Barriers to Hepatitis C Virus (HCV) Treatment Initiation in Patients With Human Immunodeficiency Virus/HCV Coinfection: Lessons From the Interferon Era

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Background. Hepatitis C is a major cause of mortality among human immunodeficiency virus (HIV)-infected patients, yet hepatitis C virus (HCV) treatment uptake has historically been low. Although the removal of interferon removes a major barrier to HCV treatment uptake, oral therapies alone may not fully eliminate barriers in this population.

Methods. Within the Johns Hopkins Hospital HIV cohort, a nested case-control study was conducted to identify cases, defined as patients initiating HCV treatment between January 1996 and 2013, and controls, which were selected using incidence density sampling (3:1 ratio). Controls were matched to cases on date of enrollment. Conditional logistic regression was used to evaluate factors associated with HCV treatment initiation.

Results. Among 208 treated cases and 624 untreated controls, the presence of advanced fibrosis (odds ratio [OR], 2.23; 95% confidence interval [CI], 1.26–3.95), recent active drug use (OR, 0.36; 95% CI, 0.19–0.69), and non-black race (OR, 2.01; 95% CI, 1.26–3.20) were independently associated with initiation of HCV therapy. An increasing proportion of missed visits was also independently associated with lower odds of HCV treatment (25%–49% missed visits [OR, 0.49; 95% CI, 0.27–0.91] and ≥50% missed visits [OR, 0.24; 95% CI, 0.12–0.48]).

Conclusions. Interferon-free treatments may not be sufficient to fully overcome barriers to HCV care in HIV-infected patients. Interventions to increase engagement in care for HIV and substance use are needed to expand HCV treatment uptake.

Keywords. Direct-acting antivirals; HIV/AIDS; HIV/HCV coinfection; HCV treatment.

Chronic hepatitis C virus (HCV) infection is a leading cause of cirrhosis and hepatocellular carcinoma, and, since 2007, HCV has superseded human immunodeficiency virus (HIV) as a cause of death in the United States [1]. Due to shared routes of transmission, HCV and HIV epidemics often overlap [2, 3]. Up to 25% of all HIV-infected individuals in the United States are coinfected with HCV, with coinfection rates as high as 90% among persons who inject drugs (PWID) [4]. When compared with HCV monoinfected individuals, coinfected patients have accelerated progression of liver disease and increased risk for liver-related morbidity and mortality [5, 6].

Hepatitis C virus treatment can eradicate infection, and sustained virological response (SVR), defined as undetectable HCV ribonucleic acid (RNA) in the blood 12 weeks after the completion of HCV treatment, is strongly associated with reduced risk of liver-related morbidity and mortality. Among HIV/HCV-coinfected patients, HCV treatment in the era of interferon-based regimens was marked by poor tolerability, frequent serious adverse events, complex drug interactions, and limited efficacy with SVR rates of 20%–29% in patients with HCV genotype 1 infection. Not surprisingly, in this context, HCV treatment uptake was limited [7–12].

In 2014, interferon-free, direct acting antiviral (DAA) regimens were approved by regulatory authorities for the treatment of HCV genotype 1 infection based on clinical trials in which more than 95% of patients achieved SVR after 12 weeks of oral treatment [13–16]. More importantly, the safety, tolerability, and efficacy of these DAA regimens have been similar in persons with and without HIV coinfection [17–20]. Although these treatments represent a significant breakthrough, the removal of interferon may not fully eliminate barriers to HCV cure in persons with HIV/HCV coinfection. To investigate potential residual barriers to HCV treatment in the oral DAA era, we conducted a nested case-control study to identify factors associated with the initiation of interferon-based HCV treatment in HIV/HCV-coinfected patients receiving primary HIV care in an urban HIV clinic. We hypothesized that although the removal of interferon is necessary to increase rates of HCV cure, other barriers to HCV treatment remain, and interferon-free, DAA
regimens alone will not be sufficient to eliminate HCV in this HIV/HCV-coinfected patient population.

