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Impact of Hepatitis Co-Infection on Healthcare Utilization among Persons Living with HIV

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Abstract

Hepatitis B (HBV) and hepatitis C (HCV) co-infection are increasingly important sources of morbidity among HIV-infected persons. We determined associations between hepatitis co-infection and healthcare utilization among HIV-infected adults at four U.S. sites during 2006–2011. Outpatient HIV visits did not differ by hepatitis serostatus and decreased over time. Mental health visits were more common among HIV/HCV co-infected persons than among HIV mono-infected (IRR 1.27 [1.08–1.50]). Hospitalization rates were higher among all hepatitis-infected groups than among HIV mono-infected (HIV/HBV IRR 1.23 [1.05–1.44], HIV/HCV 1.22 [1.10–1.36], HIV/HBV/HCV 1.31 [1.02–1.68]). These findings may inform the design of clinical services and allocation of resources.

Keywords

HIV; hepatitis B virus; hepatitis C virus; mental health; healthcare utilization; hospitalization

INTRODUCTION

With the passage of the Patient Protection and Affordable Care Act (ACA), persons living with HIV (PLWH) in the United States can expect healthcare changes that include expansion of insurance coverage, removal of lifetime coverage caps, shifting of resources to

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community health centers, and incentives to improve care coordination.[1] Updated reports of healthcare utilization by PLWH are needed to understand the healthcare needs of this population and plan for changes.

In the U.S., 5–10% of PLWH are co-infected with hepatitis B virus (HBV) and 20–33% with hepatitis C virus (HCV).[2–13] Co-infected patients are at risk of hepatic and extrahepatic complications.[13–23] Viral hepatitis has emerged as a leading cause of morbidity and mortality among PLWH.[24,25] We hypothesized that healthcare utilization among PLWH might differ according to hepatitis serostatus.

The purpose of this study is to characterize the impact of hepatitis co-infection on utilization of primary HIV care, mental health, and inpatient services in a multi-site, multi-state cohort of PLWH.

METHODS

Site Selection and Data Collection

The HIV Research Network (HIVRN) is a consortium of HIV care sites in 11 U.S. cities. Demographic, laboratory, and treatment data are abstracted from clinical records, de-identified, and consolidated into a uniform database. All sites routinely report primary HIV care visits; four also reported mental health and inpatient visits by adult participants from January 1, 2006, through December 31, 2011, and are therefore included in this analysis.

Participants in this analysis were engaged in care during ≥1 year in the study period, as defined by having ≥1 primary HIV care visit, CD4 count, and HIV-1 RNA. The unit of analysis was the patient-year (PY). Institutional review boards at each site and the data coordinating center approved the collection and use of these data for analysis and publication.

Definitions of Variables

Hepatitis serostatus was assessed using HBV surface antigen and HCV antibody. Positive results within six months of enrollment and all negative results were carried backward. Results before July 1 were used to categorize hepatitis serostatus from that year onward, while results after July 1 were used only for subsequent years. Data were censored at the time of death, loss to follow-up, or end of study.

Clinical and demographic characteristics were assessed using previously-published definitions as summarized in Table 1.[26] Time-dependent variables included age, CD4, HIV-1 RNA, ART and insurance status. Race/ethnicity, gender and HIV transmission risk factor were categorized by self-report. For secondary analyses, FIB-4 score and use of ART with HBV activity were also considered time-dependent.[27]

Outcomes

Primary HIV care visits were defined as visits to an HIV care provider, not including visits to nurses or subspecialists within multidisciplinary HIV clinics. Mental health visits were visits to a psychologist, psychiatrist or other mental health provider, not including visits to

substance abuse treatment programs such as methadone clinics. Any non-hospice acute care inpatient visit was included. Mortality was assessed by local study staff report.

Data Analysis

Unadjusted healthcare utilization rates were calculated using total number of visits as the numerator and aggregate person-time as the denominator. Person-time was accrued daily as a fraction of each calendar year, so participants contributed <1 year of observation during the year of enrollment or death.

