Integrated hepatitis C virus treatment: addressing comorbid substance use disorders and HIV infection

Marilyn S. Huckans[a,b], Aaron D. Blackwell[a,b,f], Todd A. Harms[a,b], David W. Indest[a,b,d] and Peter Hauser[a,b,c,d,e]

Objectives: To examine hepatitis C virus (HCV) and HIV testing patterns within the Northwest Veterans Integrated Service Network (VISN 20).

Methods: Using a comprehensive VISN 20 database, we retrospectively reviewed medical records of 293 445 veterans.

Results: 32.8% of patients were tested for HCV, 5.5% were tested for HIV, and 4.3% were co-tested. Of those tested, 12.3% were HCV positive, 5.4% were HIV positive, and 1.6% were co-infected. 79.1% of HIV-positive patients were tested for HCV, 29.2% of whom tested positive. 34.8% of HCV-positive patients were tested for HIV, 4.9% of whom tested positive. Of those tested, HCV-positive patients were significantly more likely than HCV-negative patients to test positive for HIV; HIV-positive patients were no more likely to test positive for HCV than HIV-negative patients. HIV-positive patients with substance use disorders (SUD) were significantly more likely to test HCV positive than those without. Within the total sample, veterans with SUD were significantly more likely to be tested for both diseases and to test positive for HCV but not HIV. After controlling for other categories of SUD, veterans with a history of cocaine abuse compared with those without were at an increased risk of HIV infection and co-infection.

Conclusion: 79.1% of HIV-positive but only 34.8% of HCV-positive veterans were co-tested, suggesting barriers to HIV testing may exist in VISN 20. Results also indicate that HCV-positive patients are at increased risk for HIV infection and that HIV-positive patients with SUD are at increased risk of HCV infection; routine co-testing for these patients is therefore warranted. Given significant co-infection rates, HCV and HIV screening and testing should be increasingly integrated. Increased infection rates among patients with SUD also warrant integration of HCV and HIV screening and testing into mental health and addiction programmes.

AIDS 2005, **19** (suppl 3):S106–S115

Keywords: Comorbidity, hepatitis C, HIV, literature review, mental disorders, prevalence, substance-related disorders

Introduction

The hepatitis C virus (HCV) is the most common bloodborne infection in the United States. At least 3.9 million Americans or 1.8% of the US population are currently infected [1]. Both the National Institutes of Health (NIH) and the US Department of Veterans Affairs (VHA) have identified HCV as a major public health priority, issuing guidelines for disease identification and management [1,2].

HCV is transmitted through infected blood, and the most common transmission route is through the sharing of needles and drug paraphernalia. Over two-thirds of new

From the [a]Northwest Hepatitis C Resource Center, the [b]Behavioral Health and Neurosciences Division, [c]The J.E.N.S. Laboratory, Portland VA Medical Center, Portland, OR, USA, the [d]Departments of Psychiatry, and [e]Behavioral Neurosciences, Oregon Health and Science University, Portland, OR, USA, and the [f]Department of Anthropology, University of Oregon, Eugene, OR, USA.
Correspondence to Peter Hauser, MD, Behavioral Health and Clinical Neurosciences Division, Portland VA Medical Center (P3MHADM), 3710 SW US Veteran's Hospital Road, Portland, OR 97239, USA.
Tel: +1 503 220 8262 (ext. 56490); fax: +1 503 721 1053; e-mail: peter.hauser2@med.va.gov

 ISSN 0269-9370 © 2005 Lippincott Williams & Wilkins

HCV infections result from injection drug use [1], and 64–77% of new injection drug users are infected with HCV within 12 months of their first injection [3]. Approximately 78–93% of those with HCV have substance use disorders (SUD) [4,5].

In addition to SUD, psychiatric comorbidites are common among HCV patients. One study [4], entailing a retrospective chart review of 33 824 HCV-positive veterans, identified 85.4% as having had a history of either SUD or psychiatric disorders; in a sub-sample of Vietnam-era veterans with HCV, 49.5% had depression, 40.8% anxiety, 33.5% post-traumatic stress disorder, 23.7% psychosis, and 16% bipolar disorder. Very few veterans in that study had a psychiatric disorder without a comorbid SUD. Individuals with serious mental illness are at a significantly increased risk of HCV. One study found that 19.6% of individuals with serious mental illness had HCV, a prevalence rate 11 times greater than that within the general population [6]. Another study found that of those tested for HCV, 9.9% of veterans with schizophrenia/schizoaffective disorder and 31.1% of veterans with comorbid schizophrenia/schizoaffective disorder and any SUD tested antibody positive [7]. Finally, IFN-α therapy is currently the only approved treatment for HCV and causes a variety of neuropsychiatric side-effects including flu-like symptoms, fatigue, depression, anxiety, and cognitive complaints; up to 44% and at least 20% of patients experience IFN-induced depression [8].