METHODS

A nested case-control study was conducted within the Johns Hopkins Hospital HIV Clinic cohort, an urban, Baltimore-based cohort with high rates of injecting drug use and low socioeconomic status. The cohort has followed approximately 8000 patients annually since 1996 [21]. Cases were defined as coinfected patients initiating their first course of HCV treatment with interferon and ribavirin between January 1996 and January 2013. Controls were selected using incidence density sampling in a ratio of 3:1 and were matched to cases on date of HIV clinic enrollment (±6 months). Controls were eligible if they had confirmed HCV infection and had not received HCV treatment at the time of matching. Hepatitis C virus infection was considered confirmed whether an individual had reactive HCV antibody and either detectable HCV RNA or no available HCV RNA testing. Patients with reactive HCV antibody and undetectable HCV RNA were excluded because they would not have been considered for HCV treatment.

Data on patient demographics, health-related behaviors (eg, drug and alcohol use), prescribed medications, and laboratory tests were abstracted from medical records. For cases and controls, time-varying characteristics were assessed within a 6-month window of the date of HCV treatment initiation of the case. Laboratory assessments, conducted by licensed clinical laboratories, included complete blood cell count, serum chemistry panel, aspartate aminotransferase and alanine aminotransferase (ALT) levels, CD4 cell count, HCV genotype, and plasma HIV-1 RNA. Aspartate aminotransferase, ALT, platelets, albumin, and bilirubin were categorized according to Division of AIDS toxicity grades for adverse events. Human immunodeficiency virus-1 RNA was defined as undetectable if values were below 400 copies/mL. To assess liver disease stage, the fibrosis (FIB)-4 index was used to categorize patients using validated criteria for minimal liver disease and cirrhosis [22].

Conditional logistic regression was used to evaluate factors associated with HCV treatment initiation. A series of multivariate models were constructed to evaluate factors that were significant (P < .05) in the univariate analysis. All models included age, sex, and race regardless of statistical significance. Due to collinearity between genotype and race, only race was included in the models. A sensitivity analysis was conducted to address the issue of missing data in the covariates included in the multivariate model. Multiple imputation with chained equations was used and 40 imputed datasets were created. Inferences from the analysis using multiple imputation did not differ from the complete case analysis. All analyses were conducted using Stata 12 (StataCorp LLC, College Station, TX).

RESULTS

Patient Population

The majority of treated patients (cases) were male (68%) and black (77%) and had a median age of 47.5 years (Table 1). Untreated patients (controls) were similar with respect to sex (male, 68%) and age (median, 46.6 years), but a higher proportion (89%) were black. Compared with untreated patients, treated patients had a higher CD4 count at time of HCV treatment initiation, 468 cells/mm$^3$ vs 339 cells/mm$^3$. Although the proportion of treated and untreated patients prescribed antiretroviral therapy (ART) was similar, 81% vs 76% (odds ratio [OR], 1.29; 95% confidence interval [CI], 0.79–2.11), HIV RNA suppression was higher in treated patients (74%) compared with untreated patients (64%) (OR, 1.78; 95% CI, 1.21–2.62).

Treated and untreated patients had a similar number of average HIV primary care visits per year before HCV treatment initiation (median 7.0 visits vs 6.1 visits; OR, 1.02; 95% CI, 0.99–1.06). However, untreated patients were significantly more likely to have missed scheduled clinic appointments in the past year compared with treated patients. Compared with treated patients, untreated patients who missed up to 25% of their scheduled visits in the preceding year were 40% less likely to be treated (OR, 0.59; 95% CI, 0.32–1.09); this increased to 67% in those who missed between 25% and 49% of their appointments (OR, 0.33; 95% CI, 0.18–0.61) and 83% in those who missed 50% or more of their appointments (OR, 0.17; 95% CI, 0.09–0.33).

