimate of the HIV seroprevalence compared with estimates determined by other methods; back-calculation models yielded estimates 1.8-fold to 4.6-fold higher than the estimate derived from the household survey even after nonresponse bias was accounted for).[76]

Fourth, while NHANES oversamples African Americans and Mexican Americans to improve representation of

these populations, it is unable to adequately sample other groups who may have elevated hepatitis C prevalence, including other ethnic minority groups and people born in high-prevalence countries.[5-9] Thus, although these groups are not excluded from the NHANES sampling frame, they are nonetheless poorly represented in the survey.[6] Hepatitis C prevalence is elevated among Puerto Rican Americans[5] and immigrants from Egypt[7] and Somalia,[8] for example; and in one study of immigrants from the former Soviet Union, of whom some 2.9 million are living in the United States, the HCV seroprevalence was 28.3%.[9] The seroprevalence among immigrants from other high-prevalence countries[77] is unknown.

Fifth, all household surveys miss people, even among groups that are not poorly represented or excluded from the sampling frame. Studies of the 2000 US census coverage, for example, estimated that ~3 million to 4 million people were uncounted.[78,79] Uncounted persons are disproportionately young, single, male, poor, of minority ethnicity, and therefore on average more likely to have hepatitis C. The coverage of national household surveys such as NHANES, with only a fraction of the resources available to the US census to reach disadvantaged groups, is likely to be at least as impaired in this regard.

Finally, NHANES has limited ability to discern new transmission patterns concentrated in specific foci in population subgroups. Increased HCV transmission is occurring in at least 30 states, especially in rural and suburban areas, on the heels of dramatic increases in opioid use among young adults during the past decade.[80-83] These new infections have yet to register in NHANES.

For these reasons, the findings presented here may still underestimate the true number of HCV-infected persons in the United States. The present study examined only one of several sources of potential underestimation. Further work is needed to assess the contributions of these other possible sources of error in the estimate, as has been done for HIV.[84] An analysis of the NHANES HIV prevalence estimate concluded that the true HIV seroprevalence was 1.4-fold to 2.0-fold higher than the NHANES estimate because of nonresponse bias and the exclusion of high-risk populations.[4,85] If HCV seroprevalence was underestimated by a similar proportion—and there is little reason to think it was not—the true seroprevalence of HCV would be 5 million to 7 million.

This study illustrates the limitations of household surveys for ascertaining sequelae of stigmatized behavior. Injection drug use is highly prevalent in prisons and marginally housed populations because our nation criminalizes and incarcerates people who inject drugs and disqualifies them from receiving public aid such as housing assistance. And because we stigmatize illicit drug use, those who have used drugs and are free and housed are understandably reluctant to disclose it. Thus, the National Household Survey on Drug Abuse estimated that 440,000 persons in the United States had injected illicit drugs in the past year, while contemporaneous estimates from other sources put the figure at 1.5 million to 2.0 million.[86,87] Over 1 million people who injected drugs were either missed or misclassified in that household survey. Because 50%-90% of people who currently inject illicit drugs have HCV antibody (depending on the duration of their use),[88,89] this provides further support for the likelihood that among current injectors alone, a million more Americans have been infected with HCV than might be detected by a household survey.

These limitations underscore the need for better assessment and monitoring of the health needs of socially marginalized populations. This problem impairs public health responses to nearly all diseases, not just hepatitis C: surveillance systems are not accurate if they overlook disenfranchised groups.[6] Hepatitis C prevalence estimates should not be based on NHANES alone but should be augmented with expanded HCV screening, case surveillance, and focused seroprevalence studies of established and emerging groups at elevated risk. These testing initiatives can provide data for surveillance purposes at the same time as they identify infected persons and link them to care and treatment.

