

Elevated Prevalence of Hepatitis C Infection in Users of United States Veterans Medical Centers

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Several studies suggest veterans have a higher prevalence of hepatitis C virus infection than nonveterans, possibly because of military exposures. The purpose of this study was to estimate the prevalence of anti-hepatitis C antibody and evaluate factors associated with infection among users of Department of Veterans Affairs medical centers. Using a two-staged cluster sample, 1,288 of 3,863 randomly selected veterans completed a survey and underwent home-based phlebotomy for serological testing. Administrative and clinical data were used to correct the prevalence estimate for nonparticipation. The prevalence of anti-hepatitis C antibody among serology participants was 4.0% (95% CI, 2.6%-5.5%). The estimated prevalence in the population of Veterans Affairs medical center users was 5.4% (95% CI, 3.3%-7.5%) after correction for sociodemographic and clinical differences between participants and nonparticipants. Significant predictors of seropositivity included demographic factors, period of military service (e.g., Vietnam era), prior diagnoses, health care use, and lifestyle factors. At least one traditional risk factor (transfusion or intravenous drug use) was reported by 30.2% of all subjects. Among those testing positive for hepatitis C antibody, 78% either had a transfusion or had used injection drugs. Adjusting for injection drug use and nonparticipation, seropositivity was associated with tattoos and incarceration. Military-related exposures were not found to be associated with infection in the adjusted analysis. **In conclusion**, the prevalence of hepatitis C in these subjects exceeds the estimate from the general US population by more than 2-fold, likely reflecting more exposure to traditional risk factors among these veterans. (HEPATOLOGY 2005;41:88–96.)

Hepatitis C virus (HCV), the most common chronic blood-borne infection in the United States and a major cause of cirrhosis and hepatocellular carcinoma, was first identified in 1989.^{1,2} Risk factors for infection include transfusion of blood products, intravenous drug use, hemodialysis, sexual promiscuity, ear piercing in men, and organ transplants from

HCV-positive donors.^{3–6} Other percutaneous exposures, including tattooing, have not been found to be associated with transmission of HCV in the United States.⁷

Throughout the 1980s, approximately 230,000 new cases of HCV per year appeared in the United States, but the incidence declined to about 38,000 cases per year in the 1990s,⁸ likely because of screening of blood donors⁹ and the institution of safer needle-using practices among injection drug users. Despite the falling incidence,⁸ the complications of chronic HCV infection are rising as a result of the long delay between acute infection and the manifestation of clinical disease.

According to the Third National Health and Nutrition Examination Survey (NHANES III), the prevalence of antibody to HCV in the general United States population was 1.8%.¹⁰ Among users of the Veterans Administration (VA) health care system, the prevalence of HCV has been estimated to significantly exceed that of the general population (ranging from 6.6% to approximately 35%^{11–15}), suggesting that the VA system could face significant challenges in caring for these veterans. Consequently, the VA embarked on a program to commit substantial new re-

Abbreviations: HCV, hepatitis C virus; NHANES III, Third National Health and Nutrition Examination Survey; VA, Veterans Administration.

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sources to identify infected veterans and to offer appropriate antiviral therapy. Moreover, these estimates raised questions regarding the possible role of military service in the acquisition of HCV infection.¹³ As a result, in 2001 the Department of Veterans Affairs commissioned a nationwide epidemiological study of HCV in veterans to help inform health policy and planning. The primary goal of this study was to estimate the prevalence of HCV in a representative national sample of veterans who use VA health care. A secondary goal was to determine associations between HCV and military and nonmilitary exposures.

Patients and Methods

Study Design/Study Site Selection. This study used a two-staged cluster sample, cross-sectional population-based design. Twenty VA medical centers were randomly selected from a list of 145 facilities with approved research programs. Sites were selected with probability proportional to the number of patients at that site. A database consisting of all 3,184,687 unique veterans seen at these facilities during fiscal years 1998–2000 was created. Using a computerized random number generator, 200 veterans were randomly selected from each of the 20 facilities.