The majority of treated (71%) and untreated (78%) patients reported ever using injection drugs and alcohol. However, at the last visit before HCV treatment initiation, treated patients were significantly less likely than untreated patients to report active drug use (OR, 0.27; 95% CI, 0.15–0.49) and were also likely to report active alcohol abuse (OR, 0.45; 95% CI, 0.25–0.82). Of note, the diagnosis of comorbid psychiatric disease was more common among treated patients (77% vs 68%); however, among all patients with psychiatric disease, treated patients were more likely to be actively engaged in psychiatric care in the colocalized mental health clinic compared with untreated patients (40% of treated vs 29% of untreated patients).

With respect to HCV infection, the majority of both treated and untreated patients were infected with HCV genotype 1 (94% vs 97%, respectively). Hepatitis C virus genotype varied according to self-reported race; the prevalence of HCV genotype 1 infection was 99% and 80% among black and non-black patients, respectively. Non-black patients were more likely to be infected with HCV genotypes 2 or 3, and patients with these genotypes were more likely to be treated. As assessed by FIB-4
| Characteristic                                      | Cases N = 208 (%) | Controls N = 624 (%) | Crude OR (95% CI) |
|---------------------------------------------------|-------------------|----------------------|-------------------|
| Male                                              | 142 (68)          | 423 (68)             | 1.02 (0.73–1.43)  |
| Age, years (median, IQR)                          | 475 (42.7–51.9)   | 46.6 (41.6–52.2)     | 1.02 (0.99–1.04)  |
| Race                                              |                   |                      |                   |
| Black                                             | 160 (77)          | 554 (89)             | 1.0               |
| White                                             | 44 (21)           | 66 (11)              | 2.31 (1.51–3.53)  |
| Other                                             | 4 (2)             | 4 (1)                | 3.44 (0.85–13.85) |
| HCV Genotype                                      |                   |                      |                   |
| 1                                                 | 196 (94)          | 480 (97)             | 1.0               |
| 2                                                 | 5 (2)             | 6 (1)                | 2.24 (1.00–4.99)  |
| 3                                                 | 7 (3)             | 4 (1)                |                   |
| 4                                                 | 0                 | 4 (1)                |                   |
| Missing                                           | 0                 | 130                  |                   |
| CD4 count at time of HCV treatment, cells/mm³ (median, IQR) | 468 (314–634) | 339 (189–530) |                   |
| <200                                              | 22 (11)           | 137 (27)             | 0.27 (0.15–0.48)  |
| 200–349                                           | 43 (21)           | 129 (25)             | 0.61 (0.40–0.95)  |
| 350–499                                           | 51 (25)           | 99 (19)              | 0.98 (0.63–1.53)  |
| ≥500                                              | 87 (43)           | 148 (29)             | 1.0               |
| Missing                                           | 5                 | 111                  |                   |
| Antiretroviral therapy at the time of HCV treatment | 168 (81)          | 472 (76)             | 1.29 (0.79–2.11)  |
| Missing                                           | 7                 | 40                   |                   |
| HIV RNA undetectable at time of HCV treatment     | 151 (74)          | 324 (64)             | 1.78 (1.21–2.62)  |
| Missing                                           | 5                 | 120                  |                   |
| Average number of visits per year before treatment (median, IQR) | 7.0 (3.9–10.2) | 6.1 (3.3–9.8) | 1.02 (0.99–1.06)  |
| Missing                                           | 3                 | 0                    |                   |
| % of missed HIV care appointments in the past year |                   |                      |                   |
| 0                                                 | 45 (25)           | 68 (14)              | 1.0               |
| 1–24                                              | 48 (27)           | 84 (17)              | 0.59 (0.32–1.09)  |
| 25–49                                             | 56 (31)           | 168 (34)             | 0.33 (0.18–0.61)  |
| >50                                               | 30 (17)           | 170 (35)             | 0.17 (0.09–0.33)  |
| Missing data                                      | 29                | 134                  |                   |
| History of psychiatric diagnosis                  | 160 (77)          | 422 (68)             | 1.58 (1.10–2.28)  |
| Visited mental health clinic in year before treatment | 65 (32)          | 130 (21)             | 1.80 (1.26–2.58)  |
| Missing                                           | 3                 | 0                    |                   |
| Self-reported alcohol abuse at last visit before treatment | 15 (8)           | 80 (16)              | 0.45 (0.25–0.82)  |
| Missing                                           | 19                | 108                  |                   |
| Self-reported illicit drug use at last visit before treatment | 14 (7)           | 120 (22)             | 0.27 (0.15–0.49)  |
| Missing                                           | 18                | 89                   |                   |
| Health Insurance                                  |                   |                      |                   |
| Commercial                                        | 118 (57)          | 326 (53)             | 1.0               |
| Medicaid/Medicare                                 | 65 (31)           | 211 (34)             | 0.85 (0.59–1.21)  |
| None                                              | 25 (12)           | 83 (13)              | 0.83 (0.51–1.36)  |
| Missing                                           | 0                 | 4                    |                   |
| FIB-4 Scorec                                      |                   |                      |                   |
| <1.45                                             | 89 (44)           | 261 (53)             | 1.0               |
| 1.45–3.25                                         | 75 (37)           | 177 (36)             | 1.27 (0.87–1.84)  |
| >3.25                                             | 39 (19)           | 56 (11)              | 2.09 (1.27–3.45)  |
| Missing                                           | 5                 | 130                  |                   |
| Alanine aminotransferase, U/L (median, IQR)       | 62 (36–97)        | 38 (25–62)           | 1.0               |
| Grade 0                                           | 80 (39)           | 328 (66)             |                   |
| Grade 1                                           | 78 (38)           | 133 (27)             | 2.23 (1.52–3.27)  |
| Grade 2                                           | 34 (17)           | 30 (6)               | 4.78 (2.63–8.70)  |
| Grade 3                                           | 8 (4)             | 6 (1)                | 6.96 (2.12–22.84) |
| Grade 4                                           | 3 (1)             | 1 (<1)               | 12.21 (1.21–123.48)|
| Missing                                           | 5                 | 126                  |                   |
| Hemoglobin, g/dL (median, IQR)                    | 13.6 (12.4–14.9)  | 13.0 (11.7–14.4)     |                   |
| <10                                               | 3 (1)             | 29 (6)               | 0.17 (0.04–0.72)  |
| ≥10                                               | 200 (99)          | 490 (94)             | 1.0               |
serum index, treated patients were more likely to be classified as having advanced liver disease than those not treated (Table 1).