Number of primary HIV care, mental health, and inpatient visits were modeled using negative binomial regression to estimate incidence rate ratios (IRRs). Age, race/ethnicity, gender, HIV risk factor, CD4, HIV-1 RNA, ART, and insurance status were pre-specified covariates of interest. Multivariable models also included categorical indicators for clinical care site to control for site-specific variability and indicators for calendar year to control for secular trends. Several secondary analyses were performed including, 1) adding number of primary HIV care visits as a predictor for mental health and inpatient visits; 2) evaluating the effects of FIB-4 score and use of ART with HBV activity (tenofovir, lamivudine, or emtricitabine) among subjects with any hepatitis and with HBV co-infection, respectively; and 3) investigating mortality using logistic regression with variables from the primary models.

To account for multiple observations involving the same individual, all models used generalized estimating equations, clustered on patient, with exchangeable working correlation and robust variance estimators. A two-sided type I error of 5% was considered statistically significant. All analyses were performed using Stata 12.0 (StataCorp LP, College Station, TX, USA).

RESULTS

Demographic and Clinical Characteristics

A total of 15,927 participants contributed 49,061 person-years of observation time. At study entry, 9,146 individuals (57.4%) had HIV mono-infection; 536 (3.4%) HIV/HBV; 2,056 (12.9%) HIV/HCV; 115 (0.7%) HIV/HBV/HCV; and 4,074 (25.6%) unknown hepatitis serostatus (Table 1). Of those with initially unknown serostatus, 89 participants later contributed person-time to the HIV/HBV co-infected group, 365 HIV/HCV co-infected, and 26 HIV/HBV/HCV tri-infected. The median age ranged from 40.4 years (IQR 32.6–47.0) in the HIV mono-infected group to 47.0 (42.0–51.9) years in the HIV/HCV co-infected group. There were higher proportions of male patients in the HIV/HBV (91.0%) and HIV/HBV/HCV groups (83.5%) than in the other hepatitis serostatus groups. IDU was reported in 5.7% of HIV mono-infected and 6.3% of HIV/HBV co-infected patients, but was reported in 60.8% of HIV/HCV and 63.5% of HIV/HBV/HCV patients.

Healthcare Utilization and Serostatus

A total of 227,618 primary HIV care visits, 24,415 mental health visits and 13,761 inpatient visits were observed. Primary HIV care visit rates were similar across all hepatitis serostatus

categories, with an average across time for the full study cohort of 4.64 visits/PY (Supplemental Digital Content Table 1). Over the five-year study period, 23.0% of participants had at least one mental health visit, including 21.2% of HIV mono-infected, 21.2% of HIV/HBV co-infected, 34.9% of HIV/HCV co-infected, 30.7% of HIV/HBV/HCV tri-infected and 18.3% of patients with unknown hepatitis serostatus (Supplemental Digital Content Table 2). Among all participants, 33.0% experienced ≥1 inpatient visits during the study period, including 31.6% of those with HIV mono-infection, 37.7% with HIV/HBV co-infection, 46.2% HIV/HCV co-infection, 49.3% HIV/HBV/HCV tri-infection and 24.6% unknown hepatitis serostatus.

In multivariable analysis, there was no association between hepatitis serostatus and number of primary HIV care visits (Table 2). Compared to the HIV mono-infected group, patients with HIV/HCV co-infection had significantly higher mental health utilization rates (IRR 1.27 [95% CI 1.08–1.50]). Inpatient utilization was higher in all hepatitis co-infected groups than with HIV mono-infection (HIV/HBV 1.23 [1.05–1.44], HIV/HCV 1.22 [1.10–1.36], HIV/HBV/HCV 1.31 [1.02–1.68]). Non-White race/ethnicity was a predictor of decreased mental health utilization as compared to White race/ethnicity. Age >50 years was associated with more primary HIV visits; age 35–64 with more mental health visits and age ≥65 with more hospitalizations. Private insurance was associated with lower primary HIV, mental health, and inpatient utilization, as compared to Medicaid, Medicare, and Ryan White/Uninsured.

Healthcare Utilization Over Time

Across all hepatitis serostatus groups, primary HIV care visits ranged from 4.5–5.5 visits/PY in 2006 and decreased to 4.0–4.6 visits/PY in 2011 (unadjusted P for decreasing trend < 0.01 for most hepatitis serostatus groups, Supplemental Digital Content Figure 1). Mental health utilization decreased from 42.1–116.7 visits/100 PY in 2006 to 21.5–67.7 visits/100 PY in 2011, with significant declines in all hepatitis serostatus groups except unknown. There were statistically significant decreases in unadjusted inpatient utilization across all groups except HIV/HBV/HCV tri-infection and unknown serostatus, from 24.2–72.4 visits/100 PY in 2006 to 19.8–34.1 visits/100 PY in 2011. In multivariable analysis, however, inpatient utilization did not decline across time for the full sample (Table 2) or for any hepatitis serostatus subgroup (Supplemental Digital Content Figure 1).

