# Analysis of a hepatitis C screening programme for US veterans

# I. A. ZUNIGA<sup>1</sup>, J. J. CHEN<sup>1\*</sup>, D. S. LANE<sup>1</sup>, J. ALLMER<sup>2</sup> and V. E. JIMENEZ-LUCHO<sup>2,3</sup>

<sup>1</sup> Department of Preventive Medicine, State University of New York at Stony Brook, Stony Brook, NY, USA

<sup>2</sup> Northport VA Medical Center, East Northport, NY, USA

<sup>8</sup> Division of Infectious Diseases, State University of New York at Stony Brook, Stony Brook, NY, USA

(Accepted 17 May 2005, first published online 18 August 2005)

### SUMMARY

This study analyses a screening programme for hepatitis C virus (HCV) infection among US veterans in a suburban Veterans Affairs Medical Center, in New York. This is the first study examining all 11 potential risk factors listed in the 2001 National U.S. Veterans Health Administration Screening Guidelines. A retrospective study was conducted of 5400 veterans 'at risk' of HCV, identified through a questionnaire in this institution's primary-care outpatient departments between 1 October 2001 and 31 December 2003. Multivariate logistic regression models were built to identify independent predictors of infection. Of 2282 veterans tested for HCV, 4·6% were confirmed by HCV PCR to be HCV infected. In the multivariate model developed, injection drug use, blood transfusion before 1992, service during the Vietnam era, tattoo, and a history of abnormal liver function tests were independent predictors of HCV infection. Our data support considering a more targeted screening approach that includes five of the 11 risk factors.

# INTRODUCTION

Hepatitis C virus (HCV), a leading cause of chronic liver disease in the United States, is a recognized public health issue among US veterans. The prevalence of HCV viraemia in published studies among veterans who use the Veterans Administration (VA) hospital system ranges from 10.6% to 17.8% [1, 2]. In comparison, a 1.3% prevalence of HCV viraemia among the general US population was reported in the Third National Health and Nutrition Examination

This study was presented in part at the 2004 Annual Meeting of the Infectious Diseases Society of America in Boston, MA, USA.

Survey (NHANES III) [3]. In 1998, the U.S. Veterans Health Administration (VHA) implemented National Guidelines for HCV screening among high-risk veterans [4]. The 2001 updated Guidelines recommend screening for HCV in the presence of at least one of 11 *identified potential* risk factors [5].

Several prior studies have examined risk factors for HCV infection among US veterans [1–2, 6–8]. The most comprehensive of these were two cross-sectional studies [1, 2]. The first was conducted at an urban VA Medical Center in San Francisco [1]. Injection drug use (IDU), tattooing, blood transfusion before 1992, incarceration, combat medical work and more than 15 lifetime sexual partners of the opposite sex were independently associated with HCV infection. The second, conducted at six VA Medical Centers in the New York Metropolitan area found that IDU, blood

<sup>\*</sup> Author for correspondence: Dr J. J. Chen, Dept. of Preventive Medicine, HSC Level 3, Rm. 086, SUNY at Stony Brook, School of Medicine, Stony Brook, NY 11794-8036, USA. (Email: John.Chen@stonybrook.edu)

exposure in combat, alcohol abuse, and service during the Vietnam era were independent risk factors for infection [2].

Gaps in these studies were: (1) the inclusion of only selected outpatient departments; (2) the inclusion on a screening questionnaire of only 8 of 11 risk factors published in the updated VHA Screening Guidelines; and, (3) the use of a non-prospectively applied screening questionnaire, which can lead to recall bias because prior knowledge of HCV status may influence individuals' recall or reporting of high-risk behaviors such as IDU [1].

In the general population, parenteral exposures (e.g. IDU and blood transfusion prior to 1992) are well recognized risk factors for infection. In contrast, the importance of sexual contact with an HCV-infected person or tattooing is less clear [9]. Several other factors, such as service in the Vietnam era, blood exposure in combat, and alcohol abuse are unique and/or highly prevalent among veterans and also warrant further investigation [2].