**Predictors of Hepatitis C Virus Treatment Initiation**

In univariate analysis, non-black race, non-HCV genotype 1 infection, and markers of more advanced liver disease (FIB-4 >3.25) were significant predictors of HCV treatment initiation (Table 1). Adherence to HIV care visits, defined as the ratio of attended to scheduled clinic visits (proportion of missed scheduled visits), successful receipt of ART defined by HIV-RNA suppression (HIV RNA <400 copies/mL), and engagement in psychiatric care were also positively associated with the initiation of HCV treatment. In contrast, self-report of active drug or alcohol use were strongly associated with not receiving treatment. After adjustment for confounders, the presence of advanced liver disease (FIB-4 score >3.25), self-reported active drug use, and non-black race were independently associated with the initiation of HCV treatment. In multivariate analysis with an increasing percentage of missed, scheduled visits (no shows) associated with a lower odds of treatment.

**Hepatitis C Virus Treatment Outcomes**

Of the 208 HIV/HCV-coinfected patients who initiated treatment with interferon/ribavirin, 17.8% achieved SVR. Among those who failed to achieve SVR, on-treatment virologic non-response was reported in 70.7% and posttreatment viral relapse was observed in 7.2% of those treated; virologic outcomes were unknown for the remaining patients (4.3%). Of note, only 3 patients had documented treatment discontinuation due to adverse events or other nonvirologic factors.

