MAJOR ARTICLE

Direct-Acting Antivirals Improve Access to Care and Cure for Patients With HIV and Chronic HCV Infection

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Background. Direct-acting antivirals (DAA) as curative therapy for hepatitis C virus (HCV) infection offer >95% sustained virologic response (SVR), including in patients with human immunodeficiency virus (HIV) infection. Despite improved safety and efficacy of HCV treatment, challenges remain, including drug-drug interactions between DAA and antiretroviral therapy (ART) and restrictions on access by payers.

Methods. We performed a retrospective cohort study of all HIV/HCV co-infected and HCV mono-infected patients captured in care at our institution from 2011–2015, reflecting the DAA era, to determine treatment uptake and SVR, and to elucidate barriers to accessing DAA for co-infected patients.

Results. We identified 9290 patients with HCV mono-infection and 507 with HIV/HCV co-infection. Compared to mono-infected patients, co-infected patients were younger and more likely to be male and African-American. For both groups, treatment uptake improved from the DAA/pegylated interferon (PEGIFN)-ribavirin to IFN-free DAA era. One-third of co-infected patients in the IFN-free DAA era required ART switch and nearly all remained virologically suppressed after 6 months. We observed SVR >95% for most patient subgroups including those with co-infection, prior treatment-experience, and cirrhosis. Predictors of access to DAA for co-infected patients included Caucasian race, CD4 count ≥200 cells/mm^3, HIV virologic suppression and cirrhosis. Time to approval of DAA was longest for patients insured by Medicaid, followed by private insurance and Medicare.

Conclusions. DAA therapy has significantly improved access to HCV treatment and high SVR is independent of HIV status. However, in order to realize cure for all, barriers and disparities in access need to be urgently addressed.

Keywords. access to care; antiretroviral therapy; direct-acting antivirals; hepatitis C virus; human immunodeficiency virus.

In the United States, approximately 30% of persons living with human immunodeficiency virus (HIV) are co-infected with hepatitis C virus (HCV), accounting for roughly 1 million individuals [1]. Liver disease is the third leading cause of death in patients with HIV [2], and it is well-established that patients with HIV/HCV co-infection, compared with those HCV mono-infected, experience an accelerated natural history of liver disease with increased morbidity and mortality [3]. Specifically, co-infected patients are less likely to naturally clear HCV infection [4, 5] and have higher rates of progression to fibrosis [6–8], hepatic decompensation [9], and hepatocellular carcinoma [10]. It is therefore imperative to prioritize HCV cure in persons living with HIV to avoid devastating clinical consequences, especially in the era of highly efficacious and tolerable antiretroviral therapy (ART).

The rapid development and implementation of curative HCV therapy with direct-acting antivirals (DAA) is dramatically changing the landscape for treating HIV/HCV co-infected patients. Prior to the approval of DAA, uptake of HCV treatment was low, particularly for co-infected patients; for example, in 1 urban HIV clinic, only 10.5% of patients with HIV/HCV co-infection referred for anti-HCV therapy actually received treatment [11]. Overall sustained virologic response (SVR) rates were lower for co-infected patients, especially in the case of infection with HCV genotype 1 [12–14]. DAA therapy offers >95% SVR for the vast majority of HCV-infected patients, regardless of HIV-1 infection [15]. Importantly, this equal opportunity for HCV cure among mono-infected and HIV/HCV co-infected patients is independent of prior treatment experience and presence of cirrhosis [16, 17].

While the safety and efficacy of HCV therapy has markedly improved, challenges have emerged for HIV/HCV co-infected patients to successfully achieve cure, including treatment uptake limited by drug-drug interactions (DDIs) between antiretrovirals (ARVs) and HCV therapeutics [18, 19], active substance abuse [20], and high rates of insurance denials [21]. The American Association for the Study of Liver Diseases (AASLD)/ Infectious Diseases Society of America (IDSA) HCV treatment and management guidance panel prioritizes HIV/HCV co-infected patients for HCV treatment access and recommends

treatment for all HCV-infected patients, independent of fibrosis score [22]. Yet many insurance companies continue to apply restrictions to access based on stage of liver disease, including in patients with HIV/HCV co-infection.