Secondary Analyses

When compared to 1–3 visits/year, increasing HIV primary care utilization was independently associated with increased mental health (4–6 visits/year IRR 1.52 [1.41–1.64], ≥7 visits/year 2.56 [2.34–2.80]) and inpatient (4–6 visits/year 1.22 [1.15–1.30], ≥7 visits/year 2.43 [2.26–2.61]) utilization. When controlling for primary HIV care visits, inferences about hepatitis serostatus and healthcare utilization were unchanged.

Among subjects with any hepatitis co-infection, increased FIB-4 score was associated with more HIV primary care visits (FIB-4 ≥3.25 IRR 1.08 [1.03–1.13], as compared to <1.45) and inpatient admissions (1.95 [1.76–2.16]), but no difference in mental health visits (0.96 [0.78–1.19]). Among subjects with HBV co-infection, use of ART with HBV activity was

associated with significantly fewer outpatient HIV primary care visits (0.83 [0.73–0.95]) and a trend towards fewer inpatient admissions (0.71 [0.48–1.05]), as compared to use of ART without HBV activity and after controlling for other covariates. With few observations, the model for mental health utilization did not converge when adjusting for use of ART with HBV activity.

In multivariable analysis, mortality was higher in all hepatitis co-infected groups than with HIV mono-infection (HIV/HBV 1.91 [1.39–2.62], HIV/HCV 1.30 [1.05–1.62], HIV/HBV/HCV 2.56 [1.70–3.85]).

DISCUSSION

Our study makes several important observations about healthcare utilization among PLWH. First, there was no difference in primary HIV care utilization according to hepatitis serostatus. Second, patients with HIV/HCV co-infection demonstrated higher rates of mental health visits than any of the other groups examined. Finally, rates of inpatient utilization were elevated across all hepatitis-infected categories as compared to HIV mono-infection.

Hepatitis co-infection was not associated with increased utilization of primary HIV care. It is possible that PLWH who are co-infected with viral hepatitis have differences in utilization of other subspecialty services, such as gastroenterology or hepatology, but data regarding subspecialty referrals were not available and further investigation is warranted. Decreasing utilization of primary HIV care services over time may be attributable to evolving guideline recommendations for less frequent monitoring for patients with well-controlled HIV disease.[28–30]

HIV/HCV co-infected participants utilized more outpatient mental health services than any other hepatitis serostatus group. Prior studies have reported that 3.2–8.8% of the general U.S. population presents for ≥1 mental health visit per year.[31,32] In our study, 12.5–16.0% of PLWH utilized mental health services during each calendar year, underscoring the high burden of mental illness among PLWH. As in the general U.S. population, non-White PLWH were less likely to utilize mental health services than were those self-reporting White race/ethnicity, potentially reflecting cultural barriers to care or other access issues.[33] Healthcare delivery systems caring for PLWH must be prepared to handle a high demand for mental health services, particularly among HIV/HCV co-infected patients.

We have previously shown that hepatitis co-infection was associated with increased inpatient utilization during a single year (2010), and here we demonstrate that this relationship has persisted over time.[26] The association between higher FIB-4 score and increased hospitalization rates suggests that hepatocellular dysfunction may directly contribute to the risk of hospitalization in co-infected patients. Use of ART with activity against HBV by persons with HBV co-infection may attenuate the risk of hospitalization.

This study has several potential limitations. First, we relied on HCV antibodies as an indirect marker of HCV co-infection, since HCV RNA levels were not available. However, spontaneous clearance of HCV occurs in less than 10% of PLWH.[34] The impact of HCV therapy was not evaluated, but prior studies have reported low treatment rates in the routine

care of co-infected PLWH.[35–37] Substance abuse is associated with both psychiatric disease and HIV/HCV co-infection, so it is possible that substance abuse contributes to differences in mental health utilization. Treatment of drug addiction was not assessed, but may play a particularly important role in the management of HIV/HCV co-infected patients. HIV/HCV co-infected patients tended to be older than patients in other hepatitis serostatus groups. While all multivariable models included age, residual confounding may have contributed to the differences observed between groups. Lower healthcare utilization among the privately insured raises the possibility that financial differences across groups, such as variable influences of lost work time, may have contributed to some of our observations. Finally, hepatitis serostatus data were not available for all participants, potentially introducing bias if there has been differential failure to capture this information.

