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ORIGINAL PAPER

Risk Factors for Hepatitis C Infection Among Vietnam Era Veterans Versus Nonveterans: Results from the Chronic Hepatitis Cohort Study (CHeCS)

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Abstract Research suggests that Vietnam era veterans have a higher prevalence of hepatitis C virus (HCV) than other veterans and nonveterans. However, the reasons for this are unclear, since this research has been conducted among Department of Veterans Affairs (VA) patients and most veterans do not use the VA. The current study compares HCV risk factors between the Vietnam era veterans and nonveterans seen in 4 large non-VA systems to explain this disparity. A total of 4,636 HCV patients completed surveys in 2011–2012. Vietnam era veterans were defined as those who served in the military any time between 1964 and 1975. Bivariate tests followed by logistic regressions, and multivariable modeling were conducted to study risk factors among Vietnam era veterans and nonveterans. Since few veterans were female ($\sim$2 %), they were excluded. Among male respondents (N = 2,638), 22.5 % were classified as Vietnam era veterans. Compared to nonveterans, these patients were older ($p < 0.001$), more educated ($p < 0.001$), less often foreign born ($p = 0.009$), more often married ($p < 0.001$), less often employed, and less likely to have a history of drug abuse treatment ($p < 0.001$). Comparison of specific risk factor differences for HCV infection by veteran status suggested that while injection drug use approached statistical significance (nonveterans = 46.1 % vs. Vietnam era veterans = 41.4 %, $p = 0.06$), only reported sex with men was significant (nonveterans = 2.4 % vs. Vietnam era veterans = 0.6 %, $p = 0.013$). In multivariate logistic regression controlling for age, education, country of birth, marital status and study site, no HCV risk factor was associated with Vietnam era veteran status. However, veterans were more likely to report "other" exposures were the source of infection than nonveterans ($p < 0.001$). While Vietnam era veterans seen in non-VA facilities do not report a higher prevalence of common HCV risk factors, such as injection drug use, they are more likely to report "other" exposures, typically associated with military service, as the source of HCV infection.

Keywords Veterans · Hepatitis C · Cohort study · Risk factors · Injection drug use

For the CheCS investigators.

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Introduction

An estimated 3.2 million persons have chronic hepatitis C virus (HCV) infection in the US [1]. In contrast to the other major chronic viral infection in the US, human immunodeficiency virus (HIV), comparatively little is known about the spectrum of disease, access to care, and the effectiveness of current therapies. In addition, compared to HIV disease, chronic viral hepatitis has not been as widely recognized as a serious public health problem and, consequently, viral hepatitis prevention, control, and surveillance has been less adequately resourced [2].

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To assess the impact of chronic hepatitis infection, the Centers for Disease Control (CDC) funded the chronic hepatitis cohort study (CHeCS). This study is being carried out during a period of development in viral hepatitis treatment alternatives and changes in healthcare financing. Thus, there is a need for information related to the burden of care, modes of transmission, effectiveness of hepatitis screening, barriers to care, and a need for information on appropriate treatments.

To assess these epidemiologic issues, the CDC designed and implemented a dynamic multicenter cohort study along principles used for a large CDC-funded study of HIV infection [3]. Chronic hepatitis patients seen at four large integrated healthcare systems have been identified, with baseline clinical and laboratory data from electronically integrated medical records examined retrospectively [4, 5]. In addition, surveys were also conducted among all chronic hepatitis patients known to be alive at the time of the surveys in 2011–2012. The purpose of these surveys was to assess hepatitis risk factors, treatment exposures, additional demographic variables, and key psychosocial measures in the course and outcome of chronic hepatitis disease. These data are important for more effective public health management of HCV disease.

The purpose of the current study is to assess reported risk factors for hepatitis C infection among US military veterans from the Vietnam era compared to nonveterans. Studies among VA patients have suggested that US veterans and, particularly, Vietnam era veterans (i.e., those who served in the military any time between 1964 and 1975, regardless of where they served), have a significantly higher prevalence of HCV infection than other groups of veterans and comparable nonveterans [6–12]. Current research suggests that the reason for this higher prevalence among the Vietnam era veterans is likely due to injection drug use (IDU) [6, 7, 9, 11]. At this time, the Department of Veterans Affairs (VA) policy is to provide compensation for service-connected disability for veterans who can make supportable claims for hepatitis C exposure related to military service [13, 14].

