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Barriers to hepatitis C direct-acting antiviral therapy among HIV/hepatitis C virus-coinfected persons

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Abstract

Background and Aim: Direct-acting antivirals (DAAs) have increased hepatitis C virus (HCV) treatment opportunities for vulnerable HIV/HCV coinfected persons. The aim of this study was to identify the frequency of and potential barriers to DAA prescription in HIV/HCV patients during the first few years of DAA availability in the United States.

Methods: The AIDS Healthcare Foundation electronic medical record system was queried to identify all HCV viremic HIV-infected patients in care at AIDS Healthcare Foundation Healthcare centers in January 2015–August 2017 and compare characteristics by receipt of a DAA prescription. Multivariate logistic regression analyses were conducted to examine factors associated with DAA prescription.

Results: Of 826 eligible patients, 355 (43%) were prescribed a DAA; among those not prescribed a DAA, 301 (64%) had well-controlled HIV (HIV RNA ≤ 200 copies per mL). In multivariate logistic regression analysis, patients with a history of substance use (odds ratio [OR], 0.51 [95% confidence interval 0.35–0.73]) or on select HIV antiretroviral regimens were less likely to be prescribed a DAA. Those who had well-controlled HIV (OR, 5.03 [3.06–8.27]), CD4 + T cell count >200 cells per mm^3 (OR, 1.85 [1.04–3.30]), estimated glomerular filtration rate >60 mL/min/1.73 m^2 (OR, 3.32 [1.08–10.15]), or established care prior to January 2015 (OR, 1.57 [1.08–2.29] were more likely to be prescribed a DAA.

Conclusions: In addition to lack of HIV suppression, select antiretroviral regimens, substance use, and kidney disease appeared to limit DAA prescription in the early interferon-free DAA era. Many were not prescribed DAAs despite HIV suppression. Further research is needed to determine if the observed associations persist today.

Introduction

It is estimated that hepatitis C virus (HCV) affects 2–15% of people living with HIV, an estimated 2.75 million people, worldwide.[1] HIV/HCV-coinfected patients suffer from more liver-related morbidity and mortality, extrahepatic end organ dysfunction, and all-cause mortality than HCV-monoinfected patients,[2,3] even in patients taking antiretroviral therapy.[4–7] For these reasons, the World Health Organization (WHO) Guidelines for HCV treatment recommend prioritizing treatment among HIV/HCV-coinfected persons.[8]

In October 2014, the Food and Drug Administration approved sofosbuvir/ledipasvir for the treatment of HCV, marking the start of the availability of single tablet direct-acting antiviral (DAA) regimens free of interferon. The availability of interferon-free regimens transformed HCV treatment for HIV/HCV-coinfected patients because of their high efficacy, minimal adverse events, and short course of treatment.[9–11] Moreover, early studies showed that the outcomes of treatment with DAA regimens in HIV/HCV-coinfected patients are similar to patients with HCV monoinfection, although more recent data suggest a possible impact of HIV coinfection on sustained virologic response rates in real world settings.[10,12–15]

Although some studies have identified barriers to DAA prescription in HCV-monoinfected patients, data are limited on the initial barriers to DAA prescription among HIV/HCV-coinfected patients in the United States (US). Identifying the key early barriers to DAA prescription may shed light on the ongoing barriers to HCV treatment in this priority population as DAA therapy is disseminated globally to achieve the WHO HCV elimination targets.[16] The purpose of this study was to (i) estimate the frequency of DAA prescription and (ii) identify barriers to HCV treatment in the early interferon-free DAA era in a geographically, socioeconomically, and ethnically diverse real-world cohort of HIV/HCV-coinfected patients.

Methods

Study population. AIDS Healthcare Foundation (AHF) operates a network of outpatient HIV clinics in 15 US states. The AHF electronic medical record (EMR) system (Centricity Practice Solution, GE Healthcare, Chicago, IL, USA) was queried for patients with a history of HCV and HIV coinfection at all AHF US healthcare centers from January 1, 2011, to August 8, 2017. HIV and HCV status were defined by International Statistical Classification of Diseases and Related Health Problems 9th Revision (ICD-9) and/or 10th Revision (ICD-10) codes. Patients with an HIV diagnosis (ICD-9 042/ICD-10 B20) and at least one HCV ICD-9 or ICD-10 code was selected. Queried ICD codes for HCV included all codes for acute, chronic, or unspecified duration of hepatitis C infection: 070.41, 070.44, 070.51, 070.70, 070.71, B17.11, B17.10, B19.20, B19.21, or Z22.52. All patients included in the study were ≥18 years old.