Our aim was to better understand how the availability of DAA has changed the landscape of treating patients with HCV, and specifically those co-infected with HIV. Our objectives included measuring DAA treatment uptake and SVR at our institution from 2011 to 2015, determining predictors of access, and investigating the role of ARV-DAA interactions and insurance status as barriers to curative HCV treatment. Elucidating the challenges and successes in treating HIV/HCV co-infected patients in the DAA era is urgently needed in order to strategize and advocate for optimized care delivery and outcomes for this special population.

METHODS

Study Population

We performed a retrospective cohort study of HCV- and HIV/HCV-infected adult patients captured in care at our center from 2011 to 2015, reflecting the DAA era. Subjects age 18 years and older with at least 1 clinical encounter in the Duke University Health System between January 1, 2011, and December 31, 2015, with HCV and/or HIV/HCV were ascertained using the Duke Enterprise Data Unified Content Explore (DEDUCE) research tool. DEDUCE is a structured query language interface used to extract data from the electronic health record (EHR) [23].

Data Procurement

Subjects were ascertained using DEDUCE by (1) searching for *International Classification of Diseases, Ninth and Tenth Revision* (ICD-9/-10) codes for HCV and HIV (Supplementary Table 1), then (2) confirming the identified subjects had a clinical encounter at our institution during the study period. For subjects ascertained to be HIV/HCV co-infected, patients were included only if both infections could be confirmed by virologic evidence (HIV-1 enzyme-linked immunosorbent assay: immunoblot or RNA; HCV antibody: RNA or genotype) or in clinical documentation by a provider. For subjects ascertained to be HCV mono-infected, HCV diagnosis was attributed to ICD-9/-10 code without additional confirmation. Prescriptions for DAA were queried to determine treatment numbers for each year, including boceprevir, daclatasvir, ledipasvir/sofosbuvir, paritaprevir/ritonavir/ombitasvir ± dasasbuvir, simeprevir, sofosbuvir, and telaprevir. Additionally, concomitant prescriptions for ribavirin (RBV) and pegylated interferon (PEGIFN)–RBV were queried to determine supplemental therapy to DAA and treatment era, respectively.

Persons with a diagnosis of HCV or HIV/HCV had demographic and clinical data extracted by DEDUCE and supplemented by manual chart review. Data elements of interest for the entire cohort included age, self-identified gender, race, and ethnicity. HIV- and HCV-specific elements for treated patients were determined by manual chart review including CD4 lymphocyte count (cells/mm^3), HIV RNA (copies/mL), ARV regimen, and need for ART switch as documented at the latest visit prior to initiation of DAA; also, HCV genotype, prior HCV treatment experience, presence of cirrhosis and/or hepatitis B virus (HBV) infection. ARV regimens were classified as non-nucleoside reverse transcriptase inhibitor (NNRTI), protease inhibitor (PI), integrase strand transfer inhibitor (INSTI), salvage (if more than 3 antiretroviral agents prescribed), or other. SVR was ascertained by manual chart review and recorded as "yes" or "no"; if no, the reason was documented as virologic breakthrough, relapse, or patient lost to follow-up. A diagnosis of cirrhosis was determined by querying DEDUCE for ICD-9/-10 codes for cirrhosis and sequelae of decompensated cirrhosis (Supplementary Table 1). HBV infection was defined as the presence of HBV surface antigen. Mortality was determined by the date of death, if listed, in the EHR.