Subject Recruitment. This study was approved by the institutional review boards at each of the 20 medical centers and the coordinating center. Sampled veterans were first sent mailed invitations. Research personnel sent nonresponders at least one additional mailing (using overnight express delivery when possible) and repeatedly attempted to make contact with them via telephone. A private investigative search firm (International Claims Specialists, Kent, WA) was employed to help find veterans who could not be reached. Whenever possible, subjects who were ineligible to participate because of death, incarceration, active duty status, or inability to give informed consent were replaced with a randomly selected veteran from the same site.

Data Collection. To maximize participation, all study procedures occurred at the subject's home or other location of their choice, and subjects received \$20 compensation. After giving informed consent, subjects completed a self-administered questionnaire and had blood drawn (Portamedic, Overland Park, KS). The study materials were then shipped via overnight express mail to the VA Puget Sound Health Care System for processing. The questionnaire included items concerning military- and nonmilitary-related exposures. Alcohol use was classified using the Alcohol Use Disorders Identification Test Consumption (AUDIT-C) questionnaire, using a cut point of

4 or more points to determine heavy alcohol use.¹⁶ Residence in an urban or rural area was classified according to the rural–urban commuting area zip code classification.¹⁷ VA administrative databases, including the patient treatment file and outpatient clinic file, were used to obtain additional information concerning patient demographics, diagnoses, treatments, and health care use for participants and nonparticipants alike.

Laboratory Measures. Serum aliquots were tested for anti-HCV antibody via second-generation enzyme immunoassay (HCV EIA 2.0; Abbott Laboratories, Abbott Park, IL). All samples were tested with both negative and positive controls (Viroclear and Virotrol I; Blackhawk BioSystems, Inc., San Ramon, CA). For those subjects with a positive or borderline positive enzyme immunoassay test, HCV RNA qualitative reverse-transcriptase–polymerase chain reaction was performed using the COBAS Amplicor HCV Test, v. 2.0 assay (Roche Molecular Systems, Pleasanton, CA) according to the manufacturer's instructions. Our laboratory was able to detect the World Health Organization international standard for HCV RNA at 100 IU/mL or more, which is identical to the manufacturer's reported limit of detection in serum. When the polymerase chain reaction test was negative, a confirmatory recombinant immunoblot assay antibody test was performed (Quest Diagnostics, San Juan Capistrano, CA). Specimens that were recombinant immunoblot assay negative or indeterminate were reported as negative. Any value of alanine aminotransferase above 39, the upper limit of normal, was considered abnormal.

Statistical Analysis. All *P* values and confidence limits were obtained using analysis methods for complex surveys. Two methods were used to evaluate and correct for nonparticipation bias. Under the first method, based on multiple imputation,^{18,19–21} a logistic regression model was developed to predict the probability (propensity) of participation from information available in VA databases. Within 20 propensity strata, imputed HCV serology values for each nonparticipant were chosen randomly using the approximate Bayesian bootstrap method.^{19,20} This process was repeated 25 times, yielding 25 complete data sets that differed from each other on the specific imputed serology result for each nonparticipant. Parallel analyses were then conducted on all 25 data sets using the same analytical methods employed to obtain the original point estimate. The results were then combined using methods described by Rubin and Schenker¹⁹ to obtain a bias-corrected summary estimate of HCV seroprevalence and confidence limits that accounted for both the sampling design and for uncertainty involved in the imputation process.

A second analytical approach employed nonparticipation weighting.²² Each subject's weight was the inverse of his/her probability of participation, as estimated by the propensity score described above. The main analysis was then conducted by applying a nonparticipation weight to each subject. The best available predictors of participation based on bivariate and multivariate analysis of administrative and clinical data were used for all subjects, depending on which data were available for use for each subject. Predictor variables were added to the logistic model in order of size of improvement in model fit according to the Akaike information criterion until no further improvement in Akaike Information Criterion was observed.

Logistic regression was used to evaluate seropositivity in relation to exposures and other variables ascertained from the survey while adjusting for injection drug use and correcting for nonparticipation bias. Given sample size limitations, adjustment was limited to injection drug use because it was a strong predictor of seropositivity and had been shown to be an important risk factor in past studies. STATA version 7.0 (College Station, TX) and SAS version 8.0 (Cary, NC) were used for all analyses. All *P* values are two-sided using an alpha of 0.05.