January 1, 2015, was defined as the start of the study period, as interferon-free DAA regimens were routinely available after this date. Patients were excluded if (i) there was no laboratory evidence of HCV infection defined as no detectable HCV ribonucleic acid (RNA) recorded in the EMR at any time; (ii) they were not actively participating in clinical care at AHF during the study period, defined as having no laboratory data of any kind in the EMR between January 1, 2015, and August 8, 2017; (iii) they were treated for HCV with a DAA as part of a clinical trial (to focus the analysis on "real world" HCV DAA prescription practices); (iv) they were prescribed a DAA before the start of the study (January 1, 2015); and (v) their HCV RNA levels before January 1, 2015, were undetectable, and all HCV RNA levels after January 1, 2015, were undetectable or missing (to exclude those who would not have been considered eligible for HCV treatment during the study period).

Definition of treatment groups and baseline date. Patients were considered to be part of the DAA prescription group if they had a record of a prescription for a DAA in the EMR with an order date on or after January 1, 2015. The DAAs included sofosbuvir (SOF), sofosbuvir/ledipasvir (SOF/LDV), ombitasvir/paritaprevir/ritonavir (OBV/PTV/r) + dasabuvir (DSV), daclatasvir (DCV), simeprevir (SMV), elbasvir/grazoprevir (EBR/GZR), and sofosbuvir/velpatasvir (SOF/VEL). Baseline date was defined as the date of DAA prescription for patients who received a DAA prescription or the last date of follow up (i.e. last known opportunity for a DAA prescription) for patients who did not receive a DAA prescription.

Variables of interest. The following variables were abstracted from the EMR: age at baseline, sex, race/ethnicity, HIV viral load, CD4 + T cell count, HIV antiretroviral regimen, insurance status/type, HCV genotype, HCV treatment history, time engaged in care at AHF prior to the study period, comorbidities (history of alcohol and other substance use, diabetes, hypertension, and hepatitis B infection), history of decompensated liver disease, creatinine level, and indicators of liver health (albumin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, and platelet count). ICD-9 codes were used to identify comorbidities and history of decompensated liver disease (Table S1). For all laboratory values except HCV RNA and genotype, the most recent laboratory value in the system up to 1 year prior to baseline was defined as the baseline measurement. For HCV RNA and HCV genotype, the most recent result at any time prior to baseline was used. HIV RNA level was categorized as ≤200 or >200 copies per mL, and patients with viral load ≤200 were considered to have well-controlled HIV. Time engaged in care at AHF prior to start of the study was calculated as the number of years between the very first laboratory value available in the AHF EMR for a patient and January 1, 2015 (e.g., ≤0 year implies the patient engaged in care at AHF on or after January 1, 2015, and >10 years implies the patient had been receiving care at AHF since before January 1, 2005). Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation.[17] The fibrosis-4 index and aspartate aminotransferase to platelet ratio index were calculated and used as surrogate measures of fibrosis using the most recent set of lab values available.[18,19] For statistical analyses, advanced fibrosis was defined as fibrosis-4 score >3.25. Antiretroviral regimens were categorized based on nucleoside backbone (tenofovir disoproxil fumarate [TDF], tenofovir alafenamide [TAF], or abacavir [ABC]/non-TAF/non-TDF) and class (integrase strand transfer inhibitor [INSTI], protease inhibitor [PI], non-nucleoside reverse transcriptase inhibitor [NNRTI]), as well as cobicistat (COBI)-containing or not, considering potential for DAA interactions: INSTI + ABC, INSTI + TDF, INSTI + TAF, INSTI + TDF + COBI, INSTI + TAF + COBI, PI + TDF, PI + TAF, PI + Other (non-TAF/non-TDF), NNRTI + TDF, NNRTI + TAF, NNRTI + Other (non-TAF/non-TDF), and no antiretroviral (ARV) regimen. For the few patients on multiple agents from multiple classes (e.g. PI + NNRTI ± other or NNRTI + INSTI ± other), they were assigned the class with the greatest potential for drug interaction, with the hierarchy being PI, then NNRTI, then INSTI (i.e. PI for the first example and NNRTI for the second example). Insurance type was classified as Medicaid, Medicare, Ryan White, private, and unknown/none.