Chronic viral hepatitis is associated with differences in mental health and inpatient utilization among PLWH, but not primary HIV care visits. Decreases in primary HIV care utilization over time among all PLWH likely reflect shifting treatment paradigms. Third-party payers and policy-makers should be aware of the high mental health service utilization by patients with HIV/HCV co-infection and heightened risk of hospitalization among PLWH with any hepatitis co-infection as they design healthcare delivery systems and allocate limited healthcare resources.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Community Health Network, Rochester, New York (Roberto Corales, D.O.)

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Table 1

Population Demographic and Clinical Characteristics at Study Entry

Characteristic	HIV Mono-infected n=9,146 (%)	HIV/HBV Co-infected n=536 (%)	HIV/HCV Co-infected n=2,056 (%)	HIV/HBV/HCV Tri-infected n=115 (%)	Unknown Serostatus n=4,074 (%)
Age [years]*					
Median (IQR)	40.4 (32.6–47.0)	41.2 (35.3–46.8)	47.0 (42.0–51.9)	45.4 (41.2–50.7)	43.0 (35.2–49.4)
18 – 34	2856 (31.2)	127 (23.7)	154 (7.5)	6 (5.2)	996 (24.4)
35 – 49	4738 (51.8)	325 (60.6)	1167 (56.8)	79 (68.7)	2154 (52.9)
50 – 64	1420 (15.5)	80 (14.9)	720 (35.0)	30 (26.1)	855 (21)
≥ 65	132 (1.4)	4 (0.8)	15 (0.7)	0 (0)	69 (1.7)
Race/Ethnicity					
White	3180 (34.8)	202 (37.7)	627 (30.5)	34 (29.6)	1637 (40.2)
Black	3750 (41.0)	252 (47.0)	1247 (60.6)	75 (65.2)	1611 (39.5)
Hispanic	1907 (20.8)	61 (11.4)	154 (7.5)	4 (3.5)	692 (17.0)
Other/Unknown	309 (3.4)	21 (3.9)	28 (1.4)	2 (1.7)	134 (3.3)
Gender					
Male	6929 (75.8)	488 (91.0)	1468 (71.4)	96 (83.5)	3255 (79.9)
Female	2217 (24.2)	48 (9.0)	588 (28.6)	19 (16.5)	819 (20.1)
HIV risk factor					
Heterosexual	3475 (38.0)	124 (23.1)	384 (18.7)	14 (12.2)	1180 (29.0)
MSM†	4807 (52.6)	359 (67.0)	357 (17.4)	26 (22.6)	1936 (47.5)
IDU‡	519 (5.7)	34 (6.3)	1251 (60.8)	73 (63.5)	776 (19.0)
Other/Unknown	342 (3.7)	19 (3.5)	64 (3.1)	2 (1.7)	182 (4.5)
CD4 count (cells/mm^3)#					
Median (IQR)	357 (175–549)	300 (106–504)	321 (155–528)	247 (95–415)	383 (212–567)
≤50	1050 (11.5)	94 (17.5)	212 (10.3)	18 (15.6)	331 (8.1)
51–200	1510 (16.5)	112 (20.9)	428 (20.8)	32 (27.8)	625 (15.3)
201–500	3813 (41.7)	194 (36.2)	857 (41.7)	45 (39.1)	1760 (43.2)
>500	2773 (30.3)	136 (25.4)	559 (27.2)	20 (17.4)	1358 (33.3)
HIV-1 RNA (copies/mL)#					
Median (IQR)	4326(UND-84200)	9465(UND-99138)	2293(UND-56350)	2650(UND-90563)	898(UND-49700)