The epidemiologic evidence suggests that HCV infection has been typically transmitted through injection drug use, blood transfusions before 1992, and medical/occupational exposures [1, 15, 16]. Given that previous reports were based on the VA healthcare data [6, 7, 9, 11], and that most veterans do not use this system for medical care [17], our hypothesis is that Vietnam era veterans do not have higher rates of HCV infection because of IDU, due to the selection bias of who uses VA medical services [18]. The majority of US veterans have private health insurance and/or Medicare and typically receive healthcare in non-VA institutions [19]. In the current study, we examine reported HCV risk factors among Vietnam era veteran and nonveteran HCV patients seen at four large non-VA health systems to test our hypothesis.

Methods

The CHeCS study methods have been previously described [4, 5]. Briefly, the cohort was created based on electronic health records (EHRs) of patients 18 years or older who had a service provided between January 1, 2006 and December 31, 2010 at one of four sites: Geisinger Health System, Danville, PA; Henry Ford Health System, Detroit MI (data coordinating center); Kaiser Permanente-Northwest, Portland, OR; and Kaiser Permanente-Honolulu, Hawaii. The electronic data collected included patient demographic information, medical encounter data, laboratory results, diagnosis and procedure data, and liver biopsy results. Electronic data used in this analysis were available retrospectively to January 1997 from the Detroit and Portland sites, to January 1998 from the Hawaii site, and to January 2001 from the Danville site [4, 5].

Patients meeting laboratory and diagnosis criteria for chronic hepatitis C were included in the cohort and were eligible for the survey, if they were known to be alive at the time of the survey. The CHeCS survey was designed to collect data on patient demographics, reported hepatitis risk factors, comorbidities, physical and mental functioning, use of alcohol and other psychoactive substances, treatment for alcohol or drug abuse, and on the patient's chronic hepatitis treatment history. Specific to this analysis, surveyed patients were asked to respond to the question: "How do you think that you may have gotten your hepatitis C infection?" Respondents could choose one or more responses from a list of known HCV risk exposures, including injection drug use or blood transfusion, or less common transmission risks, such as occupational or medical exposures, or sexual contact with infected partners. Respondents could also report or write in "other" exposures not specifically listed or mentioned in the survey. The latter responses were coded by study analysts and tabulated at survey completion. It is important to stress that for infectious diseases with long latency periods, such for HCV disease, while there are limitations, self-reported risk factor histories have been the principal method used to track risk exposures over time and been shown to be a valuable source of epidemiologic information [15, 16].

The study was funded by donations to the CDC Foundation; granting corporations did not have access to CHeCS data and did not contribute to data analysis or writing of manuscripts. The study protocol was reviewed by an Institutional Review Board approved by the Federal Office for Human Research Protections at each participating study site.

Cohort Selection

Algorithms for inclusion in the chronic hepatitis cohorts were developed and applied to the EHR data of patients aged 18 years or older from all sites with any health care utilization between January 1, 2006 and December 31, 2010 [4, 5]. Complete observation time for each patient was determined to be time from first evidence of hepatitis infection in the EHR including retrospective data prior to January 1, 2006, until either the last health system encounter or December 31, 2010. Patients were included in the hepatitis cohorts based on fulfillment of a combination of laboratory-based and ICD-9-based criteria [4, 5]. Trained medical abstractors reviewed the EHRs to collect liver biopsy results, outside system laboratory reports, detailed antiviral therapy data on all patients with treatment during 2001–2010, and to confirm chronic HCV infection status. Those charts flagged by abstractors as missing evidence of chronic HCV infection were reviewed under the supervision of a hepatitis clinician using clinician-developed criteria. Cases for which chronic HCV infection had been ruled out were excluded from the study cohort. The CHeCS study methodology has been previously described elsewhere in greater detail [4, 5].

Survey Data Collection

Altogether, we examined the records of 2,143,369 patients aged ≥18 years in the four participating health systems that had one or more services provided between January 1, 2006 and December 31, 2010. Of these patients, a total of 12,259 patients met the hepatitis C cohort inclusion criteria [4, 5]. Median time under observation for patients in the HCV cohort was 4.3 years (range 0–18 years), with a total of 90,566 person-years of observation. Across all sites approximately three-quarters of the chronic hepatitis C patients were born between 1945 through 1964 [4, 5]. In addition, payer status of patients tended to vary by site, with the percentage of patients using only public insurance (Medicaid or Medicare only) ranging from 2.3 % in Portland to 50.4 % in Danville and the percentage of uninsured ranging from 3.9 % in Danville to 10.0 % in Detroit. Additional detailed demographic information related to this cohort has been presented elsewhere [4, 5].