Results

Of the 4,000 veterans in the original sample, 86 (2.2%) were replaced because of inability to give informed consent (*n* = 36), death (*n* = 42), incarceration (*n* = 5), or active military duty status (*n* = 3). Another 93 (2.3%) were excluded (but could not be replaced during the timeframe of the study) because of inability to give informed consent (*n* = 39), death (*n* = 42), incarceration (*n* = 4), or active military duty status (*n* = 8). Finally, we excluded 44 veterans (1.1%) because of incomplete documentation of consent. Among the remaining 3,863 potential participants, HCV serology results were obtained for 1,288 (33.3%). We were unable to contact 1,325 subjects (34.3%) despite repeated mailings, phone calls, and use of a private investigative search firm. An additional 1,139 subjects declined enrollment (29.5%), 73 subjects (1.9%) died before enrollment, and 38 subjects (1.0%) agreed to participate but were unable or unwilling to have blood drawn (28 completed questionnaires). Computerized administrative data were obtained for all 3,863 potential participants; computerized data on diagnoses and health care use were available for 2,895. A variety of sociodemographic and clinical factors were significantly associated with nonparticipation, including some that are associated with HCV, such as substance abuse, prior diagnosis of HCV, homelessness, and race (data not shown).

Overall, 52 of 1,288 subjects tested positive for antibody to HCV and 39 (75.0%) of these were viremic by qualitative polymerase chain reaction. Eighty-six percent of seropositive survey respondents reported prior HCV testing; yet 46% of all seropositive veterans were unaware of the diagnosis. Serum alanine aminotransferase was elevated in 36.5% of seropositive subjects and 8.3% of seronegative subjects. The estimated seroprevalence of HCV increased with correction for nonparticipation using either multiple imputation or nonparticipation weighting (data not shown). Both methods led to very similar estimates. Using only the available serological data, the seroprevalence was 4.0% (95% CI, 2.6%-5.5%). The estimate increased to 5.4% (95% CI, 3.3%-7.5%) using the nonparticipation weighting with correction for the best available predictors of participation.

Table 1 depicts the seroprevalence of HCV in relation to demographic characteristics. Seropositivity was highest in males; veterans aged 35 to 54 years; and veterans who had never married, divorced, or separated. In addition, era of military service was associated with HCV prevalence after correcting for nonparticipation. The prevalence of HCV was significantly lower among veterans serving during World War II or the Persian Gulf War. However, the prevalence of HCV was significantly higher among Vietnam era veterans than during all other eras of service.

Table 2 shows the seroprevalence of HCV in relation to clinical diagnoses. Seropositivity was significantly higher in veterans with a prior diagnosis of HCV, hepatitis B, and drug use disorders. Half of the veterans found to be HCV seropositive had already been diagnosed with HCV in VA databases. Seropositivity was also higher in veterans with a diagnosis of alcohol abuse, cirrhosis, mental illness, and marijuana abuse, as well as veterans with liver transplantation and use of hemodialysis.

Table 3 describes the seroprevalence of HCV in relation to responses on the survey. Significant associations included never having been married or low income, air injection vaccination, tattoos, body piercing, use of illicit injection drugs, snorting of drugs, problem drinking, increased number of sex partners, unprotected sex with an intravenous drug user, exchange of sex for drugs, incarceration for more than 48 hours, or ever having slept in a public shelter or outside in the past 6 months. At least one traditional risk factor (*i.e.*, transfusion or intravenous drug use) was reported by 30.2% of subjects. If other potential risk factors are considered (*i.e.*, snorting of drugs, tattoos, incarceration, or 15 or more sexual partners), then 62.8% had at least one risk factor. Among those testing positive for HCV, 78% either had a trans-

Table 1. Prevalence of Antibody to HCV in Relation to Demographic Characteristics