Characteristic	HIV Mono-infected n=9,146 (%)	HIV/HBV Co-infected n=536 (%)	HIV/HCV Co-infected n=2,056 (%)	HIV/HBV/HCV Tri-infected n=115 (%)	Unknown Serostatus n=4,074 (%)
<400	2837 (31.0)	170 (31.7)	701 (34.1)	41 (35.6)	1364 (33.5)
≥ 400	6309 (69.0)	366 (68.3)	1355 (65.9)	74 (64.4)	2710 (66.5)
ART[§]					
No	2163 (23.6)	100 (18.7)	542 (26.4)	21 (18.3)	966 (23.7)
Yes	6983 (76.4)	436 (81.3)	1514 (73.6)	94 (81.7)	3108 (76.3)
With HBV activity	4615 (66.1)	306 (70.2)	1007 (66.5)	63 (67.0)	1857 (59.8)
Insurance[#]					
Medicaid	1307 (14.3)	81 (15.1)	721 (35.1)	41 (35.6)	684 (16.8)
Medicare/Dual eligible	1556 (17.0)	104 (19.4)	386 (18.8)	33 (28.7)	827 (20.3)
Private	1345 (14.7)	81 (15.1)	129 (6.3)	6 (5.2)	538 (13.2)
Ryan White/Uninsured	4796 (52.4)	263 (49.1)	789 (38.4)	35 (30.4)	1945 (47.7)
Unknown/Missing	142 (1.6)	7 (1.3)	31 (1.5)	0 (0)	80 (2.0)
Year of study entry					
2006	4500 (49.2)	235 (43.8)	1110 (54.0)	66 (57.4)	2000 (49.1)
2007	959 (10.5)	79 (14.7)	257 (12.5)	16 (13.9)	422 (10.4)
2008	955 (10.4)	62 (11.6)	253 (12.3)	14 (12.2)	236 (5.8)
2009	969 (10.6)	56 (10.4)	187 (9.1)	9 (7.8)	253 (6.2)
2010	1005 (11.0)	63 (11.8)	163 (7.9)	7 (6.1)	475 (11.7)
2011	758 (8.3)	41 (7.6)	86 (4.2)	3 (2.6)	688 (16.9)
Status at end of study					
Alive	8585 (93.9)	471 (87.9)	1748 (85.0)	86 (74.8)	3755 (92.2)
Deceased	561 (6.2)	65 (12.1)	308 (15.0)	29 (25.2)	319 (7.8)

[*] Age was assessed on July 1 of the year of study entry.

[†] Patients who reported sex with both men and women were categorized as MSM.

[‡] Patients who reported IDU in addition to any other risk factor were categorized as IDU.

[#] CD4, HIV-1 RNA, and insurance data are the first available for the calendar year of study entry. UND: undetectable

[§] ART refers to concurrent use of ≥3 antiretroviral medications from ≥2 classes at any time during the calendar year of study entry. HBV activity is defined by an ART regimen that contains tenofovir, lamivudine, or emtricitabine; percentages with HBV activity reflect the number prescribed one or more of these agents divided by the number prescribed ART in each hepatitis serostatus category.