Statistical approach. Descriptive statistics (mean with standard deviation, median with interquartile range, and frequency count with percent) were reported for baseline demographic and clinical characteristics by DAA prescription and overall. Two-sample t test, χ^2 test, or Fisher's exact test, as appropriate, were used for the comparison between DAA prescription groups. Multivariable logistic regression analyses were conducted to examine the association of variables with DAA prescription. Covariates considered in the multivariable model included alanine aminotransferase, age, HIV viral load, advanced fibrosis status, eGFR, CD4 + T cell count, insurance status, sex, race/ethnicity, substance use history, alcohol disorder, ARV regimen, and entry into care at AHF before or after January 2015 (the start of the study period and greater availability of DAAs). In addition, subgroup analyses were conducted restricting to the subset of patients with HIV viral load ≤200 copies per mL at baseline. Prespecified interaction analyses were conducted to examine the interaction effects on DAA prescription between (i) substance use and race/ethnicity and (ii) substance use and insurance, hypothesizing that provider bias, patient-driven engagement (or lack of engagement) in HCV treatment, and payor restrictions might modify prescription of DAAs. Significant interaction effects

were included in the final models for DAA prescription. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

Patients (2,719) with a history of HCV and HIV infection seen at an AHF clinic between January 1, 2011, and August 8, 2017, were identified from the initial data extraction. After sequentially excluding patients without a laboratory result for HCV RNA at any time available in the EMR ($n = 849$), patients with only undetectable HCV RNA results available in the EMR ($n = 441$), patients not actively involved in care during the study period ($n = 500$), patients treated with a DAA as part of a research study ($n = 10$), patients prescribed a DAA regimen prior to January 1, 2015 ($n = 42$), and patients whose last HCV RNA prior to January 1, 2015, was undetectable, without evidence of relapse or re-infection during study period ($n = 51$), 826 patients were eligible for the analysis (Fig. 1). Patients received care at AHF Healthcare Centers in 13 states/districts; the majority of patients received care in Florida (37%) and California (36%). The cohort was diverse, including 40% Black/African–American, 38% White, and 18% Hispanic patients. More than a third (42%) had Medicaid or Ryan White coverage.

Differences in baseline characteristics by direct-acting antiviral prescription. Among the 826 patients eligible for analysis, 355 (43%) were prescribed a DAA between January 1, 2015, and August 8, 2017. Some patients were prescribed more than one DAA, sequentially, likely because of insurance restrictions requiring a change in the DAA, or a change in provider preference. Of the first DAA prescribed, 76% were SOF/LDV ± RBV, 8% SOF/VEL ± RBV, 6% EBR/GZR, 5% OBV/PTV/r + DSV ± RBV, 3% SOF ± RBV, 3% SOF/DCV, and <1% OBV/PTV/r + RBV. For the first DAA prescribed, the number of prescriptions for each regimen during the study period is presented in Figure 2. Three-fourths of the total cohort (76%) demonstrated HIV control with a HIV viral load ≤200 copies per mL, including 301 of 471 (64%) not prescribed a DAA. Among patients that were HIV viremic (viral load >200 copies per mL), only 27 out of 180 (15%) received a prescription for a DAA.

Comparisons of the demographics and baseline characteristics between the DAA-prescribed and not prescribed groups are summarized in Table 1. No differences in race/ethnicity, HCV viral load, or HCV genotype were observed between the groups. Those prescribed a DAA were more likely to have previously been treated with interferon for HCV (8% *vs* 3%, $P < 0.01$). There was a higher proportion of patients with eGFR ≤60 mL/min/1.73 m^2 in the group not prescribed a DAA (4% *vs* 1%, $P = 0.03$).

Approximately half of the patients with either private insurance or Medicare were treated with a DAA (51% and 50%, respectively). In contrast, only one-third of Medicaid and Ryan White patients were prescribed a DAA (39% and 36%, respectively). A history of substance use was more common among patients that did not receive a DAA prescription when compared with patients that received a DAA prescription (42% *vs* 26%, $P < 0.01$). There