Of the 12,259 patients that met the hepatitis C cohort inclusion criteria, 7,756 were known to be alive and not institutionalized and surveyed by mail and telephone during 2011–2012. Up to 8 survey attempts were initiated in order to complete an interview with each of these patients. A small incentive was offered at each site to encourage survey response, which ranged from $10 to $25 depending on the customary practice at the study site. The survey took about 15–20 minutes to complete. Altogether, 4,636 surveys were completed by the time study data collection was ended. The overall response rate for this survey was approximately 60 % [20], after patients who were found to be deceased, incarcerated, in long-term care institutions, or who had invalid addresses or disconnected telephone numbers were excluded from the denominator. The survey was conducted in English only. It is noted that less than 5 % of the surveys (i.e., 4.5 %) were terminated due to non-English-speaking respondents.

Vietnam era veteran status was assessed by two survey questions: whether the respondent ever served in the US military and the dates they served in the military. Since only about 2 % of veterans were female in the current study, our analyses exclude female respondents. Of the 2,633 male respondents included with chronic hepatitis C infection, 1,812 indicated that they never served on active military duty in the US Armed Forces, 722 responded that they had served. In addition, 99 male respondents did not respond completely to the veteran status questions (e.g., they indicted they were veterans, but gave no service dates) and were excluded from the analyses. Of the 2,534 who responded to the military service questions, 526 (72.9 % of veterans) reported that they served in the US Military anytime between 1964 and 1975 and were, thus, classified as Vietnam era veterans. We note that military service specifically in Vietnam was not assessed in the study and this deployment status has *not* been associated with HCV infection, per se [6, 9, 10, 21]. In the current analyses, the results for the 526 male Vietnam era veterans are compared to the 1,812 males who never served on active military duty (N = 2,338). Non-Vietnam era veterans (n = 196) from other eras (e.g., Gulf War) were excluded from the current analyses to eliminate potential confounding by other service eras.

Survey data collected included demographic information (age, gender, race/ethnicity, marital status, education level, military history), substance use history (current alcohol use, current drug use, alcohol and drug abuse treatment history, illicit drug use history, injection drug use of psychoactive drugs), and other reported HCV risk factors. Specifically, respondents were first asked a close-ended question related to how they thought they contracted their HCV infection. This question included response options, such as, infected at birth, injection drug use, occupational exposure, sexual exposure, medical or surgical procedure exposure, or through blood transfusion or organ transplantation. Following this structured question, which permitted multiple responses, patients were asked if there were any "other" HCV exposures that could have resulted in their infection not listed in the survey. These responses were then recorded and later coded by study analysts at survey completion using standard survey coding methods for open-ended responses [22]. Among the

veterans, "Other" answers that specifically referenced the military (e.g., "infected in Vietnam") were excluded in order to make a valid comparison between Vietnam-era veterans and nonveterans. The remaining "Other" answers were coded into the following five descriptive subcategories: tattoo/body piercing, household contact with infected person, use of intranasal drugs, smoking or inhaling drugs, and any kind of vaccination or shot (without reference to a military venue). The survey also collected data on physical and mental health status using the SF-8 instrument [23], which provides standardized population health status data and has been widely used and validated in previous research.

Statistical Methods

Logistic regression modeling was used to study the individual risk associated with veterans and nonveterans. The variables with individual risk $p < 0.20$ were included as candidates in the first multivariable model, including "other" HCV exposures that did not include a specific military reference. The stepwise model selection was considered and the final model retained all risk factors with $p < 0.05$, with estimation of the C-index for the model goodness-of-fit assessment [24]. All statistical analyses were conducted using SAS version 9.2. Due to the nature of open-ended questions, analysis of the five descriptive subcategories of "other" was limited to descriptive analysis only. All logistic regression models were adjusted for study site.

Results

Comparison of the demographic characteristics of the survey responders and non-responders suggested that survey responders tended to be older, female, and white, consistent with the demographic biases reported as typical in US population surveys [20]. Examination of survey results by study site indicated that there were differences in veterans status by site ($p = 0.003$), with higher percentages of Vietnam era veterans included at the Kaiser Permanente-Northwest (39 %) and the Henry Ford Hospital sites (39 %), compared with the Kaiser Permanente-Hawaii (10 %) and the Geisinger (12 %) sites (Table 1). Vietnam era veterans also tended to be older ($p < 0.001$), more educated ($p < 0.001$), non-foreign born ($p = 0.009$), married ($p < 0.001$), and less often employed ($p < 0.001$) than nonveterans. In addition, the veterans were less likely to have reported being treated for drug abuse ($p < 0.001$). The veterans also had significantly higher mental health scores on the SF-8 scale ($p < 0.001$), indicating that they had better mental health than nonveterans (Table 1). Contrary to previous reports, however, there appeared to be no significant difference in the reported history of injection drug use between the Vietnam era veterans and nonveterans ($p = 0.16$) (Table 1).