HIV co-infection is also a significant risk among HCV-infected adults. Like HCV, HIV is a common blood-borne infection. Currently, 14.1 per 100 000 individuals in the general US population are infected with HIV [9], with approximately 40 000 new HIV infections each year [10]. HCV and HIV share important commonalities, including transmission routes, risk behaviors, chronic infection, extended asymptomatic periods, and increased rates of infection among certain populations, including those with SUD. Not surprisingly, HCV co-infects an estimated 25–33% of HIV-infected individuals, and 50–90% of HIV-infected injection drug users [11,12]. As with HCV, HIV is transmitted through blood-to-blood contact, and injection drug use is a primary risk behavior. Approximately 36% of all HIV cases in the USA were infected through injection drug use [13], and an estimated 14% of injection drug users are infected with HIV [14]. Unlike HCV, a significant number of HIV cases result from sexual transmission [15].

Currently, standard care in the USA does not include universal HCV or HIV screening or testing with the exception of Veterans Affairs facilities and clinics that mandate universal HCV screening, and literature on intervention patterns is sparse. For example, across national samples of substance use treatment facilities, 23% tested none of their patients [16]. One New York study [17] found that 48% of psychiatric outpatient clinics conducted HIV screening and 84% reported unmet prevention training needs. In another study [18], seven out of 11 community mental heath centers in New Hampshire reported having HIV risk-screening services. Among these, one estimated that 25–60% of patients were screened, one estimated that 10–20% were screened, three estimated that less than 10% were screened, and two did not know.

Even less clear is the extent to which programmes address both HCV and HIV simultaneously. One study used surveys and medical records to examine 881 HIV-positive patients prospectively at three VHA medical centers [19]; 79.5% of HIV-positive patients were tested for HCV. The study did not examine testing practices within the general population nor in veterans with SUD or HCV.

The 2002 Management of Hepatitis C National Institutes of Health Consensus Development Conference Statement (2002 NIH Consensus Statement) and the 2003 VHA Treatment Guidelines for Patients with Chronic Hepatitis C (2003 VHA Treatment Guidelines) state that all patients with HIV should be tested for HCV, and that all patients with HCV should be offered HIV testing and counselling [1,2]. The following study further examined current HCV and HIV testing practices among veterans with and without SUD, and assessed the prevalence of comorbidity and the characteristics associated with a co-infected population.

Methods

We collected data on patients seen at any facility in the Veterans Integrated Service Network 20 (VISN 20): eight medical centers and 17 outpatient clinics in Alaska, Washington, Oregon, and Idaho. Data came from the VISN 20 CHIPS Data Warehouse, a collection of databases extracted from the electronic patient medical records of each facility. The Portland VHA Medical Center Institutional Review Board approved data access for this project.

Using inpatient and outpatient appointment dates, we identified all patients seen between January 1998 and December 2003. We collected data on demographics, HCV and HIV laboratory results, and a history of SUD. Laboratory results included tests performed between 1994 and 2003. We excluded non-veterans who did not receive regular care from the VHA but had records in the system (i.e. VHA employees, veterans' family members, or patients receiving care as a result of humanitarian emergencies). We coded additional data as follows:

Hepatitis C virus status

We considered patients to have been tested for HCV if they had at least one HCV laboratory result in their

record. HCV-positive patients had a positive HCV antibody test, a detectable HCV viral load by polymerase chain reaction, a positive HCV recombinant immunoblot assay, or an identifiable HCV genotype. We classified patients with positive antibody tests but negative recombinant immunoblot assay confirmation as false positives and did not include them in the sample of positive patients.

HIV status

We considered patients with at least one HIV laboratory result to have been tested for HIV. HIV-positive patients had a positive HIV antibody test (including Western blot), a detectable viral load, or a positive p24 protein test. We classified patients with positive antibody tests but negative confirmatory tests as false positives and did not count them as positive patients.

Substance use disorder

We considered patients to have any SUD history if their records included a Diagnostic and Statistical Manual of Mental Disorders (DSM) version IV code for substance abuse or dependence (except nicotine dependence).

We downloaded data from the VISN 20 data warehouse into a local database using Standard Query Language (SQL) queries, where they were organized and exported to SPSS 12.0 for analysis.

Results

Demographics and characteristics

We collected data on all 293 445 patients seen between January 1998 and December 2003 at any of the VISN 20 facilities. Patients were predominately male (93.3%) and Caucasian (86.3%). Patients are not required to answer questions about race; only 44.3% had recorded race data. As a result of limited diversity we classified patients as Caucasian or non-Caucasian for analyses. The mean age was 60.3 years (± 15.7). Thirty-eight per cent served during the Vietnam war. Fifteen per cent of all patients had a documented SUD history. Table 1 includes additional demographic data.

Testing rates

Table 2 summarizes data on testing rates by age, sex, race, and SUD history. Fig. 1 and Fig. 2 further summarize testing and co-testing rates within the total sample. Overall, 32.8% of patients received HCV testing. In

Table 1. Demographic characteristics of patients tested for or positive for HIV or hepatitis C virus, and demographic characteristics of the overall Northwest Veterans Integrated Service Network (VISN 20) patient population.