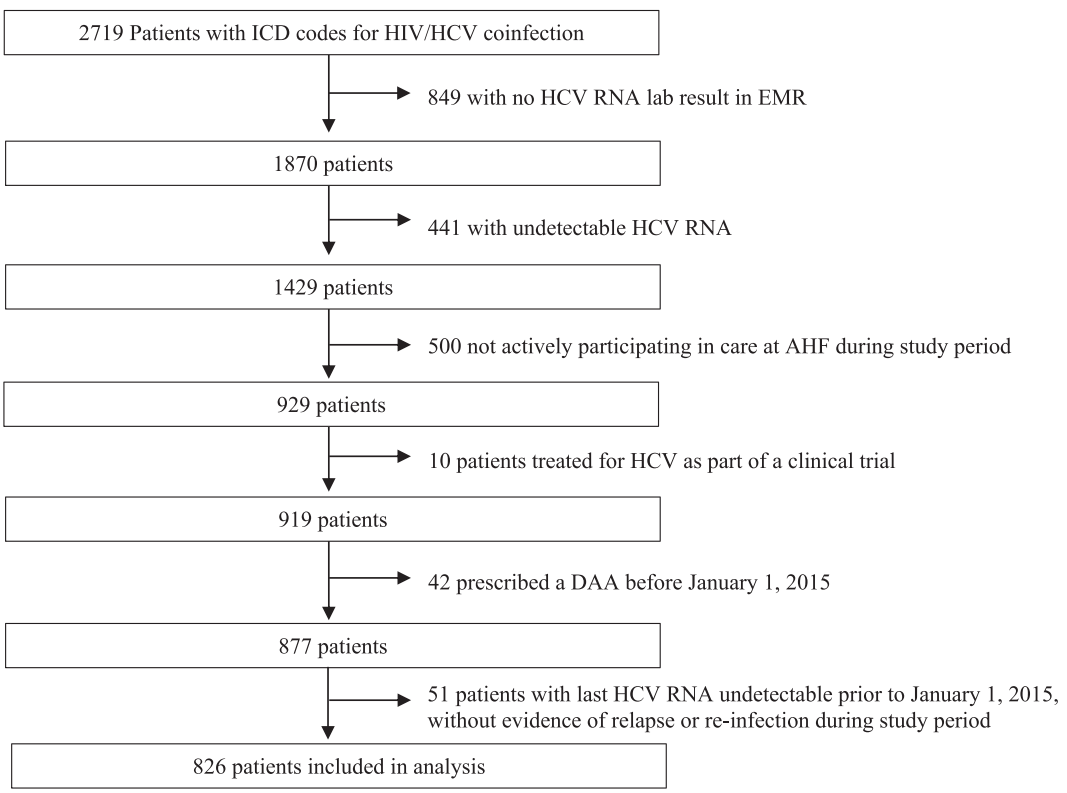

Figure 1 Study eligibility. AHF, AIDS Health Foundation; DAA, direct-acting antiviral; EMR, electronic medical record; HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICD, International Classification of Diseases.

