Previous Exposure to HCV Among Persons Born During 1945–1965: Prevalence and Predictors, United States, 1999–2008

Bryce D. Smith, PhD, Geoff A. Beckett, PA-C, MPH, Anthony Yartel, MPH, Deborah Holtzman, PhD, Nita Patel, DrPH, and John W. Ward, MD

Objectives. We examined HCV exposure prevalence and predictors among persons in the United States born during 1945–1965.

Methods. With data from the 1999–2008 National Health and Nutrition Examination Survey, we calculated the proportion of persons born during 1945–1965 who tested positive for HCV antibody (anti-HCV) and analyzed the prevalence by sociodemographic and behavioral risk factors.

Results. Anti-HCV prevalence in the 1945–1965 birth cohort was 3.2% (95% confidence interval [CI] = 2.8%, 3.8%), substantially higher than among other adults (0.9%). Within the cohort, anti-HCV prevalence was higher among non-Hispanic Blacks (6.4%; 95% CI = 5.3%, 7.7%), persons with injection drug use histories (56.8%; 95% CI = 48.4%, 64.8%), and persons with elevated alanine aminotransferase levels (12.7%; 95% CI = 10.7%, 15.1%). Injection drug use (adjusted odds ratio = 98.4; 95% CI = 58.8, 164.5) was the strongest anti-HCV prevalence predictor. Among anti-HCV–positive persons, 57.8% reported having 2 or more alcoholic drinks daily.

Conclusions. With the high prevalence of HCV among persons born during 1945–1965, the increasing morbidity and mortality associated with HCV, and reductions in liver cancer and HCV-related mortality when HCV is eradicated, it is critically important to identify persons with HCV and link them to appropriate care. (*Am J Public Health.* 2014;104:474–481. doi:10.2105/AJPH.2013.301549)

In the United States, the incidence of HCV infection rose dramatically through the 1970s and 1980s reaching more than 200 000 new infections per year through the mid- to late-1980s.[1] This high incidence resulted in a disproportionately high burden of HCV infection among Americans who were born between the mid-1940s and the mid-1960s, a birth cohort popularly referred to as the baby boom generation.[2] Alter et al. first documented the relatively high prevalence of HCV infection among this cohort in their analysis of 1988–1994 National Health and Nutrition Examination Survey (NHANES) data, reporting that 65% of persons with HCV infection were aged 30 to 49 years during the survey period.[3] In an analysis of NHANES data from 1999 to 2002, a similarly high proportion of all persons with HCV antibody had been born from 1945 through 1964.[1] This cohort effect on the high prevalence of HCV infection in the baby boom generation has been attributed largely to exposures (principally injection drug use [IDU] and blood transfusion before 1992) that occurred many years before the survey periods.[1,3] However, a significant proportion of HCV-infected persons do not report any risk factors,[4–6] perhaps because of fear of being stigmatized,[7] or simply lack of recall or knowledge of exposures such as those that may occur in health care settings.[8,9]

A validated Markov model forecasting lifetime morbidity and mortality attributable to HCV infection projected that of 2.9 million persons with untreated HCV infection who did not have cirrhosis of the liver in 2005, 1 071 000 (36.8%) will die from complications of HCV.[10] In the United States, HCV-associated disease is the leading indication for liver transplantation and HCV infection is a leading cause of hepatocellular carcinoma.[11–14] Approximately 73.9% of HCV-associated mortality occurs among persons born from 1945 to 1965.[15]

In 1998, the Centers for Disease Control and Prevention recommended[16] that persons with certain risk factors (e.g., any history of IDU) or medical conditions (e.g., persistently elevated alanine aminotransferase [ALT] levels) be tested for HCV infection. Despite these recommendations, testing practices over the past decade have had limited success in identification of HCV infection in the United States as estimates of the proportion of persons who are unaware of their infection range from 40% to 85%.[17–20] Contributing to the limited success of the recommendations is the difficulty in obtaining risk behavior history that occurred in the distant past, the primarily asymptomatic nature of the infection, and a less than optimal level of physician knowledge regarding the natural history and prevalence of infection, the current recommendations for testing, and interpretation of test results.[21–24]

In 2011, the prospects for successful medical treatment of HCV infection were significantly improved with the US Food and Drug Administration licensure of 2 direct-acting antiviral medications, both in the protease inhibitor class. In clinical trials, the rates of sustained viral response—equivalent to a "virological cure"—increased from 44% with use of the current standard regimen, to 75% when a direct-acting antiviral medication was added to that regimen in treatment of persons infected with HCV genotype 1, the genotype that is most common in the United States.[25] Since this article was accepted for publication, the US Food and Drug Administration has approved new HCV medications[26,27] that have further increased cure rates to as high as 90% in clinical trials.

Persons who achieve a sustained viral response after treatment experience significantly less liver-related morbidity (including hepatocellular carcinoma),[28] less liver-related mortality,[29] and reductions in all-cause mortality.[30] However, the

potential population benefits from these improvements in treatment effectiveness will be limited unless there are concurrent increases in the rate of identification and treatment of HCV-infected persons.[31]

Because of the limited effectiveness of risk-based testing strategies to date and the high prevalence of HCV infection and projected disease burden, the Centers for Disease Control and Prevention recently issued the Recommendations for the Identification and Initial Care of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965[32] with the goal of identifying persons with HCV infection who are undiagnosed. The recommendation was subsequently made by the US Preventive Services Task Force.[33] The purpose of the current study was to determine the proportion of persons in the birth cohort who were positive for antibody to HCV (anti-HCV), and to examine the sociodemographic and behavioral risk factors associated with anti-HCV prevalence.