			HIV				Hepatitis C			
Characteristic or variable	Overall		Tested		Positive		Tested		Positive	
Number (%) of patients	293 445	(100.0)	16 171	(5.5)[a]	874	(5.4)[a]	96291	(32.8)[a]	11 854	(12.3)[a]
Sex										
Male	273 786	(93.3)	14 859	(91.9)	854	(97.7)	90 446	(93.9)	11 496	(97.0)
Female	19 622	(6.7)	1312	(8.1)	20	(2.3)	5845	(6.1)	358	(3.0)
Unknown	37	(0.0)								
Age										
Mean (SD)	60.3 (± 15.7)	–	52.6 (± 11.6)	–	50.0 (± 9.6)	–	60.9(± 16.9)	–	53.7 (± 7.9)	–
Race[b]										
Not recorded	163 595	(55.7)	4721	(29.2)	297	(34.0)	40 916	(42.5)	3579	(30.2)
Recorded	129 850	(44.3)	11 450	(70.8)	577	(66.0)	55 375	(57.5)	8275	(69.8)
White	112 019	(86.3)	9326	(81.4)	445	(77.1)	47 163	(85.2)	6790	(82.1)
Non-white	17 831	(13.7)	2124	(18.6)	132	(22.9)	8212	(14.8)	1485	(17.9)
Period of service										
Vietnam era	111 929	(38.1)	8381	(51.8)	427	(48.9)	47 613	(49.4)	8261	(68.7)
Post-Vietnam	33 224	(11.3)	3408	(21.1)	252	(28.8)	11 214	(11.6)	2128	(18.0)
Persian Gulf war	36 327	(12.4)	2256	(14.0)	137	(15.7)	9796	(10.2)	399	(3.4)
World War II	50 375	(17.2)	584	(3.6)	7	(0.8)	10 549	(11.0)	274	(2.3)
Korean war	32 726	(11.2)	737	(4.6)	24	(2.7)	9755	(10.1)	338	(2.9)
Post-Korean war	16 962	(5.8)	610	(3.8)	19	(2.2)	6053	(6.3)	370	(3.1)
Other	11 902	(4.1)	195	(1.2)	8	(0.9)	1311	(1.4)	84	(0.7)
History of substance abuse or dependence										
Yes	44 124	(15.0)	8460	(52.3)	319	(36.5)	26 290	(27.3)	7591	(64.0)
No	249 321	(85.0)	7711	(47.7)	555	(63.5)	70 001	(72.7)	4263	(36.0)
Alcohol	39 629	(13.5)	7721	(47.7)	262	(30.0)	23 888	(24.8)	6842	(57.7)
Opioids	4094	(1.4)	1555	(9.6)	50	(5.7)	3017	(3.1)	1850	(15.6)
Cocaine	5973	(2.0)	2294	(14.2)	99	(11.3)	4439	(4.6)	2097	(17.7)
Amphetamines	3536	(1.2)	1494	(9.2)	58	(6.6)	2647	(2.7)	1235	(10.4)
Other	17 044	(5.8)	5084	(31.4)	187	(21.4)	12 010	(12.5)	4739	(40.0)
Polysubstance	17 930	(6.1)	5589	(34.6)	193	(22.1)	12 824	(13.3)	5200	(43.9)

[a]Numbers in parentheses are percentages within each group (e.g. of those tested for HIV, 91.9% were men and 8.1% were women), except for the top row, in which numbers in parentheses are percentage tested of the overall total, or percentage infected of those tested, respectively.
[b]Patients are not required to answer questions about race and the race of many patients is not recorded.

comparison, only 5.5% received HIV testing. Only 4.3% received co-testing for both HIV and HCV, and 66% were not tested for either disease. Compared with patients without SUD histories, patients with any history of SUD were significantly more likely to receive testing: 59.6% received HCV testing, 19.2% received HIV testing, 16.3% received co-testing for both HCV and HIV, and 37.6% were not tested for either disease.

Men were more likely than women to be tested for HCV; however, men were less likely to be tested for HIV. Although women were significantly more likely to be co-tested than men, the magnitude of this difference was not large. Patients tested for HIV tended to be younger than those who were not tested for HIV, and those co-tested for both HCV and HIV were also younger than those not co-tested. HCV-tested patients were slightly older than those not tested; although this difference reached statistical significance, the magnitude was not large. Compared with Caucasian patients, non-Caucasian patients were significantly more likely to be tested and co-tested for HCV and for HIV.

Infection rates

Table 2 summarizes infection rates by age, sex, race, and SUD history. Fig. 1 and Fig. 2 summarize infection rates for the total sample (whether or not they were tested) versus only those who were tested.

Hepatitis C virus

Of those tested for HCV, 12.3% tested positive, representing 4.0% of the total sample. Men, non-Caucasian patients, younger patients, and veterans with any SUD history were significantly more likely to test positive.

HIV

Of those tested for HIV, 5.4% were positive (0.3% of the total sample). Similar to the HCV results, men, non-Caucasian patients, and younger patients were more likely

Table 2. Relationships between demographic variables and hepatitis C virus/HIV testing and infection rates.

