Factors Associated with Testing for Hepatitis C Infections Among a Commercially Insured Population of Persons with HIV, United States 2008–2016

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Keywords: hepatitis C; hepatitis C virus (HCV) infection; HIV, Co-Infection

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Key points: Because HIV infection can accelerate hepatitis C related morbidity and mortality, national guidelines recommend hepatitis C testing for patients with HIV. Overall, 50% of newly diagnosed HIV patients were tested for hepatitis C within 12 months of HIV diagnosis.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

ABSTRACT

Background: Hepatitis C virus (HCV) infection is an important public health problem among people living with HIV. People with HIV who are coinfected with HCV infection are at increased risk for cirrhosis, liver failure, and hepatitis C–related mortality, as such national guidelines recommend persons with HIV should be tested for HCV infection.

Methods: Data from the 2003–2017 IBM Watson® Health MarketScan® database were used for this study. We used diagnostic, procedural, and drug codes to identify patients with ≥1 inpatient or outpatient medical claim of HIV diagnosis. Patients with prior HIV or hepatitis C diagnosis were excluded. We calculated hepatitis C testing rates among newly diagnosed HIV–infected persons within 12 months of the initial HIV diagnosis date (January 1, 2008– December 31, 2016). We used Poisson regression to identify the factors associated with hepatitis C testing. Lastly, we assessed hepatitis C testing trends using the Cochran–Armitage test.

Results: The prevalence of testing for hepatitis C in newly identified persons with HIV (N=46, 277) was 50% within 12 months of the index HIV diagnosis. From 2008–2017 the testing rate increased by 13%. Significant predictors of hepatitis C testing were age, sex and urbanicity. Women with HIV were less likely to have been tested compared with men (RR: 0.79 95% CI 0.77–0.81). Only 40% of patients between 50–59 years of age were tested for hepatitis C within 12 months of the index HIV diagnosis, while 56% of persons with HIV aged 20–29 years were tested for hepatitis C.

Conclusions: Overall, 50% of newly diagnosed HIV patients were tested for hepatitis C within 12 months of HIV diagnosis. Although there were increases in hepatitis C testing rates over the study period, there were missed opportunities to detect HCV infection among people newly diagnosed with HIV.

Introduction

Hepatitis C virus (HCV) infection is an important public health problem among people living with human immunodeficiency virus (HIV) Worldwide, approximately, 2.2 million persons were estimated to have been co-infected with HIV and HCV infection in 2015 [1–2]. In the United States, estimates of the proportion of persons with HIV who were ever exposed to HCV range from 16–30% [2–8]. Both HIV and HCV are transmitted through exposure to blood or body fluids of an infected person [9–11]. In the United States, the most common modes of HIV transmission are through sexual contact and injection drug use (IDU) [9–10]; whereas, HCV transmission is primarily spread through IDU [1]. Although, sexual transmission of HCV is rare, there is an increased risk for men who have sex with men (MSM) who are infected with HIV [10, 12–14]. Because HIV infection can accelerate the natural history of HCV infection leading to increased risk for cirrhosis, liver failure, and hepatitis C–related mortality, all individuals living with HIV should be tested for hepatitis C and linked to care were appropriate [15–17]. Since 1998, CDC has recommended hepatitis C testing for persons at increased risk for HCV infection, including persons who (a) are currently or have ever injected drugs; (b) were ever on chronic hemodialysis; (c) received blood transfusions or organ transplants before July 1992; (d) received clotting factor concentrates produced before 1987; (e) had a recognized exposure (e.g., healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures and children born to hepatitis C-infected mothers); and (f) had laboratory evidence of liver inflammation (i.e., persistently elevated alanine aminotransferase levels) [18]. In 1999, hepatitis C testing also was recommended for persons with HIV [19]. In 2012, CDC expanded hepatitis C testing recommendations to include one–time testing for persons born during 1945–1965 [20]. Similarly, the American Associations and Society for Liver Disease (AASLD) and

United States Preventative Services Task Forces USPTF) recommend hepatitis C testing in person who are at increased risk for hepatitis C and one–time testing for persons born during 1945–1965 [21–22]. Despite these long-standing recommendations, limited studies have assessed hepatitis C testing among HIV infected persons who have initiated HIV care [8]. Therefore, we sought to explore the frequency and rates of hepatitis C testing among a large sample of commercially insured, newly diagnosed HIV–infected individuals. The specific aims of the study were to: (1) determine rates of hepatitis C testing during the 12–month period following the diagnose of HIV and (2) examine demographic, regional, and healthcare related factors associated with hepatitis C testing.