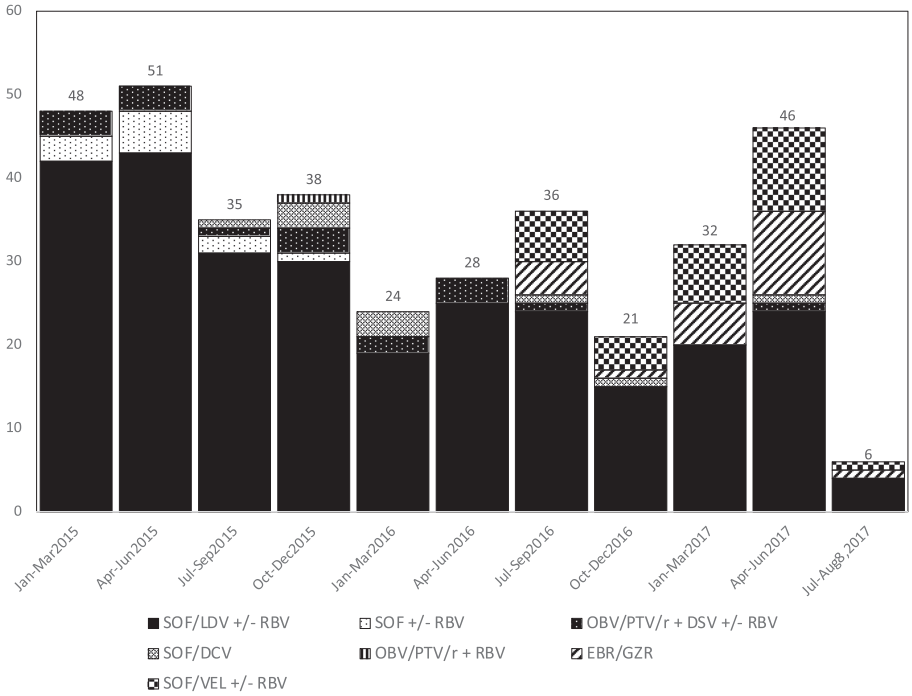

Figure 2 Total number and type of HCV DAA prescriptions at AIDS Healthcare Foundation over time (by quarter, January 2015–August 2017). DAA, direct-acting antiviral; DCV, daclatasvir; DSV, dasabuvir; EBR, elbasvir; GZR, grazoprevir; HCV, hepatitis C virus; LDV, ledipasvir; OBV, ombitasvir; PTV/r, paritaprevir/ritonavir; RBV, ribavirin; SOF, sofosbuvir; VEL, velpatasvir. ■, SOF/LDV ± RBV; ▩, SOF/DCV; ▪, SOF/VEL ± RBV; ⊡, SOF ± RBV; ▯, OBV/PTV/r + RBV; ▪, OBV/PTV/r + SDV ± RBV; ◪, EBR/GZR.

were no significant differences in the prevalence of alcohol use disorders between groups. The distribution of ARV regimens was significantly different between the groups (see Table 1).

Predictors of receiving a direct-acting antiviral prescription. The final model for the overall cohort is presented in Figure 3. Interaction terms for substance use and race and substance use and insurance were not included in the final model as no significant interaction effects were observed in interaction analyses.

Patients with well-controlled HIV (odds ratio (OR), 5.03 [95% confidence interval 3.06–8.27], $P < 0.0001$), and a CD4 + T cell count >200 cells per mm^3 (OR, 1.85 [1.04–3.30], $P = 0.036$), eGFR >60 (OR, 3.31 [1.08–10.15], $P = 0.036$), or established in care at AHF prior to January 2015 (OR, 1.57 [1.08–2.29], $P = 0.019$) were more likely to be prescribed a DAA. ARV regimen was significantly associated with DAA prescription (overall P value <0.0001). Characteristics associated with lower odds of being prescribed a DAA included having a history of substance use (OR, 0.51 [0.35–0.73], $P < 0.001$) and being on select ARV regimens (compared with INSTI + ABC) including: INSTI + TAF (OR, 0.18 [0.08–0.39]), INSTI + TDF + COBI (OR, 0.46 [0.21–0.98]), INSTI + TAF + COBI (OR, 0.36 [0.19–0.67]), NNRTI + TAF (OR, 0.24 [0.08–0.68]), PI + other (non-TAF/non-TDF) (OR, 0.49 [0.25–0.93]), PI + TDF (OR, 0.41 [0.22–0.77]), PI + TAF (OR, 0.24 [0.10–0.57]), and no ARV regimen (OR, 0.15 [0.04–0.61]). Restricting the analysis to HIV-suppressed patients, we found similar associations as in the overall cohort, with an additional significant interaction effect of history of substance use and race on DAA prescription (Fig. S1).

Discussion

In this diverse cohort study of HIV/HCV-coinfected patients, we found that less than half of the patients received a prescription for a DAA during the study period (January 2015–August 2017). The rate of HCV DAA prescription (43%) was higher than two published estimates from studies of HIV/HCV-coinfected cohorts conducted from 2014 to 2015 (19% and 23%) and lower than two recently reported studies from 2014 to 2016 and 2014 to 2017 (51% and 60%).[20–23] The higher rates of prescription seen in the studies conducted in more recent years may be because of expanded DAA options, greater provider-driven uptake of DAAs, increased patient demand for treatment, and changes in payor-imposed restrictions (i.e. fewer restrictions) over time.

Poor HIV control was one of the strongest predictors of not being prescribed a DAA. However, nearly two-thirds (64%) of patients that were not prescribed a DAA had well-controlled HIV and would have been ideal candidates for HCV treatment from an adherence standpoint, as they had already demonstrated the ability to adhere to a daily therapy (antiretrovirals).