For the meantime, projections based on NHANES data may underestimate current health disparities and the burden of liver disease that can be expected in the coming decades. Most models projecting the future disease burden use NHANES estimates without correction for the excluded populations or other sources of underestimation.[90-93] As new highly effective antiviral regimens offer the hope of transforming the hepatitis C epidemic, it will be important to plan appropriately.[89,94]

These findings may heighten concern about the affordability of providing antiviral treatment to all who need it. Only an estimated 5%-6% of infected people in the United States have been successfully treated.[11] It is important to realize, however, that curative antiviral treatment, and the associated costs, will occur over many years. Most people with hepatitis C do not yet know their status,[11,95] and many of the groups discussed in this article have substantial barriers to health care access.[94] Resources for addressing these deficiencies have not kept pace with the need.[89] It will take years of concerted effort before most infected people, especially

those in underserved groups, are tested, engaged in care, and referred for treatment. Indeed, a national commitment will be needed to bring screening, treatment, and prevention services to these populations.[11,89,94,95]

Currently, however, public and private payers are limiting access to the new, high-priced oral drugs for hepatitis C, requiring abstinence from drugs and alcohol and the presence of advanced liver disease,[96,97] which means that HCV will continue to spread among the highly affected groups most in need, such as young people who inject drugs.[80,81] More accurate estimates of hepatitis C prevalence and incidence can help inform the planning and negotiation of strategies to reach, test, treat, cure, and prevent every case of hepatitis C.[94]

Appendix A: Sex Ratio Methods

Where sex-specific prevalence rates were available, we calculated the M:F ratio of infected persons by multiplying the M:F prevalence in each study with sex-specific prevalence data[20,28,32-36,38,41-45,49,52,53,64,65] by the sex ratio of the population:

M:F ratio of infected persons = M:F prevalence ratio × M:F sex ratio of population

This is true because:

$$\frac{\text{No. infected women in population}}{\text{No. infected men in population}} = \frac{\text{HCV prevalence in women}}{\text{HCV prevalence in men}} \times \frac{\text{Total no. women in population}}{\text{Total no. men in population}}$$

For prison studies we used the sex ratio of the respective state prison system. For homeless studies we used the estimated overall national sex ratio.

We then converted the M:F ratio of infected persons to the percentage of men over the percentage of women. For prison and homeless studies we averaged the percentages, weighting prison studies by the total prison population for the respective state and homeless studies by the sample size of the study. For the military population, we used the one representative national study[64] (self-weighted with respect to sex ratios) and calculated the M:F ratio of infected persons directly.

Appendix B: Projected Seroprevalence of People Living in Prison Versus People Entering Prison

Background. Entrants to prison are younger than the overall prison population. This is true not only because persons age while they serve time in prison but also because prison populations are enriched with people serving longer terms, in proportion to the length of time they serve. The mean age of people entering prison in the United States in 2012 was 33 years, while the mean age of people living in prison was 36 years.[98] Thus, because HCV prevalence is strongly associated with older age in people <65 years (the age of 98% of prisoners), the HCV prevalence of prison entrants underrepresents the HCV prevalence of people serving time in prison.

Methods and Results. To determine the effect on HCV seroprevalence of the age difference between people entering prison and people living in prison, we used published data on HCV prevalence rates by birth cohort of entrants to prison in Pennsylvania.[41] The age distribution of entrants to prison in Pennsylvania was similar to that of entrants to prison nationwide.[98] While the HCV prevalence of persons entering prison in Pennsylvania might not represent the prevalence of persons entering prison nationwide, we used the distribution of rates by birth cohort as a proxy for the distribution by birth cohort nationwide. (For example, the peak prevalences in Pennsylvania entrants were in the 1945-1965 birth cohort, similar to the national household survey data).[10] When we applied the birth cohort–specific prevalence data from Pennsylvania to the age distribution of entrants in 2012 nationwide, we obtained an overall HCV prevalence similar to that reported from Pennsylvania (17.9% versus 18.1%). When we then applied the same prevalence data to the age distribution of persons serving time in prison in 2012 nationwide, the calculated prevalence was 20.3%. The difference in projected HCV prevalence between the entrants (17.85%) and persons serving time (20.30%) was 2.45%.

Summary. To adjust the projected seroprevalence of prisoners for the difference between the age of people entering prison and the age of people living in prison, we applied the birth cohort–specific HCV prevalences of persons entering prison in Pennsylvania[41] to the age distributions of persons entering prison and persons living in prison nationwide. The projected prevalence of persons serving time was 2.45% greater than the projected prevalence among entrants.

References

1. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. http://www.cdc.gov/nchs/nhanes.htm. Accessed September 22, 2014.
2. Zipf G, Porter KS, Ostchega Y, Lewis BG, Dostal J. National Health and Nutrition Examination Survey: Plan and operations, 1999-2010. National Center for Health Statistics. Vital Health Stat 2013;1(56):1-28. http://www.cdc.gov/nchs/data/series/sr_01/sr01_056.pdf.
3. Denniston MM, Jiles RB, Drobeniuc J, Klevens RM, Ward JW, McQuillan GM, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. Ann Intern Med 2014;160:293-300.