In terms of HCV risk exposures, initially Vietnam era veterans appeared less likely to report that they contracted HCV infection from injection drug use (41.4 vs. 46.1 %, $p = 0.06$) or through male sexual exposures (0.6 vs. 2.4 %, $p = 0.013$), but more likely to report some other exposure as the reason for infection (19.4 vs. 9.0 %, $p < 0.001$) (Table 2). However, after excluding all "other" answers that referenced military exposures, which only veterans could experience and was therefore confounded with veteran status (n = 55), reporting other exposures as the reason for infection was no longer significant (8.9 vs. 9.0 %, $p = 0.68$) (Table 2). Altogether, 11 variables with the bivariate effects ($p < 0.20$) were candidates for the multivariable model (Tables 1, 2). After multivariable analysis, 4 variables (age, education, birth place, marital status) were retained in the final model (Table 3) with a C-index of 0.74. The results of the final model indicate that those who are older ($p < 0.001$), have greater than a high school education ($p < 0.001$), are from North America ($p < 0.001$), and are married ($p < 0.001$), are more likely to be Vietnam era veterans (Table 3). Neither drug abuse treatment history nor injection drug use history is associated with Vietnam era veteran status in this regression model predicting Vietnam era status.

The self-reported HCV exposures volunteered by nonveterans and Vietnam era veterans are summarized in Table 4, using Fisher's Exact Tests. These tests showed that Vietnam era veterans were also significantly more likely to report vaccinations or shots as the source of infection (5.9 vs. 0.30 %, $p < 0.001$) (Table 4), while no other reasons for infection differed between the groups. It is important to note that these tests were unable to be adjusted for study site or other confounding variables, due to small cell sizes.

It is noted that a sensitivity analysis was conducted comparing veterans overall (i.e., veterans of all eras, not just Vietnam era veterans) versus nonveterans. Comparing to the results from Table 2, the same risk exposures that were significantly different between Vietnam era veterans and nonveterans were also significant between all veterans and nonveterans, suggesting that singling out Vietnam era veterans as a group did not substantially bias the risk-factor comparisons with nonveterans.

Discussion

Previous studies suggest that Vietnam era veterans have a higher prevalence rate of HCV infection than other veterans and nonveterans [6–12]. The reason for this higher prevalence among the Vietnam era veterans, compared to

Table 1 Overall demographic and health status factors by veteran status, males only (N = 2,338)

Variable	Categories	Overall mean or % and 95 % CI	Nonveterans N = 1,812	Vietnam era veterans N = 526	*p* value
Site code	KPNW	37 (35.1, 39)	659 (36 %)	207 (39 %)	0.003
	KPHI	9 (7.8, 10.1)	157 (9 %)	53 (10 %)	
	HFHS	36.8 (34.9, 38.8)	657 (36 %)	204 (39 %)	
	GHS	17.2 (15.6, 18.7)	339 (19 %)	62 (12 %)	
Age	Mean ± SD	57.2 (56.9, 57.5)	56.0 ± 8.7	61.2 ± 3.9	<0.001
Race	White	71.9 (70.1, 73.8)	1,309 (72 %)	373 (71 %)	0.34
	Black	19 (17.4, 20.5)	331 (18 %)	112 (21 %)	
	AI/Asian/PI	7.6 (6.5, 8.6)	143 (8 %)	34 (6 %)	
	Unknown	1.5 (1, 2)	29 (2 %)	7 (1 %)	
Hispanic	No	87 (85.7, 88.4)	1,581 (87 %)	454 (86 %)	0.85
	Yes	4.7 (3.8, 5.5)	83 (5 %)	26 (5 %)	
	Unknown	8.3 (7.2, 9.4)	148 (8 %)	46 (9 %)	
Education	Less high school	12.6 (11.2, 14.1)	243 (15 %)	24 (5 %)	<0.001
	HS grad or GED	29.1 (27.2, 31)	480 (29 %)	135 (29 %)	
	Some college/tech	38.1 (36, 40.2)	590 (36 %)	215 (45 %)	
	College graduate or higher	20.2 (18.5, 21.9)	328 (20 %)	99 (21 %)	
Country of birth	USA/Canada	93.3 (92.3, 94.3)	1,667 (93 %)	501 (96 %)	0.009
	Other country	6.7 (5.7, 7.7)	134 (7 %)	22 (4 %)	
Married	Yes	60.7 (58.7, 62.7)	1,031 (57 %)	374 (72 %)	<0.001
Employment status	Full or part time	49.5 (47.5, 51.6)	883 (51 %)	219 (44 %)	<0.001
	Unemployed	6.8 (5.7, 7.8)	128 (7 %)	23 (5 %)	
	Retired	19.5 (17.8, 21.1)	280 (16 %)	153 (31 %)	
	Disabled	24.2 (22.4, 26)	435 (25 %)	104 (21 %)	
Ever treated for alcohol abuse	Yes	35.9 (34, 37.9)	662 (37 %)	172 (33 %)	0.11
Ever treated for drug abuse	Yes	35.7 (33.7, 37.7)	669 (38 %)	140 (28 %)	<0.001
Ever injected psychoactive drugs	Yes	57 (55, 59)	1,032 (58 %)	279 (54 %)	0.16
SF-8 physical health score	Mean ± SD	44.4 (43.9, 44.9)	44.4 ± 10.9	44.6 ± 11.0	0.71
SF-8 mental health score	Mean ± SD	47.3 (46.9, 47.7)	46.9 ± 10.6	48.7 ± 9.8	<0.001