METHODS

We analyzed NHANES data collected from 1999 to 2008. NHANES is an annual nationally representative multistage, stratified probability cluster survey of the US civilian, noninstitutionalized population. Information on the survey design and implementation, including institutional review board approval and consent, is detailed in the survey documentation.[34,35]

Anti-HCV testing is administered to NHANES participants aged 6 years or older. We restricted our analysis to adult participants born from 1945 to 1965 who were interviewed and provided serum samples for anti-HCV testing. Birth year was estimated by subtracting participant age at time of survey from estimated year in which participant was surveyed. Because NHANES does not release data on participant birth year or the actual year in which a participant was interviewed or examined, we estimated the earliest survey year for each participant according to the variable, "six month time period when the examination was performed: November 1 through April 30, May 1 through October 31." As an example, for the 1999–2000 survey cycle, participants examined from November 1 to April 30 were assigned an earliest survey year of 1999 and those examined from May 1 through October 30 were assigned to the 2000 survey year. We excluded participants without specimens for testing and those with indeterminate anti-HCV results from the final analytic sample.

Outcome Variable

The outcome measure was anti-HCV prevalence as determined by serologic testing. We chose anti-HCV status as an endpoint because HCV RNA testing was not performed for the 2003–2004 NHANES cycle, and we determined that combining data from all 10 years (1999–2008) was necessary to achieve sufficient subdomain sample sizes for improved precision and reliability of point estimates.

Specimens were tested for antibodies to HCV by repeated enzyme-linked immunosorbent assay (ELISA version 3.0, Ortho Diagnostic Systems Inc, Raritan, NJ). Reactive specimens were confirmed by recombinant immunoblot assay (RIBA version 3.0, Chiron Corporation, Emeryville, CA). Participants who tested positive by both ELISA and RIBA were categorized as anti-HCV–positive.

Independent Variables

We examined the following independent variables as potential predictors or confounders of anti-HCV prevalence within the birth cohort: race/ethnicity, gender, country of birth, veteran status, marital status, educational attainment, family income, health insurance status, daily alcohol consumption within the past 12 months, age at first sexual intercourse, number of lifetime sexual partners, lifetime IDU (cocaine, heroin, and methamphetamine), history of blood transfusion before 1992, and ALT level.[1,3] We categorized race/ethnicity as non-Hispanic White, non-Hispanic Black, Mexican American, and other. We categorized educational attainment as completed less than high school and completed high school or more; marital status as married or living with partner, divorced or separated or widowed, and never married; and family income as greater than 2 times federal poverty threshold, 1 to 2 times federal poverty threshold, and less than the federal poverty threshold. We defined elevated ALT as 40 or more international units per liter. For independent variables with 10% or more of observations with missing values, we created an "unknown" category to include those missing values as valid for analysis. Accordingly, we categorized alcohol consumption as 0 or 1, 2 or more, and unknown number of drinks per day within the past year; age at first sexual intercourse as 17 years or younger, 18 years or older, and unknown; number of lifetime sexual partners as 0 to 9, 10 to 19, 20 or more, and unknown; lifetime drug use as never, non–injection drug use, IDU, and unknown.

NHANES questions related to sexual behavior and history of IDU are restricted to adult participants younger than 60 years. Thus, all analyses involving these variables in the current study were similarly restricted.

Statistical Analysis

We generated proportions and 95% confidence intervals (CIs) to describe the characteristics of the 1945–1965 birth cohort. We also produced estimates of anti-HCV prevalence in the birth cohort and by subgroups. We specified linear contrasts of estimates to test for statistical differences in characteristics between anti-HCV–positive participants and all participants, and to test for differences in anti-HCV prevalence between subgroups. We assessed statistical reliability of estimated proportions by evaluating relative standard errors (< 30%) and by ensuring that subdomains met NHANES minimum sample size requirements. We generated unadjusted odds ratios from univariate logistic regression models. We defined statistical significance as P value less than .05.

We developed a multivariate logistic regression model to identify independent risk factors associated with anti-HCV positivity within the birth cohort after we controlled for covariates. We specified an estimated full model by including all independent variables with a P value of less than .1 from the univariate analyses. Using a backward elimination procedure, we removed variables with the lowest observed partial F-statistic at a predetermined P value of less than .1. We simultaneously tested for 2-way interaction effects between race and IDU or gender and IDU, by using multiple partial F-tests. We assessed multicollinearity among covariates by review of diagnostic statistics including variance

inflation factors (> 2.5), condition indices (> 15), and variance proportions (> 0.5; SAS version 9.3, SAS Institute, Cary, NC). In deciding whether to exclude a covariate because of collinearity, we also considered the relative importance of the covariate, its relationship with key variables such as IDU, and its contribution to the overall model fit. We used the Hosmer–Lemeshow goodness-of-fit test to evaluate the overall fit of the final model. Except as otherwise specified, we analyzed all data with SAS-callable SUDAAN to account for the complex survey design (version 10.0.1, Research Triangle Institute, Research Triangle Park, NC). We rescaled sample weights after combining data across multiple survey years. We estimated variance and standard errors by using the Taylor series (linearization) method.