Table 2

Multivariable Analysis of Risk Factors for Healthcare Utilization

Characteristic	Primary HIV CareVisits IRR (95% CI)	Mental Health Visits IRR (95% CI)	InpatientVisits IRR (95% CI)
Hepatitis Serostatus			
HIV mono-infection	1.0 (REF)	1.0 (REF)	1.0 (REF)
HIV/HBV co-infection	1.02 (0.97–1.07)	0.86 (0.69–1.06)	**1.23 (1.05–1.44)**
HIV/HCV co-infection	1.02 (0.99–1.05)	**1.27 (1.08–1.50)**	**1.22 (1.10–1.36)**
HIV/HBV/HCV tri-infection	0.93 (0.86–1.00)	0.82 (0.57–1.18)	**1.31 (1.02–1.68)**
Unknown serostatus	1.01 (0.99–1.03)	**1.24 (1.03–1.48)**	0.93 (0.85–1.03)
Age (years)*			
18 – 34	1.0 (REF)	1.0 (REF)	1.0 (REF)
35 – 49	**0.94 (0.92–0.96)**	**1.26 (1.05–1.50)**	0.94 (0.86–1.02)
50 – 64	**1.03 (1.00–1.06)**	**1.34 (1.10–1.64)**	1.08 (0.97–1.20)
≥ 65	**1.08 (1.02–1.15)**	1.08 (0.76–1.53)	**1.49 (1.21–1.83)**
Race/Ethnicity			
White	1.0 (REF)	1.0 (REF)	1.0 (REF)
Black	**1.04 (1.01–1.06)**	**0.60 (0.53–0.69)**	1.07 (0.98–1.17)
Hispanic	**1.04 (1.01–1.07)**	**0.50 (0.41–0.60)**	1.03 (0.93–1.15)
Other/Unknown	0.98 (0.93–1.04)	**0.47 (0.33–0.68)**	0.77 (0.58–1.02)
Gender			
Male	1.0 (REF)	1.0 (REF)	1.0 (REF)
Female	**1.09 (1.07–1.12)**	**1.54 (1.29–1.84)**	**1.16 (1.06–1.26)**
HIV risk factor			
Heterosexual	1.0 (REF)	1.0 (REF)	1.0 (REF)
MSM†	1.02 (1.00–1.05)	**1.65 (1.41–1.93)**	**0.90 (0.82–1.00)**
IDU‡	**1.04 (1.01–1.08)**	**1.49 (1.24–1.79)**	**1.28 (1.14–1.43)**
Other/Unknown	0.98 (0.93–1.04)	1.34 (0.58–3.10)	**1.54 (1.27–1.87)**
CD4 count (cells/mm^3)#			
>500	1.0 (REF)	1.0 (REF)	1.0 (REF)
201–500	**1.07 (1.05–1.08)**	0.96 (0.88–1.04)	**1.53 (1.41–1.65)**
51–200	**1.20 (1.18–1.23)**	0.95 (0.83–1.08)	**3.15 (2.86–3.47)**
≤ 50	**1.49 (1.44–1.54)**	**0.80 (0.67–0.95)**	**7.49 (6.79–8.26)**
HIV-1 RNA (copies/mL)#			
<400	1.0 (REF)	1.0 (REF)	1.0 (REF)
≥400	**1.21 (1.19–1.22)**	**1.09 (1.00–1.18)**	**1.71 (1.60–1.82)**
ART§			
No	1.0 (REF)	1.0 (REF)	1.0 (REF)
Yes	**1.20 (1.18–1.23)**	1.10 (0.97–1.25)	0.94 (0.86–1.03)
Insurance#			
Private	1.0 (REF)	1.0 (REF)	1.0 (REF)

Characteristic	Primary HIV CareVisits IRR (95% CI)	Mental Health Visits IRR (95% CI)	InpatientVisits IRR (95% CI)
Medicaid	**1.17 (1.13–1.20)**	**1.66 (1.42–1.94)**	**1.82 (1.60–2.07)**
Medicare/Dual eligible	**1.16 (1.13–1.19)**	**1.46 (1.24–1.72)**	**1.75 (1.53–2.01)**
Ryan White/Uninsured	**1.22 (1.19–1.25)**	**1.63 (1.36–1.95)**	**1.21 (1.07–1.38)**
Unknown/Missing	**0.69 (0.66–0.72)**	**0.70 (0.55–0.88)**	**0.65 (0.50–0.85)**
Year			
2006	1.0 (REF)	1.0 (REF)	1.0 (REF)
2007	**0.93 (0.91–0.95)**	1.07 (0.98–1.16)	**1.14 (1.05–1.24)**
2008	**0.93 (0.91–0.94)**	**1.12 (1.01–1.24)**	1.05 (0.97–1.14)
2009	**0.93 (0.92–0.95)**	**0.90 (0.82–0.99)**	**1.20 (1.11–1.31)**
2010	**0.93 (0.91–0.95)**	**0.71 (0.64–0.79)**	**1.17 (1.07–1.27)**
2011	**0.85 (0.83–0.87)**	**0.66 (0.60–0.73)**	1.06 (0.96–1.16)

* Age was assessed annually on July 1.

† Patients who reported sex with both men and women were categorized as MSM.

‡ Patients who reported IDU in addition to any other risk factor were categorized as IDU.

CD4, HIV-1 RNA, and insurance data are the first available for each year.

§ ART refers to concurrent use of ≥3 antiretroviral medications from ≥2 classes at any time during the calendar year.

The unit of analysis for all models was person-year. Incidence rate ratios (IRRs) are interpreted as the relative number of visits compared to the reference group after adjusting for other listed characteristics and clinical care site. Statistically significant results ($p \leq 0.05$) are shown in bold.