KPNW Kaiser Permanente-Northwest, *KPHI* Kaiser Permanente-Hawaii, *HFHS* Henry Ford Health System, *GHS* Geisinger Health System, *CI* confidence interval, SF-8 Short Form-8

other veteran groups and nonveterans, is thought to be due to higher rates of injection drug use [6, 7, 9, 11]. However, most previous studies of veterans have been conducted among those who used the VA healthcare system. Problematic is that the majority of US veterans do not use the VA healthcare system and veterans who do are typically different [18]. Within this context, it is noteworthy that while Vietnam veterans have been reported to be at higher risk of illicit drug use in the some studies [25], research with representative samples of community-based veterans has not supported this finding [26, 27]. Noteworthy is that the majority of US veterans today have private health insurance and/or Medicare insurance and typically receive healthcare in non-VA institutions [17, 19]. In the current study, we saw that Vietnam era veterans seen in non-VA facilities were less likely to report ever being treated for drug abuse (28 vs. 38 %, $p < 0.001$) and did not have a higher reported prevalence of injection drug use overall compared to nonveterans (54 vs. 58 %, $p = 0.16$). While IDU was the most prevalent conventional HCV risk factor self-reported by the veterans overall, with 54 % reporting this exposure (Table 1), there were no significant differences reported for the other known HCV risk factors between the Vietnam era veterans and nonveterans, including occupational ($p = 0.18$), medical procedure ($p = 0.61$), and blood transfusion/organ transplant exposures ($p = 0.94$) (Table 2). While nonveterans were more likely to report sex with men than veterans as a risk factor ($p = 0.013$), the prevalence of this risk factor was low (nonveterans = 2.4 % vs. veterans = 0.6 %) (Table 2).

As suggested, among veterans reporting "other" exposures, the reason for this was primarily due to veterans

Table 2 Logistic regressions predicting risk exposures reported per standard survey answer categories by veteran status, males only (N = 2,338)

Variable	Categories	Overall N = 2,338	Nonveterans N = 1,812	Vietnam era veterans N = 526	OR (95 % CI)
Common transmission modes: survey answer options for self-reported source of HCV infection					
Injection drug use	Yes	1,054 (45.1 %)	836 (46.1 %)	218 (41.4 %)	0.83 (0.68, 1.01)
Occupational exposure	Yes	175 (7.5 %)	129 (7.1 %)	46 (8.7 %)	1.27 (0.89, 1.81)
Medical procedure exposure	Yes	236 (10.1 %)	186 (10.3 %)	50 (9.5 %)	0.92 (0.66, 1.28)
Blood transfusion, organ transplant, etc.[b]	Yes	401 (17.2 %)	312 (17.2 %)	89 (16.9 %)	0.99 (0.76, 1.28)
Rare transmission modes: survey answer options for self-reported source of HCV infection					
Infected at birth	Yes	21 (0.9 %)	19 (1.0 %)	2 (0.4 %)	–[a]
Sex with men	Yes	46 (2.0 %)	43 (2.4 %)	3 (0.6 %)	0.23 (0.07, 0.73)†
Sex with women	Yes	299 (12.8 %)	237 (13.1 %)	62 (11.8 %)	0.89 (0.66, 1.20)
Other exposure mentioned	Yes	264 (11.3 %)	162 (9.0 %)	102 (19.4 %)	2.63 (2.00, 3.46)†††
Other exposure mentioned: without military reference[c]	Yes	209 (9.0 %)	162 (9.0 %)	47 (8.9 %)	1.08 (0.76, 1.52)
Exposure unknown mentioned	Yes	461 (19.7 %)	356 (19.6 %)	105 (20.0 %)	0.99 (0.78, 1.27)

