



Hepatitis C Virus Testing in Adults Living with HIV: A Need for Improved Screening Efforts

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Abstract

Objectives: Guidelines recommend hepatitis C virus (HCV) screening for all people living with HIV (PLWH). Understanding HCV testing practices may improve compliance with guidelines and can help identify areas for future intervention.

Methods: We evaluated HCV screening and unnecessary repeat HCV testing in 8,590 PLWH initiating care at 12 U.S. HIV clinics between 2006 and 2010, with follow-up through 2011. Multivariable logistic regression examined the association between patient factors and the outcomes: HCV screening (≥ 1 HCV antibody tests during the study period) and unnecessary repeat HCV testing (≥ 1 HCV antibody tests in patients with a prior positive test result).

Results: Overall, 82% of patients were screened for HCV, 18% of those screened were HCV antibody-positive, and 40% of HCV antibody-positive patients had unnecessary repeat HCV testing. The likelihood of being screened for HCV increased as the number of outpatient visits rose (adjusted odds ratio 1.02, 95% confidence interval 1.01–1.03). Compared to men who have sex with men (MSM), patients with injection drug use (IDU) were less likely to be screened for HCV (0.63, 0.52–0.78); while individuals with Medicaid were more likely to be screened than those with private insurance (1.30, 1.04–1.62). Patients with heterosexual (1.78, 1.20–2.65) and IDU (1.58, 1.06–2.34) risk compared to MSM, and those with higher numbers of outpatient (1.03, 1.01–1.04) and inpatient (1.09, 1.01–1.19) visits were at greatest risk of unnecessary HCV testing.

Conclusions: Additional efforts to improve compliance with HCV testing guidelines are needed. Leveraging health information technology may increase HCV screening and reduce unnecessary testing.

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Introduction

Up to 25% of people living with HIV (PLWH) in the United States (U.S.) are coinfecting with hepatitis C virus (HCV). [1] HIV/HCV coinfection accelerates progression to liver fibrosis, end-stage liver disease, and death compared to HCV mono-infection. [2] Consequently, guidelines recommend that all PLWH be screened for HCV infection upon initiation of HIV care [3–6].

Despite these recommendations, HCV screening rates have varied for PLWH. [7–10] Among a random sample of 1,329 HIV-infected men who have sex with men (MSM) in care at 8 U.S. HIV clinics between 2004 and 2007, only 54% were ever tested

for HCV. [7] Conversely, the U.S. Veterans Health Administration (VA) reported that 96% of the 23,463 HIV-infected veterans in care in 2008 received HCV screening [9].

Screening for HCV is performed by testing for HCV antibody; positive results should be followed by measurement of HCV RNA to differentiate chronic infection from resolved infection. [11] HCV antibody testing in individuals with a prior positive result is unnecessary, as the antibody test remains reactive regardless of whether the infection has cleared. [11] However, PLWH may be at increased risk of unnecessary HCV testing due to the high prevalence of HCV infection and their more frequent use of medical services compared to the general population [3].

Understanding HCV testing practices is important to improving compliance with national guidelines and can help identify areas for future intervention. The goal of this study was to estimate the proportion of PLWH screened for HCV and to identify groups at risk of not being screened. We also assessed unnecessary repeat HCV testing among patients with a prior positive HCV antibody test.

Methods

The HIV Research Network (HIVRN) is a consortium of clinics that provide care to people living with HIV. [12,13] Data from 12 sites treating adults, located in the Northeastern (6), Midwestern (1), Southern (2), and Western (3) U.S., were included in this analysis. All patients establishing care at these sites are offered enrollment in the HIVRN; 99% of patients consent to participate. Sites abstract data from medical records and send them to a data-coordinating center after removing personal identifying information. Following quality control and verification, data are combined across sites to produce a uniform database. Institutional review boards (IRBs) at each site (complete list of sites can be found in the acknowledgments) and the data coordinating center at Johns Hopkins University approved the collection and analyses of these data. IRBs at some clinics required written informed consents, while others waived the requirement because only existing anonymized and de-identified data were collected.

HIV-infected adults (age ≥ 18 years) new to care at HIVRN sites and seen at least twice between January 1, 2006 and December 31, 2010 were included and followed through December 31, 2011. The two-visit criterion was employed to capture patients establishing regular care. To exclude those who may have received care previously, we excluded patients with first recorded HIV RNA ≤ 400 copies/mL ($n = 2,665$) and individuals with a history of outpatient HIV visits or use of antiretroviral therapy (ART) prior to HIVRN enrollment ($n = 916$).