Characteristic	No. HCV-Positives/ Total	Unadjusted			Adjusted for Nonparticipation*		
		Prevalence per 100	95% CI	P Value	Prevalence per 100	95% CI	P Value
Overall	52/1288	4.0	2.6-5.5		5.4	3.3-7.5	
Age (yr)				<.001			<.001
<35	0/47	0.0	—		0.0	—	
35-54	31/347	8.9	5.6-12.2		11.5	6.9-16.1	
55-74	19/633	3.0	1.4-4.6		3.7	1.5-5.9	
75+	2/261	0.8	0.0-1.9		0.9	0.0-2.4	
Sex				.41			.09
Female	1/51	2.0	0.0-5.8		1.2	0.0-3.6	
Male	51/1,237	4.1	2.6-5.6		5.6	3.4-7.7	
Marital status				.036			.046
Married/widowed	27/892	3.0	1.5-4.5		3.5	1.7-5.2	
Divorced/separated	15/265	5.7	2.3-9.1		7.5	2.1-12.9	
Never married	7/85	8.2	2.6-13.8		11.7	1.5-22.0	
Race				.18			.06
White	29/1,005	2.9	1.7-4.0		3.2	1.9-4.4	
Black	11/144	7.6	2.2-13.0		11.0	2.9-19.1	
Asian/Pacific Islander	0/25	0.0	—		0.0	—	
American Indian/Alaskan Native	1/9	11.1	0.0-34.8		32.7	0.0-84.7	
Other	9/69	13.0	0.1-26.0		15.3	1.8-28.7	
Hispanic				.39			.33
No	40/1,118	3.6	2.2-4.9		4.9	3.0-6.8	
Yes	7/102	6.9	0.0-17.5		9.6	0.0-23.1	
Education				.24†			.15†
Elementary	1/75	1.3	0.0-4.3		2.6	0.0-8.1	
Some high school	4/110	3.6	0.0-7.3		5.0	0.0-10.2	
High school graduate	19/357	5.3	3.0-7.6		7.3	3.0-11.5	
Some college	23/483	4.8	2.9-6.7		6.0	3.4-8.7	
College graduate	2/227	0.9	0.0-2.1		1.0	0.0-2.3	
Annual household income				<.001†			.002†
<\$10,000	16/142	11.3	6.0-16.6		17.1	6.6-27.7	
\$10,000-\$20,000	16/291	5.5	1.5-9.5		6.6	1.1-12.1	
\$20,000-\$35,000	10/354	2.8	1.1-4.5		2.6	1.0-4.2	
>\$35,000	6/393	1.5	0.0-3.0		2.0	0.1-4.0	
Era of service							
World War II				.015			.018
No	50/1,058	4.7	3.0-6.5		6.4	3.8-9.0	
Yes	2/230	0.9	0.0-2.2		1.0	0.0-2.6	
Pre-Korean War				.62			.56
No	52/1,277	4.1	2.6-5.6		5.4	3.3-7.5	
Yes	0/11	0.0	—		0.0	—	
Korean War				.042			.07
No	48/1,071	4.5	2.9-6.1		5.9	3.7-8.0	
Yes	4/217	1.8	0.0-3.7		2.7	0.0-5.5	
Post-Korean War				.27			.37
No	49/1,156	4.2	2.6-5.9		5.6	3.3-8.0	
Yes	3/132	2.3	0.0-4.8		3.0	0.0-6.9	
Vietnam War				<.001			<.001
No	14/774	1.8	0.7-2.9		2.2	0.9-3.4	
Yes	38/514	7.4	4.8-9.9		11.0	6.7-15.3	
Post-Vietnam War				.70			.94
No	45/1,136	4.0	2.5-5.5		5.4	3.2-7.6	
Yes	7/152	4.6	0.9-8.3		5.2	0.2-10.2	
Persian Gulf War				.20			.029
No	50/1,177	4.2	2.7-5.8		5.8	3.4-8.1	
Yes	2/111	1.8	0.0-4.4		1.3	0.0-3.0	
Other era				.08			.10
No	50/1,273	3.9	2.5-5.3		5.2	3.2-7.2	
Yes	2/15	13.3	0.0-32.8		18.2	0.0-46.2	

*Using nonparticipation weights based on best available predictors of participation.