RESULTS

We identified a total of 8167 participants estimated to be born from 1945 to 1965 who were both interviewed and examined. After we excluded participants without specimens (n = 411) and those with indeterminate anti-HCV results (n = 33), the final analytic sample for the birth cohort was 7723 (95% of those examined). Table 1 shows the demographic, behavioral, and clinical characteristics of the birth cohort population and those in the cohort who were anti-HCV–positive. Relative to the total birth cohort population, a greater proportion of anti-HCV–positive participants were male, non-Hispanic Black, had a family income below the poverty threshold, and had no health insurance coverage. Among anti-HCV–positive participants, 41.9% reported a history of IDU, 16.2% received a blood transfusion before 1992, 57.8% consumed 2 or more alcoholic drinks per day, and 51.3% had elevated ALT levels. Combined, persons with a history of IDU or blood transfusion accounted for 51.7% of anti-HCV–positive participants; 48.3% reported no known exposure risks.

Prevalence of Anti-HCV in the Birth Cohort

Prevalence estimates for the birth cohort and subgroups are presented in Table 2. The overall prevalence of anti-HCV in the birth cohort was estimated at 3.2% (95% CI = 2.8%,

TABLE 1—Characteristics of Participants Born From 1945 to 1965: National Health and Nutrition Examination Survey, 1999–2008

Characteristic	All Participants Tested		Anti-HCV–Positive		P[a]
	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)	
Overall	7723	100	308	100	
Gender					
Female	3911	50.8 (49.7, 51.9)	104	34.3 (27.5, 41.9)	< .001
Male	3812	49.2 (48.1, 50.3)	204	65.7 (58.1, 72.5)	< .001
Race/ethnicity					
Non-Hispanic White	3648	72.8 (70.0, 75.4)	124	64.8 (58.3, 70.8)	.01
Non-Hispanic Black	1700	10.7 (9.2, 12.4)	110	21.2 (16.9, 26.3)	< .001
Mexican American	1564	6.2 (5.1, 7.5)	49	6.25 (4.3, 8.9)	.99
Other	811	10.3 (8.7, 12.1)	25	7.7 (4.6, 12.7)	.22
Marital status					
Married or living with partner	5170	72.4 (70.6, 74.1)	170	60.2 (52.6, 67.4)	.002
Divorced, separated, or widowed	1640	19.2 (17.8, 20.7)	80	25.2 (19.3, 32.15)	.07
Never married	747	8.4 (7.4, 9.4)	52	14.6 (10.5, 20.0)	.009
Country of birth					
United States	5836	84.9 (82.7, 86.8)	284	94.7 (91.2, 96.9)	< .001
Other	1884	15.1 (13.2, 17.3)	24	5.3 (3.1, 8.8)	< .001
Education level					
≤ high school	3838	40.8 (38.6, 43.0)	199	60.5 (53.0, 67.6)	< .001
> high school	3879	59.2 (57.0, 61.4)	109	39.5 (32.4, 47.0)	< .001
Family income to poverty threshold					
> 2 times	4464	74.6 (72.5, 76.5)	113	48.6 (42.1, 55.3)	< .001
1–2 times	1524	15.0 (13.8, 16.3)	82	26.1 (20.0, 33.4)	.002
Below	1183	10.5 (9.4, 11.6)	93	25.2 (20.1, 31.2)	< .001
Health insurance coverage					
Yes	5919	83.6 (82.0, 85.0)	205	68.5 (61.6, 74.6)	< .001
No	1757	16.4 (15.0, 18.0)	100	31.5 (25.4, 38.4)	< .001
Served in the US armed forces					
No	6765	87.0 (85.9, 87.9)	242	79.6 (73.2, 84.8)	.01
Yes	955	13.0 (12.1, 14.1)	65	20.4 (15.2, 26.8)	.01
Average no. of alcoholic drinks/d, last y					
0–1	2492	33.4 (32.0, 35.0)	37	12.4 (8.5, 17.8)	< .001
≥ 2	3272	43.4 (41.7, 45.1)	166	57.8 (50.8, 64.5)	< .001
Unknown	1959	23.2 (21.5, 24.9)	105	29.8 (24.2, 36.0)	.02
Age at first sexual intercourse (up to 59[b] y; n = 7210), y					
≤ 17	3258	45.5 (43.7, 5.4)	202	69.3 (62.7, 75.2)	< .001
≥ 18	2871	42.8 (41.0, 44.7)	49	18.3 (13.2, 24.9)	< .001
Unknown	1081	11.6 (10.7, 12.7)	44	12.4 (8.7, 17.3)	.74
No. of lifetime sexual partners (up to 59[b] y; n = 7210)					
0–9	4507	63.2 (61.5, 64.8)	87	26.5 (20.0, 34.1)	< .001
10–19	916	13.0 (12.1, 14.0)	49	15.3 (11.0, 20.9)	.38
≥ 20	1133	15.9 (14.8, 17.1)	124	47.7 (40.4, 55.0)	< .001
Unknown	654	7.8 (7.0, 8.7)	35	10.6 (7.2, 15.2)	.16

Continued

3.8%) or approximately 2.8 million (2.4 million to 3.2 million) persons with anti-HCV. Anti-HCV prevalence was higher among men (4.3%; 95% CI = 3.6%, 5.2%), non-Hispanic Blacks (6.4%; 95% CI = 5.3%, 7.7%), and persons with a family income below the poverty threshold (7.8%; 95% CI = 6.3%, 10.0%), respectively, compared with women, non-Hispanic Whites, and persons with a family income of more than 2 times the poverty threshold.