Variables

Demographic and clinical characteristics (age, sex, race/ethnicity, HIV transmission risk, insurance coverage, CD4 count) at the time of the first outpatient visit were collected for each patient. Patients' age was divided into 4 groups: 18–29, 30–39, 40–49, and over 50 years old. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Hispanic, and other/unknown. Self-reported HIV transmission behavior categories were MSM, heterosexual transmission (HET), injection drug use (IDU), and other/unknown. Patients who had IDU in combination with another risk factor (e.g. MSM, heterosexual transmission) were classified as IDU. Insurance was categorized as private, Medicaid, Medicare, uninsured, or other/unknown. Patients whose care was funded by Ryan White, those recorded as self-pay, and those covered by local governmental programs were considered to be uninsured. CD4 cell count was categorized as ≤ 350 , 351–500, >500 cells/mm³, or missing.

The numbers of outpatient, inpatient, and emergency department visits over the entire study period were collected for each patient. Outpatient visits refer only to primary HIV care appointments made to an HIVRN clinic, and do not include nursing or pharmacy visits, consultations, or other types of appointments.

Dichotomous outcomes were (1) performance of any HCV screening and (2) unnecessary repeat HCV testing, during the observation period. We defined the observation period as the time from date of enrollment to date of last outpatient visit, transfer of care, or death, whichever occurred first. Patients were considered screened for HCV if they had one or more HCV antibody test(s)

during the observation period. Unnecessary repeat HCV testing was defined as one or more HCV antibody tests in patients with a prior positive test result.

Statistical Analysis

We compared demographic and clinical differences in the proportion of patients screened for HCV, HCV antibody positive, and unnecessarily tested for HCV using χ^2 tests. Multivariable logistic regression was used to estimate the association between patient factors and the two outcomes. Analyses of unnecessary repeat HCV testing were restricted to patients with a prior positive HCV test, for whom unnecessary testing could be measured. In secondary analyses, multivariable logistic regression was used to estimate the association between patient factors and repeat HCV testing (>1 HCV antibody tests) among HCV antibody negative patients. All regression models included indicators for each HIVRN site and length of observation period. Analyses were conducted in STATA 12.1 (College Station, TX).

Results

Table 1 presents descriptive information for the 8,590 patients new to care at the 12 HIVRN sites in 2006–2010. Median age at presentation was 39 years, with 16% aged 50 years or older. The sample comprised high proportions of patients who were male (75%), of minority race/ethnicity (71%), and who had either no health insurance or Medicaid at the time of their first outpatient visit (66%). The most common HIV transmission behavior was MSM (46%), followed by HET (37%) and IDU (11%). Excluding patients with missing data ($N = 607$), the mean first CD4 cell count was 318 cells/mm³.

In total, 7,023 patients (82% of 8,590) were screened for HCV. (**Table 2**) Among those screened, 92% were tested within 1 year of entering care, 96% within 2 years, and 98% within 3 years. HCV screening rates varied ($P < 0.05$) by HIV transmission behavior: 84% for MSM, 83% for heterosexual (HET), and 73% for injection drug use (IDU). (**Figure 1**) Individuals with Medicaid (84%) or Ryan White/uninsured (85%) were more likely to be tested ($P < 0.05$) than those with private insurance (79%) and Medicare (80%). Using the mean number of outpatient visits during the study period as a divider, 79% of patients with ≤ 14 visits were screened compared to 86% of patients who attended more than 14 visits ($P < 0.05$). (**Figure 2**).

In multivariate analyses, the likelihood of being screened for HCV increased as the number of outpatient visits rose (adjusted odds ratio (AOR) = 1.02; 95% confidence interval (CI) = 1.01–1.03). Compared to MSM, patients with IDU risk were less likely to be screened (AOR = 0.63, 95% CI 0.52–0.78). Individuals with Medicaid were more likely to be screened than those with private insurance (AOR = 1.30, 95% CI = 1.04–1.62). (**Table 3**).

Among patients screened for HCV, 1,283 (18% of 7,023) had a positive test result. (**Table 2**) The percentage of patients identified as HCV antibody positive varied ($P < 0.05$) by age, sex, and HIV transmission behavior. Persons with public insurance and greater numbers of outpatient and inpatient visits had higher proportions of HCV antibody positivity than those with private insurance and lower numbers of outpatient and inpatient visits, respectively ($P < 0.05$).

Of patients with a positive HCV antibody, 510 (40% of 1,283) had an unnecessary repeat HCV test. (**Table 2**) Sixty-five percent had one unnecessary test, 19% had two, 10% had three, and 6% had four or more unnecessary tests. Unnecessary testing varied by HIV risk behavior, with 35% of MSM, 46% of HET, and 39% of IDU undergoing repeat testing ($P < 0.05$). (**Figure 1**) Individuals

Table 1. Demographic and Clinical Characteristics of HIV-infected Patients.

