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

Baligh R. Yehia1,2*, Ramin S. Herati3, John A. Fleishman3, Joel E. Gallant4, Allison L. Agwu5, Stephen A. Berry5, P. Todd Korthuis6, Richard D. Moore5, Joshua P. Metlay7, Kelly A. Gebo5 for the HIV Research Network

1 Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, United States of America, 2 Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America, 3 Center for Financing, Access, and Cost Trends, Agency for Healthcare Research and Quality, Rockville, Maryland, United States of America, 4 Southwest Care Center, Santa Fe, New Mexico, United States of America, 5 Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States of America, 6 Department of Medicine, Oregon Health and Sciences University, Portland, Oregon, United States of America, 7 General Medicine Division, Massachusetts General Hospital, Boston, Massachusetts, United States of America

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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* Email: byehia@upenn.edu

Introduction

Up to 25% of people living with HIV (PLWH) in the United States (U.S.) are coinfected with hepatitis C virus (HCV). [1] HIV/HCV coinfected accelerates progression to liver fibrosis, end-stage liver disease, and death compared to HCV monoinfection. [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 χ² 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
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% 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).

### 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 deviation12.03), 0.75 (1.86), and 1.41 (3.70), respectively.

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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.

1P≤0.05 when comparing differences in the proportion screened for HCV using the χ² test.

2P≤0.05 when comparing differences in the proportion HCV antibody positive using the χ² test.

3P≤0.05 when comparing differences in the proportion unnecessary tested for HCV using the χ² test.

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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].

![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)

![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                        | 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 (1.17–2.78)     |
| 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. doi:10.1371/journal.pone.0102766.t003
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

HIVRN Participating Sites:
- Alameda County Medical Center, Oakland, California (Howard Edelstein, M.D.).
- Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania (Richard Rutstein, M.D.).
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Author Contributions
Conceived and designed the experiments: BRY 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 JAF JEG ALA SAB PTK RDM JPM KAG.

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