Among participants reporting a history of IDU, 56.8% (95% CI = 48.4%, 64.8%) were anti-HCV–positive compared with 1.2% (95% CI = 0.9%, 1.6%) for those who had never used any illicit drugs. Persons who received a blood transfusion before 1992 had a higher prevalence of anti-HCV (6.7%; 95% CI = 4.8%, 9.4%) than did those without this history (2.9%; 95% CI = 2.5%, 3.5%). Among persons with elevated ALT levels, 12.7% (95% CI = 10.7%, 15.1%) were anti-HCV–positive relative to 1.8% (95% CI = 1.5%, 2.2%) for those with normal ALT levels.

TABLE 1—*Continued*

Lifetime illicit drug use (up to 59[b] y, n = 7210)					
Never	5101	70.8 (68.9, 72.6)	72	25.9 (20.3, 32.4)	< .001
Non-IDU	1280	18.9 (17.6, 20.2)	70	21.0 (16.9, 25.7)	.34
IDU	187	2.4 (2.0, 3.1)	116	41.9 (36.1, 47.9)	< .001
Unknown	642	7.9 (7.0, 8.8)	37	11.2 (6.9, 8.7)	.1
Blood transfusion before 1992					
No	7030	92.3 (91.6, 92.9)	260	83.8 (78.2, 88.1)	.001
Yes	581	7.7 (7.1, 8.4)	40	16.2 (11.9, 21.8)	.001
Serum alanine aminotransferase level, U/L					
< 40	6599	87.1 (86.1, 87.9)	143	48.7 (42.1, 55.4)	< .001
≥ 40	1056	12.9 (12.1, 13.9)	158	51.3 (44.6, 57.9)	< .001

Note. Anti-HCV = HCV antibody; CI = confidence interval; HCV = hepatitis C virus; IDU = injection drug use.
[a]Obtained from linear contrasts comparing anti-HCV–positive participants to all participants and accounting for the covariance induced by the presence of anti-HCV–positive participants in the total population of participants.
[b]National Health and Nutrition Examination Survey data collection on certain risk factors was limited to participants aged 20–59 years at time of survey; accordingly the 2005–2006 and 2007–2008 National Health and Nutrition Examination Survey cycles do not contain risk factor data for participants born in 1945–1946 and 1945–1948, respectively.

Factors Associated With Anti-HCV Prevalence Within the Birth Cohort

Unadjusted odds ratios (ORs) and 95% CIs for characteristics associated with anti-HCV prevalence are displayed in Table 2. Men, non-Hispanic Blacks, and persons with a family income below the poverty threshold, respectively, were more likely to be anti-HCV–positive compared with women, non-Hispanic Whites, and persons with family income of more than 2 times the poverty level. Injection drug use was the strongest predictor of anti-HCV prevalence among the birth cohort. Other characteristics significantly associated with anti-HCV prevalence were elevated ALT level, consumption of 2 or more alcoholic drinks per day, sexual intercourse before age 18 years, 20 or more lifetime sexual partners, and blood transfusion before 1992.

After we controlled for covariates in a multivariate logistic regression model (Table 3), IDU (adjusted OR = 98.4; 95% CI = 58.8, 164.5) remained the strongest predictor of anti-HCV prevalence. We also identified the following variables as significant risk factors for anti-HCV prevalence in the multivariate model: elevated ALT level (9.0; 95% CI = 6.0, 13.7), a family income below the poverty threshold (4.7; 95% CI = 3.0, 7.4), US-born (3.2; 95% CI = 1.7, 6.1), non-Hispanic Black race (2.3; 95% CI = 1.7, 3.2), and blood transfusion before 1992 (2.3; 95% CI = 1.3, 4.0). We removed number of sexual partners and age at first sexual intercourse from the multivariate model because of collinear relationships with IDU. No interaction terms were significant.

DISCUSSION

These findings highlight the relatively high prevalence of anti-HCV (3.2%) among persons in the 1945–1965 birth cohort compared with the prevalence among adults aged 20 to 70 years during the 1999–2008 survey period, but born before 1945 or after 1965 (0.9%; unpublished Centers for Disease Control and Prevention data); persons in the birth cohort were 4 times more likely to be anti-HCV–positive than adults outside the cohort. Our finding that history of IDU, blood transfusion, elevated ALT, Black race, and poverty were associated with HCV infection within the birth cohort is consistent with previous findings based on the general US adult population.[1,3] However, IDU and blood transfusions before 1992, the most common exposure risks reported by persons infected with HCV, account for only 52% of infections and the remaining 48% report no known exposure risk and may not be identified through risk-based testing approaches. Testing for HCV infection on the basis of the birth cohort presents an opportunity to identify a significant proportion of cases that may otherwise go undetected in a subpopulation that accounts for approximately 75% of the burden of HCV infection in the adult US population.[5] The 1945–1965 birth cohort has the highest incidence of HCV-related liver disease and death, which is projected to increase sharply over the next 2 decades.[10,36,37]

Most persons in the birth cohort are likely to have been infected for 20 to 40 years or more, and multiple models have indicated that there will be dramatic increases in the numbers of HCV-infected persons with significant liver disease over the next 10 to 20 years[31,38] without effective public health interventions. Even with declining prevalence in the overall US population, HCV disease burden is expected to increase significantly because of the aging of the infected population.[10,36] Identification of HCV-infected persons and planning for care and therapy now, however, will improve efforts for long-term care and management of the infected population.[39] Although treatment response is better among persons younger than 40 years than those aged 40 years or older, persons older than 65 years have been shown