Characteristics	HIV-Infected Patients N = 8,590 (%)
Age (years)	
18–29	2,134 (24.84)
30–39	2,355 (27.42)
40–49	2,743 (31.93)
≥50	1,358 (15.81)
Sex	
Male	6,481 (75.45)
Female	2,109 (24.55)
Race/Ethnicity	
White	2,202 (25.63)
Black	4,142 (48.22)
Hispanic	1,926 (22.42)
Other/Unknown	320 (3.73)
HIV Risk Factor	
MSM	3,913 (45.55)
HET	3,180 (37.02)
IDU	977 (11.37)
Other/Unknown	520 (6.05)
Insurance	
Private	1,270 (14.78)
Medicaid	2,334 (27.17)
Medicare	630 (7.33)
Ryan White/Uninsured	3,334 (38.81)
Other/Unknown	1,022 (11.90)
First CD4 Cell Count (cell/mm³)	
≤350	4,795 (55.82)
351–500	1,501 (17.47)
>500	1,687 (19.64)
Missing	607 (7.07)
Number of Outpatient HIV Visits per Year, mean (SD)*	5.03 (3.12)
Number of Inpatient Visits per Year, mean (SD)*	0.34 (0.93)
Number of Emergency Department Visits per Year, mean (SD)*	0.60 (1.61)
Observation Time (years)	
1	2,338 (27.22)
2	2,010 (23.40)
3	1,486 (17.30)
4	1,220 (14.20)
5	968 (11.27)
6	569 (6.61)

Abbreviations: HET, heterosexual transmission; IDU, injection drug use; MSM, men who have sex with men.

*Mean number of outpatient, inpatient, and emergency department visits over the observation period were: 13.92 (standard deviation 12.03), 0.75 (1.86), and 1.41 (3.70), respectively.

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with greater numbers of outpatient, inpatient, and emergency department visits had higher proportions of unnecessary testing than those with lower numbers of outpatient, inpatient, and emergency department visits, respectively ($P < 0.05$) (**Figure 2**).

In multivariate logistic regression analysis, persons with HET (AOR = 1.78, 95% CI = 1.20–2.65) and IDU (AOR = 1.58, 95% CI = 1.06–2.34) risk and those with higher numbers of outpatient (AOR = 1.03, 95% CI = 1.01–1.04) and inpatient (AOR = 1.09,

95% CI = 1.01–1.19) visits were more likely to be tested unnecessarily (**Table 3**).

We identified 5,740 patients who were HCV antibody negative throughout the observation period. Of these, 2,447 (43% of 5,740) had a repeat HCV test. Fifty-five percent had one repeat test, 24% had two, 11% had three, and 10% had four or more repeat tests. In multivariate analyses, the likelihood of having a repeat HCV test increased as the number of outpatient visits (AOR = 1.03, 95%

Table 2. Proportion of Patients Screened for HCV Infection, HCV Antibody Positive, and Unnecessarily Tested for HCV Infection (2006–2011).

Characteristics	Screened N = 7,023 (%)	Antibody Positive N = 1,283 (%)	Unnecessarily Tested N = 510 (%)
Age (years)[†]			
18–29	1,766 (82.76)	93 (5.27)	33 (35.48)
30–39	1,946 (82.63)	248 (12.74)	97 (39.11)
40–49	2,229 (81.26)	562 (25.21)	232 (41.28)
≥50	1,082 (79.68)	380 (35.12)	148 (38.95)
Sex[†]			
Male	5,304 (81.84)	933 (17.59)	369 (39.55)
Female	1,719 (81.51)	350 (20.36)	141 (40.29)
Race/Ethnicity			
White	1,804 (81.93)	336 (18.63)	119 (35.42)
Black	3,373 (81.43)	627 (18.59)	264 (42.11)
Hispanic	1,578 (81.93)	284 (18.00)	116 (40.85)
Other/Unknown	268 (83.75)	36 (13.43)	11 (30.56)
HIV Risk Factor^{†‡§}			
MSM	3,273 (83.64)	295 (9.01)	104 (35.25)
HET	2,630 (82.70)	424 (16.12)	195 (45.99)
IDU	714 (73.08)	493 (69.05)	194 (39.35)
Other/Unknown	406 (78.08)	71 (17.49)	17 (23.94)
Insurance^{†‡}			
Private	999 (78.66)	82 (8.21)	26 (31.71)
Medicaid	1,963 (84.10)	534 (27.20)	214 (40.07)
Medicare	508 (80.63)	119 (23.43)	47 (39.50)
Ryan White/Uninsured	2,835 (85.03)	408 (14.39)	171 (41.91)
Other/Unknown	718 (70.25)	140 (19.27)	52 (37.14)
First CD4 Cell Count (cell/mm³)^{†‡}			
≤350	4,038 (84.21)	778 (19.27)	318 (40.87)
351–500	1,252 (83.41)	192 (15.34)	81 (42.19)
>500	1,388 (82.28)	247 (17.80)	87 (35.22)
Missing	345 (56.84)	66 (19.13)	24 (36.36)
Number of Outpatient HIV Visits^{*†‡§}			
≤14	4,153 (79.21)	806 (16.64)	201 (27.72)
>14	2,870 (85.75)	477 (21.90)	309 (55.38)
Number of Inpatient Visits^{*‡§}			
0	4,845 (81.35)	725 (17.46)	290 (35.98)
≥1	2,178 (82.69)	558 (19.44)	220 (46.12)
Number of Emergency Department Visits^{*§}			
0	4,434 (81.34)	785 (17.70)	286 (36.43)
≥1	2,589 (82.48)	498 (19.24)	224 (44.98)
Observation Time (years)^{†‡§}			
1	1,812 (77.50)	368 (20.31)	75 (20.38)
2	1,617 (80.45)	226 (13.98)	75 (33.98)
3	1,261 (84.86)	225 (17.84)	98 (43.56)
4	1,062 (87.05)	200 (18.83)	102 (51.00)
5	802 (82.85)	152 (18.95)	93 (63.18)
6	469 (82.57)	112 (23.88)	67 (59.82)