Based on logistic regression; p values adjusted for study site. † $p < 0.05$; ††† $p < 0.001$

[a] Inestimable, due to a small cell count

[b] Any blood transfusions (n = 401), by year reported: before 1992, all cases (n = 285), 71.1 %, Nonveterans (n = 221), 70.8 %, Vietnam era veterans (n = 64), 71.9 %; 1992 or later, all cases (n = 27), 6.7 %, Nonveterans (n = 20), 6.4 %, Vietnam era veterans (n = 7), 7.9 %; Year unknown, all cases (n = 89), 22.2 %, Nonveterans (n = 71), 22.8 %, Vietnam era veterans (n = 18), 20.2 %

[c] The original standard survey answer "other" was re-coded to exclude those who made a military reference (n = 55), in order to make an unbiased comparison between veteran and nonveteran groups

HCV hepatitis C virus, *CI* confidence interval

Table 3 Multivariate logistic regression: significant predictors of Vietnam veteran status, males only (N = 2,338)

Predict variable	Adjusted OR (95 % CI)
Age (in years)	1.12 (1.10, 1.14)†††
Education: college grad or higher versus < HS	3.19 (1.85, 5.50)†††
Education: HS grad or equivalent versus < HS	3.18 (1.87, 5.40)†††
Education: some college/tech versus < HS	3.82 (2.28, 6.40)†††
Country of birth: other versus USA/Canada	0.31 (0.17, 0.57)†††
Marital status: married versus not married	1.56 (1.21, 2.00)†††

Model includes the variables shown, as well as variables coded for the four study sites: Kaiser Permanente-Northwest, Kaiser Permanente-Hawaii; Henry Ford Health System; Geisinger Health System. This regression model also assessed employment status, drug treatment history, SF-8 mental health score, and each of the possible modes of self-reported hepatitis infection, but these predictors were dropped from the final model due to non-significance

††† $p < 0.001$

reporting exposure to vaccinations or shots in the military (or military service, generally), as the "other" source of HCV infection. It is noted that vaccinations in the military during the Vietnam War era were often done with pneumatic air-guns, en masse, during military induction and prior to overseas deployments. Typically, service members received multiple injections as they moved through these vaccination lines [13, 14]. Given this vaccination method, it was not uncommon for veterans to be bleeding by the time they reached the end of the line [13]. These injector systems were widely used in the 1960s and phased out by the military in later years [28]. Although some have suggested service members may have acquired their HCV infections from the pneumatic immunization systems used by the services during the Vietnam War era or through exposure to blood or medical procedures in the military during this timeframe [13, 14], these assertions have never been proven [28].

Limitations with this study include that the study survey was based on self-reported responses to survey question and the survey response rate was less optimal (~60 %). These factors could have biased our study results. It is noted that "self-report" is the chief method used by the CDC to monitor risk factors for HCV infection in the US [1]. This surveillance method has consistently suggested that IDU and transfusions/transplants before 1992 were the major risk factors for HCV infection in the US [1]. Also, we note that HCV infection is currently recognized as a potential "service-connected" disability by the VA and, thus, can be a

Table 4 Differences in other exposures volunteered as self-report or write-in answers by veteran status, males only (N = 2,338)

Variable	Categories	Nonveterans N = 1,812	Vietnam era veterans N = 526	*p* value[†]
Tattoo/body piercing	No	1,727 (95.3 %)	499 (94.9 %)	0.64
	Yes	85 (4.7 %)	27 (5.1 %)	
Household contact w/infected person	No	1,805 (99.6 %)	524 (99.6 %)	1.00
	Yes	7 (0.4 %)	2 (0.4 %)	
Intranasal drugs	No	1,803 (99.5 %)	524 (99.6 %)	1.00
	Yes	9 (0.5 %)	2 (0.4 %)	
Smoking/inhaling drugs	No	1,811 (99.9 %)	525 (99.8 %)	0.40
	Yes	1 (0.1 %)	1 (0.2 %)	
Any kind of vaccination or shot	No	1,807 (99.7 %)	495 (94.1 %)	<0.001
	Yes	5 (0.3 %)	31 (5.9 %)	

[†] Using Fisher's exact test, unadjusted results

VA-compensated disorder for veterans [13, 14]. Many Vietnam era veterans are likely aware of this compensation issue and this may have biased their recall. The survey response rate and selection bias may have also prejudiced our study findings, given that younger persons, nonwhites, and men were less likely to respond to the survey [20]. Some of these subgroups may have different HCV risk factor profiles. Finally, since our study was based on a limited number of study sites located in Danville, PA, Detroit MI, Portland, OR, and Honolulu, HI, our results may not be representative of the chronic HCV population in the US.