**DISCUSSION**

With the advent of safe and efficacious DAA regimens, there is great potential to increase the proportion of HIV/HCV-coinfected patients who achieve HCV cure, leading to decreased risk of liver-related morbidity and mortality. Indeed, based on the achievement of SVR in more than 95% of HCV genotype

### Table 1. Multivariate Analysis of HCV-Treated Patients (Cases) vs HCV Untreated Patients (Controls)

| Characteristic | Cases N = 208 (%) | Controls N = 624 (%) | Crude OR (95% CI) |
|---------------|------------------|---------------------|------------------|
| Male          | 0.95 (0.61–1.50) | 0.89 (0.62–1.29)    |                  |
| Age           | 0.98 (0.94–1.02) | 0.99 (0.97–1.02)    |                  |
| Non-black race| 2.47 (1.36–4.47) | 2.01 (1.26–3.20)    |                  |
| % missed illicit drug use at last visit | 0.52 (0.25–1.08) | 0.36 (0.19–0.69)    |                  |
| % missed primary care visits in last year |                |                     |                  |
| 0             | 1.0              | 1.0                 |                  |
| 1–24          | 0.78 (0.38–1.60) | 0.76 (0.41–1.42)    |                  |
| 25–49         | 0.41 (0.20–0.83) | 0.49 (0.27–0.91)    |                  |
| ≥50           | 0.21 (0.09–0.46) | 0.24 (0.12–0.48)    |                  |
| Undetectable HIV-RNA | 1.26 (0.77–2.06) | 1.43 (0.93–2.20)    |                  |
| FIB-4 Score |                |                     |                  |
| <1.45         | 1.0              | 1.0                 |                  |
| 1.45–3.25     | 1.10 (0.68–1.80) | 1.27 (0.84–1.93)    |                  |
| ≥3.25         | 2.25 (1.13–4.47) | 2.23 (1.26–3.95)    |                  |

**Table 2. Multivariate Analysis of HCV-Treated Patients (Cases) vs HCV Untreated Patients (Controls)**

| Variable        | Complete Case Analysis Adjusted OR (95% CI) | Multiple Imputation Adjusted OR (95% CI) |
|-----------------|---------------------------------|----------------------------------------|
| Male            | 0.95 (0.61–1.50)                | 0.89 (0.62–1.29)                        |
| Age             | 0.98 (0.94–1.02)                | 0.99 (0.97–1.02)                        |
| Non-black race  | 2.47 (1.36–4.47)                | 2.01 (1.26–3.20)                        |
| % missed illicit drug use at last visit | 0.52 (0.25–1.08) | 0.36 (0.19–0.69)                        |
| % missed primary care visits in last year |                |                                         |
| 0               | 1.0                             | 1.0                                    |
| 1–24            | 0.78 (0.38–1.60)                | 0.76 (0.41–1.42)                        |
| 25–49           | 0.41 (0.20–0.83)                | 0.49 (0.27–0.91)                        |
| ≥50             | 0.21 (0.09–0.46)                | 0.24 (0.12–0.48)                        |
| Undetectable HIV-RNA | 1.26 (0.77–2.06) | 1.43 (0.93–2.20)                        |
| FIB-4 Score     |                                |                                         |
| <1.45           | 1.0                             | 1.0                                    |
| 1.45–3.25       | 1.10 (0.68–1.80)                | 1.27 (0.84–1.93)                        |
| ≥3.25           | 2.25 (1.13–4.47)                | 2.23 (1.26–3.95)                        |

**Table 1. Continued**

| Characteristic               | Cases N = 208 (%) | Controls N = 624 (%) | Crude OR (95% CI) |
|------------------------------|------------------|---------------------|------------------|
| Platelet, count/mm³ (median, IQR) | 188 (139–232) | 201 (154–248) |                  |
| Serum Creatinine, mg/dL      |                  |                     |                  |
| ≤1.1                        | 168 (86)         | 410 (79)            | 1.0              |
| 1.2–2.0                     | 26 (13)          | 94 (18)             | 0.69 (0.43–1.11) |
| >2.0                        | 2 (1)            | 15 (3)              | 0.34 (0.08–1.57) |
| Missing                     | 12               | 105                 |                  |

**Abbreviations:** ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; FIB, fibrosis; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; OR, odds ratio; PLT, platelet; ULN, upper limit of the normal.