Abbreviations: HET, heterosexual transmission; IDU, injection drug use; MSM, men who have sex with men.

*Continuous variables were dichotomized to facilitate calculation of proportions. The mean value divided the number of outpatient HIV visits during the observation period into two groups; whereas the number of inpatient and emergency department visits during the observation period differentiated between 0 and 1 or more visits.

[†] $P < 0.05$ when comparing differences in the proportion screened for HCV using the χ^2 test.

[‡] $P < 0.05$ when comparing differences in the proportion HCV antibody positive using the χ^2 test.

[§] $P < 0.05$ when comparing differences in the proportion unnecessarily tested for HCV using the χ^2 test.

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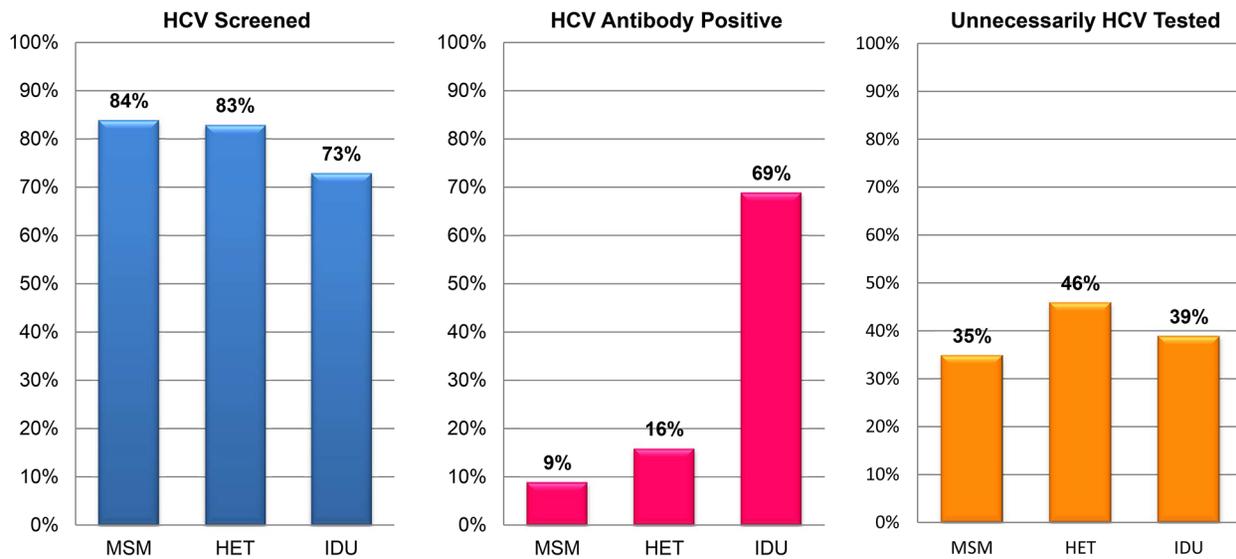


Figure 1. Proportion of Patients Screened for HCV Infection, HCV Antibody Positive, and Unnecessarily Tested for HCV Infection by HIV Transmission Behavior. Abbreviations: HET, heterosexual transmission; IDU, injection drug use; MSM, men who have sex with men. doi:10.1371/journal.pone.0102766.g001

CI = 1.02–1.04) and inpatient visits (AOR = 1.14, 95% CI = 1.08–1.20) increased. Compared to MSM, patients with IDU risk were more likely to have repeat testing (AOR = 1.54, 95% CI = 1.04–2.29). Similarly, individuals with Medicaid were more likely to have repeat testing than those with private insurance (AOR = 1.54, 95% CI = 1.10–2.17). (Appendix S1).