Methods

Data from 2003–2017 IBM Watson® Health MarketScan® (IBM, Incorporated, Armonk, New York) Commercial Research Database were used for this study [23]. The database includes a convenience sample of medical claims, including inpatient, outpatient and prescription drug claims from approximately 21 different commercial health insurance plans. We measured HIV and hepatitis C testing rates by examining the occurrence of testing-related codes from the *International Classification of Diseases, Ninth Revision, Clinical Modifications* (ICD–9–CM) or *Tenth Revision* (ICD–10–CM), *Current Procedural Terminology* (CPT), and National Drug Codes (NDC) Directory. Patient–level data were de-identified in the MarketScan database in compliance with the Health Insurance Portability and Accountability Act regulations.

Patient Selection

Enrollment included patients who were identified with one or more medical claim(s) (either inpatient or outpatient) with ICD–9–CM or ICD–10–CM codes indicative of an HIV diagnosis (ICD9: 042, 079.53, 0795.71,V08, ICD10:B20, B9735, R75, Z21,O9872, O9873, O98711,

O98712, O98713, O98719) from January 1, 2008 to December 31, 2016. Our study population was composed of patients who were continuously enrolled for at least 6 months prior to the index event (HIV diagnosis) and 12 months after the index event from June 2007 through December 2017.

Exclusion criteria included patients with prior HIV or hepatitis C diagnoses. All patients had no HIV diagnostic, procedural, or antiretroviral drug codes for at least 6 months prior to the index HIV diagnosis date. Although we limited the study period for an index event to 2008–2016, we examined all available patient data in the database, which spanned 2003–2017, for medical and prescription records and excluded patients if they had a documented HIV diagnosis or hepatitis C diagnosis or a prescription for antiretroviral therapy (ART) prior to the index date. Patients were excluded if information was missing on age, sex, U.S. region of residence, metropolitan statistical area (MSA), or health plan type.

Study Variables

The primary outcome was persons with HIV that were tested for hepatitis C, as identified by current CPT codes for testing procedures (V73.89, G0472, 80074, 86803, 86804, 87520–87522, 87902, 3266F) within 12 months of the HIV index diagnosis.

Selected sociodemographic, regional, and healthcare–related variables were examined, including age group (less than 20, 20–29, 30–39, 40–49, 50–59, 60+ years); sex (male, female); U.S. geographic region (Northeast, Midwest, South, and West), and MSA location (resided in a U.S. Census Bureau–designated rural or urban area).

Statistical Analysis

We computed frequencies and percentages describing characteristics of persons with HIV from 2008–2017. Next, we used the chi-square statistic to examine the likelihood of hepatitis C testing by year, patient demographics, U.S. region, and metropolitan status (urban vs rural) (See Appendix 1 Supplementary Material). Multicollinearity was tested with Variance Inflation Factor (VIF). Variables that were significantly associated in the bivariate analysis were included in a multivariate modified Poisson regression with robust error variance [24] to estimate the relative risk, where hepatitis C testing (yes, no) was the dependent variable. The lowest Akaike Information criteria (AIC) was used to identify the most parsimonious model. The association between the independent variables and the dependent variable was estimated and presented using adjusted risk ratios and 95% confidence intervals. The Cochran–Armitage test for trend was used assess trends in hepatitis C testing by year. P values <.05 were considered significant. All analyses were performed using SAS® version 9.4 (SAS Institute, Inc., Cary, North Carolina).

Results

From 2008 through 2016, a total of 46,277 commercially insured persons were identified as newly diagnosed with HIV in the MarketScan® database. The frequency of new HIV diagnoses varied by an average of 728 patients from year to year. The number of new HIV diagnoses ranged from 6,838 in 2011 to 3,464 in 2016 patients. Among those identified across all years, 64% were male (Table 1). Most patients were aged 30–49 years (50%), the mean and median age was 38 years. Most of the persons diagnosed with HIV resided in the Southern region of the U.S. (39%), followed by the Northeast (32%). Only 15% of patients were in the Midwest and 14% were in the Western region. Most patients received care in urban areas (95%).