Study Definitions

Treatment uptake was defined as the proportion of patients who were prescribed DAA each year per total number of patients with a clinical encounter for HCV that year. Patients who achieved SVR or died during the study period were excluded from the uptake analysis in all subsequent years following SVR or death, respectively. Treatment era was defined as "DAA/PEGIFN-RBV" or "IFN-free DAA." The prior era included patients treated with PEGIFN-RBV along with a single DAA including telaprevir, simeprevir, boceprevir, or sofosbuvir. The "IFN-free DAA" era included patients treated with 1 of the following oral combination DAA regimens: daclatasvir + sofosbuvir, ledipasvir/sofosbuvir, simeprevir + sofosbuvir, or paritaprevir/ritonavir/ombitasvir ± dasabuvir (± ribavirin). Treatment experience was defined as documentation of any HCV therapy prior to the regimen prescribed during the study period. SVR was defined as an undetectable (<lower limit of quantification target not detected) HCV RNA at ≥10 weeks following completion of HCV treatment. HIV viral suppression was defined as HIV RNA <200 copies/mL. "ART switch" was defined as a change in the ARV regimen prior to the initiation of DAA due to a potential DDI, as documented by the provider.

Time to DAA Approval

Records of insurance approval of DAA were available for a subset of patients who had their initial DAA prescription sent to the Duke specialty pharmacy. For these patients, median time to DAA approval was calculated by the number of days between first receipt of the DAA prescription from provider to pharmacy and the date of final approval. For patients missing a final approval date, a date was applied using the median number of days between the approval and initial DAA fill date based on the remainder of the cohort. Insurance status was classified as North Carolina Medicaid, Medicare, or Private.

Statistical Analysis

Descriptive statistics were calculated for demographic and clinical characteristics. Comparisons were performed using chi-square tests or Fisher exact tests for categorical variables and *t* tests or Wilcoxon tests for continuous variables, as appropriate. Univariate logistic regression was performed independently for each candidate covariate (age, gender, race, CD4 count, HIV viral suppression, PI-based ART, presence of cirrhosis and/or HBV infection); each was identified a priori as a potential predictor based on prior studies [24–26]. All covariates with *P* values <.05 were selected into a multivariate logistic regression model for further analysis using backward selection. The point estimation and 2-sided 95% confidence intervals of odds ratios were calculated. All statistical analysis was performed using Statistical Analysis System, version 9.4.

Human Subjects

This retrospective cohort study was conducted under an approved human subjects protocol by the Duke University Medical Center Institutional Review Board.

RESULTS

Treatment Uptake

We identified 9290 patients with HCV mono-infection and 506 with HIV/HCV co-infection seen for an HCV care–related encounter within the Duke University Health System between 2011 and 2015 (Supplementary Table 2). Patients with HIV/HCV co-infection, compared with those with HCV mono-infection, were younger (median age, 58 vs 60 years; *P* < .0001) and more likely to be male (67.0% vs 60.1%; *P* < .0001) and African American (75.9% vs 35.9%; *P* < .0001). Treatment uptake did not significantly differ between African American and Caucasian patients with HCV mono-infection (11.8% vs 12.7%; *P* = .296); however, it was significantly lower in African Americans compared with Caucasians with HIV/HCV co-infection (16.1% vs 33.3%; *P* = .003). Of the 9290 HCV mono-infected patients with at least 1 HCV care encounter during the study period, 1125 (12.1%) received DAA-based therapy. For the 506 HIV/HCV co-infected patients with at least 1 HCV care encounter during the study period, 97/506 (19.2%) received DAA-based therapy. Figure 1 displays DAA-based treatment uptake from 2011 to 2015 for all patients with HCV and HIV/HCV who had an HCV encounter in the health system for each respective year and highlights the more rapid rate of uptake for co-infected patients over time, reaching nearly 40% by 2015.

HIV/HCV Co-infected Patients and ART Switching

HIV/HCV co-infected patients treated with DAA compared with those co-infected and not treated with DAA were more likely to be male (78.4% vs 68.0%; *P* = .049), to be Caucasian (33.0% vs 15.7%; *P* = .001), to be HIV virologically suppressed (95.9% vs 69.2%; *P* < .0001), and to have cirrhosis (36.1% vs 14.9%; *P* < .0001) (Table 1). Nearly a quarter of HIV/HCV co-infected patients not treated with DAA were deceased by the end of the study period compared with co-infected patients treated with DAA (*P* < .0001).