4. McQuillan GM, Khare M, Karon JM, Schable CA, Vlahov D. Update on the seroepidemiology of human immunodeficiency virus in the United States household population: NHANES III, 1988-1994. J Acquir Immune Defic Syndr Hum Retrovirol 1997;14:355-360.
5. Kuniholm MH, Jung M, Everhart JE, Cotler S, Heiss G, McQuillan G, et al. Prevalence of hepatitis C virus infection in US Hispanic/Latino adults: results from the NHANES 2007-2010 and HCHS/SOL studies. J Infect Dis 2014;209:1585-1590.
6. Waksberg J, Levine D, Marker D. Assessment of Major Federal Data Sets for Analyses of Hispanic and Asian or Pacific Islander Subgroups and Native Americans. Table 3-3. Rockville MD: Westat; 2000. http://aspe.hhs.gov/hsp/minority-db00/task3/section3.htm.
7. Perumalswami P, Factor S, Kapelusznik L, Friedman SL, Pan CQ, Chang C, et al. Hepatitis Outreach Network: a practical strategy for hepatitis screening with linkage to care in foreign-born communities. J Hepatol 2013;58:890-897.
8. Shire AM, Sandhu DS, Kaiya JK, Oseini AM, Yang JD, Chaiteerakij R, et al. Viral hepatitis among Somali immigrants in Minnesota: association of hepatitis C with hepatocellular carcinoma. Mayo Clin Proc 2012;87:17-24.
9. Batash S, Khaykis I, Raicht RF, Bini EJ. High prevalence of hepatitis C virus infection among immigrants from the former Soviet Union in the New York City metropolitan area: results of a community-based screening program. Am J Gastroenterol 2008;103:922-927.
10. Armstrong G, Wasley A, Simard E, McQuillan G, Kuhnert W, Alter M. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med 2006;144:705-714.
11. Holmberg S, Spradling P, Moorman A, Denniston MM. Hepatitis C in the United States. N Engl J Med 2013;368:1859-1861.
12. Glaze LE, Herberman EJ. Correctional Populations in the United States, 2012. Washington, DC: Bureau of Justice Statistics; 2013. http://www.bjs.gov/content/pub/pdf/cpus12.pdf.
13. National Alliance to End Homelessness. The state of homelessness in America 2013. Washington, DC: National Alliance to End Homelessness. http://www.endhomelessness.org/library/entry/the-state-of-homelessness-2013. Published April 8, 2013.
14. Centers for Disease Control and Prevention. National Hospital Discharge Survey. Atlanta, GA: Centers for Disease Control and Prevention; 2010. http://www.cdc.gov/nchs/nhds.htm.
15. National Center for Veterans Analysis and Statistics. Selected Veterans Health Administration Characteristics: FY2002 to FY2013. Washington, DC: Department of Veterans Affairs; 2013. https://catalog.data.gov/dataset/selected-veterans-health-administration-characteristics-fy2002-fy2013.
16. Jones AL, Dwyer LL, Bercovitz AR, Strahan GW. The National Nursing Home Survey: 2004 overview. Vital Health Stat 2009;13(167):1-155.
17. US Census. National security and veterans affairs. In: Statistical Abstract of the United States: 2012. Washington, DC: US Census Bureau; 2012. http://www.census.gov/prod/2011pubs/12statab/defense.pdf.
18. US Census. Health and nutrition. In: Statistical Abstract of the United States: 2012. Washington DC: United States Census Bureau; 2012. http://www.census.gov/compendia/statab/cats/health_nutrition.html.
19. Norris T, Vines PL, Hoeffel EM. The American Indian and Alaska Native population: 2010. Washington, DC: US Census Bureau; 2012. http://www.census.gov/prod/cen2010/briefs/c2010br-10.pdf.
20. Varan AK, Mercer DW, Stein MS, Spaulding AC. Hepatitis C seroprevalence among prison inmates since 2001: still high but declining. Public Health Rep 2014;129:187-195.
21. Harrison PM, Beck AJ. Prison and jail inmates at midyear 2005. Washington, DC: Bureau of Justice Statistics; 2006. http://www.bjs.gov/content/pub/pdf/pjim05.pdf.
22. West HC, Sabol WJ. Prison inmates at midyear 2008—statistical tables. Washington, DC: Bureau of Justice Statistics; 2009. http://www.bjs.gov/content/pub/pdf/pim08st.pdf.
23. Tseng FC, Edlin BR, Zhang M, Kral A, Busch MP, Ortiz-Conde BA, et al. The inverse relationship between chronic HBV and HCV infections among injection drug users is associated with decades of age and drug use. J Viral Hepat 2008;15:690-698.