The overall prevalence of testing for hepatitis C in the newly diagnosed persons with HIV was 50% within a year of the index HIV diagnosis. There was a significant increasing trend in testing for hepatitis C over the study period (p<0.001), where overall testing increased by 13% over the study period. However, the increase was not consistent. Patients diagnosed in 2014 were 1.45 times more likely to have been tested than persons diagnosed in 2008 (RR: 1.45 95% CI 1.33–1.57); however, after 2015 the rates leveled off and then began to decline (Table 1, Figure 1). Hepatitis C testing was significantly associated with age group, sex, and MSA (Table 1). Patients aged 20–29 years were more likely to have been tested as those aged 50–59 years of age (**RR**: 1.25 95% CI 1.20–1.31). Newly diagnosed women with HIV were less likely to have been tested for hepatitis C compared to newly identified men with HIV (**RR**: 0.79 95% CI 0.77–0.81). Patients with HIV who received care in rural areas were also less likely to have been tested for hepatitis C than persons with HIV in urban areas (**RR**: 0.85 95% CI 0.80–0.91). Region was statistically significant in the bivariate analysis (p-value=<0.001)) but was removed out of concerns for collinearity and to create a more stable, parsimonious model.

Discussion

Using 2007–2017 IBM® MarketScan® data, we reported that in this large sample of commercially insured persons, only half of persons with newly diagnosed HIV were tested for hepatitis C within 12 months of their index HIV diagnosis. There was an improvement in 12-month post HIV diagnosis hepatitis C testing rates for those diagnosed 2008 through 2014 but after 2015 the rates leveled off and then began to decline. Males and persons aged 20–29 years had the highest rates of testing compared with all other age groups, including patients in the birth cohort age range (50–65 years). Patients who resided in a rural area were least likely tested for hepatitis C compared to urban area.

National elimination goals necessitate increased testing for hepatitis C as a priority activity and early detection of persons coinfected with HIV and hepatitis C improves both individual and population health outcomes. The passage of the Affordable Care Act in the United States in 2010 was designed to remove impediments to testing and encourage optimal care for at–risk populations. However, our findings indicate a less than optimal uptake of CDC recommendations and are similar to previously published estimates of hepatitis C testing of persons with HIV. Hoover et al., reported similar testing rates, with 54% of MSM with HIV tested for hepatitis C infection in HIV clinics in the United States [25]. While, Freiman et al., reported overall higher rates of testing, in the Center for AIDS Research Network of Integrated Clinical Systems (CFAR CNICS), where 85% of the cohort were tested for hepatitis C, but there was a large variation of testing rates between sites (35%–87%) from 2000 to 2011 [5]. These findings underscore the need to implement effective and sustainable interventions to increase hepatitis C testing among people living with HIV, especially in the era of effective hepatitis C direct–acting antiviral agents (DAA) [26]. As such, the low testing rates reported in this study may be the result of limited awareness of hepatitis C testing recommendations among providers caring for commercially insured patients compared to providers caring for persons in the CFAR CNICS cohort. While the hepatitis C testing rates increased unevenly over the study period, the greatest increase was among patients diagnosed with HIV in 2011 (46%), compared to those diagnosed in 2012 (52%), after the new treatment regimens were approved by the FDA. Isenhour et al., reported similar increases in testing for hepatitis C in the general patient population [27]. Testing increased overall from 1.1% to 2.5% in the 10–year study period (2005–2014), but most dramatically in the persons aged 50–69 years from 2012 through 2014. In our study, testing rates began to level off in 2014 and 2015 and then decreased slightly in 2015–2016. This may be a

result of stabilizing of testing rates after an initial change in policy or treatment. Further research is needed to understand this finding but continued programmatic targeting of the need for hepatitis C testing to providers caring for patients who have commercial insurance, may be beneficial. Despite the increases in testing, these data continue to suggest that hepatitis C testing of persons with HIV was lower than recommended and that hepatitis C testing rates need to increase.

Interestingly, there were significant differences in testing rates between age groups and HIV–infected men and women. Given the recommendations for testing of the CDC–designated "birth cohort" (1945–1965), more frequent hepatitis C testing of persons aged 20–29 years with HIV than aged 50–65 years was unexpected. National surveillance data have revealed an increase in reported cases of new HCV infection every year since 2009 through 2017 among persons aged 20–39 years [11]. Similarly, the annual number of new HIV diagnoses in the U.S. decreased 9 percent from 2010-2016 [28]. This may be a result of increased testing among people less than 30 years of age who inject drugs. Zibbell et al. reported that young persons, 30 years or younger, from nonurban areas contributed to the majority of hepatitis cases related to injection drug use [29]. We also found that women were less likely to have been tested for hepatitis C compared to men. The sex differences identified in our study are consistent with published research and may be associated with other identified risk factors for substance use disorder or sexual risk behavior. Wurchel et al. reported that while 85% of persons with HIV had repeat syphilis testing, only 62% had repeat hepatitis C testing, and that men had significantly greater odds of hepatitis C testing [30]. In a study examining hepatitis C testing in community health clinics, Cook et al. reported that 49% of women and 51% of men were tested for hepatitis C [31]. A recent study of hepatitis C virus incident cases among persons with HIV found that most cases were predominately

among men (80%) [32]. Koneru reported that from 2011–2014 incident hepatitis C cases in women of reproductive years increased 22%, and there is a growing body of literature encouraging development of public health policies for routine hepatitis C testing of pregnant women and reporting of pregnancy status in hepatitis C surveillance data [33]. Low testing results from the current study support the need to increase testing in women of childbearing age, including those with HIV.