Thirty-one of the 97 co-infected patients (32%) treated with DAA required a switch in their ARV regimen due to predicted DDI with DAA therapy. Figure 2 shows the proportion of patients who switched their ART stratified by baseline ARV regimen. The majority of ART switches occurred on PI-based regimens (60.7% switched), followed by salvage- (33.3%), NNRTI- (27.3%), and INSTI-based (5.6%) regimens. The most common reasons cited by providers for switching ARVs were (1)
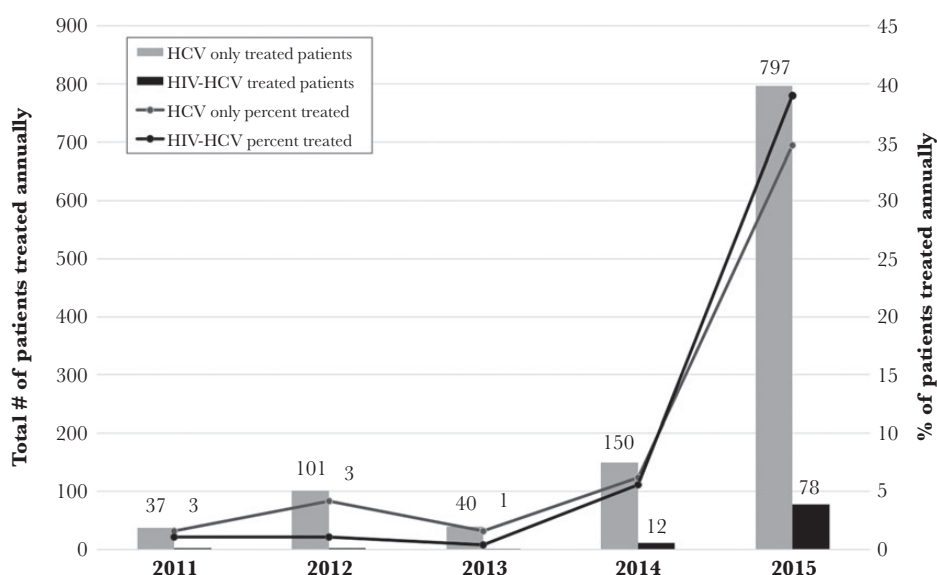

Figure 1. Treatment uptake with direct-acting antiviral therapy for all patients with hepatitis C virus (HCV) and HIV/HCV presenting to care by study year.

Table 1. Demographic and Clinical Characteristics of Patients With HIV/HCV Co-infection Stratified by Treatment Uptake With Direct-Acting Antiviral Therapy

	HIV/HCV		
	Not Treated With DAA (n = 409)	Treated With DAA (n = 97)	P Value
Age, median (IQR), y	58 (53–62)	55 (51–62)	.46
% male	68.0%	78.4%	.049
Race, No. (%)			
African American	322 (78.7)	62 (63.9)	.004
Caucasian	64 (15.7)	32 (33.0)	.001
Other	18 (4.4)	1 (1.0)	N/A
Unknown/declined	5 (1.2)	2 (2.1)	N/A
Ethnicity			
Hispanic, No. (%)	15 (3.7)	1 (1.0)	N/A
Non-Hispanic, No. (%)	384 (93.9)	94 (96.9)	.33
Unknown/declined, No. (%)	10 (2.4)	2 (2.1)	N/A
CD4 count, median (IQR)	411.5 (230–718)	561.5 (403–910)	<.0001
HIV viral suppression, No. (%)			
<200 copies/mL	283 (69.2)	93 (95.9)	<.0001
≥200 copies/mL	114 (27.9)	3 (3.1)	<.0001
Unknown	12 (2.9)	1 (1.0)	N/A
ARV regimen,[a] No. (%)			
PI	115 (28.1)	28 (28.9)	.90
NNRTI	81 (19.8)	33 (34.0)	.004
INSTI	106 (25.9)	19 (19.6)	.23
Salvage	75 (18.3)	12 (12.4)	.18
Other	4 (1.0)	0 (0)	N/A
No ARV regimen, No. (%)			
Elite controller	4 (1.0)	5 (5.1)	.02
Poor adherence	24 (5.9)	0 (0)	.007
ARV switched	---	31 (32.0)	N/A
% Cirrhosis	14.9	36.1	<.0001
% HBV infection	2.7	6.2	.11
% Mortality at study end	23.2	0	<.0001