To analyse an existing hepatitis C screening programme and help clarify the relative contribution of various risk factors for HCV infection, we carried out a 2-year retrospective study among 5400 veterans with risk factors for HCV on a prospectively applied screening questionnaire. This is the first study to include all primary-care outpatient departments of a suburban VA Medical Center and to examine all 11 identified potential risk factors outlined in the 2001 updated National VHA Screening Guidelines [5].

# METHODS

# Study population and setting

The study population included all 5400 veterans with one or more risk factors for HCV infection on a screening questionnaire administered between 1 October 2001 and 31 December 2003 in all primarycare outpatient departments of the Northport VA Medical Center (NVAMC). The NVAMC is a suburban VA hospital located in Suffolk County, Long Island that provides care to  $\sim$  200 000 veterans throughout Long Island, NY. A self-administered risk assessment questionnaire for HCV has been used at this institution since 1999 to prospectively identify HCV-infected veterans. Veterans with one or more risk factors on the questionnaire are offered serological testing for HCV whereas testing of veterans without risk factors is not routinely performed.

# Screening questionnaire

All 11 identified potential risk factors for HCV listed in the 2001 updated National VHA Screening Guidelines [5] were assessed through this institution's screening questionnaire. Specifically, veterans were evaluated for the following potential risk factors: (1) 'Vietnam era veteran'; (2) 'transfusion of blood products prior to 1992'; (3) 'IDU (past or present)'; (4) 'blood exposure in or through skin or mucous membranes (e.g. medical worker, combat needle stick injury)'; (5) 'multiple sexual partners (past or present)'; (6) 'haemodialysis'; (7) 'tattoo or repeated body piercing'; (8) 'intranasal cocaine use (past or present)'; (9) 'unexplained liver disease'; (10) 'having been told that he/she has abnormal liver function tests (LFTs)'; and (11) 'intemperate alcohol use (more than seven alcoholic beverages per week)'.

# Laboratory testing and definition of HCV infection

Anti-HCV serology was performed at this institution using the second-generation ELISA for antibody (EIA 2.0). HCV EIA(+) samples were confirmed at the Bronx VA Medical Center by qualitative reverse-transcriptase HCV polymerase chain reaction (RT–PCR) testing (COBAS AMPLICOR<sup>TM</sup> HCV test, version 2.0; Roche Diagnostics, Indianapolis, IN, USA). We defined hepatitis C infection as having a positive PCR test result. For HCV EIA(+), PCR(-) samples, we ensured that these individuals had not previously received therapy for HCV by reviewing their medical charts. Recombinant immunoblot assay testing (RIBA) was not performed on these individuals, which were categorized as HCV noninfected for purposes of analysis.

# **Data collection**

The 5400 veterans with risk factors for HCV infection were identified through administrative data using all primary-care outpatient department stop codes. Risk factors, HCV testing data, and demographic information (date of birth, ethnicity, gender, marital status, employment status and Medicaid eligibility) were collected through this institution's electronic and paper medical record system. Age was calculated by subtracting the veteran's date of birth from the questionnaire date. The study protocol was approved by the NVAMC Institutional Review Board and Research and Development Committee.

### Statistical methods

Data are reported as frequencies and percentages unless otherwise noted. Associations between two categorical variables were studied using the  $\chi^2$  test and Fisher's exact test, when applicable. Odds ratios (ORs) and their 95% confidence intervals (CIs) were reported.

Data-driven analysis was used to categorize age into low prevalence (<40 or  $\geq 55$  years) and high prevalence (40-54 years) groups. Due to the possibility that the 8.2% missing values for ethnicity (among tested individuals) might occur nonrandomly, these missing values were classified as an 'unknown' category and included in the analysis. American Indian or Alaska Natives, Asians, Hispanics, Native Hawaiian or Pacific Islanders constituted only 3.7% of the tested population. Therefore, they were combined into the 'unknown' category.