We also identify regional disparities related to hepatitis C testing in the MarketScan® data, indicating patients with residence in rural areas were 15% less likely to have been tested compared to patients in urban areas. Unfortunately, rural areas maybe the most vulnerable to outbreaks of blood born infections like HIV and hepatitis C [34]. These findings demonstrate important missed opportunities for testing of viral hepatitis in rural areas. During 2006–2012, four rural states (Kentucky, Tennessee, Virginia, and West Virginia) had the greatest combined incidence of new HCV infection (364%) among persons aged ≤30 years [29]. Most persons with HIV live in urban and metropolitan areas and therefore HIV prevention efforts, including testing for hepatitis C, have been focused in urban communities [35]. Although rural populations have lower rates of HCV infections, persons with HIV were less likely to be tested and therefore linked to care for monitoring and effective DAA treatment. The new CDC recommendations to implement universal testing among adults 18 and older may impact HCV testing rates. Research shows that only half of people in U.S. were diagnosed and aware of their HCV infection, despite CDC recommendation since 1998 for hepatitis C testing [36–37]. Thus, we are hopeful the new CDC recommendations with further remove stigma associated with hepatitis C testing.

Our study has limitations. Our study included commercially insured persons, so our findings cannot be generalized to other populations of persons with HIV, such as those who utilize Ryan

White Services or have Medicaid insurance. We also required patients to have been continuously enrolled for several months to be included in our study, which might have resulted in a selection bias that included persons with stable health insurance coverage. Hepatitis C testing might have been performed but not billed to the health insurance plan and would result in an underestimation of the testing prevalence. Future studies should examine the differences in hepatitis C testing at 12 months compared tested anytime for new diagnosed HIV patients. Identifying patients using ICD–9–CM and ICD–10–CM diagnostic codes might result in misclassification, and an underestimation of the overall prevalence of persons with HIV. Finally, the MarketScan commercial database does not include a variable for race and ethnicity, so we were unable to evaluate potential associations between race and ethnicity on hepatitis C testing practices.

In conclusion, hepatitis C testing is suboptimal among commercially insured persons with HIV in the United States as only 50% of newly diagnosed HIV patients were tested for hepatitis C within 12 months of their HIV diagnosis. Although there were increases in hepatitis C testing rates over the study period, there remain missed opportunities to detect and treat HCV infection among people newly diagnosed with HIV. Because HIV infection can accelerate hepatitis C related morbidity and mortality additional efforts are needed to improve hepatitis C testing among people newly diagnosis with HIV.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest: The authors have no conflicts of interest to disclose.

Acknowledgement: none.

Financial disclosure: The authors have no financial relationships relevant to this research to disclose.

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Figure 1 Legend. Persons tested for hepatitis C within a year of a clinical diagnosis of HIV infection (ICD-9–CM ǂ, ICD-10–CM ǂ and procedural† codes), United States 2008–2016

Source: 2007–2017 IBM MarketScan® Commercial Claims, new HIV diagnosis 2008–2016

*Urban or rural designation based on Metropolitan Statistical Area (MSA) of the primary beneficiary at the point of clinical diagnosis.

ǂDiagnosis codes based on the International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) or Tenth Revision (ICD-10-CM) billing claim codes.

†Diagnosis codes based on Current Procedural Terminology (CPT)