24. Edlin BR. Five million Americans infected with the hepatitis C virus: a corrected estimate. Hepatology 2005;42(4 Suppl. 1):213A.
25. Ruiz JD, Molitor F, Sun RK, Mikanda J, Facer M, Colford JM Jr, et al. Prevalence and correlates of hepatitis C virus infection among inmates entering the California correctional system. West J Med 1999;170:156-160.
26. Ruiz JD, Molitor F, Plagenhoef JA. Trends in hepatitis C and HIV infection among inmates entering prisons in California, 1994 versus 1999. AIDS 2002;16:2236-2238.
27. Hennessey K, Kim A, Griffin V, Collins NT, Weinbaum CM, Sabin K. Prevalence of infection with hepatitis B and C viruses and co-infection with HIV in three jails: a case for viral hepatitis prevention in jails in the United States. J Urban Health 2009;86:93-105.
28. Fox RK, Currie SL, Evans J, Wright TL, Tobler L, Phelps B, et al. Hepatitis C virus infection among prisoners in the California State correctional system. Clin Infect Dis 2005;41:177-186.
29. Spaulding A, Greene C, Davidson K, Schneidermann M, Rich J. Hepatitis C in state correctional facilities. Prev Med (Baltim) 1999;28:92-100.
30. Fennie K, Selwyn P, Stephens P, Balacos K, Altice F. Hepatitis C virus prevalence and incidence in a cohort of HIV^+ and HIV^- female prisoners [Abstract]. In: Program and Abstracts of the XI International Conference on AIDS. Geneva: International AIDS Society; 1996. Abstract Tu.C.2655.
31. Spaulding A, Bowden C, Miller L, Mbaba M, Church J. An IID-DEALL program for jails: integrating infectious disease detection at entry and linkage to care. Presentation at National HIV Prevention Conference, Atlanta, Georgia, August 14-17, 2011.
32. Solomon L, Flynn C, Muck K, Vertefeuille J. Prevalence of HIV, syphilis, hepatitis B, and hepatitis C among entrants to Maryland correctional facilities. J Urban Health 2004;81:25-37.
33. Cocoros N, Nettle E, Church D, Bourassa L, Sherwin V, Cranston K, et al. Screening for Hepatitis C as a Prevention Enhancement (SHAPE) for HIV: an integration pilot initiative in a Massachusetts County correctional facility. Public Health Rep 2014;129:S5-S11.
34. Lincoln T, Tuthill RW, DePietro SL, Tocco MJ, Keough K, Conklin TJ. Viral hepatitis, risk behaviors, aminotransferase levels, and screening options at a county correctional center. J Correct Health Care 2006;12:249-261.
35. Eastman E, Rappaport E, DeMaria A, Werner B. Validation of self-reported risk as a method for identifying anti–hepatitis C positive individuals at time of intake physical examination at Massachusetts Department of Correction facilities [Abstract]. In: Program and Abstracts of the 129th Annual Meeting of the American Public Health Association. Washington, DC: American Public Health Association; 2001. Abstract 30003. https://apha.confex.com/apha/129am/techprogram/paper_30003.htm.
36. Wenger PJ, Rottnek F, Parker T, Crippin JS. Assessment of hepatitis C risk factors and infection prevalence in a jail population. Am J Public Health 2014;104:1722-1727.
37. Chen L, Salcido B, Whitley R, Forero M. Seroprevalence of hepatitis B and C markers among inmates entering Nevada State Correctional system [Abstract]. In: Program and Abstracts of the 130th Annual Meeting of the American Public Health Association. Washington, DC: American Public Health Association; 2002. Abstract 48667. https://apha.confex.com/apha/130am/techprogram/paper_48667.htm.
38. Alvarez KJ, Befus M, Herzig CT, Larson E. Prevalence and correlates of hepatitis C virus infection among inmates at two New York State correctional facilities. J Infect Public Health 2014;7:517-521.
39. Wang L, Smith L, Wright LN, Birkhead GS, Zhu B, Young ME, et al. Changing dynamics of hepatitis C virus (HCV) and injection drug use (IDU) as predictors of HIV infection among inmates entering the New York State (NYS) prison system from 2000 to 2007 [Abstract]. Am J Epidemiol 2010;171(Suppl.):S134. Abstract 536.
40. Smith L, Wang L, Wright L, Sabin K, Glebatis D, Smith P. Hepatitis C virus (HCV) seroprevalence in incoming inmates in New York State