Discussion

Despite recommendations that all HIV-infected patients be screened for HCV infection upon initiation of HIV care, [3–6] only 82% of patients were screened. This screening rate is higher than the 16–54% found in some prior studies but is lower than the

VA (96%). [7–10] The VA has prioritized HCV screening, [14] as veterans have a higher prevalence of HCV infection compared to the general population. [15] The VA also uses an integrated electronic medical record system that is easily accessible by practitioners at multiple sites and generates preventive care and screening reminders. This combination of prioritized HCV screening and sophisticated health information technology may serve as a model for other HIV clinics. In addition, alerting patients and providers when screenings are due, evaluating provider performance and offering feedback, delivering one-on-one and group education to patients, and using patient and provider incentives have been identified as additional tools for improving compliance with screening guidelines [16–20].

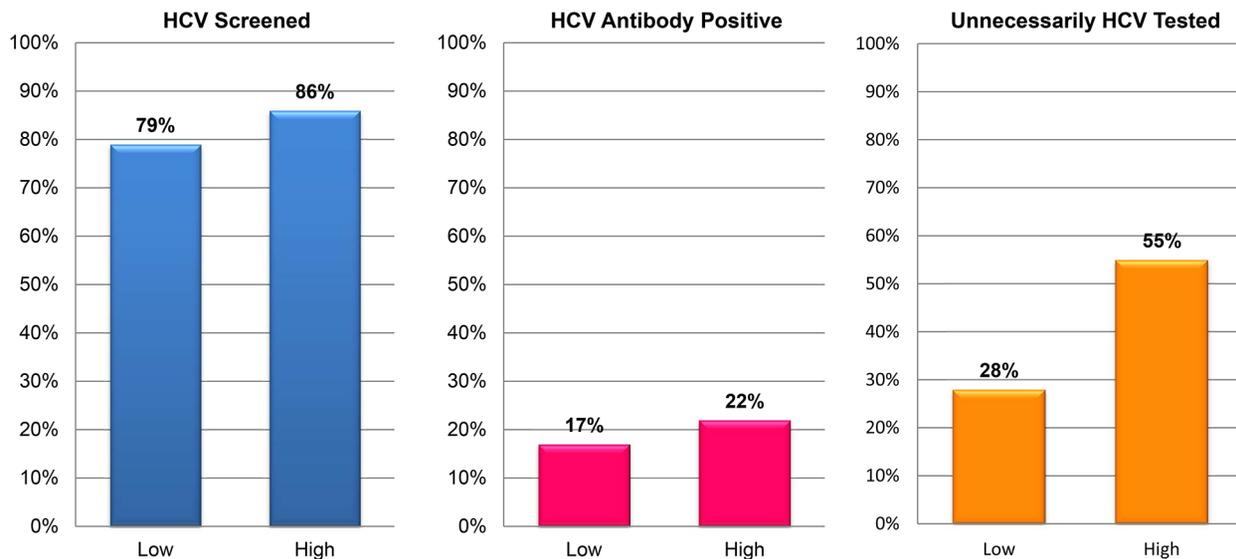


Figure 2. Proportion of Patients Screened for HCV Infection, HCV Antibody Positive, and Unnecessarily Tested for HCV Infection by HIV Outpatient Utilization. Note: The mean value divided the number of outpatient HIV visits during the observation period (13.92) into two groups – low and high. doi:10.1371/journal.pone.0102766.g002

Similar to unnecessary HCV testing rates reported among non-HIV infected individuals, [21] 40% of HIV-infected HCV antibody positive patients in this study had unnecessary duplicate HCV tests. Multiple factors could contribute to the high number of inappropriate tests, including failure to check previous test results, lack of awareness that a test has already been performed, and inadequate distribution of patient information across multiple medical record systems. [22,23] In a survey of 283 primary care

physicians and residents, 17–32% reported having no reliable method to track test results, suggesting the need to develop effective and user-friendly methods for monitoring test results [23].

Computer provider order entry (CPOE) with embedded decision-support tools may provide one solution for reducing repetitive testing. [24,25] In one study, point-of-care prompts decreased redundant testing by 24%, demonstrating the feasibility of CPOE decision-support tools to reduce unnecessary testing.

Table 3. Factors Associated with HCV Screening and Unnecessary Repeat HCV Testing.