TABLE 2—Characteristics and Risk Factors Associated With HCV Antibody Prevalence Among Adults Born From 1945 to 1965: National Health and Nutrition Examination Survey, 1999–2008

Characteristic	Participants Tested, No.	Prevalence of Anti-HCV		Unadjusted Odds Ratios	
		% (95% CI)	P[a]	Unadjusted OR (95% CI)	P
Overall	7723	3.2 (2.8, 3.8)		. . .	. . .
Gender					
Female (Ref)	3911	2.2 (1.7, 2.9)	. . .	1.0	. . .
Male	3812	4.3 (3.6, 5.2)	< .001	2.0 (1.4, 2.8)	< .001
Race/ethnicity					
Non-Hispanic White (Ref)	3648	2.9 (2.3, 3.6)	. . .	1.0	. . .
Non-Hispanic Black	1700	6.4 (5.3, 7.7)	< .001	2.3 (1.7, 3.0)	< .001
Mexican American	1564	3.3 (2.4, 4.4)	.51	1.1 (0.8, 1.6)	.5
Marital status					
Married or living with partner (Ref)	5170	2.7 (2.2, 3.4)	. . .	1.0	. . .
Divorced, separated, or widowed	1640	4.3 (3.3, 5.5)	.24	1.6 (1.1, 2.3)	.02
Never married	747	5.7 (4.0 8.0)	.004	2.2 (1.4, 3.3)	< .001
Country of birth					
United States	5836	3.6 (3.1, 4.2)	< .001	3.3 (1.9, 5.6)	< .001
Other (Ref)	1884	1.1 (0.7, 1.8)	. . .	1.0	. . .
Education level					
≤ high school	3838	4.8 (4.0, 5.9)	< .001	2.3 (1.7, 3.1)	< .001
> high school (Ref)	3879	2.2 (1.8, 2.7)	. . .	1.0	
Family income to poverty threshold					
> 2 times (Ref)	4464	2.1 (1.7, 2.7)	. . .	1.0	. . .
1–2 times	1524	5.6 (4.2, 7.5)	< .001	2.8 (1.9, 4.1)	< .001
Below	1183	7.8 (6.3, 9.6)	< .001	3.9 (2.9, 5.3)	< .001
Health insurance coverage					
Yes (Ref)	5919	2.7 (2.3, 3.1)	. . .	1.0	. . .
No	1757	6.2 (4.8, 8.0)	< .001	2.4 (1.8, 3.3)	< .001
Served in the US armed forces					
No (Ref)	6765	3.0 (2.5, 3.5)	. . .	1.0	. . .
Yes	955	5.1 (3.7, 6.9)	.01	1.7 (1.2, 2.5)	.004
Average no. of alcoholic drinks/d, last y					
0–1 (Ref)	2492	1.2 (0.8, 1.8)	. . .	1.0	. . .
≥ 2	3272	4.3 (3.6, 5.3)	< .001	3.7 (2.3, 5.9)	< .001
Unknown	1959	4.2 (3.3, 5.2)	< .001	3.6 (2.3, 5.6)	< .001
Age at first sexual intercourse (up to 59[b] y; n = 7210), y					
≤ 17	3258	5.0 (4.3, 5.9)	< .001	3.7 (2.5, 5.5)	< .001
≥ 18 (Ref)	2871	1.4 (1.0, 2.1)	. . .	1.0	. . .
Unknown	1081	3.5 (2.5, 5.0)	.004	2.5 (1.5, 4.4)	< .001
No. of lifetime sexual partners (up to 59[b] y; n = 7210)					
0–9 (Ref)	4507	1.4 (1.0, 2.0)	. . .	1.0	. . .
10–19	916	3.9 (2.6, 5.7)	.001	2.9 (1.8, 4.6)	< .001
≥ 20	1133	9.9 (8.2, 11.9)	< .001	7.8 (5.2, 11.8)	< .001
Unknown	654	4.5 (3.1, 6.5)	.001	3.3 (1.9, 5.7)	< .001
Lifetime drug use (up to 59[b] y; n = 7210)					
Never (Ref)	5101	1.2 (0.9, 1.6)	. . .	1.0	. . .
Non-IDU	1280	3.7 (2.8, 4.8)	< .001	3.1 (2.1, 4.5)	< .001
IDU	187	56.8 (48.4, 64.8)	< .001	107.0 (69.3, 165.1)	< .001
Unknown	642	4.7 (3.3, 6.8)	< .001	4.0 (2.5, 6.6)	< .001

Continued

TABLE 2—*Continued*

Blood transfusion before 1992					
No (Ref)	7030	2.9 (2.5, 3.5)	. . .	1.0	. . .
Yes	581	6.7 (4.8, 9.4)	.002	2.4 (1.6, 3.5)	< .001
Serum alanine aminotransferase level, U/L					
< 40 (Ref)	6599	1.8 (1.5, 2.2)	. . .	1.0	. . .
≥ 40	1056	12.7 (10.7, 15.1)	< .001	8.0 (6.0, 10.5)	< .001

Note. Anti-HCV = HCV antibody; CI = confidence interval; IDU = injection drug use; OR = odds ratio.
[a]Obtained by specifying linear contrasts of proportions among the levels of the subgroups.
[b]National Health and Nutrition Examination Survey data collection on certain risk factors was limited to participants aged 20–59 years at time of survey; accordingly the 2005–2006 and 2007–2008 National Health and Nutrition Examination Survey cycles do not contain data risk factor for participants born in 1945–1946 and 1945–1948, respectively.

to respond as well to therapy as those between the ages of 40 and 65 years, a fact that will become increasingly important as the birth cohort ages into retirement.[40]

For HCV-infected persons for whom antiviral treatment is indicated,[41] there have been recent medical advances that significantly improve the efficacy of therapy. Unfortunately, HCV treatment rates are low.[42] We found that almost one third of anti-HCV–positive persons in this cohort report being uninsured, a problem that certainly contributes to low treatment rates and difficulty accessing care. Expansion of coverage for medical care could increase access to care and treatment.