To study the association between risk factors and the binary outcome variable of HCV infection (infected vs. not infected), multiple logistic regression models were built to determine the independent contribution of individual risk factors, adjusting for others. Demographic variables (age, ethnicity, Medicaid eligibility, employment and marital status) were adjusted for in all models. Gender was not included in the model because of the low percentage, 3.9%, of female veterans. Haemodialysis was excluded from the multivariate analysis because only 0.7% of tested veterans reported this risk factor. Interactive effects between two risk factors and between a demographic variable and a risk factor variable were explored by cross-tabulation. Potential interactions with P < 0.1, based on the Breslow–Day statistic, were considered for entry into logistic regression models. Multivariate modeling was developed through a combination of forward and backward selection, using Wald and likelihood ratio test results. Based on the final model and the interactive effects observed, adjusted ORs and 95% CIs were derived for meaningful comparisons between subgroups of veterans. Sensitivity analyses (e.g. different age and ethnicity breakdowns, etc.) were performed to check on the stability of the final model. A twotailed P < 0.05 was considered statistically significant.



Fig. 1. Flow diagram outlining the testing sequence, test results and infection status of veterans 'at risk' of hepatitis C virus (HCV) infection. EIA, Enzyme immunoassay; PCR, polymerase chain reaction. HCV infection was defined as having a positive PCR. Of seven individuals tested only by PCR (without prior EIA), four individuals had hepatitis C by history of whom three had confirmatory positive PCR results. No reason for initial testing by PCR was established for the other three individuals, all of whom had negative PCR results. Nineteen individuals with positive EIA test results lacked a confirmatory PCR at the time of data analysis. Of these, 14 individuals were lost to follow-up, three individuals underwent PCR testing subsequent to data analysis and were found to be PCR-positive, and two individuals lacked confirmatory PCR testing for unknown reasons.

Statistical analyses were conducted using SPSS 11.0 (SPSS Inc., Chicago, IL, USA) and SAS 8.2 (SAS Institute, Cary, NC, USA).

### RESULTS

### Sequence of HCV testing and HCV test results

Of 5400 veterans with one or more potential risk factors for HCV,  $42 \cdot 3\%$  were tested for HCV (Fig. 1). Nineteen individuals with positive EIA results in whom confirmatory PCR testing was not performed were excluded from analyses of infected *vs.* non-infected veterans. The rate of HCV infection was 103 out of 2263, i.e.  $4 \cdot 6\%$ .

# Demographic characteristics of infected and non-infected veterans

Table 1 compares infected and non-infected veterans by demographic characteristics. While only 2.2% of veterans <40 or  $\ge 55$  years of age were HCV infected, 9.8% of those aged 40–54 years were infected (P < 0.001). Black veterans were more likely than white veterans to be infected (9.4% vs. 4.2%; P = 0.001). Other demographic variables significantly associated with infection in univariate analysis were: Medicaid eligibility; single or divorced marital status; and, unemployed or part-time status.

### Potential risk factors

Service during the Vietnam era was reported most commonly, by 50.1% of tested veterans, while only 4.5% reported past or present IDU (Fig. 2). Fiftyeight per cent of tested veterans had more than one potential risk factor for HCV infection. The mean number of reported risk factors per veteran was 3.54 (s.D. = 1.8, range 1-8) in the infected group and 2.02 (s.D. = 1.2, range 1-8) in the non-infected group (P < 0.001, based on a non-parametric *t* test) (data not shown).

#### Risk factors for HCV infection in univariate analysis

Table 2 compares infected and non-infected veterans on the presence of potential risk factors. The most important risk factor for HCV infection was IDU (crude OR 24·67, 95% CI 15·23–39·96). Other risk factors significantly associated with HCV infection were: unexplained liver disease; a history of abnormal LFTs; intranasal cocaine use; tattoo or repeated body piercing; and, intemperate alcohol use. Service during the Vietnam era, blood transfusion prior to 1992, blood exposure in or through mucous membranes, haemodialysis, and multiple sexual contacts were not significantly associated with HCV infection in univariate analysis.

