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MAJOR ARTICLE

Implementing a Comprehensive Hepatitis C Virus (HCV) Clinic Within a Human Immunodeficiency Virus Clinic: A Model of Care for HCV Microelimination

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Background. Among the 1.2 million people with human immunodeficiency virus (HIV) in the United States, 25% are coinfected with hepatitis C virus (HCV). The availability of effective direct acting antivirals (DAAs) makes the goal of HCV elimination feasible, but implementation requires improvements to the HCV treatment cascade, especially linkage to and initiation of treatment in underserved populations.

Methods. In this retrospective review, a cohort of patients receiving care at a hospital-based HIV clinic in New Haven, Connecticut (January 1, 2014–March 31, 2017) with chronic HCV infection not previously treated with DAAs were followed longitudinally. Patients were referred to a colocated multidisciplinary team. Standardized referral and treatment algorithms and electronic medical record templates were developed, monthly meetings were held, and a registry was created to review progress.

Results. Of 173 patients, 140 (80.9%) were 50–70 years old, 115 (66.5%) were male, 99 (57.2%) were African American, 43 (24.9%) were white, and 23 (13.3%) were Hispanic. Comorbidities included the following: cirrhosis (25.4%), kidney disease (17.3%), mental health issues (60.7%), alcohol abuse (30.6%), and active drug use (54.3%). Overall, 161 (93.1%) were referred, 147 (85%) were linked, 122 (70.5%) were prescribed DAAs, and 97 (56.1%) had sustained viral response at 12 weeks posttreatment or cure (SVR12). Comparison between those with SVR12 and those unsuccessfully referred, linked, or treated, showed that among those not engaged in HCV care, there was a higher proportion of younger (mean age 54.2 vs 57 years old, P = .022), female patients (P = .001) and a higher frequency of missed appointments.

Conclusions. Establishing a colocated HCV clinic within an HIV clinic resulted in treatment initiation in 70.5% of patients and SVR12 in 56.1%. This success in a hard-to-treat population is a model for achieving microelimination goals set by the World Health Organization.

Keywords. care cascade; HCV; HIV.

It is estimated that, worldwide, 71 million people are chronically infected with hepatitis C virus (HCV) [1]. The World Health Organization (WHO) has set the goal of global HCV elimination by 2030 by defining the following targets: an 80% reduction in new infections, and a 65% reduction in deaths [2]. This goal is predicated on the availability of effective HCV treatment. Since 2011, multiple new direct-acting antivirals (DAAs) have made HCV treatment easier due to shorter durations of therapy, less toxicity, and improved efficacy with greater than 95% sustained viral response at 12 weeks posttreatment or cure (SVR12) [3]. Current scale-up attempts are not on pace to meet these goals; therefore, more aggressive efforts are underway that target microelimination within smaller high-risk communities, such as people coinfected with human immunodeficiency virus (HIV) and HCV. This prioritization is justified given that HCV infection progresses more rapidly to liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) and contributes significantly to mortality in people infected with HIV [4]. In 2015, worldwide, it was estimated that 2.3 million people with HIV (PWH) were seropositive for HCV (6.2% of prevalent HIV cases) [2]. Within the United States, it is estimated that of 1.2 million prevalent HIV cases, approximately 25% are coinfected with HCV, although prevalence estimates vary widely by region [5]. Among PWH with injection drug use (IDU) as a risk factor, approximately 75% are coinfected with HCV [6].

Multiple studies have demonstrated that DAA treatment is equally effective in PWH compared with monoinfected patients [7]. The current WHO and US guidelines reiterate that PWH should be treated for HCV at any stage of disease with caution given to accommodating drug-drug interactions with

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antiretroviral medications [2, 8]. These guidelines emphasize that active substance use should not be a contraindication to initiating HCV treatment [9–11]. Real-world implementation of these guidelines remains suboptimal.