	Women ($n = 19\,622$)		Men ($n = 273\,786$)				
Sex (unknown $n = 37$)	*N* (total)	% Tested or infected[a]	*N* (total)	% Tested or infected[a]	OR	95% CI	*P*
HCV tested	5845	29.8	90 446	33.0	1.16	1.13–1.20	< 0.001
HCV infected	358	6.1	11 496	12.7	2.23	2.00–2.49	< 0.001
HIV tested	1312	6.7	14 859	5.4	0.80	0.76–0.85	< 0.001
HIV infected	20	1.5	854	5.7	3.94	2.52–6.16	< 0.001
Co-tested	913	4.7	11 820	4.3	0.92	0.86–0.99	0.026
Co-infected	7	0.8	195	1.6	2.17	1.02–4.63	0.045
Race (unknown $n = 163\,595$)	Caucasian ($n = 112\,019$)		Non-Caucasian ($n = 17\,831$)				
HCV tested	47 163	42.1	8212	46.1	1.17	1.13–1.22	< 0.001
HCV infected	6790	14.4	1485	18.1	1.31	1.23–1.39	< 0.001
HIV tested	9326	8.3	2124	11.9	1.49	1.41–1.56	< 0.001
HIV infected	445	4.8	132	6.2	1.31	1.09–1.62	0.006
Co-tested	7641	6.8	1701	9.5	1.44	1.37–1.52	< 0.001
Co-infected	112	1.5	38	2.2	1.54	1.06–2.22	0.024
Any substance use disorder history	No ($n = 249\,321$)		Yes ($n = 44\,124$)				
HCV tested	70 001	28.1	26 290	59.6	3.78	3.70–3.86	< 0.001
HCV infected	4263	6.1	7591	28.9	6.26	6.01–6.52	< 0.001
HIV tested	7711	3.1	8460	19.2	7.43	7.19–7.68	< 0.001
HIV infected	555	7.2	319	3.8	0.51	0.44–0.58	< 0.001
Co-tested	5522	2.2	7211	16.3	8.62	8.31–8.95	< 0.001
Co-infected	75	1.4	127	1.8	1.30	0.98–1.74	0.072[ns]

	Yes		No			
Age[b]	*N* (total)	Mean age	*N* (total)	Mean age	*t*	*P*
HCV tested	96 291	60.9	197 154	59.3	26.1	< 0.001
HCV infected	11 854	53.7	84 437	60.0	50.0	< 0.001
HIV tested	16 171	52.6	277 274	60.8	64.9	< 0.001
HIV infected	874	50.0	15 297	52.7	6.9	< 0.001
Co-tested	12 733	52.8	280 712	60.7	55.9	< 0.001
Co-infected	202	51.8	12 531	52.8	1.3	0.192[ns]

CI, Confidence interval; HCV, hepatitis C virus; OR, odds ratio.

[a]Odds ratios were calculated to determine whether infection and testing rates differed on the basis of sex, race, and history of any substance use disorder. Testing rates (%) were based on the number tested out of the total group sample (e.g. men tested/all men). Infection rates (%) were based on the number who tested positive out of those who were tested (e.g. men who tested positive/all men who were tested).

[b]*t* Tests were calculated to determine whether infection and testing rates differed on the basis of age. Mean ages for those tested versus not tested, and infected versus not infected are listed and compared.

[ns]Not significant. All other between-group comparisons were significant ($P < 0.05$).

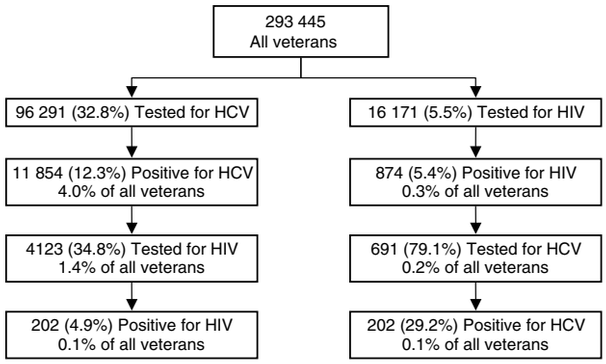

Fig. 1. Testing, infection, and co-infection rates among Northwest Veterans Integrated Service Network (VISN 20) veterans. Data are numbers of patients in each category. The percentage listed in parentheses is the percentage in the group that is shown one step higher in the flow chart [e.g. of those tested for hepatitis C virus (HCV), 12.3% tested positive for HCV].

to test positive. Within the group of tested veterans, veterans with any SUD history were significantly less likely to test positive compared with those without any SUD history.

Co-infection

Of those co-tested for both diseases, 1.6% were co-infected. Non-Caucasian patients and men were significantly more likely to be co-infected. Co-infected and non-co-infected patients did not differ in age. Within the group of co-tested patients, co-infection rates did not significantly differ between those with and without SUD histories.