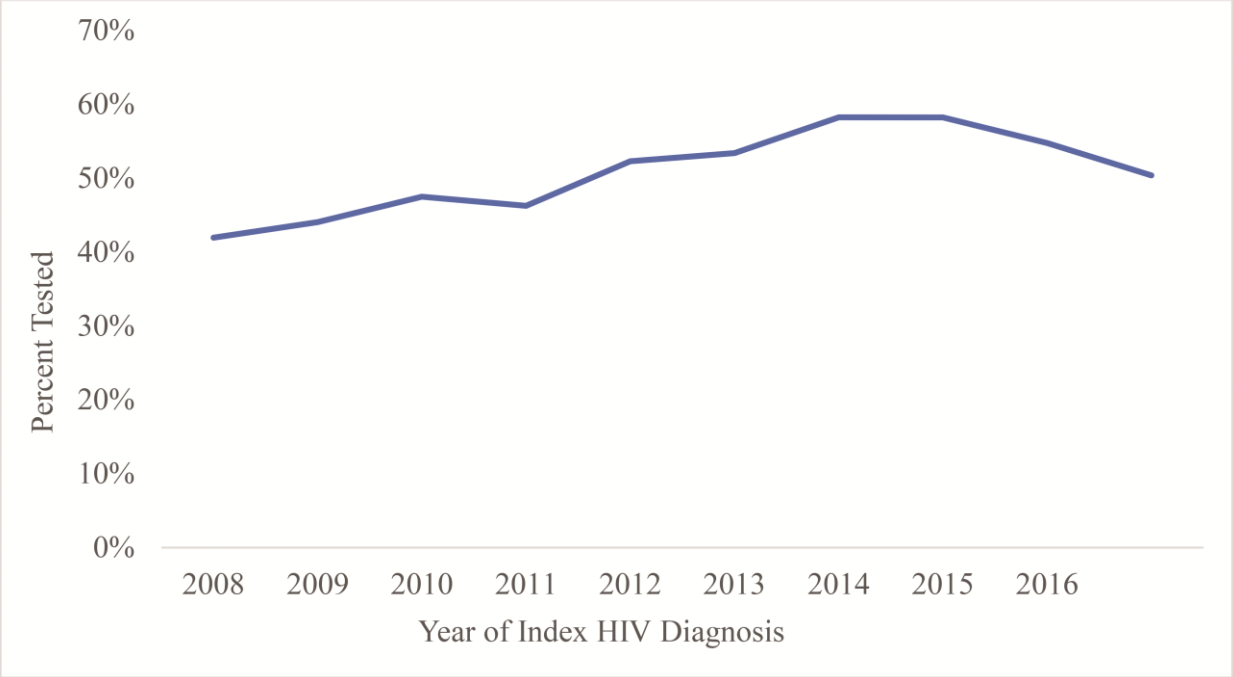

Table 1. Characteristics and adjusted risk ratios (aRR) among persons tested for hepatitis C within a year of a new clinical diagnosis of HIV infection (ICD-9–CM ‡, ICD-10–CM ‡ and procedural† codes), United States 2008–2016

		Total Number of HIV-infected Persons	Number Tested for Hepatitis C within 12 months of HIV diagnosis (n=23,307, (50%))		aRR ^	95% CI	P value
Year							
	2008	4491	1884	42%	REF		
	2009	4874	2148	44%	1.08	(1.02 to 1.14)	0.008
	2010	5934	2817	47%	1.05	(0.99 to 1.11)	0.087
	2011	6838	3164	46%	1.18	(1.12 to 1.25)	<0.001
	2012	5921	3097	52%	1.21	(1.15 to 1.28)	<0.001
	2013	6002	3205	53%	1.45	(1.34 to 1.57)	<0.001
	2014	4502	2621	58%	1.45	(1.33 to 1.57)	<0.001
	2015	4251	2475	58%	1.37	(1.26 to 1.50)	<0.001
	2016	3464	1896	55%	1.05	(0.99 to 1.11)	0.087
Age Group							
	<20	2962	1210	41%	0.96	(0.90 to 1.02)	0.173
	20-29	10432	5831	56%	1.25	(1.20 to 1.31)	<0.001
	30-39	11558	6290	54%	1.26	(1.21 to 1.31)	<0.001
	40-49	11674	5879	50%	1.15	(1.10 to 1.20)	<0.001
	50-59	7968	3502	44%	REF		
	60+	1683	595	35%	0.81	(0.74 to 0.88)	<0.001
Sex							
	Male	29603	16130	54%	REF		
	Female	16674	7177	43%	0.79	(0.77 to 0.81)	<0.001
U.S. Geographic Region							
	Northeast	15016	8089	54%			
	North Central	6729	2895	43%			
	South	18235	9386	51%			
	West	6300	2940	47%			
MSA							
	Urban	43853	22298	51%	REF		
	Rural	2424	1009	42%	0.85	(0.80 to 0.91)	<0.001

Source: 2007–2017 IBM MarketScan® Commercial Claims, new HIV diagnosis 2008–2016

*Urban or rural designation based on Metropolitan Statistical Area (MSA) of the primary beneficiary at the point of clinical diagnosis.

ǂDiagnosis codes based on the International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) or Tenth Revision (ICD-10-CM) billing claim codes. † diagnosis codes based on Current Procedural Terminology (CPT)

^Modified Poisson regression model adjusted for year, age group, sex, and MSA region