†From test for trend.

Table 2. Prevalence of Antibody to HCV in Relation to Clinical Diagnoses

Characteristic	No. HCV-Positives/ Total	Unadjusted			Adjusted for Nonparticipation*		
		Prevalence per 100	95% CI	P Value	Prevalence per 100	95% CI	P Value
Overall	52/1,288	4.0	2.6-5.5		5.4	3.3-7.5	
Hepatitis C				<.001			<.001
No	26/1,253	2.1	0.9-3.2		2.7	1.0-4.4	
Yes	26/35	74.3	60.2-88.4		77.5	60.4-94.5	
Hepatitis B				<.001			<.001
No	49/1,280	3.8	2.4-5.3		4.9	2.9-6.9	
Yes	3/8	37.5	2.6-72.4		61.1	20.6-100.0	
Alcohol abuse				<.001			<.001
No	34/1,148	3.0	1.6-4.3		3.7	1.7-5.6	
Yes	18/140	12.9	7.2-18.6		15.1	7.3-23.0	
Cirrhosis				<.001			<.001
No	47/1,273	3.7	2.2-5.2		4.8	2.7-6.8	
Yes	5/15	33.3	6.3-60.3		44.3	10.0-78.6	
Mental illness				<.001			<.001
No	24/960	2.5	1.1-3.9		3.2	1.1-5.2	
Yes	28/328	8.5	5.6-11.5		11.4	6.4-16.5	
Drug disorder				<.001			<.001
No	42/1,235	3.4	2.1-4.7		3.9	2.4-5.4	
Yes	10/53	18.9	5.9-31.8		22.6	5.0-40.2	
Marijuana abuse				<.001			.040
No	47/1,262	3.7	2.2-5.2		5.1	3.0-7.2	
Yes	5/26	19.2	5.3-33.2		15.4	0.0-31.2	
Homeless				.013			.28
No	48/1,256	3.8	2.3-5.3		5.1	3.0-7.3	
Yes	4/32	12.5	2.1-22.9		9.9	0.0-21.4	
HIV				.49			.91
No	51/1,276	4.0	2.5-5.5		5.4	3.2-7.5	
Yes	1/12	8.3	0.0-26.4		4.7	0.0-15.5	

*Using nonparticipation weights based on best available predictors of participation.

fusion or had used injection drugs, while all had one or more of the broader risk factors listed above.

Finally, Table 4 shows the results of logistic regression models of seropositivity in relation to exposures ascertained on the survey, adjusting for injection drug use and correcting for nonparticipation. The odds of seropositivity were increased among veterans with prior testing for HCV and human immunodeficiency virus, tattoos, and incarceration for 48 or more hours. We found no evidence of significant multicollinearity between injection drug use, tattoos, and incarceration.

Discussion

We found the prevalence of past infection with HCV to be 4.0% among participants who used VA medical centers. Correcting for nonparticipation raised the estimated prevalence among all such users to 5.4%. Although these estimates exceed the estimate of 1.8% among non-institutionalized residents of the United States, they are somewhat lower than the prior national estimate of 6.6% among veterans undergoing phlebotomy¹¹ and sharply lower than the 17.7% to 35% estimates from selected patients.^{13, 15}

These earlier studies led to speculation that factors associated with military service may be strongly related to HCV infection. Several pieces of evidence now suggest that military exposures *per se* are not dominant risk factors. First, in the NHANES III study, the HCV prevalence was actually lower for those with prior military service (1.7%) when compared with those who had never been in the military (2.2%).¹⁰ Second, the HCV prevalence in active duty military personnel (0.48%) has been found to be lower than in the general population.²³ Although combat medic work was an independent risk factor in the study by Briggs et al.,¹³ most infections were associated with traditional risk factors. Finally, our study found no association between military-related exposures and HCV infection after adjusting for intravenous drug use.