(NYS), 2000-2001 [Abstract]. In: Programs and Abstracts of the 40th Annual Meeting of the Infectious Diseases Society of America. Alexandria, VA: Infectious Diseases Society of America; 2002. Abstract 793.
41. Larney S, Mahowald MK, Scharff N, Flanigan TP, Beckwith CG, Zaller ND. Epidemiology of hepatitis C virus in Pennsylvania state prisons, 2004-2012: limitations of 1945-1965 birth cohort screening in correctional settings. Am J Public Health 2014;104:e69-e74.
42. Macalino GE, Vlahov D, Dickinson BP, Schwartzapfel B, Rich JD. Community incidence of hepatitis B and C among reincarcerated women. Clin Infect Dis 2005;41:998-1002.
43. Macalino GE, Vlahov D, Sanford-Colby S, Patel S, Sabin K, Salas C, et al. Prevalence and incidence of HIV, hepatitis B virus, and hepatitis C virus infections among males in Rhode Island prisons. Am J Public Health 2004;94:1218-1223.
44. Baillargeon J, Wu H, Kelley MJ, Grady J, Linthicum L, Dunn K. Hepatitis C seroprevalence among newly incarcerated inmates in the Texas correctional system. Public Health 2003;117:43-48.
45. Pfister JR, Haase B, State W, Hurie M. Targeted hepatitis C virus screening of inmates on admission to the Wisconsin adult correctional system. Wisconsin AIDS/HIV Update 2001;(spring):43-46.
46. Desai RA, Rosenheck RA, Agnello V. Prevalence of hepatitis C virus infection in a sample of homeless veterans. Soc Psychiatry Psychiatr Epidemiol 2003;38:396-401.
47. Nyamathi AM, Dixon EL, Wiley D, Christiani A, Lowe A. Hepatitis C virus infection among homeless men referred from a community clinic. West J Nurs Res 2006;28:475-488.
48. Cheung RC, Hanson AK, Maganti K, Keeffe EB, Matsui SM. Viral hepatitis and other infectious diseases in a homeless population. J Clin Gastroenterol 2002;34:476-480.
49. Rosenblum A, Nuttbrock L, McQuistion HL, Magura S, Joseph H. Hepatitis C and substance use in a sample of homeless people in New York City. J Addict Dis 2001;20:15-25.
50. Schwarz KB, Garrett B, Alter MJ, Thompson D, Strathdee SA. Seroprevalence of HCV infection in homeless Baltimore families. J Health Care Poor Underserved 2008;19:580-587.
51. Stein JA, Nyamathi A. Correlates of hepatitis C virus infection in homeless men: a latent variable approach. Drug Alcohol Depend 2004; 75:89-95.
52. Gelberg L, Robertson MJ, Arangua L, Leake BD, Sumner G, Moe A, et al. Prevalence, distribution, and correlates of hepatitis C virus infection among homeless adults in Los Angeles. Public Health Rep 2012; 127:407-421.
53. Strehlow AJ, Robertson MJ, Zerger S, Rongey C, Arangua L, Farrell E, et al. Hepatitis C among clients of health care for the homeless primary care clinics. J Health Care Poor Underserved 2012;23:811-833.
54. Boyce DE, Tice AD, Ona F, Akinaka K, Lusk H. Viral hepatitis in a homeless shelter in Hawai'i. Hawaii Med J 2009;68:113-115.
55. Austin GE, Jensen B, Leete J, De l'Aune W, Bhatnagar J, Racine M, et al. Prevalence of hepatitis C virus seropositivity among hospitalized US veterans. Am J Med Sci 2000;319:353-359.
56. Pham D, Walshe D, Montgomery J, Buskell-Bales Z, Collier K. Seroepidemiology of hepatitis C and B in an urban VA medical center. Hepatology 1994;20(Suppl.):236A.
57. Cheung RC. Epidemiology of hepatitis C virus infection in American veterans. Am J Gastroenterol 2000;95:740-747.
58. Brillman JC, Crandall CS, Florence CS, Jacobs JL. Prevalence and risk factors associated with hepatitis C in ED patients. Am J Emerg Med 2002;20:476-480.
59. Meyer JM. Prevalence of hepatitis A, hepatitis B, and HIV among hepatitis C-seropositive state hospital patients: results from oregon state hospital. J Clin Psychiatry 2003;64:540-545.
60. Tabibian JH, Wirshing D, Pierre JM, Guzik LH, Kisicki MD, Danovitch I, et al. Hepatitis B and C among veterans on a psychiatric ward. Dig Dis Sci 2008;53:1693-1698.
61. Hall MR, Ray D, Payne J. Prevalence of hepatitis C, hepatitis B, and human immunodeficiency virus in a Grand Rapids, Michigan emergency department. J Emerg Med 2010;38:401-405.