#### Predictors of HCV infection by multivariate analysis

In the multivariate model developed, IDU, service during the Vietnam era, blood transfusion prior to 1992, tattoo or repeated body piercing (OR 2·12, 95% CI 1·28–3·49), and a history of abnormal LFTs (OR 5·36, 95% CI 3·10–9·27) were independent predictors of HCV infection (Table 3). Two statistically significant interactive effects were identified: an interaction between service during the Vietnam era and IDU

Table 1.	Demographic	characteristics	of infected and
non-infec	ted veterans		

Characteristic	Infected $(n=103)$	Non-infected $(n=2160)$	<i>P</i> *
Age (years)			
40-54	69 (67.0)	635 (29.4)	<0.001
$<40 \text{ or } \ge 55$	34 (33.0)	1525 (70.6)	
Race/ethnicity			
White	73 (70.9)	1685 (78.0)	
Black	22 (21.4)	211 (9.7)	0.001
Unknown	8 (7.8)	264 (12.2)	0.345
Gender			
Male	99 (96.1)	2075 (96.1)	
Female	4 (3.9)	85 (3.9)	1.000
Marital status			
Married or widowed	33 (32.0)	1186 (55.0)	
Single-never married	23 (22.3)	369 (17.1)	0.004
Divorced or separated	47 (45.6)	600 (27.8)	< 0.001
Employment			
Full time	26 (25.2)	656 (30.4)	
Unemployed or part	61 (59.2)	822 (38.1)	0.009
time			
Retired	16 (15.5)	679 (31.5)	0.107
Medicaid			
Non-eligible	95 (94.1)	2054 (98.9)	
Eligible	6 (5.9)	23 (1.1)	0.002

Data are no. (%). Denominators may change because of missing data, and percentages may not add up to 100% because of rounding.

\* Statistical analyses were performed using  $\chi^2$  tests and Fisher's exact tests, when applicable.

(P=0.003) and, an interaction between blood transfusion prior to 1992 and IDU (P = 0.005). Because of these interactive effects, reporting single ORs for IDU, service during the Vietnam era or blood transfusion prior to 1992 was not meaningful. Therefore, estimated ORs were derived in Table 4 for subgroups of IDU vs. non-IDU veterans; in Figure 3 for subgroups of Vietnam era vs. non-Vietnam era veterans; and, in Figure 4 for subgroups of veterans with a history of blood transfusion prior to 1992 vs. veterans without a history of blood transfusion prior to 1992. The estimated OR for IDU vs. non-IDU individuals was highest for non-Vietnam era veterans who did not receive a blood transfusion prior to 1992 (OR 78.79, 95% CI 28·42-218·50; comparison 1, Table 4), followed by Vietnam era veterans who were not transfused prior to 1992 (OR 12.61, 95% CI 6.04-26.36; comparison 2), and non-Vietnam era veterans who were transfused prior to 1992 (OR 3.00, 95% CI 0.28-32.45; comparison 3). However, the same effect



Fig. 2. Percentages of tested veterans (n = 2263) reporting each of the 11 potential risk factors for HCV. Percentages do not add up to 100% because veterans may have multiple risk factors. The denominator for the per cent calculations excludes 106 individuals because of missing questionnaire data. IDU, injection drug use.

was not seen for Vietnam era veterans who were transfused prior to 1992 (OR 0·48, 95% CI 0·05–4·30; comparison 4). Figure 3 compares the effect of service during the Vietnam era as a risk factor for HCV infection, between non-IDU and IDU veterans. Service during the Vietnam era was a *risk* factor for infection for non-IDU veterans (OR 1·91, 95% CI 1·04–3·50), but not for IDU veterans (OR 0·31, 95% CI 0·11–0·88). Similarly, Figure 4 compares the effect of blood transfusion prior to 1992 as a risk factor for infection, between non-IDU and IDU veterans. Blood transfusion prior to 1992 was a *risk* factor for infection for non-IDU veterans (OR 3·15, 95% CI 1·67–5·93), but not for IDU veterans (OR 0·12, 95% CI 0·01–1·06).