*The grade of the ALT levels was based on an ULN range of 40 U/L as follows: Grade 0 <1.25 × ULN; Grade 1 = 1.25 to 2.5 × ULN; Grade 2 = 2.6 to 5.0 × ULN; Grade 3 = 5.1 to 10 × ULN; Grade 4 ≥10 × ULN.}

*Odd ratio is for the comparison of HCV genotype 1 to all other HCV genotypes.

*FIB-4 score was calculated using the following formula: age [years] × AST [U/L]/PLT [10⁹/L] × (ALT [U/L])¹/².

*Significant adjusted ORs are presented in bold.

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1/HIV-coinfected patients treated with interferon-free, oral DAA regimens in clinical trials, the American Association for the Study of Liver Disease/Infectious Diseases Society of America HCV guidance panel recommended that all coinfected patients be treated for hepatitis C, including those at high risk for transmission of HCV to others [18, 19, 23, 24]. Although the selection of coinfected patients for HCV treatment has been markedly simplified in the DAA era, our findings on treatment initiation in the interferon era may have important implications for the potential elimination of HCV in populations with HIV/HCV coinfection.

First, we did not find evidence that psychiatric disease or medical comorbidities such as chronic kidney disease were associated with decreased uptake of interferon-based therapy. On the contrary, we found that a higher percentage of treated patients had been previously diagnosed with comorbid psychiatric disease; engagement in mental healthcare available onsite in the HIV clinic was associated with greater likelihood of initiating HCV treatment. This finding suggests that mental illness did not represent an independent barrier to HCV treatment in the interferon era in this particular clinic, because mental health services were integrated with HIV care. In other settings where mental health services are not as accessible, the removal of interferon may have an even larger beneficial effect, because DAAs provide more tolerable and safer treatment in persons with depression and other psychiatric conditions.

Second, we observed a strong dose-response relationship between the proportion of missed visits (no shows) and the likelihood of HCV treatment. After adjustment for confounders, compared with treated patients who kept scheduled visits in the preceding year, patients who missed between 25% and 49% of their scheduled visits and those who missed 50% or more of scheduled visits were 67% and 83% less likely to start HCV treatment. Indeed, this measure of missed visits was a stronger predictor of HCV treatment initiation than actual attendance at clinic visits, and mirrors previous observations in HIV care, where missed clinic visits has been linked to lack of HIV suppression with ART. For example, in the Johns Hopkins HIV clinic, Lucas et al [25] demonstrated that missed visits were associated with HIV treatment failure in the early ART era. More recently, in the Centers for AIDS Research Network of Integrated Clinical Systems multisite HIV cohort, Mugavero et al [26] found that missed primary HIV care visits after ART was a strong predictor of retention in HIV care and, more importantly, of mortality.

The finding that increasing numbers of missed HIV care visits strongly predicts low HCV treatment initiation has implications for the DAA HCV treatment era because the removal of interferon from the regimen will not address this important barrier to HCV treatment uptake. This observation also highlights the need to focus on linking and retaining coinfected patients in HIV care by working to reduce missed visits for both HIV and concurrent mental health conditions. In addition, along with measures of adherence to HIV treatment (eg, viral suppression, or an undetectable HIV RNA), the rate of missed visits may be useful in clinical practice to identify persons for whom additional support may be needed to successfully engage in HCV care.

Third, coinfected patients who were not treated for HCV were more likely to have recently used illicit drugs and/or alcohol. These factors are known to be associated with poor adherence to clinic visits and medical treatment [27]. The impact of this barrier on HCV care may be mitigated by the short duration of HCV treatment (12 weeks) needed to achieve HCV cure in most coinfected patients. However, the HCV care continuum extends beyond the short treatment course for HCV, and patients with cured HCV continue to require monitoring for liver disease progression and reinfection. Ongoing alcohol use may contribute to progressive liver disease despite HCV cure. In addition, patients who engage in high-risk behaviors such as unprotected sex or injection drug use after SVR are at risk for HCV reinfection. In a meta-analysis examining rates of HCV reinfection after curative treatment, Simmons et al [28] reported that the 5-year risk of reinfection may be as high as 21.8% among HIV/HCV-coinfected patients. More importantly, in one study of young PWID, opioid substitution therapy was independently associated with a lower hazard of incident HCV infection even after adjustment for incarceration and homelessness [29]. Our finding suggests that drug and alcohol abuse will continue to be important issues in the era of oral DAAs both as major contributors to missed appointments and as risk factors for ongoing liver disease (alcohol) and reinfection (injection drug use) after HCV cure is achieved. Taken together, our data strongly support the close linkage of programs to treat HIV, hepatitis C, and addiction; more importantly, harm reduction interventions must extend beyond the short HCV treatment period.