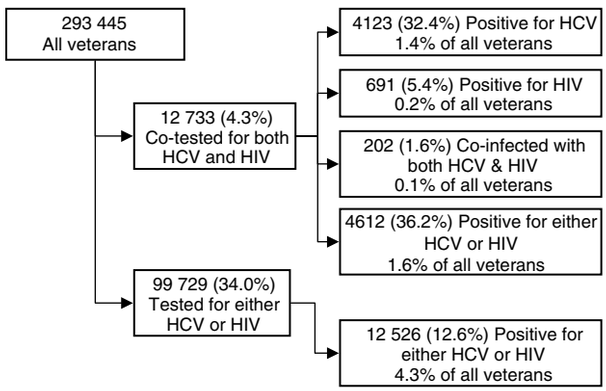

Fig. 2. Infection rates among VISN 20 veterans tested for both hepatitis C virus and HIV. Data are numbers of patients in each category. The percentage listed in parentheses is the percentage in the group that is shown one step higher in the flow chart [e.g. of those tested for either hepatitis C virus (HCV) or HIV, 12.6% tested positive for either HCV or HIV.

HIV testing in hepatitis C virus-positive patients

Only 34.8% of HCV-positive veterans received HIV testing, and of those tested, 4.9% tested positive for HIV (see Fig. 1). The rate of HIV infection was not significantly different among HCV-positive patients versus the total sample of HIV-tested patients [4.9 versus 5.4%, odds ratio (OR) 0.90, 95% confidence interval (CI) 0.77–1.05, $P = 0.21$]. However, compared with HCV-negative veterans, HCV-positive veterans were significantly more likely to receive HIV testing (tested for HCV, 34.8 versus 10.2%, OR 4.70, 95% CI 4.50–4.91, $P < 0.001$) and to test HIV positive (tested for HCV, 1.7 versus 0.6%, OR 2.98, 95% CI 2.52–3.52, $P < 0.001$). Of the HCV-positive patients, those with any SUD history were significantly more likely to receive HIV testing (42.6 versus 20.8%, OR 2.83, 95% CI 2.60–3.09, $P < 0.001$) but were no more likely to test HIV positive than those without any SUD history (1.7 versus 1.8%, OR 0.95, 95% CI 0.71–1.27, $P = 0.728$). Controlling for SUD in a logistic regression analysis of HCV-tested patients, HCV-positive status is a significant predictor of HIV status (OR 2.69, 95% CI 2.25–3.22, $P < 0.001$), whereas a history of SUD made a significant but less substantial contribution (OR 1.26, 95% CI 1.07–1.50, $P = 0.006$). Overall, these results suggest that HCV-positive status was a significant predictor of HIV infection, more so than a history of any SUD.

Hepatitis C virus testing in HIV-positive patients

Of those who tested positive for HIV, 79.1% received HCV testing, and of those tested, 29.2% tested HCV positive. Of those tested for HIV, HIV-positive patients were no more likely than HIV-negative patients to receive HCV testing (79.1 versus 78.7%, OR 1.02, 95% CI 0.86–1.21, $P = 0.81$), indicating that most patients tested for HIV were also tested for HCV, irrespective of HIV status. The rate of HCV infection among HIV-positive patients was significantly higher than among the total sample of HCV-tested patients (29.2 versus 12.3%, OR 2.14, 95% CI 1.83–2.51, $P < 0.001$). However, the percentage of HCV-positive patients within the HIV-positive population was not significantly different from the percentage of HCV-positive patients within the HIV-tested-but-negative population (23.1 versus 25.6%). HIV-positive veterans with SUD histories were significantly more likely to be tested for HCV (84.3 versus 76.0%, OR 1.70, 95% CI 1.18–2.43, $P = 0.004$) and to test HCV-positive (39.8 versus 13.5%, OR 4.23, 95% CI 3.04–5.89, $P < 0.001$) than those without SUD histories. Overall, these results suggest that HIV patients with SUD histories are at an increased risk of HCV infection.

Testing and infection prevalence associated with substance use disorders

Table 3 summarizes data from logistic regression analyses completed to determine whether various SUD were independently predictive of testing and infection status. Patients were categorized as having or not having a

Table 3. Odds ratios associated with substance abuse diagnoses.