Abbreviations: ARV, antiretroviral therapy; CD4, cluster of differentiation 4; DAA, direct-acting antiviral therapy; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; NNRTI, non-nucleoside analogue reverse transcriptase inhibitor; PI, protease inhibitor.

[a]Original antiretroviral regimen prior to any switching to accommodate DAA.

pharmacologic boosting agent, (2) increased tenofovir exposure, and (3) DDI between efavirenz and DAA. Of note, 20/31 co-infected patients (64.5%) switched to an INSTI-based ARV regimen. Of the 31 patients requiring ART switch, 29 were HIV virologically suppressed at 6 months postswitch. One patient's HIV RNA was 202 copies/mL at 6 months (though undetectable at 1 year postswitch), and the other patient did not have a repeat viral load during the remainder of the study period.

SVR by Treatment Era

During the study period, 185/9290 (2.0%) of patients with HCV mono-infection and 7/506 (1.4%) of HIV/HCV co-infected patients were prescribed a DAA/PEGIFN-RBV regimen. The SVR in this era was 62.7% (116/185) for patients with HCV mono-infection and 85.7% (6/7) for those with HIV/HCV co-infection. Comparatively, 940/9174 (10.2%) of mono-infected and 90/500 (18.0%) of co-infected patients were treated with IFN-free DAA regimens. The SVR in this era was 90.9% (854/940) for HCV mono-infected patients and 96.7% (87/90) for HIV/HCV co-infected patients (Table 2). In the IFN-free DAA era, 383/436 (87.8%) patients with HCV mono-infection and cirrhosis achieved SVR. For HIV/HCV co-infected patients with cirrhosis, 30/32 (93.8%) achieved SVR. The reason for treatment failure in all patients was relapse, with the exception of 1 HCV mono-infected patient in the IFN-free DAA era who was lost to follow-up.

Predictors of Access to DAA in HIV/HCV Co-infected Patients

We constructed a multivariable logistic regression model comprised of demographic and clinical characteristics to determine predictors of access to DAA for patients with HIV/HCV co-infection. As shown in Table 3, Caucasian race, CD4 count ≥200 cells/mm³, HIV viral suppression, and the presence of cirrhosis were identified as predictors of access to DAA for co-infected patients. Age, gender, PI-based ART, and HBV infection did not play a significant role in influencing access to DAA. Supplementary Table 3 lists barriers to initiation of DAA for treatment of HCV as documented by the provider for all 409 co-infected patients not yet prescribed DAA. Thirty-seven percent of co-infected patients were undergoing evaluation for DAA at the close of the study period, 31% were not yet evaluated, and nearly 25% not treated with DAA died over the course of the study period. As documented by providers, specific barriers limiting access to DAA for HIV/HCV co-infected patients included active mental health and/or substance abuse issues, newly diagnosed or uncontrolled HIV, other medical comorbidities. For those who had been referred to an infectious diseases or hepatology subspecialist for DAA initiation, the majority of patients at the end of the study period were awaiting their appointment, results of HCV genotype or liver fibrosis assessment, and/or HIV viral suppression after ART switch.