Even so, HCV prevalence in users of VA facilities was found to be considerably higher than in the general population. This finding may be at least partially explained by differences between veterans who do and do not use VA facilities. It is estimated that only 17% of the nearly 27 million United States veterans use the VA for their health care.²⁴ VA users have been shown to be demographically

Table 3. Prevalence of Antibody to HCV in Relation to Selected Responses on Questionnaire

Characteristic	No. HCV-positives/ Total	Unadjusted			Adjusted for Nonparticipation*		
		Prevalence per 100	95% CI	P Value	Prevalence per 100	95% CI	P Value
Overall	52/1,288	4.0	2.6-5.5		5.4	3.3-7.5	
Ever in combat				.90			.23
No	25/660	3.8	2.1-5.5		6.1	3.3-8.9	
Yes	23/588	3.9	2.0-5.8		4.1	1.6-6.6	
Ever wounded in combat				.29			.83
No	41/1,088	3.8	2.4-5.2		5.2	3.2-7.3	
Yes	8/155	5.2	1.6-8.7		5.6	1.5-9.7	
Exposed to another person's blood in combat				.007			.07
No	31/962	3.2	1.8-4.7		4.9	2.7-7.1	
Yes	12/133	9.0	3.8-14.2		9.6	3.7-15.6	
Ever had blood transfusion				.53			.23
No	27/703	3.8	1.7-5.9		4.4	1.7-7.2	
Yes	16/335	4.8	2.2-7.3		7.0	3.4-10.5	
Ever received air injection				.026			.018
No	7/338	2.1	0.5-3.7		2.6	0.7-4.5	
Yes	43/862	5.0	3.1-6.9		6.8	4.0-9.6	
Ever had test for hepatitis C				<.001			<.001
No	6/513	1.2	0.1-2.3		1.5	0.0-3.0	
Yes	37/204	18.1	11.1-25.2		21.7	14.9-28.6	
Ever had test for HIV				<.001			<.001
No	10/607	1.6	0.6-2.7		1.7	0.6-2.9	
Yes	36/439	8.2	5.5-10.9		11.0	7.4-14.6	
Ever a health care worker				.059			.13
No	35/978	3.6	2.1-5.1		4.9	2.7-7.0	
Yes	15/271	5.5	3.2-7.9		6.9	3.9-10.0	
Ever had a needle stick				.13			.39
No	39/1,098	3.6	1.8-5.3		5.0	2.6-7.3	
Yes	10/146	6.8	2.8-10.9		7.0	2.2-11.8	
Ever had acupuncture				.64			.52
No	45/1,138	4.0	2.6-5.3		5.2	3.3-7.1	
Yes	5/103	4.9	0.2-9.6		7.1	0.0-14.7	
Ever had a tattoo				<.001			.001
No	22/1,006	2.2	1.0-3.4		3.3	1.2-5.4	
Yes	28/247	11.3	6.9-15.8		13.4	7.2-19.7	
Ever had body piercing				<.001			<.001
No	27/1,070	2.5	1.3-3.7		3.3	1.4-5.2	
Yes	23/178	12.9	7.3-18.6		15.1	8.3-21.9	
Ever injected illicit drugs				<.001			<.001
No	19/1,191	1.6	0.8-2.4		1.7	0.8-2.6	
Yes	31/59	52.5	41.5-63.6		56.3	43.5-69.1	
Ever snorted drugs				<.001			<.001
No	15/1,091	1.4	0.5-2.2		1.6	0.4-2.8	
Yes	35/159	22.0	14.6-29.4		23.3	14.2-32.4	
Problem drinker (AUDIT-C score >3)				.015			.035
No	22/772	2.8	1.7-4.0		3.5	2.0-5.0	
Yes	28/468	6.0	2.8-9.1		8.1	3.1-13.1	
Number of sex partners				.025†			.020†
0-1	1/134	0.7	0.0-2.3		0.5	0.0-1.7	
2-49	27/663	4.1	2.1-6.0		5.6	2.4-8.9	
50+	7/86	8.1	1.6-14.7		9.5	1.5-17.6	
Ever had unprotected sex with injection drug user				<.001			<.001
No	19/863	2.2	0.9-3.5		2.9	0.8-5.0	
Yes	18/48	37.5	25.7-49.3		42.3	28.4-56.2	
Ever exchanged sex for drugs				.005			.009
No	47/1,242	3.8	2.4-5.2		5.0	3.1-6.9	
Yes	3/12	25.0	0.0-56.0		28.2	0.0-63.2	
Man who had sex with men				.52			.44
No	43/1,050	4.1	2.6-5.6		5.5	3.4-7.7	
Yes	1/47	2.1	0.0-6.6		2.5	0.0-7.8	
Ever in jail for >48 hours				<.001			<.001
No	18/1,016	1.8	0.8-2.7		1.7	0.7-2.7	
Yes	32/206	15.5	9.0-22.1		19.9	11.3-28.5	
Ever slept in public shelter, etc., in last 6 mo				.16			.014
No	46/1,220	3.8	2.3-5.3		4.6	2.5-6.6	
Yes	3/32	9.4	0.0-20.5		23.6	0.0-50.3	