# Application of the multivariate model to the screening strategy

Results of the multivariate model were used to examine whether a more selective screening strategy might be warranted. By screening only for IDU, 40.8% of infected individuals would have been identified, and 97% fewer individuals would have required testing. By screening only for the five risk factors that were significant in the multivariate model, 97% of infected individuals would have been identified, and 21.5% fewer individuals would have required testing (data not shown).

# DISCUSSION

The 4.6% rate of HCV infection among veterans 'at risk' of HCV at this institution is lower than the

10.6–17.8% prevalence of HCV infection reported in prior published studies among US veterans [1, 2]. The actual prevalence of infection among veterans at this institution may in fact approach the prevalence of HCV infection in the general US population, assuming a low rate of infection among the large proportion of veterans without reported risk factors. Veterans who receive their care through the outpatient departments of this suburban VA may differ from veterans seen primarily in urban VA Medical Centers in terms of their demographic characteristics and/or their general health status.

In the context of this relatively low HCV prevalence, the current strategy of screening for all 11 risk factors listed in the National VHA Screening Guidelines may not be necessary or cost-effective, especially since only five of 11 risk factors were independent predictors of HCV infection. Moreover, screening for these five risk factors only would have allowed this institution to identify 97% of infected individuals while testing 21.5% fewer individuals. In its 2004 published recommendations, the U.S. Preventive Services Task Force concluded that there is insufficient evidence to show that the benefits of testing high-risk individuals for HCV outweigh the potential costs [10]. However, because it would take decades to find conclusive evidence that HCV-related chronic disease rates decrease with early identification [11], a screening programme targeted to those most likely to be HCV infected would seem justified.

As prior studies among veterans have found [1-2, 6], IDU was the most important risk factor for HCV infection. We found an interactive effect between IDU and service during the Vietnam era and between IDU

### I. A. Zuniga and others

	Infected	Non-infected		
Risk factor present	(n = 103)	(n = 2160)	OR†	95% CI
Service during Vietnam era	58 (59.2)	1022 (49.6)	1.47	(0.97 - 2.22)
Blood transfusion prior to 1992	18 (18.4)	356 (17.3)	1.08	(0.64 - 1.82)
Injection drug use	40 (40.8)	56 (2.7)	24.67	(15.2–39.96)***
Blood exposure	14 (14.3)	253 (12.3)	1.19	(0.67 - 2.13)
Multiple sexual partners	35 (35.7)	697 (33.9)	1.09	(0.71 - 1.65)
Haemodialysis	0 (0.0)	16 (0.8)	0.63	(0.04 - 10.56)
Tattoo/body piercing	47 (48.0)	634 (30.8)	2.07	(1.38–3.11)***
Intranasal cocaine use	44 (44.9)	280 (13.6)	5.18	(3·41–7·86)***
Unexplained liver disease	16 (16.3)	53 (2.6)	7.39	(4.05–13.47)***
Abnormal liver function tests	35 (35.7)	161 (7.8)	6.55	(4.20–10.20)***
Alcohol abuse	40 (40.8)	621 (30.2)	1.60	(1.06-2.42)*

Table 2. Risk factors for hepatitis C infection among infected and non-infected veterans, by univariate analysis

Data are no. of veterans with potential risk factors. Numbers do not add up to totals of infected and non-infected individuals because veterans can have multiple risk factors. Missing questionnaires were excluded from the denominator for per cent calculations.

OR, Odds ratio; CI, confidence interval.

<sup>†</sup> Crude OR, calculated by  $\chi^2$  tests and Fisher's exact tests, when applicable.

\* P < 0.05, \*\*\* P < 0.001.