Despite these limitations, there may be merit for further investigation related to HCV infection risks among Vietnam era veterans. As shown, we found few differences in the known conventional HCV risk factors between veterans and nonveterans. In fact, when self-reported injection drug use risk was examined by veteran status, veterans appeared to report lower HCV exposure risk than nonveterans (41.4 vs. 46.1 %, $p = 0.06$) (Table 2) and there was no difference in overall reported injection drug use rates between Vietnam era veterans and nonveterans (54 vs. 58 %, $p = 0.16$) (Table 1). Furthermore, history of drug abuse treatment was more common among nonveterans than the era veterans (38 vs. 28 %, $p < 0.001$) (Table 1). Additionally, very few nonveterans reported vaccination-related risk factor exposures compared to veterans (0.3 vs. 5.9 %, $p < 0.001$) (Table 4). Finally, as was seen, multivariate logistic regression predicting Vietnam era veteran status from key study variables, including study site, age, education, birth place, and marital status, suggested that Vietnam era veteran status was not significantly associated with any known HCV risk factors. As discussed, it is noteworthy that neither history of drug abuse treatment nor history of injection drug use was associated with Vietnam era veteran status.

In summary, our findings do not appear to be consistent with the findings often reported for Vietnam era veterans included in VA-based studies. As indicated, most veterans do not use the VA healthcare system. Thus, past studies related to the prevalence of risk factors for HCV among veterans may be biased. While our findings are not conclusive and may reflect recall, response, and/or sampling biases [22], they may justify the need for additional research. It is important to stress that the military service exposure findings found for the Vietnam era veterans was not part of our original survey design, but emerged from the coding and analysis of open-ended responses after survey completion. Given our findings, and the adverse legacy of the Vietnam War in general [18], additional research may be warranted and important for future surveillance and management of HCV disease. The problem with the current study, of course, is that it is also potentially limited by selection bias as well, whereby higher-functioning, higher SES, and higher-educated veterans, than those who receive medical care from the VA, were overrepresented. A future study that could more accurately answer the question about the relative frequency of injection drug use and other HCV risk factors among veterans, compared to nonveterans with HCV, would need to include data on veterans treated in both VA and non-VA facilities. We are currently planning such research.

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Conflict of interest Stuart C. Gordon receives grant/research support from AbbVie Pharmaceuticals, Bristol-Myers Squibb, Gilead Pharmaceuticals, GlaxoSmithKline, Intercept Pharmaceuticals,

Merck, and Vertex Pharmaceuticals. He is also a consultant for Amgen, Bristol-Myers Squibb, CVS Caremark, Gilead Pharmaceuticals, Merck, Novartis, and Vertex and is on the Data Monitoring Board for Janssen Pharmaceuticals. The other authors have no conflict of interests associated with this research study.

Ethical standard The investigation followed the guidelines of the U.S. Department of Health and Human Services regarding protection of human subjects. The study protocol was approved and renewed annually by each participating institution's institutional review board.