Abbreviation: AUDIT-C, Alcohol Use Disorders Identification Test Consumption.

*Using nonparticipation weights based on best available predictors of participation.

†From test for trend.

Table 4. Seropositivity in Relation to Exposure Ascertained on Questionnaire, Adjusting for Intravenous Drug Use and Nonparticipation

Exposure	Adjusted for					
	Unadjusted		Intravenous Drug Use		Intravenous Drug Use + Nonparticipation*	
	OR	95% CI	OR	95% CI	OR	95% CI
Ever in combat	1.0	0.6-1.8	1.4	0.7-2.7	1.0	0.5-2.0
Ever wounded in combat	1.4	0.7-2.6	1.3	0.5-3.1	1.1	0.5-2.7
Exposed to another person's blood in combat	3.0	1.4-6.5	1.8	0.5-5.9	1.5	0.5-4.9
Ever had surgery	1.0	0.3-3.9	1.3	0.5-3.5	1.1	0.4-3.2
Ever had blood transfusion	1.3	0.6-2.6	1.1	0.5-2.5	1.2	0.5-2.7
Ever received air injection	2.5	1.1-5.6	1.3	0.6-2.7	1.1	0.5-2.5
Ever had test for hepatitis C	18.7	7.2-48.9	11.1	4.0-31.2	10.0	3.1-32.0
Ever had test for HIV	5.3	2.9-9.8	2.3	1.0-5.6	2.2	1.0-5.1
Ever a health care worker	1.6	1.0-2.6	0.8	0.3-1.8	0.7	0.3-1.7
Ever had a needle stick	2.0	0.8-5.0	0.8	0.3-2.7	0.9	0.3-2.5
Ever had acupuncture	1.2	0.5-3.2	1.1	0.4-3.3	1.1	0.3-3.3
Ever had a tattoo	5.7	2.8-11.7	3.8	2.0-7.1	3.2	1.6-6.4
Ever had a body piercing	5.7	2.9-11.2	2.2	0.7-6.8	1.5	0.4-5.1
Ever snorted drugs	20.2	10.3-39.9	3.8	1.4-10.5	2.5	0.9-7.1
Ever had unprotected sex with HCV-positive person	3.9	0.3-46.1	0.3	0.0-6.3	0.1	0.0-2.6
Ever had unprotected sex with injection drug user	26.7	12.8-55.3	1.8	0.5-6.6	1.7	0.5-6.0
Ever exchanged sex for drugs	8.5	1.6-45.4	1.2	0.2-8.5	0.8	0.1-6.5
Ever exchanged sex for money, food, etc.	1.0	0.4-2.6	0.5	0.2-1.3	0.6	0.2-1.8
Man who had sex with men	0.5	0.0-4.5	0.2	0.0-5.7	0.2	0.0-4.2
Ever in jail for >48 hours	10.2	4.7-22.0	3.1	1.3-7.2	4.2	1.7-10.1
Ever slept in public shelter, etc., in last 6 mo	2.6	0.6-11.1	1.4	0.3-6.2	3.0	0.7-12.0

*Using nonparticipation weights based on best available predictors of participation.

very different from the general United States population as well as from veterans who do not use the VA,²⁵ with an overrepresentation of higher-risk groups for HCV infection, including men and minorities. Poverty is also relatively common, with 44.3% of those who used VA hospitals and 32% of those using VA outpatient services having annual incomes less than \$10,000, as opposed to only 11.2% of all United States veterans and 14.6% of United States adult residents.