Our finding that a history of substance use was associated with a decreased likelihood of DAA prescription is consistent with previous studies.[23,24] The decreased likelihood of DAA prescriptions among patients with a history of substance use might reflect provider reluctance as a result of concern about non-adherence,

Table 1 Baseline characteristics

Variable	All subjects $N = 826$	No DAA $N = 471$	DAA $N = 355$	*P* value
Age[†]	49.2 ± 11.1	48.1 ± 11.4	50.7 ± 10.7	**<0.01**
Sex: Male	672 (81)	374 (79)	298 (84)	0.34
Race/ethnicity				
Black/AA	334 (40)	188 (40)	146 (41)	0.45
White	318 (38)	190 (40)	128 (36)	
Hispanic[‡]	150 (18)	78 (17)	72 (20)	
Other/unknown	24 (3)	15 (3)	9 (3)	
HIV viral load ≤200 copies per mL	625 (76)	301(64)	324(91)	**<0.01**
Missing	21 (3)	17(4)	4(1)	
CD4 + T cell count >200 cells per mm^3	703 (85)	377 (80)	326 (92)	**<0.01**
Missing	30 (4)	24 (5)	6 (2)	
HIV Antiretroviral regimen				
INSTI + ABC	166 (20)	76 (16)	90 (25)	**<0.0001**
INSTI + TDF	99 (12)	43 (9)	56 (16)	
NNRTI + TDF	91 (11)	45 (10)	46 (13)	
INSTI + TDF + COBI	50 (6)	31 (7)	19 (5)	
INSTI + TAF	54 (7)	40 (8)	14 (4)	
NNRTI + TAF	22 (3)	15 (3)	7 (2)	
INSTI + TAF + COBI	85 (10)	57 (12)	28 (8)	
PI + Other (non-TAF/non-TDF)	77 (9)	40 (8)	37 (10)	
PI + TDF	89 (11)	58 (12)	31 (9)	
PI + TAF	45 (5)	35 (7)	10 (3)	
NNRTI + Other (non-TAF/non-TDF)	18 (2)	5 (1)	13 (4)	
No ARV regimen	30 (4)	26 (6)	4 (1)	
Insurance category				
Private	193 (23)	95 (20)	98 (28)	**<0.01**
Medicaid	264 (32)	161 (34)	103 (29)	
Medicare	185 (22)	92 (20)	93 (26)	
Ryan White	81 (10)	52 (11)	29 (8)	
Unknown/none	103 (12)	71 (15)	32 (9)	
HCV Genotype				
1	536 (65)	284 (60)	252 (71)	0.74
2	39 (5)	22 (5)	17 (5)	
3	44 (5)	25 (5)	19 (5)	
4	16 (2)	8 (2)	8 (2)	
6	1 (0.1)	0 (0)	1 (0.1)	
1/6	1 (0.1)	0 (0)	1 (0.1)	
Missing	189 (23)	132 (28)	57 (16)	
Prior HCV treatment with interferon	43 (5)	16 (3)	27 (8)	**<0.01**
Time engaged in clinical care at AHF prior to start of the study				
≤0 year[§]	277 (34)	181 (38)	96 (27)	**<0.01**
0–5 years	287 (35)	155 (33)	132 (37)	
5–10 years	153 (19)	80 (17)	73 (21)	
>10 years	109 (13)	55 (12)	54 (15)	
Comorbidities				
History of alcohol use disorder	64 (8)	40 (8)	24 (7)	0.36
Decompensated liver disease	9 (1)	8 (2)	1 (0.1)	**0.05**
Diabetes	75 (9)	40 (8)	35 (10)	0.50
Hepatitis B	52 (6)	29 (6)	23 (6)	0.85
Hypertension	261 (32)	147 (31)	114 (32)	0.78
History of substance use	290 (35)	197 (42)	93 (26)	**<0.01**
Indicators of liver health				
Albumin (g/dL)[¶]	4.2 (3.9–4.4)	4.2 (3.9–4.4)	4.3 (4.0–4.5)	**<0.01**
Missing	42 (5)	27 (6)	15 (4)	
ALT (U/L)[¶]	44 (27–74)	39 (23–69)	50 (33–84)	0.14
Missing	24 (3)	17 (4)	7 (2)	

(Continues)

Table 1 (Continued)