Characteristics	HCV Screening	Unnecessary Testing
	Adjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Age (years)		
18–29	1.00 (reference)	1.00 (reference)
30–39	1.04 (0.87–1.24)	1.33 (0.73–2.42)
40–49	0.91 (0.77–1.09)	1.26 (0.72–2.21)
≥50	0.88 (0.72–1.08)	1.00 (0.56–1.83)
Sex		
Male	1.00 (reference)	1.00 (reference)
Female	1.00 (0.85–1.18)	0.92 (0.68–1.25)
Race/Ethnicity		
White	1.00 (reference)	1.00 (reference)
Black	1.01 (0.84–1.20)	1.13 (0.79–1.62)
Hispanic	0.85 (0.70–1.04)	0.98 (0.65–1.47)
Other/Unknown	1.36 (0.94–1.97)	1.64 (0.57–4.73)
HIV Risk Factor		
MSM	1.00 (reference)	1.00 (reference)
HET	0.96 (0.81–1.14)	1.78 (1.20–2.65)
IDU	0.63 (0.52–0.78)	1.58 (1.06–2.34)
Other/Unknown	1.08 (0.81–1.43)	1.34 (0.63–2.82)
Insurance		
Private	1.00 (reference)	1.00 (reference)
Medicaid	1.30 (1.04–1.62)	1.17 (0.64–2.14)
Medicare	1.01 (0.76–1.33)	1.13 (0.56–2.27)
Ryan White/Uninsured	1.21 (0.97–1.50)	1.23 (0.66–2.30)
Other/Unknown	0.93 (0.70–1.23)	0.74 (0.35–1.54)
CD4 Cell Count (cell/mm³)		
≤350	1.00 (reference)	1.00 (reference)
351–500	0.98 (0.83–1.17)	1.18 (0.81–1.71)
>500	0.90 (0.76–1.06)	0.82 (0.56–1.17)
Missing	0.22 (0.17–0.29)	0.65 (0.33–1.29)
Number of Outpatient HIV Visits		
	1.02 (1.01–1.03)	1.03 (1.01–1.04)
Number of Inpatient Visits		
	0.99 (0.95–1.03)	1.09 (1.01–1.19)
Number of Emergency Department Visits		
	0.99 (0.97–1.01)	0.96 (0.91–1.01)
Observation Time (years)		
1	1.00 (reference)	1.00 (reference)
2	1.26 (1.07–1.50)	1.80 (1.17–2.76)
3	1.70 (1.39–2.10)	2.68 (1.73–4.16)
4	2.14 (1.67–2.73)	3.64 (2.25–5.88)
5	1.73 (1.31–2.29)	4.18 (2.37–7.39)
6	1.20 (0.86–1.67)	3.96 (2.17–7.25)

Abbreviations: CI, confidence interval; HET, heterosexual transmission; IDU, injection drug use; MSM, men who have sex with men.

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[24] However, given the widespread adoption of electronic health records and the U.S. government's emphasis on health information technology, many practices may already have access to these resources [26,27].

Injection drug users are at increased risk of HCV and disproportionately account for 80% of new infections and 60% of existing cases in developed countries. [28] Despite this risk, in our cohort, injection drug users were less likely to be screened for HCV than MSM. This finding may be due, in part, to the multiple comorbidities and psychosocial barriers facing many people with IDU. Providers are challenged with managing drug addiction; treating co-occurring conditions, including HIV infection and mental illness; and addressing competing needs (e.g. lack of housing, insurance, social support) during a 20–30 minute office visit. [29–33] Deferral of preventative care services, as typically occurs during complicated visits, and the need to review lengthy medical records to verify prior test results may lead to lower HCV screening. Conversely, the recent emergence of sexually transmitted acute HCV infection may influence HCV testing in MSM. [34] Increased awareness of HCV transmission in this group by both patients and providers may have contributed to the higher screening rate [35].

In our study, greater use of health care services was significantly associated with increased HCV testing, both appropriate and unnecessary. Prior research demonstrates that the number of laboratory tests performed rises with the number of health system interactions. [29] In addition, higher health care utilization can compromise care coordination, which may lead to over treatment and testing. [36–39] Accordingly, improving care coordination and addressing the needs of high users of health care services have been identified as key targets for reducing waste in the U.S. health care system [36,40–42].

The current analysis has several limitations. First, sites in our sample are not nationally representative, although they do encompass a broad geographic distribution and a variety of demographic and clinical characteristics of patients, thereby improving generalizability compared to single-site studies. Second, our data only capture laboratory tests performed at or reported to the site of care. It is possible that patients may be tested for HCV during consultation with other physicians or during hospitalization at outside institutions. Third, some patients may have been tested for HCV prior to entering HIV care. If the results of these test(s) are accurately documented and reported, some providers may not pursue HCV testing. Lastly, our analyses did not focus on the cost of unnecessary HCV testing. Additional studies are needed to estimate how repeat HCV testing impacts health expenditures. These studies should not only consider the added cost of HCV antibody testing but also potential downstream costs (e.g. HCV viral load testing, genotype testing, radiologic studies, and provider referrals).

In summary, 82% of HIV-infected patients were screened for HCV, 18% of those screened were HCV antibody-positive, and 40% of HCV antibody-positive patients had unnecessary repeat HCV testing. Additional efforts are needed to increase HCV screening, particularly for PLWH with IDU risk. In low prevalence populations, serum-pooling strategies may represent

cost-effective techniques to improve screening. [43,44] Leveraging health information technology may be useful for both increasing screening and reducing unnecessary testing.

Supporting Information

Appendix S1 Proportion of HCV Antibody Negative Patients with Repeat HCV Testing and Factors Associated with Repeat HCV Testing.