Finally, our data reveal racial disparity in the provision of HCV treatment in the interferon era. Lower treatment uptake among black patients in our cohort could in part be due to the greater prevalence of genotype 1 infection, which was more difficult to treat with interferon. Genotype notwithstanding, black patients were also less likely to respond to interferon-based treatments than white patients due, in part, to the presence of unfavorable interferon lambda 4 polymorphism [30, 31]. In this context, many healthcare providers and black patients with HCV genotype 1 infection may have been unwilling to initiate treatment with interferon/ribavirin. Other medical factors may also have precluded HCV treatment with interferon. In the IDEAL study of peginterferon/ribavirin, blacks were less likely than non-blacks to meet eligibility criteria, largely due to higher prevalence of neutropenia and uncontrolled medical conditions such as diabetes or chronic renal insufficiency [32]. Thus, it is possible that the observed racial disparity in our study is explained by the inability of blacks to use interferon-based
treatments due to unfavorable genotypes or polymorphisms and/or medical comorbidities. If this is the case, the removal of interferon and the use of highly effective, oral DAA regimens may result in similar treatment uptake among blacks and non-blacks [33]. However, it is also possible that the observed disparity in HCV treatment initiation may not be fully explained by the use of interferon alone. In the Veterans Affairs healthcare system, black veterans were still less likely to undergo HCV treatment compared with non-black veterans in the DAA era [34]. Similar racial disparities have been observed in the treatment of HIV infection and may in part be explained by a higher rate of missed visits among black patients in HIV care [35]. Other factors, including general mistrust of the medical system, providers, and treatments, have also been associated with lower adherence to antiretrovirals among black patients and may also be important contributors to decreased HIV engagement in care [36]. Thus, although more effective interferon-free HCV treatments are necessary, they may not fully overcome racial disparities in HCV care, highlighting the need for targeted, culturally appropriate interventions to engage black patients with HIV/HCV coinfection.

This study has some limitations. First, alcohol and illicit drug use were self-reported, and chart review noted that data were missing for both cases and controls when the physician did not actively include these in documentation. Second, the decision to initiate or forego HCV treatment is complex and likely subject to additional factors from both the provider and patient perspective that we were unable to measure. Furthermore, these intangible factors underlying the selection of patients for HCV treatment are likely to be different in the DAA era. Nonetheless, the barriers that we observed to HCV treatment are consistent with previously reported barriers to engagement in HIV and HCV care and support the validity of our findings. Third, access to HCV treatment was generally not restricted by payers in the interferon era, and we did not note a difference in type of health insurance coverage between treated and untreated patients in our study. In contrast, in the DAA era, limited access by payers is undoubtedly an important barrier to HCV treatment. Lastly, our findings are derived from a single, urban HIV clinic; however, the demographics of our cohort is similar to that of many inner city HIV-infected populations, to which our study findings may be generalizable.

CONCLUSIONS

In conclusion, although the availability of safe and effective, interferon-free HCV treatment regimens is necessary to increase the rate of HCV treatment in coinfected patients, our findings indicate that DAA regimens alone cannot be expected to completely overcome barriers to HCV cure in this patient population. To improve the HCV care continuum and prevent ongoing HCV transmission, efforts may be best focused on increasing the engagement of coinfected patients in medical care for their HIV infection, comorbid mental illness, and/or active drug or alcohol abuse. In the United States, further research is also needed to address the potential for the persistence of racial disparities in the delivery and uptake of highly effective, all-oral, interferon-free HCV treatment.

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