62. Calore BL, Cheung RC, Giori NJ. Prevalence of hepatitis C virus infection in the veteran population undergoing total joint arthroplasty. J Arthroplasty 2012;27:1772-1776.
63. Chien NT, Dundoo G, Horani MH, Osmack P, Morley JH, Di Bisceglie AM. Seroprevalence of viral hepatitis in an older nursing home population. J Am Geriatr Soc 1999;47:1110-1113.
64. Hyams KC, Riddle J, Rubertone M, Trump D, Alter MJ, Cruess DF, et al. Prevalence and incidence of hepatitis C virus infection in the US military: a seroepidemiologic survey of 21,000 troops. Am J Epidemiol 2001;153:764-770.
65. Hakre S, Peel S, O'Connell RJ, Sanders-Buell EE, Jagodzinski LL, Eggleston JC, et al. Transfusion-transmissible viral infections among US military recipients of whole blood and platelets during Operation Enduring Freedom and Operation Iraqi Freedom. Transfusion 2011;51:473-485.
66. Neumeister AS, Pilcher LE, Erickson JM, Langley LL, Murphy MM, Haukaas NM, et al. Hepatitis C prevalence in an urban Native American clinic: a prospective screening study. J Natl Med Assoc 2007;99:389-392.
67. Burt M. Helping America's Homeless: Emergency Shelter or Affordable Housing? Washington, DC: Urban Institute Press; 2001.
68. Grant R, Gracy D, Goldsmith G, Shapiro A, Redlener I. Twenty-five years of child and family homelessness: where are we now? Am J Public Health 2013;103(Suppl. 2):e1-e10.
69. US Census Bureau. Accuracy and Limitations of Census Data. In: 2007 American Indian and Alaska Native Tribal Consultations Final Report. Washington, DC: US Census Bureau; 2008:13-17.
70. DeWeaver N. American community survey data on the American Indian/Alaska Native population: a look behind the numbers. Washington, DC: National Congress of American Indians; 2013. http://www.ncai.org/policy-research-center/initiatives/ACS_data_on_the_AIAN_Population_paper_by_Norm_DeWeaver.pdf.
71. Montana 2008 annual report: STDs including HIV/AIDS and hepatitis C. Helena, MT: Montana Department of Public Health and Human Services; 2009. http://www.dphhs.mt.gov/Portals/85/publichealth/documents/HIVSTD/HIVSTD2008AnnualReport.pdf.
72. Division of Viral Hepatitis. Viral Hepatitis Surveillance, United States, 2012. Atlanta, GA: Centers for Disease Control and Prevention; 2014. http://www.cdc.gov/hepatitis/Statistics/2012Surveillance/index.htm.
73. Burgard S, Seefeldt KS, Zelner S. Housing instability and health: findings from the Michigan recession and recovery study. Soc Sci Med 2012;75:2215-2224.
74. Witte P. The State of Homelessness in America 2012. Washington, DC: National Alliance to End Homelessness. http://www.endhomelessness.org/library/entry/the-state-of-homelessness-in-america-2012. Published January 17, 2012.
75. Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, et al. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. MMWR Recomm Rep 2012;61:1-32.
76. Centers for Disease Control and Prevention. Pilot study of a household survey to determine HIV seroprevalence. MMWR Morb Mortal Wkly Rep 1991;40:1-5.
77. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57:1333-1342.
78. Ericksen E. An evaluation of the 2000 census. In: Final Report to Congress. Suitland, MD: US Census Monitoring Board; 2001:15-85.
79. Bell RM, Cohen ML, National Research Council, eds. Coverage Measurement in the 2010 Census. Washington, DC: National Academies Press; 2009. http://www.nap.edu/catalog/12524/coverage-measurement-in-the-2010-census.
80. Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, et al. Emerging epidemic of hepatitis C virus infections among young non-urban persons who inject drugs in the United States, 2006-2012. Clin Infect Dis 2014;59:1411-1419.
81. Zibbell JE, Hart-Malloy R, Barry J, Fan L, Flanigan C. Risk factors for HCV infection among young adults in rural New York who inject prescription opioid analgesics. Am J Public Health 2014:e1-e7.