Variable	**All subjects** $N = 826$	**No DAA** $N = 471$	**DAA** $N = 355$	***P* value**
APRI Score[¶]	0.49 (0.31–0.93)	0.44 (0.28–0.87)	0.55 (0.35–0.99)	0.58
Missing	34 (4)	24 (5)	10 (3)	
AST U/L[¶]	43 (29–71)	39 (26–68)	46 (32–74)	0.62
Missing	25 (3)	17 (4)	8 (2)	
Bilirubin (Total) (mg/dL)[¶]	0.4 (0.3–0.7)	0.4 (0.3–0.6)	0.4 (0.3–0.7)	0.16
Missing	51 (6)	34 (7)	17 (5)	
Advanced Fibrosis (FIB-4 > 3.25)	127 (15)	74 (16)	53 (15)	0.65
Missing	34 (4)	24 (5)	10 (3)	
eGFR ≤ 60 mL/min/1.73 m^2	23 (3)	18 (4)	5 (1)	**0.03**
Missing	35 (4)	23 (5)	12 (3)	
Platelets $\times 10^3/\mu L$[¶]	220 (174–265)	221 (171–266)	219 (175–260)	0.86
Missing	26 (3)	20 (4)	6 (2)	

[†]Variable reported as Mean ± standard deviation.
[‡]Includes Hispanic/Black participants.
[§]Started engagement in clinical care at AHF on or after January 1, 2015.
[¶]Variable reported as: median, (quartile 1–3).
Statistically significant values are bolded. AA, African–American; ABC, abacavir; AHF, AIDS Health Foundation; ALT, alanine aminotransferase; APRI, aspartate aminotransferase to platelet ratio index; AST, Aspartate aminotransferase; COBI, cobicistat; DAA, direct-acting antiviral; GFR, glomerular filtration rate; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INSTI, integrase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

stigma against substance use, and concern about the risk of reinfection, as well as abstinence policies required by payors.[25,26] However, recent modeling data suggest that increasing HCV treatment of injection drug users is key to HCV elimination; specifically, data suggest that high treatment coverage of drug users is cheaper and more effective than a less intensive intervention because transmission is reduced more rapidly and fewer courses of treatment are needed.[27,28]

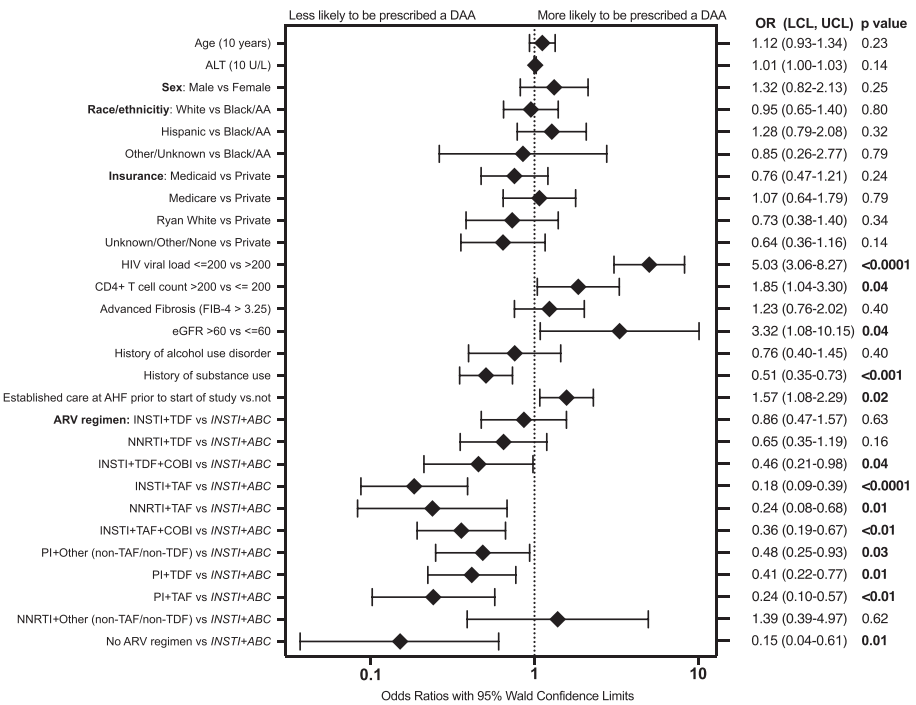

Figure 3 Multiple logistic regression model for the odds of a patient being prescribed a DAA by patient characteristic ($n = 727$). AA, African–American; ABC, abacavir; AHF, AIDS Health Foundation; ALT, alanine aminotransferase; COBI, cobicistat; eGFR, estimated glomerular filtration rate; HIV, human immunodeficiency virus; INSTI, integrase strand transfer inhibitor; LCL, lower confidence limit; NNRTI, non-nucleoside reverse transcriptase inhibitor; OR, odds ratio; PI, protease inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; UCL, upper confidence limit.