TC 11	1 2	D	1· .	C 1	. • . •	~ ·	C	, •	1	1	1	1 • .•		•	1	•
Ign	e 4	Prod	lictore	nt h	onatitie	1 1	nto	ction .	$h_{1}$	multi	nla	10010tic	roaro	CCION	anal	12070
тан	10.2.	1 100	u u u v s	$o_I m$	SDULLIN	V 11	ne	cuon.	11	mann	ne $i$	$O_{2}I_{M}I_{U}$	16216	sston	anai	VALA
				- J · · ·	· · · · · · · · · · · · · · · · · · ·				~		r	0.0				,~-~

Variables	Coefficient	S.E.	OR	95% CI	Р	
Age 40–54 years	0.92	0.27	2.51	(1.47-4.28)	0.001	
Black race	0.70	0.33	2.01	(1.05 - 3.86)	0.036	
Other/unknown race	-0.36	0.49	0.70	(0.27 - 1.83)	0.467	
Divorced/separated	0.47	0.29	1.61	(0.92 - 2.81)	0.098	
Single-never married	0.47	0.35	1.60	(0.81 - 3.16)	0.176	
Medicaid eligible	1.09	0.64	2.96	(0.85–10.33)	0.089	
Unemployed/part time	0.42	0.30	1.52	(0.84 - 2.76)	0.167	
Retired	0.14	0.40	1.14	(0.53 - 2.49)	0.734	
Tattoo/body piercing	0.75	0.26	2.12	(1.28 - 3.49)	< 0.001	
Abnormal LFTs	1.68	0.28	5.36	(3.10 - 9.27)	< 0.001	
IDU†	4.37	0.52				
Vietnam era†	0.65	0.31	_	_	_	
Blood transfusion prior to 1992†	1.15	0.32	—	_	—	
IDU × Vietnam era	-1.83	0.63		_	0.003	
$IDU \times transfusion$	-3.27	1.16		—	0.002	

s.E., Standard error; OR, odds ratio; CI, confidence interval; LFT, liver function test; IDU, injection drug use; IDU × Vietnam era, interactive effect between IDU and service during the Vietnam era; IDU × transfusion, interactive effect between IDU and blood transfusion prior to 1992. Referent group was <40 or  $\geq$ 55 years for age, white for ethnicity, married for marital status, and full-time employed for employment status.

<sup>†</sup> Due to the interactive effects, estimated ORs were derived in Table 4, Figure 3 and Figure 4 for various subgroups of veterans.

and blood transfusion prior to 1992. Service during the Vietnam era and blood transfusion prior to 1992 were found to be *risk* factors for HCV infection only among veterans who reported *no* IDU, past or present. Conversely, IDU was strongly associated with infection in non-Vietnam era veterans who did not receive a blood transfusion prior 1992.

Blood transfusion prior to 1992, before universal screening of blood products for HCV, is a well known risk factor for HCV infection in the general

Table 4. Effect of IDU as a risk factor for HCV infection, for subgroups of veterans stratified by era of service and history of blood transfusion prior to 1992

_								
Con	nparisons (l	Adjusted OR (95% CI)						
1	IDU	Non-VE	No TF	vs.	No IDU	Non-VE	No TF	78.79 (28.42–218.50)***
2	IDU	VE	No TF	vs.	No IDU	VE	No TF	12.61 (6.04–26.36)***
3	IDU	Non-VE	TF	vs.	No IDU	Non-VE	TF	3.00 (0.28-32.45)
4	IDU	VE	TF	VS.	No IDU	VE	TF	0.48 ( 0.05–4.30)

OR, Odds ratio; CI, confidence interval; IDU, injection drug use; VE, Vietnam era; TF, blood transfusion prior to 1992. The multivariate model adjusted for all demographic variables, tattoo, a history of abnormal liver function tests, IDU, service during the Vietnam era and blood transfusion prior to 1992. \*\*\*P < 0.001.