	HCV testing				HIV testing				Both tested			
	Raw		Adjusted		Raw		Adjusted		Raw		Adjusted	
(a)	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Alcohol	3.80	3.72–3.89	2.64	2.57–2.71	7.03	6.80–7.26	3.30	3.14–3.46	8.12	7.83–8.42	3.54	3.35–3.73
Opioids	5.89	5.49–6.32	1.49	1.38–1.62	11.51	10.78–12.29	1.64	1.51–1.77	12.87	12.03–13.76	1.66	1.54–1.80
Cocaine	6.16	5.81–6.54	1.35	1.26–1.45	12.29	11.64–12.99	1.63	1.52–1.75	13.58	12.84–14.38	1.61	1.50–1.74
Amphetamine	6.24	5.78–6.74	1.34	1.23–1.46	13.72	12.81–14.70	1.85	1.71–2.01	15.13	14.10–16.23	1.85	1.71–2.01
Other	5.44	5.26–5.63	2.27	2.16–2.40	10.17	9.79–10.56	2.37	2.19–2.55	11.64	11.18–12.12	2.40	2.21–2.61
Polysubstance	5.78	5.59–5.96	1.10	1.03–1.17	11.34	10.93–11.77	1.42	1.30–1.56	13.09	12.58–13.62	1.52	1.38–1.68
	HCV positive				HIV positive				Both positive			
	Raw		Adjusted		Raw		Adjusted		Raw		Adjusted	
(b)	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Alcohol	5.40	5.18–5.61	2.55	2.41–2.69	0.45	0.39–0.52	0.47	0.38–0.58	1.18^{ns}	0.89–1.56	0.79^{ns}	0.51–1.23
Opioids	13.20	12.23–14.24	3.44	3.15–3.76	0.56	0.42–0.74	0.78^{ns}	0.56–1.08	1.83	1.27–2.62	1.45^{ns}	0.95–2.22
Cocaine	7.53	7.08–8.02	1.30	1.20–1.41	0.76	0.62–0.94	1.57	1.18–2.10	1.82	1.32–2.51	1.58	1.04–2.38
Amphetamine	6.84	6.32–7.40	1.25	1.14–1.38	0.69	0.52–0.90	1.15^{ns}	0.84–1.57	1.08^{ns}	0.70–1.68	0.78^{ns}	0.48–1.25
Other	7.07	6.77–7.39	2.18	2.01–2.37	0.58	0.49–0.68	0.92^{ns}	0.71–1.20	1.34	1.01–1.78	0.99^{ns}	0.62–1.59
Polysubstance	7.87	7.54–8.22	1.35	1.22–1.49	0.52	0.44–0.61	0.84^{ns}	0.59–1.20	1.43	1.09–1.90	1.31^{ns}	0.70–2.44

CI, Confidence interval; HCV, hepatitis C virus; OR, odds ratio. Raw odds ratios were calculated for each substance use disorder (SUD) group separately, comparing those with that SUD to those without that SUD, irrespective of membership in another SUD group. Adjusted odds ratios were estimated using a logistic regression model to correct for membership in any other SUD group. (a) Odds ratios for HCV and HIV testing. (b) Odds ratios for HCV and HIV infection. Infection odds were calculated within the group of individuals tested, rather than using the entire sample population.
^{ns}Not significant. All other values for between-group differences (tested versus not-tested, positive versus negative) were significant to $P < 0.05$.

DSM-IV code for each of the following types of SUD: alcohol, opioid, cocaine, amphetamines, other (any other substance excluding nicotine), or polysubstance (polysubstance dependence was documented in the chart without specifying the substances) abuse or dependence. Most patients had a history of multiple SUD, so SUD groups were largely overlapping (see Table 4). Analyses of only non-overlapping monodiagnostic groups were non-interpretable as a result of small cell sizes.

Raw odds ratios were calculated for each SUD group separately, comparing those with that particular SUD with those without that particular SUD, irrespective of membership in another SUD group. These analyses revealed that relative to patients without these SUD, all SUD groups were significantly more likely to receive HCV and HIV testing and co-testing. Of those tested, all SUD groups were significantly more likely to test HCV positive, but they were significantly less likely to test HIV positive. Of those co-tested, the following SUD groups were significantly more likely to be co-infected: opioid, cocaine, other, and polysubstance groups. The alcohol and amphetamine groups were no more likely to be co-infected than those without these diagnoses.

Because SUD groups were largely overlapping, adjusted odds ratios were then calculated using a binary logistic regression model to correct for membership in any other

Table 4. Overlap between substance use disorder diagnosis groups.

	Group two					
Group one	Alcohol %	Opioids %	Cocaine %	Amphetamine %	Other %	Polysubstance %
Alcohol	100	9	14	8	34	43
Opioids	84	100	44	23	69	91
Cocaine	93	30	100	23	72	97
Amphetamine	90	26	39	100	77	96
Other	79	17	25	16	100	83
Polysubstance	95	21	32	19	79	100

Patients were classified into substance use disorder groups based on the presence of one or more Diagnostic and Statistical Manual of Mental Disorders version IV diagnosis codes within a patient's chart. The table indicates the percentage of individuals within the indicated first group who also belong to the indicated second group. Other, Any substance use disorder other than alcohol, opioid, cocaine, or amphetamine (excluding nicotine abuse); polysubtance, polysubstance dependence was documented in their record without designation of a particular substance.

SUD group. After isolating the contribution of each SUD as a risk factor, all SUD groups were still significantly more likely to receive HCV and HIV testing and co-testing. Of those tested for HCV, all SUD groups were significantly more likely to test HCV positive after controlling for other SUD. Of those tested for HIV, only patients in the cocaine group were significantly more likely to test HIV positive after controlling for other SUD, and patients in the alcohol group were significantly less likely to test HIV positive after controlling for other SUD. Of those co-tested, only those in the cocaine group were significantly more likely to be co-infected.

Discussion

Individuals with SUD and HIV infection are at an increased risk of HCV infection, and these comorbidities pose a variety of medical management complications. Research and clinical experience clearly demonstrate that to prevent and treat HCV, we must address simultaneously these highly prevalent comorbid conditions across the disciplines of hepatology, infectious disease, mental health, and substance use treatment.