References

1. Armstrong, G. L., Wasley, A., Simard, E. P., McQuillan, G. M., Kuhnert, W. L., & Alter, M. J. (2006). The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Annals of Internal Medicine, 144*, 705–714.
2. Mitchell, A. E., Colvin, H. M., & Beasley, R. P. (2010). Institute of medicine recommendations for the prevention and control of hepatitis B and C. *Hepatology, 51*, 729–733.
3. Moorman, A. C., Holmberg, S. D., Marlowe, S. I., et al. (1999). Changing conditions and treatments in a dynamic cohort of ambulatory HIV patients: The HIV outpatient study (HOPS). *Annals of Epidemiology, 9*, 349–357.
4. Moorman, A. C., Gordon, S. C., Rupp, L. B., et al. (2013). Baseline characteristics and mortality among people in care for chronic viral hepatitis: The chronic hepatitis cohort study. *Clinical Infectious Diseases, 56*, 40–50.
5. Spradling, P. R., Rupp, L., Moorman, A. C., et al. (2012). Hepatitis B and C virus infection among 1.2 million persons with access to care: Factors associated with testing and infection prevalence. *Clinical Infectious Diseases, 55*, 1047–1055.
6. Dominitz, J. A., Boyko, E. J., Koepsell, T. D., et al. (2005). Elevated prevalence of hepatitis C infection in users of United States veterans medical centers. *Hepatology, 41*, 88–96.
7. Briggs, M. E., Baker, C., Hall, R., et al. (2001). Prevalence and risk factors for hepatitis C virus infection at an urban veterans administration medical center. *Hepatology, 34*, 1200–1205.
8. Yee, H. S., Chang, M. F., Pocha, C., et al. (2012). Update on the management and treatment of hepatitis C virus infection: Recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program Office. *American Journal of Gastroenterology, 107*, 669–689.
9. Cheung, R. C. (2000). Epidemiology of hepatitis C virus infection in American veterans. *American Journal of Gastroenterology, 95*, 740–747.
10. Brau, N., Bini, E. J., Shahidi, A., et al. (2002). Prevalence of hepatitis C and coinfection with HIV among United States veterans in the New York City metropolitan area. *American Journal of Gastroenterology, 97*, 2071–2078.
11. Mishra, G., Sninsky, C., Roswell, R., Fitzwilliam, S., & Hyams, K. C. (2003). Risk factors for hepatitis C virus infection among patients receiving health care in a Department of Veterans Affairs hospital. *Digestive Diseases and Sciences, 48*, 815–820.
12. Calore, B. L., Cheung, R. C., & Giori, N. J. (2012). Prevalence of hepatitis C virus Infection in the veteran population undergoing total joint arthroplasty. *The Journal of Arthroplasty*, 27(10), 1772–1776.
13. Gary, C. (2009). A race against time: Hepatitis C diagnosis and treatment. *The VVA Veteran*. *29*(5): 37–38. http://vva.org/veteran/1009/veteran1009.html. Accessed 3/9/2014.
14. Hunt, C. F. (2004). Relationship between immunization with jet injectors and hepatitis C infection as it relates to service connection. Washington, DC: Department of Veterans Affairs, Veterans Benefits Administration:1–2.
15. Tohme, R. A., & Holmberg, S. D. (2012). Transmission of hepatitis C virus infection through tattooing and piercing: A critical review. *Clinical Infectious Diseases, 54*, 1167–1178.
16. Tohme, R. A., & Holmberg, S. D. (2010). Is sexual contact a major mode of hepatitis C virus transmission? *Hepatology, 52*, 1497–1505.
17. US Department of Veterans Affairs. (2002). *2001 National Survey of Veterans (NSV): Final report*. Washington, DC: US Department of Veterans Affairs.
18. Boscarino, J. A. (2007). Vietnam veterans, postwar experiences and health outcomes. In G. Fink (Ed.), *Encyclopedia of stress* (2nd ed., Vol. 3, pp. 830–838). New York, NY: Academic Press.
19. US Department of Veterans Affairs. (2010). *National Survey of Veterans, Active Duty Services Members, Demobilized National Guard and Reserve Members, Family Members, and Surviving Spouses.* Final Report ed. Washington, DC: Department of Veterans Affairs.
20. Centers for Disease Control and Prevention (CDC). (2013). Locations and reasons for initial testing for hepatitis C infection—chronic hepatitis cohort study, United States, 2006–2010. *MMWR. Morbidity and Mortality Weekly Report, 62*, 645–648.
21. Roselle, G. A., Danko, L. H., Kralovic, S. M., Simbartl, L. A., & Kizer, K. W. (2002). National hepatitis C surveillance day in the Veterans Health Administration of the Department of Veterans Affairs. *Military Medicine, 167*, 756–759.
22. Groves, R. M., Fowler, F. J., Couper, M. P., Lepkowski, J. M., Singer, E., & Tourangeau, R. (2009). *Survey methodology* (2nd ed.). New York, NY: Wiley.
23. Ware, J. E., Kosinski, M., Turner-Bowker, D. M., & Gandek, B. (2001). *How to Score the SF-8 Health Survey*. Boston, MA: Quality metric incorporated; Health Assessment Lab.
24. Harrell, F. E. (2001). *Regression modeling strategies: With applications to linear models, logistic regression, and survival analysis*. New York, NY: Springer.
25. Robins, L. N. (1974). *The Vietnam drug user returns*. Washington, DC: U.S. Government Printing Office.
26. Kulka, R. A., Schlenger, W. E., Fairbank, J. A., et al. (1990). *The national Vietnam veterans readjustment study: Tables of findings and technical appendices*. New York, NY: Brunner/Mazel.
27. Boscarino, J. (1979). Current drug involvement among vietnam and non-Vietnam veterans. *American Journal of Drug and Alcohol Abuse, 6*, 301–312.
28. US Department of Veterans Affairs. (2014). Hepatitis C: Military-related blood exposures, risk factors, VA care. http://www.hepatitis.va.gov/provider/policy/military-blood-exposures.asp. Accessed 3/9, 2014.