Time to DAA Approval by Insurance Status

For patients who had a DAA prescription sent to the Duke Specialty Pharmacy, insurance status and time to approval of DAA were available for analysis. Figure 3 shows median time to approval of DAA in days stratified by infection and insurance status for 508 patients with HCV mono-infection and 40 with HIV/HCV co-infection. Median times to approval for patients with HCV compared with HIV/HCV were 23 vs 29 days for private insurance (P = .321), 12 vs 21 days for Medicare (P = .412), and 52 vs 40.5 days for NC Medicaid (P = .769). Time to approval differed by insurance status for HCV mono-infected patients (NC Medicaid vs private, P = .0002; NC Medicaid vs Medicare, P < .0001; Medicare vs private, P = .001), however, not significantly for HIV/HCV co-infected patients (NC Medicaid vs private, P = .300; NC Medicaid vs Medicare, P = .378; Medicare vs private, P = .544).
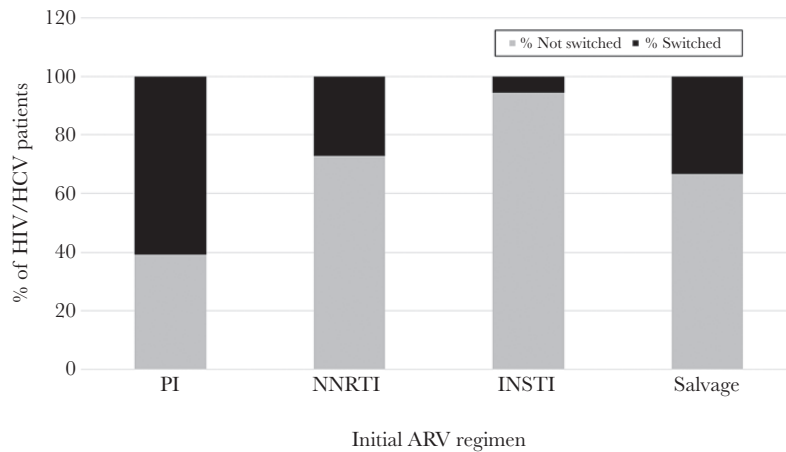
Figure 2. Antiretroviral switching prior to initiation of direct-acting antiviral therapy for hepatitis C virus (HCV) treatment in patients with HIV/HCV.

DISCUSSION

DAAs are safer, better tolerated, and more efficacious than interferon-based therapies. Our single-center findings highlight the impact of DAAs on access to HCV therapy and cure for patients with HCV mono- and HIV/HCV co-infection, with HIV/HCV co-infected patients realizing a substantial increase in access to cure. We found that treatment uptake has markedly improved from the DAA/PEGIFN-RBV to IFN-free DAA era, and loss to follow-up was very low. However, access to cure remains much lower than desired for both mono- and co-infected populations, especially given SVR rates of >95% for nearly all patient groups. We identified a multitude of barriers limiting DAA access for co-infected patients, which reflect bias and disparities that need confronting so that an HCV cure can be realized for all.

In our cohort, HIV/HCV co-infected patients were younger and more likely to be male and African American than HCV mono-infected patients, although these demographics were not different between patients treated with DAA and those not treated. This suggests an alternate etiology for the higher treatment uptake in co-infected vs mono-infected patients in the IFN-free DAA era. One possibility is that co-infected patients are already engaged in care for a chronic infection and more readily identified for HCV treatment. In addition, the increased liver-related morbidity and mortality in HIV/HCV co-infection may have been a strong motivator for DAA initiation by both patient and provider.

Overall, treatment uptake for HIV/HCV co-infected patients at our institution is low (<20% of the total study cohort), which is especially problematic given the accelerated natural history of liver disease [2, 3]. Per AASLD/IDSA HCV treatment guidance, a well-recognized challenge when treating HCV in patients co-infected with HIV is the potential for DDIs between DAA and ART [22]; however, this did not pose a significant barrier to achieving SVR in our cohort. Thirty-two percent of our HIV/HCV co-infected patients required ART switch, which is a lower proportion than that reported for other real-world cohorts [19, 27]. Importantly, 30/31 (96.8%) co-infected patients requiring ART switch achieved SVR, which was similar to those not switched (96.9%) in our cohort. This is in contrast to the Johns Hopkins HIV/HCV cohort, which demonstrated a lower SVR rate in co-infected patients requiring ART switch compared with those who remained on their baseline ARV regimen [28]. Our findings suggest that the need for ART switch to safely tolerate DAA should not serve as a barrier to initiation of curative HCV therapy in patients co-infected with HIV/HCV.