The current study examines HCV and HIV testing and the rates of co-infection. We have evaluated demographic risk factors associated with both infections in a veteran population and found that, although differences exist (such as mean age), similar demographic features identify at-risk populations for both diseases. In general, both testing practices and infection results reflect these findings, suggesting that VISN 20 has directed testing towards high-risk populations. In particular, male sex, non-Caucasian race, and younger age are associated with HCV and HIV infection in veteran populations.

Veterans with any SUD history were at a significantly increased risk of HCV infection relative to those without any SUD history; this was true for patients with a history of alcohol, opioid, cocaine, amphetamine, polysubstance, or other abuse or dependence. Unexpectedly, of those tested, patients with, as compared with those without, any SUD history did not differ in terms of HIV infection or co-infection rates. Several issues may have contributed to this finding. First, our data do not distinguish between injection drug users and patients with other SUD; therefore, we are unable to assess the association between injection drug use and HIV infection. Second, after controlling for other categories of SUD, only those patients with a history of cocaine abuse or dependence were at an increased risk of HIV infection and HCV/HIV co-infection, suggesting that not all categories of SUD history contribute to HIV infection risk. The reasons for this finding are unclear from the current design, but future studies could explore whether cocaine use is associated with increased HIV transmission risk behaviors such as unprotected sexual activity and injection drug use. This finding also illustrates a fundamental limitation of a retrospective chart review: the data did not allow us to evaluate patient screening or account for reasons why individual patients were or were not tested.

This limitation precludes us from making an exact estimate of HCV, HIV, and co-infection rates in this population. However, we can set logical limits (see Fig. 1). At a minimum, we must count patients with positive tests for either disease. For HCV, the lower limit is 4.0% of the total VISN 20 population. If we assume a higher infection rate in the tested versus the untested population as a result of the preferential testing of veterans with risk factors, then we can use the percentage positive of those tested as an upper limit, or 12.3% for HCV. Similarly, we can establish that the rate of HIV infection lies between 0.3 and 5.4%, and that the rate of co-infection lies between 0.1 and 1.6%. For veterans with histories of SUD, infection rates are even higher (see Table 1).

In addition to determining the rates of HCV and HIV infection, our study examines VISN 20 HCV/HIV testing practices among at-risk populations. VISN 20 tested more than half the veterans with SUD for HCV (59.6%); in contrast, VISN 20 tested relatively few for HIV (19.2%). Consistent with previous findings [19], VISN 20 tested most HIV-positive veterans (79.1%) for HCV. However, VISN 20 tested only 34.8% of HCV-positive veterans for HIV. From 1999 to 2004, VHA policy mandated universal screening for HCV risk factors and testing of those at risk; however, as is clearly reflected in these testing practices, there was no similar mandate for HIV screening and testing. This trend is concerning because HCV and HIV have similar transmission routes, and the 2002 NIH Consensus Statement and 2003 VHA Treatment Guidelines clearly recommend that individuals with one infection be offered testing for the other [1,2]. HCV programmes within the VHA may need to pursue stronger efforts to comply with these recommendations and improve HIV disease identification.

Of note is the fact that current Centers for Disease Control and Prevention Guidelines do not specifically recommend for or against HIV testing of individuals testing positive for HCV [15,20,21]. Our results indicate that HCV and HIV share common risk factors, in particular SUD history, and as two-thirds of HCV cases result from injection drug use [1], it would be reasonable to assume that HCV-positive patients would be at an increased risk of contracting HIV as a result of high injection drug use rates. Our results indicate that HCV-positive patients are probably at an increased risk of HIV infection and that HIV-positive patients with SUD are probably at an increased risk of HCV infection. However, our results do not make clear whether targeting all

HCV-infected patients for HIV testing would increase HIV detection rates. On the one hand, relative to patients who test HCV negative, HCV-positive veterans are at a significantly increased risk of HIV infection (1.7 versus 0.6%). On the other hand, the rate of HIV infection was not significantly different among HCV-positive patients versus the total sample of HIV-tested patients (4.9 versus 5.4%). In addition, barriers may currently impede routine HIV testing; for example, healthcare providers may not have the time and personnel necessary to provide informed consent and confidential pre- and post-test HIV counselling as recommended by the Centers for Disease Control and Prevention [22].

Our study had several limitations. Typical of retrospective database designs, possible documentation errors and inconsistencies, missing data points, and predefined variables limited the scope and interpretations of our study. First, our design did not allow us to differentiate between infrequent and consistent healthcare recipients. Future studies could examine whether regular attendance at a particular clinic (e.g. psychiatric, substance use, primary care) increases a patient's chance of receiving HIV or HCV testing. Second, the database also did not include information about the care veterans may have received from non-VHA facilities, so it is unclear to what extent veterans may have been tested by outside providers. Third, we could not confirm the accuracy of a patient's SUD diagnosis. VISN 20 has instituted a performance measure whereby providers are annually required to complete a standard substance abuse screening questionnaire that automatically appears in each patient's record as a clinical reminder. Although the VHA is perhaps more likely to detect SUD than other institutions without standard screening procedures, the brief screening is probably insufficient to detect all substance abuse cases. Therefore this study probably underestimates the true rates of SUD. Future studies, using a thorough medical record review in selected diagnostic groups could better address these issues.