Efforts to achieve HCV elimination have been measured by progress along the HCV care cascade. Analogous to the widely used HIV treatment cascade [12], progress has been mapped to success in achieving HCV testing, referral to and linkage to care, HCV treatment initiation, and documentation of SVR12. Published HCV care cascades in the United States have shown overall poor rates along the entire care cascade. Before DAA introduction, the systematic review and meta-analysis by Yehia et al [13] showed that in the United States, among those with chronic HCV monoinfection, only 50% were diagnosed and aware of their infection, 43% had access to outpatient care, 27% had HCV ribonucleic acid (RNA) confirmed, 16% were prescribed treatment, and 9% achieved SVR12.

Several studies have shown concerted efforts within clinics targeting HIV/HCV-coinfected persons. Cachay et al [14] showed that within an HIV clinic, 54% of patients were referred for HCV treatment, 16% initiated treatment, and 7% achieved SVR12. Several international studies have shown greater success towards microelimination primarily in the setting of universal access to DAAs [15–17].

In this paper, we describe specific clinical practices using a model of care in a colocated HCV clinic within a University-affiliated hospital-based clinic in New Haven, Connecticut that serves PWH. This model consists of a dedicated management team that includes a cadre of HCV-trained Infectious Disease (ID) prescribers, a mid-level provider, a nurse, specialty pharmacy staff, and data support staff. The team met regularly to monitor progress and provide flexible and innovative approaches to facilitate engagement in HCV care. We describe the strengths of this approach and assessed for factors affecting the HCV treatment cascade.

MATERIALS AND METHODS

Study Population

Eligible participants were adults (>18 years old) with documented HIV infection and chronic HCV (reactive HCV antibody with detectable HCV RNA), who were receiving continuity HIV care at the Nathan Smith Clinic (NSC), from January 1, 2014 to March 31, 2017. Inclusion criteria included patients who were DAA treatment-naive (including patients who had previously failed interferon-based regimens). The NSC is a Ryan White-funded, academically affiliated, hospital-based HIV specialty clinic (Yale New Haven Hospital, New Haven, CT). It is staffed by Yale School of Medicine Infectious Disease and General Medicine HIV providers, and it is the training site for primary care residents within a specialized HIV primary care track. All patients receive a HCV antibody test after enrollment, per protocol, and a polymerase chain reaction (PCR) test is given to those who test antibody positive.

Hepatitis C Virus Model of Care

In response to the newly available HCV DAAs, in mid-2012, clinic leadership decided to proactively convene a multidisciplinary team that would focus on the onsite management of HCV among patients with HIV/HCV coinfection. The multidisciplinary team included the following: (1) 3 physicians who received additional HCV training through national courses provided by International Antiviral Society (IAS) and Infectious Disease Society of America (IDSA) courses and were designated DAA prescribers; (2) 1 physician assistant who provided face-to-face, follow-up evaluations during treatment courses as needed and served as liaison with the specialty pharmacy; (3) 1 registered nurse who communicated with patients and who provided treatment adherence assistance and contacted patients who were not linked to care; (4) 1–2 pharmacists who were employed by the affiliated specialty pharmacy (initially outside pharmacy, but then a hospital-based 340B pharmacy); and (5) data managers who ensured timely entry of relevant data and generated updated reports. Standardized screening, referral, and treatment algorithms were created. Uniform EPIC templates for initial and follow-up evaluations that contained all pertinent HCV-specific information (eg, HCV genotype, viral load, results of noninvasive testing such as fibrosis [FIB]-4, aspartate aminotransferase-to-platelet ratio index [APRI], Model for End-Stage Liver Disease score, and relevant imaging) were created.

All eligible patients were recommended to undergo referral for consultation to the onsite HCV coinfection clinic. Referrals were made by the HIV primary care provider or HCV nurse to a weekly HCV clinic that was staffed by 3 ID physicians. After treatment initiation, patients were seen at 4 weeks, at the end of treatment, and at 12 weeks posttreatment. Criteria for referrals to the Hepatology clinic included cirrhosis (variceal and HCC screening) and evaluation for liver transplant for those with decompensated cirrhosis. Regular meetings for all team members were initially held on a monthly basis, then changed to quarterly to review progress and treatment outcomes. The patient registry was regularly updated, and patients who were not being referred, linked, or treated were reviewed to assess barriers and to customize individual plans to promote engagement in HCV care.