(DOC)

Acknowledgments

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Author Contributions

Conceived and designed the experiments: BRY RSH JAF JEG ALA SAB PTK RDM JPM KAG. Analyzed the data: BRY JAF KAG. Contributed reagents/materials/analysis tools: ALA PTK RDM KAG. Contributed to the writing of the manuscript: BRY RSH JAF JEG ALA SAB PTK RDM JPM KAG.

References

- Kim AY, Onofrey S, Church DR (2007) An epidemiologic update on hepatitis C infection in persons living with or at risk of HIV infection. *J Infect Dis Suppl* 1: S1–6.
- Operskalski EA, Kovacs A (2011) HIV/HCV co-infection: pathogenesis, clinical complications, treatment, and new therapeutic technologies. *Curr HIV/AIDS Rep* 8(1): 12–22.
- Kaplan JE, Benson C, Holmes KH, Brooks JT, Pau A, et al. (2009) Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR Recomm Rep* 58: 1–207.

4. Aberg JA, Kaplan JE, Libman H, Emmanuel P, Anderson JR, et al. (2009) Primary care guidelines for the management of persons infected with human immunodeficiency virus: 2009 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis* 49(5): 651–681.
5. Centers for Disease Control and Prevention (2012) Recommendations for the Identification of Hepatitis C Virus Infection among Persons Born from 1945 through 1965. *Morb Mortal Wkly Rep* 61: 1–32.
6. Department of Health and Human Services (2013) Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Available at: <http://www.aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf>. Accessed May 15, 2014.
7. Hoover KW, Butler M, Workowski KA, Follansbee S, Gratzner B, et al. (2012) Low rates of hepatitis screening and vaccination of HIV-infected MSM in HIV clinics. *Sex Transm Dis* 39: 349–353.
8. Jonckheere S, Vincent A, Belkhir L, Wilmes D, Vandercam B, et al. (2013) Adherence to Screening Guidelines for Hepatitis C Among HIV-Positive Patients. *AIDS Patient Care STDS* 27: 317–319.
9. Veterans Health Administration (2009) The State of Care for Veterans with HIV/AIDS. 2009. Available at <http://www.hiv.va.gov/HIV/provider/state-of-care/index.asp>. Accessed May 15, 2014.
10. Linas BP, Hu H, Barter DM, Horberg M (2014). Hepatitis C screening trends in a large integrated health system. *Am J Med* 127: 398–405.
11. Centers for Disease Control and Prevention (2013) Testing for HCV infection: an update of guidance for clinicians and laboratorians. *MMWR Morb Mortal Wkly Rep* 62: 362–365.
12. Yehia BR, Gebo KA, Hicks PB, Korhuit PT, Moore RD, Ridore M, et al. (2008) Structures of care in the clinics of the HIV Research Network. *AIDS Patient Care STDS* 22: 1007–1013.
13. Yehia BR, Agwu AL, Schranz A, Korhuit PT, Gaur AH, Rutstein R, et al. (2013) Conformity of pediatric/adolescent HIV clinics to the patient-centered medical home care model. *AIDS Patient Care STDS* 27: 272–279.
14. Veterans Health Administration (2013) Veterans Health Administration Directive 1300.01: National Viral Hepatitis Program. Available at http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=1586. Accessed May 15, 2014.
15. Chak E, Talal AH, Sherman KE, Schiff ER, Saab S (2011) Hepatitis C virus infection in USA: an estimate of true prevalence. *Liver Int* 31: 1090–1101.
16. Baron RC, Medillo S, Rimer BK, Coates RJ, Kerner J, Habarta N, et al (2010) Intervention to increase recommendation and delivery of screening for breast, cervical, and colorectal cancers by healthcare providers a systematic review of provider reminders. *Am J Prev Med* 38: 110–117.
17. Legorreta AP, Hasan MM, Peters AL, Pelletier KR, Leung KM (1997) An intervention for enhancing compliance with screening recommendations for diabetic retinopathy. A bicoastal experience. *Diabetes Care* 20: 520–523.
18. White P, Kenton K (2013) Use of electronic medical record-based tools to improve compliance with cervical cancer screening guidelines: effect of an educational intervention on physicians' practice patterns. *J Low Genit Tract Dis* 17: 175–181.
19. Asonganyi E, Vaghiasa M, Rodrigues C, Phadtare A, Ford A, et al. (2013) Factors affecting compliance with clinical practice guidelines for pap smear screening among healthcare providers in africa: systematic review and meta-summary of 2045 individuals. *PLoS One* 8(9): e72712.
20. Community Preventive Services Task Force (2012) Updated recommendations for client- and provider-oriented interventions to increase breast, cervical, and colorectal cancer screening. *Am J Prev Med* 43: 92–96.