Our study also has several strengths. With the VHA's computerized medical record system, we were able to collect data on a large and representative number (293 445) and percentage (virtually 100%) of veterans who received care through VISN 20 over a 6-year period. Although HCV and HIV are national public health priorities, relatively few studies evaluate disease management patterns. Our study is among the first to examine testing patterns with a focus on comorbid and co-infected populations, and many questions remain unanswered. We are currently collecting data to evaluate other areas of disease management not addressed in this study: whether individuals with psychiatric disorders are being routinely tested for HCV and HIV, whether co-infected populations are being routinely treated for HIV and HCV, and whether mandated risk factor screening facilitates disease identification.

Although results may not entirely generalize to non-VHA facilities, other healthcare systems may still benefit from understanding relevant trends, barriers, and practices. During the study period the VHA implemented performance measures, universal risk-factor screening, and the mandatory testing of high-risk patients in order to increase HCV detection. Two VISN 20 sites also house the Northwest Hepatitis C Resource Center, a nationally funded center charged with developing HCV best practices. Compared with institutions that lack standard HCV screening procedures and HCV resource centers, testing rates are probably higher within VISN 20. In contrast, HIV testing rates within VISN 20 may be lower than in institutions that have formal HIV testing policies or resource centers.

Infection rates may also differ for populations outside VISN 20. Consistent with this study's findings, previous studies have found veterans to be at an increased risk of both HCV and HIV. One study found that US veterans had an HCV infection rate of approximately 5.4% compared with the general US population rate of 1.8% [23]. Another study found a 2.5-fold increase in the incidence of HIV among US veterans versus non-veterans [24]. Therefore, the present study may not provide an accurate estimate of HCV and HIV infection rates within non-veteran facilities. Of note is the fact that Vietnam veterans comprised the majority of the total sample (38.1%) as well as HIV-positive and HCV-positive patients (48.9 and 68.7%, respectively); therefore, infection risk may vary to some extent on the basis of combat history as well as age. In addition, compared with other facilities, VISN 20 may be less diverse as it serves a primarily male and Caucasian population. Consistent with the present findings, higher rates of both HIV and HCV are found among men compared with women [1,9]. Higher HIV and HCV rates have also been reported among African Americans compared with Caucasians [1,9]. At least one study [6], however, found that after controlling for increased HCV infection rates among metropolitan versus non-metropolitan residents, race did not relate to infection status. VISN 20 includes both urban and rural populations, but infection rates may be lower than those found in more ethnically diverse or metropolitan regions.

The present findings should also be considered in the context of a middle-aged and older adult population. Up to 15% of all US AIDS cases occur in older adults, and the number of individuals diagnosed with AIDS over 65 years of age has increased 10-fold in the past 10 years [25]. This is because highly active antiretroviral therapies have prolonged HIV survival, but also because a greater proportion of older adults are becoming newly infected. Growing evidence suggests that older adults with HIV have a more severe disease course, more opportunistic infections and complications, and shorter survival rates [25]. Older adults also experience high rates of age-specific

concomitant medical conditions such as Alzheimer's disease, Parkinson's disease, diabetes, heart disease, hypertension, stroke, cancer, osteoporosis, and arthritis. How the natural aging process and these concomitant conditions interact with the disease course of HIV and HCV is poorly understood, but may relate to shorter survival rates and increased neuropsychological problems in older adults with HIV [26]. As the highest rates of HIV infection are found among younger adults, the present sample with a mean age of 60.3 ± 15.7 years is a somewhat unique HIV sample. In contrast, the highest rates of HCV infection are found among individuals 40–59 years of age [1]. Therefore, the present findings may overestimate HCV infection rates and underestimate HIV infection rates for younger populations.

In conclusion, current HCV knowledge and our own results strongly indicate the need for better integrated HCV and HIV programmes. Although many facilities continue to implement HCV and HIV programmes separately, these infections affect groups with similar risk behaviors and comorbid conditions. Although psychiatric and substance use programmes are not designed to implement education and treatment of infectious diseases such as HCV and HIV, the increasing number of HCV- and HIV-infected patients, particularly in SUD populations, suggests that programmes should be developed that integrate mental health, substance abuse, and medical care.

In summary, the most effective and efficient approach to the HCV and HIV epidemics may not be through independent HCV and HIV clinics, but through the development of an integrated care model. Although disease management studies are needed to evaluate further the cost effectiveness and efficacy of integrated interdisciplinary approaches, there are several that can be suggested: psychiatric and substance use programmes could staff an infectious disease specialist who could provide concurrent screening, testing, education, and treatment services for HCV, HIV, and other common concerns (e.g. hepatitis A and B, sexually transmitted infections). Primary care clinics could routinely screen and test for both diseases. Specialty HCV and HIV clinics could be combined or affiliated in order to coordinate care. In addition, infectious disease providers should routinely screen for SUD and psychiatric comorbidities, because they are important factors related to HCV and HIV disease identification, treatment management, and compliance.

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