Even for those infected persons who do not receive antiviral medication, because of treatment contraindications or for other reasons, interventions are available that may limit disease progression and decrease HCV transmission to other persons. Reducing alcohol use can prevent exacerbation of liver disease. In our analysis, however, we found that nearly 58% of anti-HCV–positive persons in the birth cohort reported drinking 2 or more alcoholic drinks per day on average. Alcohol use is associated with development and progression of fibrosis and significant increase in liver-related and overall mortality.[41,43,44] Among HCV-infected persons, history of and current moderate alcohol use (approximately 2 drinks/day or less) have been found to be associated with a 2-fold increase in all-cause mortality and 7-fold increase for those who report drinking 2 or 3 drinks per day.[43] The prevalence of alcohol use among anti-HCV–positive birth cohort members suggests that use of Screening and Brief Interventions for Referral for Treatment of the Reduction of Alcohol Use as recommended by the US Preventive Services Task Force may be beneficial.[45] It has furthermore been suggested that, among heavy drinkers, knowledge of HCV-positive status and brief counseling received from health care providers upon diagnosis may be important factors in the reduction of alcohol use.[46,47]

Limitations

There are limitations in this study. First, NHANES samples include only the US civilian, noninstitutionalized population. A large number of high-risk persons who are incarcerated, institutionalized, or homeless are excluded; thus, these analyses are likely to result in an underestimate of anti-HCV prevalence. Second, behavioral risk-factor data were limited to participants aged 60 years or younger. As a consequence, for the 2005–2006 NHANES cycle, no risk-factor information was available for participants born during 1945–1946 (who would have been aged 60–61 years during the 2005–2006 cycle). Likewise, there were no risk factor data for participants born during 1945–1948 in the 2007–2008 cycle. Third, nearly all risk-factor data used in this analysis were self-reported. Participants may overreport or underreport behaviors in response to questions such as IDU or number of lifetime sexual partners, which might bias our results. Fourth, participant birth year was approximated from estimated year of interview and age at survey.

Finally, we did not examine differences by sociodemographic and risk characteristics between persons who knew and those who did not know their HCV-infection status (positive or negative) before testing because prior knowledge of HCV-infection status is not assessed for NHANES participants. However, among participants who test positive for anti-HCV or those with an indeterminate test result for anti-HCV plus a positive HCV-RNA, NHANES conducts a separate follow-up survey to ascertain knowledge of HCV infection status before receiving notification of results from NHANES. Although analyses[31,48] of the follow-up survey data have suggested differences—by age, access to health care, knowledge of risk factors—between HCV-positive persons who were aware of their status versus those who were unaware, those findings are by themselves limited by small sample sizes, low survey response rates, and their lack of generalizability to all persons, HCV-positive or -negative.

Conclusions

This study provides additional evidence of the high prevalence of anti-HCV among persons in the 1945–1965 birth cohort consistent with earlier studies of infection prevalence. Considerable racial and socioeconomic disparities by anti-HCV positivity status also are apparent within the cohort. High rates of alcohol use reported by anti-HCV–positive respondents suggest the importance of diagnosing infection and providing effective interventions to decrease alcohol consumption and slow the progression of liver disease. In light of the high prevalence of HCV infection among persons born during 1945–1965, the increasing morbidity and mortality associated with HCV infection, and reductions in liver cancer and HCV-related mortality when HCV infection is eliminated, it is critically important to identify

TABLE 3—Adjusted Odds Ratios for Risk Factors Associated With Hepatitis C Virus Antibody Prevalence Among Adults Born From 1945 to 1965, National Health and Nutrition Examination Survey 1999–2008

Characteristic	Adjusted OR (95% CI)[a]	*P*
Race/ethnicity		
Non-Hispanic White (Ref)	1.0	. . .
Non-Hispanic Black	2.3 (1.7, 3.2)	< .001
Mexican American	1.1 (0.7, 2.0)	.64
Country of birth		
Other (Ref)	1.0	. . .
United States	3.2 (1.7, 6.1)	< .001
Family income to poverty threshold		
> 2 times (Ref)	1.0	. . .
1–2 times	2.3 (1.4, 3.7)	.001
Below	4.7 (3.0, 7.4)	< .001
Served in the US armed forces		
No (Ref)	1.0	. . .
Yes	1.6 (1.0, 2.6)	.06
Lifetime drug use (up to 59[b] y)		
Never (Ref)	1.0	. . .
Non-IDU	2.8 (1.9, 4.2)	< .001
IDU	98.4 (58.8, 164.5)	< .001
Unknown	3.7 (2.2, 6.3)	< .001
Blood transfusion before 1992		
No (Ref)	1.0	. . .
Yes	2.3 (1.3, 4.0)	.005
Serum alanine aminotransferase level, U/L		
< 40 (Ref)	1.0	. . .
≥ 40	9.0 (6.0, 13.7)	< .001