82. Zibbell JE, Iqbal K, Patel RC, Suryaprasad A, Sanders KJ, Moore-Moravian L, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years—Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. MMWR Morb Mortal Wkly Rep 2015;64:453-458.
83. Conrad C, Bradley HM, Broz D, Buddha S, Chapman EL, Galang RR, et al. Community outbreak of HIV infection linked to injection drug use of oxymorphone—Indiana, 2015. MMWR Morb Mortal Wkly Rep 2015;64:443-444.
84. Lansky A, Brooks JT, DiNenno E, Heffelfinger J, Hall HI, Mermin J. Epidemiology of HIV in the United States. J Acquir Immune Defic Syndr 2010;55(Suppl. 2):S64-S68.
85. Karon JM, Rosenberg PS, McQuillan G, Khare M, Gwinn M, Petersen LR. Prevalence of HIV infection in the United States, 1984 to 1992. JAMA 1996;276:126-131.
86. Tempalski B, Pouget ER, Cleland CM, Brady JE, Cooper HL, Hall HI, et al. Trends in the population prevalence of people who inject drugs in US metropolitan areas 1992-2007. PLoS One 2013;8: e64789.
87. Mathers BM, Degenhardt L, Phillips B, Wiessing L, Hickman M, Strathdee SA, et al. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. Lancet 2008; 372:1733-1745.
88. Tseng F-C, O'Brien TR, Zhang M, Kral AH, Ortiz-Conde BA, Lorvick J, et al. Seroprevalence of hepatitis C virus and hepatitis B virus among San Francisco injection drug users, 1998 to 2000. HEPATOLOGY 2007;46:666-671.
89. Edlin BR. Perspective: test and treat this silent killer. Nature 2011;474: S18-S19.
90. Rein DB, Wittenborn JS, Weinbaum CM, Sabin M, Smith BD, Lesesne SB. Forecasting the morbidity and mortality associated with prevalent cases of pre-cirrhotic chronic hepatitis C in the United States. Dig Liver Dis 2011;43:66-72.
91. Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)–infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. Gastroenterology 2010;138:513-521.
92. Kabiri M, Jazwinski AB, Roberts MS, Schaefer AJ, Chhatwal J. The changing burden of hepatitis C virus infection in the United States: model-based predictions. Ann Intern Med 2014;161:170-180.
93. Razavi H, Elkhoury AC, Elbasha E, Estes C, Pasini K, Poynard T, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. HEPATOLOGY 2013;57:2164-2170.
94. Edlin BR, Winkelstein ER. Can hepatitis C be eradicated in the United States? Antiviral Res 2014;110:79-93.
95. Institute of Medicine. Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C. Washington, DC: National Academies Press; 2010.
96. Barua S, Greenwald R, Grebely J, Dore GJ, Swan T, Taylor LE. Restrictions for medicaid reimbursement of sofosbuvir for the treatment of hepatitis C virus infection in the United States. Ann Intern Med 2015 Jun 30. doi: 10.7326/M15-0406. [Epub ahead of print].
97. Canary LA, Klevens RM, Holmberg SD. Limited access to new hepatitis C virus treatment under state Medicaid programs. Ann Intern Med 2015 Jun 30. doi: 10.7326/M15-0320. [Epub ahead of print]
98. Carson EA. Prisoners in 2013. Washington, DC: Bureau of Justice Statistics; 2014. http://www.bjs.gov/content/pub/pdf/p13.pdf. Published September 2014.