In the IFN-free DAA era, HIV/HCV co-infected patients in our cohort achieved a high rate of SVR. This study adds to the growing body of literature reporting that co-infected patients in a real-world setting with treatment experience, cirrhosis, and/

Table 2. Treatment Success in Patients With HCV and HIV/HCV Treated in the Era of Interferon-Free Direct-Acting Antivirals

	IFN-Free DAA Era		
	HCV (n = 940), No. (%)	HIV/HCV (n = 90), No. (%)	P Value
SVR, all genotypes	854 (90.9)	87 (96.7)	.074
SVR, by genotype			
1	95/98 (96.9)	12/12 (100)	1.00
1a	449/463 (97.0)	47/49 (95.9)	.659
1b	197/203 (97.0)	19/20 (95.0)	.487
2	53/54 (98.2)	2/2 (100)	N/A
3	47/47 (100)	1/1 (100)	N/A
4	12/13 (92.3)	1/1 (100)	N/A
6	1/1 (100)	N/A	N/A
Unknown	0/61 (0)	5/5 (100)	N/A
SVR, by condition			
Cirrhosis	383/436 (87.8)	30/32 (93.8)	.566
Tx-experienced	196/211 (92.9)	3/3 (100)	N/A
Cirrhosis/Tx-experienced	121/133 (91.0)	1/1 (100)	N/A

Abbreviations: DAA, direct-acting antivirals; HCV, hepatitis C virus; HIV, human immunodeficiency virus; SVR, sustained virologic response at ≥10 weeks after therapy completion; Tx, treatment.

Table 3. Stepwise Multivariable Logistic Regression Model Assessing Predictors of HCV Treatment With Direct-Acting Antiviral Therapy in Patients With HIV/HCV

| | Likelihood HIV/HCV Patient Treated With DAA | | | |
| | Univariate Analysis | | Multivariate Analysis | |
	OR	95% CI	OR	95% CI
Age <55 y	0.56	0.35–0.89	---	---
Male	1.75	1.02–3.00	---	---
Caucasian race	2.87	1.71–4.82	2.68	1.54–4.68
CD4 count ≥200 cells/mm^3	4.74	2.00–11.21	3.65	1.41–9.43
HIV viral load <200 copies/mL	11.76	3.64–37.98	6.64	1.99–22.16
PI-based ART	1.03	0.62–1.72	---	---
Cirrhosis	3.08	1.84–5.16	3.12	1.77–5.51
HBV infection	1.89	0.64–5.56	---	---

Abbreviations: ART, antiretroviral therapy; CD4, cluster of differentiation 4; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; OR, odds ratio; PI, protease inhibitor.

or requiring ART switch can realize a cure rate on par with that reported in clinical trials, and similar to that achieved by HCV mono-infected patients [15–17]. The high mortality observed in the untreated group (25%) highlights the gravity of HIV/HCV co-infection, especially in patients with poorly controlled HIV, and identifies a subgroup of HIV-infected patients who could benefit from a more personalized approach to HIV management.

Likelihood of DAA access for co-infected patients in our cohort increased with Caucasian race, CD4 count ≥200 cells/mm^3, HIV viral suppression, and the presence of cirrhosis. Racial disparity in accessing HCV treatment existed in the IFN era, which could be explained by providers less frequently offering therapy due to poorer clinical outcomes with IFN therapy in African American compared with Caucasian patients, at least in part attributed to a higher prevalence of genotype 1 and the presence of unfavorable interferon lambda 4 polymorphism in blacks [20]. However, this racial disparity has persisted into the DAA era [29], suggesting that nonmedical barriers may hinder black patients in accessing curative HCV therapy. Such structural obstacles are likely multifactorial and interrelated [30, 31]. As seen with racial disparity challenging cancer care access and outcomes [32], it is possible that more African Americans in our cohort were insured by Medicaid, which has the strictest approval criteria for HCV treatment with DAA compared with Medicare or private insurance [21, 33, 34], thus further limiting treatment uptake for black patients.