Our study confirms and extends what is known about HCV risk factors. While intravenous drug use is believed to be the major source of HCV infection in the United States,²⁶⁻²⁸ and cocaine use may result in transmission through contaminated straws or other devices,³ the association between seropositivity and marijuana or alcohol use likely reflects confounding with other risk behaviors, as suggested by our multivariate analyses. Although the NHANES III study excluded homeless or incarcerated persons, studies of homeless veterans found that approximately 40% were anti-HCV positive,^{29,30} and among California inmates, 39% were seropositive for HCV.³¹ Our study found that both homelessness and incarceration were associated with seropositivity, though only incarceration remained significantly associated after adjustment for intravenous drug use. Although a direct causal association between incarceration and HCV is un-

likely, it is conceivable that incarceration is a marker for other high-risk behaviors that either were underreported by subjects or were not assessed. Although tattoos have not been designated as a risk factor in the United States,⁷ we found that tattoos were associated with seropositivity, even after adjusting for intravenous drug use. Unfortunately, we do not have information about how tattoos were acquired (*e.g.*, professional facility vs. prison tattoo vs. other, United States vs. abroad). In a *post hoc* analysis, tattoos remained significantly associated with HCV seropositivity after adjusting for injection drug use, incarceration, and nonparticipation (odds ratio, 2.9 [95% CI, 1.4-5.8]). Four subjects who had tattoos and HCV did not report blood transfusions, injection drug use, or incarceration. Future studies should attempt to determine the specific risk factors for tattoo-associated HCV. Also, like incarceration and homelessness, it is possible that receipt of a tattoo is a marker for another risk factor for which we are unable to adjust.

The veterans' self-reported prevalence of known risk factors for HCV was remarkable. Although some military-related risk factors were associated with seropositivity in bivariate analyses, none was significant after adjusting for intravenous drug use and nonparticipation. Likewise, despite reports of hepatitis B transmission with air injection,³² this common exposure was

not significantly associated with HCV in our multivariate analysis.

Despite extensive efforts to contact all potential subjects, including mailings, multiple calls and several messages (mean 8.7 calls per veteran not reached), and use of private investigators, 34.3% could not be contacted to determine their willingness to participate. Although we went to considerable lengths to minimize study burden (*e.g.*, sending phlebotomists to the subject's home) and compensated subjects, serum was obtained from only 52.2% of those veterans we contacted. This highlights some of the challenges of conducting population-based epidemiological research on veterans. There are important strengths to this study. First, it targeted a randomly identified population of users of VA medical facilities from across the United States and Puerto Rico and tested them for HCV. Unlike prior clinic-based studies, this design provides a more accurate estimate of the true prevalence of HCV infection in users of VA facilities through a reduction in the effect of sampling bias. Furthermore, the availability of demographic and clinical data from nonparticipants allowed use of advanced statistical techniques in an attempt to minimize bias. Because nonparticipation was related to factors that are associated with HCV, it is not surprising that this correction resulted in an increased prevalence estimate. Unfortunately, other studies of the prevalence of HCV, including the NHANES III, lack access to this informative data on nonparticipants. Therefore, if predictors of nonparticipation are generalizable, then these studies may underestimate the true prevalence of HCV.

In summary, we estimate that 5.4% of VA users are HCV-seropositive, exceeding the estimate from the general population by more than 2-fold. Although Vietnam veterans had the highest prevalence (11%) in our sample, military-related exposures were not found to be significant risk factors. That this estimate differs considerably from some prior estimates used to determine health policy underscores the need for methodologically sound epidemiological research to guide health policy decision makers. Given the relatively high prevalence of HCV, the Department of Veterans Affairs should continue to support prevention, screening, counseling, and treatment efforts to reduce the frequency of HCV complications. Moreover, the VA should prepare for the expected increase in veterans experiencing complications of HCV, including end-stage liver disease and hepatocellular carcinoma.

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