**Fig. 3.** Differential effect of service during the Vietnam era as a risk factor for HCV infection, for non-injection drug use (non-IDU) and IDU veterans. Point estimates for adjusted odds ratios (ORs) (solid squares) and 95% confidence intervals (CIs) (vertical bars) are shown. The multivariate model adjusted for all demographic variables, tattoo, a history of abnormal liver function tests, IDU, service during the Vietnam era and blood transfusion prior to 1992 (\* P < 0.05).

population [12]. Also, several studies found that service during the Vietnam era was an independent predictor of infection [2, 7], and undisclosed IDU was proposed as a possible explanation for this association [2]. Other candidate explanations related to military service include blood exposure in combat [2] or exposure to HCV through jet injectors (i.e. multi-dose vaccination instruments) [13].

We hypothesize that the timing of IDU among Vietnam era veterans in relation to the HCV epidemic may explain why service during the Vietnam era was not found to be a *risk* factor for HCV infection in IDU veterans. According to estimates by the Centers for Disease Control and Prevention (CDC) in the United States, the incidence of HCV infection was low before 1965, increased steadily from the late 1960s to the 1980s and peaked in the mid-late 1980s [14]. It is possible that IDU among Vietnam era veterans



**Fig. 4.** Differential effect of blood transfusion prior to 1992 as a risk factor for HCV infection, for non-injection drug use (non-IDU) and IDU veterans. Point estimates for adjusted odds ratios (ORs) (solid squares) and 95% confidence intervals (CIs) (vertical bars) are shown. The multivariate model adjusted for all demographic variables, tattoo, a history of abnormal liver function tests, IDU, service during the Vietnam era and blood transfusion prior to 1992 (\*\*\* P < 0.001).

occurred primarily in the late 1960s-early 1970s preceding the peak of the HCV epidemic among injecting drug users in the United States. These individuals may have injected drugs at a time when the incidence/ prevalence of HCV was low, and, therefore, may not have become HCV infected. On the other hand, non-Vietnam era veterans with IDU could represent a distinct sociological niche of injecting drug users; these individuals may have injected drugs closer to the peak of the HCV epidemic, thus acquiring HCV infection. The literature seems to support this hypothesis. While heroin use was common during the Vietnam War, only a minority of Vietnam era veterans used injected heroin upon their return to the United States [15]. Also, rapid recovery from heroin addiction by the great majority of Vietnam era veterans was reported [16]. Similarly confounding, due to the timing of blood transfusion in relation to the HCV

epidemic, could explain why blood transfusion prior to 1992 was found to be a *risk* factor for HCV infection only for *non*-IDU veterans. Unfortunately, we cannot provide additional data to support or refute this hypothesis, because the timing of exposures to various risk factors was not collected in the questionnaire.

This study has limitations. The use of a prospectively applied screening questionnaire minimized but did not completely eliminate recall bias. However, supporting the validity of our results, the final multivariate model did not change qualitatively when we excluded individuals who were known to be positive prior to the risk assessment (data not shown). Second, because RIBA testing on EIA(+), HCV PCR(-) samples is not routinely performed at this institution, we were unable to distinguish false-positive samples from samples indicative of resolved infection. For the purposes of analysis, these individuals were indiscriminately categorized as non-infected. A separate analysis was conducted using antibody status as the outcome indicator, and no qualitative changes were found in the results (data not shown).

Selection bias is a potential limitation since over half of veteran 'at risk' of HCV infection at this institution were not tested. If non-tested veterans differed significantly from tested veterans in terms of demography and/or risk factors, our estimation of the rate of HCV infection among veterans screened at this institution and the validity of our final multivariate model could be affected in an unknown direction. The reasons for not being tested may include both patientrelated factors (e.g. the veteran declined testing) and/ or provider-related reasons (e.g. the provider did not follow through with the guidelines because a given risk factor was assumed to be 'low risk'). Analyses of the tested vs. non-tested groups are in progress. If significant differences are found, certain subgroups of patients (and/or their providers) may need to be targeted for more intensive counselling regarding HCV testing. Although the results of this study may not be generalizable to veterans as a whole, they may be of interest to other institutions implementing similar screening programmes for HCV.