Note. CI = confidence interval; IDU = injection drug use; OR = odds ratio. The sample size was n = 6554.
[a]Adjusted for all variables included in multivariate logistic regression model as shown in the table.
[b]National Health and Nutrition Examination Survey data collection on certain risk factors was limited to participants aged 20–59 years at time of survey; accordingly the 2005–2006 and 2007–2008 National Health and Nutrition Examination Survey cycles do not contain data risk factor for participants born in 1945–1946 and 1945–1948, respectively.

those persons living with hepatitis C and link them to appropriate care and treatment. ■

About the Authors

Bryce D. Smith, Geoff A. Beckett, Deborah Holtzman, and John W. Ward are with the Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, GA. Anthony Yartel and Nita Patel are with the Centers for Disease Control and Prevention Foundation, Atlanta, GA.

Correspondence should be sent to Bryce D. Smith, 1600 Clifton Rd, MS: G-37, Atlanta, GA 30333 (e-mail: bsmith6@cdc.gov). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

This article was accepted July 3, 2013.

Contributors

B. D. Smith contributed to the original conceptualization, study design, first draft of article, data analysis direction and interpretation, and critical article revisions. G. A. Beckett contributed to the study design, data interpretation, and critical article revisions. A. Yartel contributed to the study design; data management, analysis, and interpretation; first draft of article; and critical article revisions. D. Holtzman contributed to data analysis, data interpretation, and critical article revisions. N. Patel contributed to data analysis and interpretation. J. W. Ward contributed to critical article revisions and data interpretation.

Acknowledgments

Some of the results in the current study were presented previously at The Liver Meeting in 2011 and published in part in the Centers for Disease Control and Prevention's *Morbidity and Mortality Weekly Report* (Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. *MMWR Recomm Rep.* 2012;61[RR-4]:1–32) and the *Annals of Internal Medicine* (Smith BD, Morgan RL, Beckett GA, et al. HCV testing of persons born during 1945–1965: recommendations from the Centers for Disease Control and Prevention. *Ann Intern Med.* 2012;157:817–822).

Human Participant Protection

The National Health and Nutrition Examination Survey has received institutional review board approval and all participants provided informed consent. Detailed institutional review board documentation can be found at http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm.

References

1. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med.* 2006;144(10):705–714.

2. Vincent GK, Velkoff VA. *The Next Four Decades, The Older Population in the United States: 2010 to 2050.* Washington, DC: US Census Bureau; 2010.

3. Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med.* 1999;341(8):556–562.

4. Drainoni ML, Litwin AH, Smith BD, et al. Effectiveness of a risk screener in identifying hepatitis C virus in a primary care setting. *Am J Public Health.* 2012;102(11):e115–e121.

5. Tomaszewski KJ, Deniz B, Tomanovich P, Graham CS. Comparison of current US risk strategy to screen for hepatitis C virus with a hypothetical targeted birth cohort strategy. *Am J Public Health.* 2012;102(11):e101–e106.

6. Rosen HR. Clinical practice. Chronic hepatitis C infection. *N Engl J Med.* 2011;364(25):2429–2438.

7. O'Brien SF, Xi G, Yi QL, Goldman M. Understanding non-disclosure of deferrable risk: a study of blood donors with a history of intravenous drug use. *Transfus Med.* 2010;20(1):15–21.

8. Williams IT, Perz JF, Bell BP. Viral hepatitis transmission in ambulatory health care settings. *Clin Infect Dis.* 2004;38(11):1592–1598.

9. Thompson ND, Hellinger WC, Kay RS, et al. Healthcare-associated hepatitis C virus transmission among patients in an abdominal organ transplant center. *Transpl Infect Dis.* 2009;11(4):324–329.

10. 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(1):66–72.

11. Yang JD, Kim WR, Coelho R, et al. Cirrhosis is present in most patients with hepatitis B and hepatocellular carcinoma. *Clin Gastroenterol Hepatol.* 2011;9(1):64–70.

12. Sanyal AJ. The Institute of Medicine report on viral hepatitis: a call to action. *Hepatology.* 2010;51(3):727–728.

13. Velázquez RF, Rodriguez M, Navascues CA, et al. Prospective analysis of risk factors for hepatocellular carcinoma in patients with liver cirrhosis. *Hepatology.* 2003;37(3):520–527.

14. Freeman RB Jr, Steffick DE, Guidinger MK, Farmer DG, Berg CL, Merion RM. Liver and intestine transplantation in the United States, 1997–2006. *Am J Transplant.* 2008;8(4 pt 2):958–976.

15. Moorman AC, Gordon SC, Rupp LB, et al. Baseline characteristics and mortality among people in care for

chronic viral hepatitis: the chronic hepatitis cohort study. *Clin Infect Dis.* 2013;56(1):40–50.

16. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. *MMWR Recomm Rep.* 1998;47(RR-19):1–39.

17. Roblin DW, Smith BD, Weinbaum CM, Sabin ME. HCV screening practices and prevalence in an MCO, 2000–2007. *Am J Manag Care.* 2011;17(8):548–555.

18. Southern WN, Drainoni ML, Smith BD, et al. Hepatitis C testing practices and prevalence in a high-risk urban ambulatory care setting. *J Viral Hepat.* 2011;18 (7):474–481.