Additionally, this study found that patients on select HIV ARV regimens were less likely to be prescribed a DAA. As expected, not being on antiretroviral therapy was strongly associated with decreased likelihood of DAA prescription. Patients on ARV regimens that included cobicistat or a PI, regardless of the other components, were less likely to be prescribed a DAA. This was not surprising given that both cobicistat and PIs have known interactions with some DAAs.[29] Patients on TDF were less likely to be prescribed a DAA if they were also on cobicistat or a PI, but not in combination with other ARVs such as INSTIs or NNRTIs. This was also expected given the potential increased risk of renal toxicity with the combination of TDF, certain DAAs, and HIV PIs or cobicistat. This combination is not recommended by US guidelines for patients with eGFR ≤60 mL/min/1.73 m^2.[29] Notably, eGFR ≤60 was associated with lower odds of DAA prescription in our cohort, possibly reflecting limited availability of compatible DAAs for renal insufficiency and complexity of treatment in this population. Unexpectedly, there was a strong association between TAF and decreased likelihood of DAA prescription across all ARV regimens that included TAF. There are no known significant interactions between TAF and DAAs. As a newer HIV agent, the association of TAF may reflect temporal influences on DAA prescription, such as later engagement in care at AHF with less time in care to address HCV treatment (although the association with TAF persisted after adjusting for entry into care before or after the onset of the study observation period), more recent HIV diagnosis with similarly less time engaged in care to address HCV treatment and establish HIV suppression, or delay in DAA prescription because of providers first optimizing or changing patients' ARV regimen (e.g. TDF to TAF switch). Use of TAF may also reflect other, still to be delineated, patient, provider, or system-based characteristics that are a barrier to DAA prescription.

We found no differences in prescription rates based on race or ethnicity. Early studies among both HCV-monoinfected and HIV/HCV-coinfected patients found that Hispanic Whites and Blacks were less likely to be treated.[21,24,30–32] Our finding of a lack of race/ethnicity-based effect modification in the overall cohort is similar to more recent studies, which may be explained by the changing treatment environment, with more aggressive treatment of HIV/HCV-coinfected patients.[22,23]

One unique characteristic of this cohort is that all patients were receiving primary care from a physician trained in HIV care, many of whom are infectious disease physicians. As has been encouraged by others, co-location of HIV and HCV treatment services may improve HCV treatment rates, particularly in populations such as this cohort, which may experience more patient-level barriers to treatment; co-location and treatment by an infectious diseases specialist also allows potential drug–drug interactions between ARVs and DAAs to be more easily addressed and eliminate the barrier imposed by some insurance companies requiring DAAs be prescribed by a specialist.[33]

Strengths of this study include the diversity of insurance plans among the patients, diverse geographic locations of the clinics, and the diverse racial/ethnic make-up of the study population. Limitations of this study include the reliance on ICD-9 codes to identify comorbid conditions, use of prescription rates and not treatment initiation rates, and the inability to identify patients who might have been treated with a DAA at a clinic outside of AHF Healthcare Centers.

In conclusion, this study demonstrates that HIV/HCV-coinfected patients, in the period studied of January 2015 to August 2017, remained undertreated for HCV with DAA therapy despite national recommendations to prioritize treatment for this vulnerable population. Potentially modifiable barriers were identified. First, substance use history, even among well-controlled HIV patients, appeared to be a persistent barrier that might be addressed by eliminating payor restrictions or provider biases that inhibit treatment for these patients. Second, the potential barrier of select ARV regimens on DAA prescription should be addressable today with the greater availability of compatible DAAs and experience with DAA treatment in HIV-coinfected persons. Further research is needed to determine if the negative predictors of DAA prescription identified in this analysis persist today and inhibit the scale-up of HCV treatment and elimination.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Multiple logistic regression model of the odds of being prescribed a DAA among patients with well-controlled HIV (n = 574)† ALT: alanine aminotransferase; AA: African-American; eGFR: Estimated Glomerular filtration rate; AHF: AIDS Health Foundation; INSTI: integrase strand transfer inhibitor; TDF: tenofovir disoproxil fumarate; ABC: abacavir; COBI: cobicistat; TAF: tenofovir alafenamide; PI: protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; OR: odds ratio; LCL: lower confidence limit; UCL: upper confidence limit. †Model includes interaction effects between substance use and race/ethnicity.

Table S1. ICD 9 Codes used to identify comorbidities.