In summary, screening for HCV risk factors may provide an effective strategy for identification of infected patients in low-prevalence settings. Five of 11 potential risk factors identified in the National VHA Screening Guidelines may be independent predictors of HCV infection, and IDU is by far the most important risk factor. A cost-effectiveness analysis could help decide whether a more targeted screening approach should broadly be recommended.

# ACKNOWLEDGEMENTS

We thank Dr Asrat Tesfa for editing and recommending changes to the study protocol and for providing guidance with IRB submission. We also thank Michael Schulman, Gina Maurer and the medical records team at the Northport VA Medical Center for their participation in data retrieval.

### **DECLARATION OF INTEREST**

None.

# REFERENCES

- 1. Briggs ME, Baker C, Hall R, et al. Prevalence and risk factors for HCV virus infection at an urban veterans administration medical center. Hepatology 2001; 34: 1200–1205.
- Bräu N, Bini EJ, Shahidi A, et al. Prevalence of hepatitis C and co-infection with HIV among United States veterans in the New York City Metropolitan Area. Am J Gastroenterol 2002; 97: 2071–2078.
- 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: 556–562.
- 4. US Department of Veterans Affairs. Hepatitis C: Standards for provider evaluation and testing. Washington, DC, Department of Veterans Affairs 1998: IL 10-98-013 (http://vhaaidsinfo.cio.med.va.gov/ ils/1098013.doc). Accessed 13 April 2004.
- 5. US Department of Veterans Affairs. Hepatitis C testing and prevention counseling guidelines for VA health care practitioners (information letter). Washington, DC: US Department of Veterans Affairs 2001: IL-10-2001-009 (http://www.hepatitis.va.gov/vahep?page=tp05-01-02-01). Accessed 2 April 2005.
- Cheung RC. Epidemiology of hepatitis C virus infection in American veterans. Am J Gastroenterol 2000; 95: 740–747.
- Roselle GA, Danko LH, Kralovic SM, Simbartl LA, Kizer KW. National hepatitis C surveillance day in the veterans health administration of the department of veterans affairs. Mil Med 2002; 167: 756–759.
- 8. Mishra G, Sninsky C, Roswell R, Fitzwilliam S, Hyams KC. Risk factors for hepatitis C infection among patients receiving health care in a department of veterans affairs hospital. Dig Dis Sci 2003; **48**: 815–820.
- Conry-Cantilena C, VanRaden M, Gibble J, et al. Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. N Engl J Med 1996; 334: 1691–1696.

- U.S. Preventive Task Force. Screening for Hepatitis C virus infection in adults: recommendation statement. Ann Intern Med 2004; 140: 462–464.
- 11. Alter MJ, Seeff LB, Bacon BR, Thomas DL, Rigsby MO, Di Bisceglie AM. Testing for hepatitis C virus infection should be routine for persons at increased risk for infection. Ann Intern Med 2004; 141: 715–717.
- 12. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus infection and HCV-related chronic disease. MMWR Recomm Rep 1998; 47: 1–39.
- 13. **Dimache G, Croitoru M, Balteanu M, et al.** A clinical, epidemiological and laboratory study on avoiding the risks of transmitting viral hepatitis during vaccinations

with the Dermojet protected by an anticontaminant disposable device. Vaccine 1997; **15**: 1010–1013.

- Armstrong GL, Alter MJ, McQuillan GM, Margolis HS. The past incidence of hepatitis C virus infection: Implications for the future burden of chronic liver disease in the United States. Hepatology 2000; 31: 777–782.
- Robins LN, Slobodyan S. Post-Vietnam heroin use and injection by returning US veterans: clues to preventing injection today. Addiction 2003; 98: 1053–1060.
- 16. Robins LN, Davis DH, Goodwin DW. Drug use by U.S. Army enlisted men in Vietnam: a follow up on their return home. Am J Epidemiol 1974; 99: 235–249.