This study has several limitations, including the single clinical site and retrospective nature. The study population was identified by an internal research tool (DEDUCE), which primarily queries the EHR by ICD-9/-10 codes. Given the smaller sample size of HIV/HCV co-infected patients (and that this population was our study focus), we confirmed both infections by direct virologic evidence or confirmation in clinical documentation by a provider; however, this was not done for the 9290 patients identified by DEDUCE as HCV mono-infected. Treatment uptake for both mono- and co-infected patients is likely underestimated given that we included patients with any clinical encounter at our institution from 2011 through 2015. Duke is a tertiary referral center for a large catchment area; thus our cohort included patients who were seen at Duke only once for subspecialty consultation as an inpatient or outpatient encounter. Overall treatment numbers were particularly low in the DAA/PEGIFN-RBV era, which may reflect patient and provider anticipation of all oral combination therapy, but also the use of clinical prescriptions to identify patients receiving HCV therapy did not include patients at the institution who were enrolled in clinical trials of DAA therapies, which represents a significant number of patients with both HCV mono-infection and HIV/HCV co-infection. Another limitation is that we
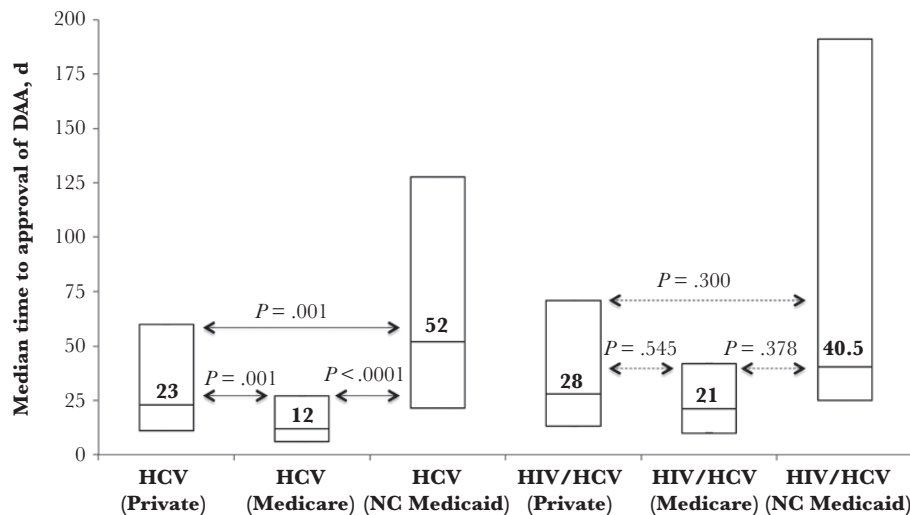

Figure 3. Time to approval of direct-acting antiviral therapy for patients with hepatitis C virus (HCV) and HIV/HCV stratified by insurance status.

only had access to the insurance status of patients with DAA prescriptions through the Duke specialty pharmacy, which was less commonly used for HIV/HCV co-infected patients. Furthermore, this did not consistently include information on insurance denials, so time to approval of DAA was used as a surrogate.

CONCLUSIONS

The introduction of DAA therapy has significantly improved access to HCV treatment, and SVR is high in HIV/HCV co-infected patients. Meanwhile <20% of all HCV-infected patients at Duke have received curative therapy. We identify several barriers to access, including racial disparity, possible bias against treating patients with substance abuse, and strict Medicaid criteria for funding DAA, all of which need to be urgently addressed so that HCV cure can be realized for all.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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