21. Groom H, Dieperink E, Nelson DB, Garrard J, Johnson JR, et al. (2008) Outcomes of a Hepatitis C screening program at a large urban VA medical center. *J Clin Gastroenterol* 42: 97–106.
22. Kwok J, Jones B (2005) Unnecessary repeat requesting of tests: an audit in a government hospital immunology laboratory. *J Clin Pathol* 58: 457–462.
23. Boohaker EA, Ward RE, Uman JE, McCarthy BD (1996) Patient notification and follow-up of abnormal test results. A physician survey. *Arch Intern Med* 156: 327–331.
24. Bates DW, Kuperman GJ, Rittenberg E, Teich JM, Fiskio J, et al. (1999) A randomized trial of a computer-based intervention to reduce utilization of redundant laboratory tests. *Am J Med* 106(2): 144–150.
25. Nies J, Colombet I, Zapletal E, Gillaizeau F, Chevalier P, et al. (2010) Effects of automated alerts on unnecessarily repeated serology tests in a cardiovascular surgery department: a time series analysis. *BMC Health Serv Res* 10: 70.
26. Reed M, Huang J, Brand R, Graetz I, Neugebauer R, Fireman B, et al (2013) Implementation of an outpatient electronic health record and emergency department visits, hospitalizations, and office visits among patients with diabetes. *JAMA* 310: 1060–1065.
27. Hsiao CJ, Hing E (2012) Use and characteristics of electronic health record systems among office-based physician practices: United States, 2001–2012. *NCHS data brief*, no 111. Hyattsville, MD: National Center for Health Statistics.
28. Grebely J, Matthews GV, Lloyd AR, Dore GJ (2013) Elimination of hepatitis C virus infection among people who inject drugs through treatment as prevention: Feasibility and future requirements. *Clin Infect Dis* 57(7): 1014–20.
29. Valenstein P, Leiken A, Lehmann C (1998) Test-ordering by multiple physicians increases unnecessary laboratory examinations. *Arch Pathol Lab Med* 112: 238–241.
30. Kerr T, Wood E, Grafstein E, Ishida T, Shannon K, et al (2005) High rates of primary care and emergency department use among injection drug users in Vancouver. *J Public Health* 27: 62–66.
31. Knowlton AR, Hoover DR, Chung SE, Celentano DD, Vlahov D, Latkin CA (2011) Access to medical care and service utilization among injection drug users with HIV/AIDS. *Drug Alcohol Depend* 64: 55–62.
32. Chander G, Himelhoch S, Moore RD (2006) Substance abuse and psychiatric disorders in HIV-positive patients: epidemiology and impact on antiretroviral therapy. *Drugs* 66: 769–789.
33. Krusi A, Wood E, Montaner J, Kerr T (2010) Social and structural determinants of HAART access and adherence among injection drug users. *Int J Drug Policy* 21: 4–9.
34. Yaphe S, Bozinoff N, Kyle R, Shivkumar S, Pai NP, Klein M (2012) Incidence of acute hepatitis C virus infection among men who have sex with men with and without HIV infection: a systematic review. *Sex Transm Infect* 88: 558–564.
35. Lambers FA, Prins M, Davidovich U, Stolte IG (2014) High awareness of hepatitis C virus (HCV) but limited knowledge of HCV complications among HIV-positive and HIV-negative men who have sex with men. *AIDS Care* 26: 416–424.
36. Berwick DM, Hackbarth AD (2012) Eliminating waste in US health care. *JAMA* 307: 1513–1516.
37. McGregor MJ, Martin D (2012) Testing 1, 2, 3: is overtesting undermining patient and system health? *Can Fam Physician* 58: 1191–1193.
38. Yehia BR, Kangovi S, Frank I (2013) Patients in transition: avoiding detours on the road to HIV treatment success. *AIDS* 27: 1529–1533.
39. Yehia BR, Schranz AJ, Momplaisir F, Keller SC, Gross R, Frank I, et al. (2013) Outcomes of HIV-Infected Patients Receiving Care at Multiple Clinics. *AIDS Behav* Epub ahead of press Sept 28, 2013.
40. Lefevre F, Reifler D, Lee P, Sbhenge M, Nwadiaro N, Verma S, et al. (1999) Screening for undetected mental disorders in high utilizers of primary care services. *J Gen Intern Med* 14: 425–431.
41. Neal RD, Heywood PL, Morley S (2000) Frequent attenders' consulting patterns with general practitioners. *Br J Gen Pract* 50: 972–976.
42. Scaife B, Gill P, Heywood P, Neal R (2000) Socio-economic characteristics of adult frequent attenders in general practice: secondary analysis of data. *Fam Pract* 17: 298–304.
43. Liu P, Shi ZX, Zhang YC, Xu ZC, Shu HS, Zhang XY (1997) A prospective study of a serum-pooling strategy in screening blood donors for antibody to hepatitis C virus. *Transfusion* 37: 732–736.
44. Taylor LE, DeLong AK, Maynard MA, Chapman S, Gholam P, Blackard JT, et al. (2011) Acute hepatitis C virus in an HIV clinic: a screening strategy, risk factors, and perception of risk. *AIDS Patient Care STDS* 25: 571–577.