19. Spradling PR, Rupp L, Moorman AC, et al. Hepatitis B and C virus infection among 1.2 million persons with access to care: factors associated with testing and infection prevalence. *Clin Infect Dis.* 2012;55(8):1047–1055.

20. Hagan H, Campbell J, Thiede H, et al. Self-reported hepatitis C virus antibody status and risk behavior in young injectors. *Public Health Rep.* 2006;121(6):710–719.

21. Shehab TM, Sonnad S, Gebremariam A, Schoenfeld P. Knowledge of hepatitis C screening and management by internal medicine residents: trends over 2 years. *Am J Gastroenterol.* 2002;97(5):1216–1222.

22. Shehab TM, Sonnad SS, Jeffries M, Gunaratnum N, Lok AS. Current practice patterns of primary care physicians in the management of patients with hepatitis C. *Hepatology.* 1999;30(3):794–800.

23. Shehab TM, Sonnad SS, Lok AS. Management of hepatitis C patients by primary care physicians in the USA: results of a national survey. *J Viral Hepat.* 2001; 8(5):377–383.

24. Ferrante JM, Winston DG, Chen PH, de la Torre AN. Family physicians' knowledge and screening of chronic hepatitis and liver cancer. *Fam Med.* 2008;40(5): 345–351.

25. Jacobson IM, McHutchison JG, Dusheiko G, et al. Telaprevir for previously untreated chronic hepatitis C virus infection. *N Engl J Med.* 2011;364(25):2405–2416.

26. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. *N Engl J Med.* 2013;368(20):1878–1887.

27. US Food and Drug Administration. FDA approves new treatment for hepatitis C virus. 2013. Available at: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm376449.htm. Accessed December 16, 2013.

28. Morgan RL, Baack B, Smith BD, Pitasi M, and Falck-Ytter Y. Eradication of hepatitis C virus (HCV) infection and the development of hepatocellular carcinoma (HCC): a meta-analysis of observational studies. *Ann Intern Med.* 2013;158(5):329–337.

29. Berenguer J, Alvarez-Pellicer J, Martin PM, et al. Sustained virological response to interferon plus ribavirin reduces liver-related complications and mortality in patients coinfected with human immunodeficiency virus and hepatitis C virus. *Hepatology.* 2009;50(2):407–413.

30. Backus LI, Boothroyd DB, Phillips BR, Belperio P, Halloran J, Mole LA. A sustained virologic response reduces risk of all-cause mortality in patients with hepatitis C. *Clin Gastroenterol Hepatol.* 2011;9(6):509–516.e1.

31. Volk ML, Tocco R, Saini S, Lok AS. Public health impact of antiviral therapy for hepatitis C in the United States. *Hepatology.* 2009;50(6):1750–1755.

32. Smith BD, Morgan RL, Beckett GA, et al. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. *MMWR Recomm Rep.* 2012;61(RR-4):1–32.

33. Moyer VA. Screening for hepatitis C virus infection in adults: US Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2013;159(5): 349–357.

34. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey Questionnaire. Available at: http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm. Accessed March 1, 2012.

35. Centers for Disease Control and Prevention. NHANES analytic and reporting guidelines Available at: http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/nhanes_analytic_guidelines_dec_2005.pdf. Accessed March 1, 2012.

36. 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(2):513–521.e1–e6.

37. Ly KN, Xing J, Klevens R, Jiles R, Ward J, Holmberg S. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med.* 2012;156(4):271–278.

38. McHutchison JG, Bacon BR. Chronic hepatitis C: an age wave of disease burden. *Am J Manag Care.* 2005; 11(10 suppl):S286–S295; quiz S307–S311.

39. Knickman JR, Snell EK. The 2030 problem: caring for aging baby boomers. *Health Serv Res.* 2002;37(4): 849–884.

40. Antonucci G, Longo MA, Angeletti C, et al. The effect of age on response to therapy with peginterferon alpha plus ribavirin in a cohort of patients with chronic HCV hepatitis including subjects older than 65 yr. *Am J Gastroenterol.* 2007;102(7):1383–1391.

41. Ghany MG, Strader DB, Thomas DL, Seeff LB, American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology.* 2009;49(4):1335–1374.

42. Holmberg SD, Spradling PR, Moorman AC, Denniston MM. Hepatitis C in the United States. *N Engl J Med.* 2013;368(20):1859–1861.

43. Younossi ZM, Zheng L, Stepanova M, Venkatesan C, Mir HM. Moderate, excessive or heavy alcohol consumption: each is significantly associated with increased mortality in patients with chronic hepatitis C. *Aliment Pharmacol Ther.* 2013;37(7):703–709.

44. McMahon BJ, Bruden D, Bruce MG, et al. Adverse outcomes in Alaska natives who recovered from or have chronic hepatitis C infection. *Gastroenterology.* 2010; 138(3):922–931.e1.

45. Whitlock EP, Polen MR, Green CA, Orleans T, Klein J. Behavioral counseling interventions in primary care to reduce risky/harmful alcohol use by adults: a summary of the evidence for the US Preventive Services Task Force. *Ann Intern Med.* 2004;140(7):557–568.

46. McCusker M. Influence of hepatitis C status on alcohol consumption in opiate users in treatment. *Addiction.* 2001;96(7):1007–1014.

47. Beich A, Thorsen T, Rollnick S. Screening in brief intervention trials targeting excessive drinkers in general practice: systematic review and meta-analysis. *BMJ.* 2003;327(7414):536–542.

48. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001–2008. *Hepatology.* 2012;55(6):1652–1661.