Design

This paper is a retrospective review of a clinical program aimed at treating persons with HIV/HCV coinfection, with data collection spanning January 1, 2014 to August 31, 2018. The Yale Institutional Review Board approved the study.

Data Collection

The list of coinfected patients was generated using both the CAREWare database, an electronic health system developed by the Health Resources and Service Administration for Ryan White Grant recipients, and the electronic medical record ([EMR] EPIC) based on *International Classification of Diseases* (ICD)-9/10 codes relevant to HCV. Basic demographics, laboratory results, and clinic visit dates were extracted from EPIC (cutoff date August 31, 2018) by the Joint Data Analytics Team of the Yale Center for Clinical Investigation and coded using R version 3.5.1 before importing into REDCap [18–21]. A chart review was performed to confirm patient eligibility, and comorbidity data were manually entered into REDCap, a secure web-based application designed to support data capture for research studies, providing the following: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources [22]. Specific data elements included the following: race/ethnicity, gender, age, date of birth, clinical data (including HIV- and HCV-related data), screening and diagnosis, medications (HIV and HCV specific), treatment parameters, and other relevant clinical data such as presence of kidney disease and stage of liver disease. Cirrhosis was defined based on the active problem list and calculation of noninvasive scoring (FIB-4 >3.25, APRI >1.0) [23] or a liver biopsy and/or elastography (if available) that was positive for liver cirrhosis. Comorbidities, including alcohol use, substance use, and mental health disorders, were recorded based on their being recorded on the active problem list in EPIC (based on ICD-9/10 codes). Additional comorbidities reflected diagnoses specified in the electronic problem list. Chart review using EPIC and CAREWare was performed as needed to elicit laboratory, insurance, and housing status parameters.

Definition of Hepatitis C Virus Treatment Cascade Parameters

We are using a "diagnosis-based" HCV cascade of care, as opposed to a prevalence-based cascade of care, due to our inability to definitively quantify the number of unique active PWH in the clinic in the study period. All patients received a baseline HCV antibody test; however, there are limitations in our ability to track patients who relocate (to other states, clinics, or incarceration), so clinic-level data on follow-up PCR testing for those with HCV antibody positivity may be incomplete. Using the subset of PWH with documented chronic HCV in this time period as a starting point, we used the following definitions for our diagnosis-based HCV treatment cascade: (1) referral to HCV care - referral for HCV DAA treatment evaluation based on documentation in clinic office note, EPIC referrals tab, or date scheduled for HCV coinfection clinic within scheduling tab; (2) linkage to HCV care - successful attendance at clinic visit for HCV treatment evaluation as documented by specific provider note; (3) DAA treatment initiation - documented prescription for DAA treatment as per provider and/or pharmacy note; and (4) treatment outcomes - based on treatment status as of August 31, 2018, ie, currently on treatment, treatment completed awaiting SVR12 documentation, SVR12 (negative HCV viral load at least 12 weeks after end of treatment), treatment stopped early, lost to follow-up (patient did not attend any HCV visits after starting therapy), or relapse (patient completed therapy but did not achieve SVR12).

Statistical Analysis

Categorical variables were described using frequencies and percentages; continuous variables were characterized as means with standard deviations. Pearson's χ^2 test or Fisher's exact test were used to analyze frequency distributions; the Student's *t* test was used for analyzing continuous variables. Data analysis was performed using SAS software (version 9.4, SAS System for Windows).

RESULTS

Demographics

Patient characteristics are shown (see Table 1) at baseline and according to HCV treatment stage. During the study period, 173 patients were eligible for inclusion; 140 (80.9%) were between 50 and 70 years old with a mean age of 55.9 years; 115 (66.5%) were male; 99 (57.2%) were African American; 43 (24.9%) were white; and 23 (13.3%) were Hispanic. The majority, 140 (80.9%), had HCV genotype 1. Comorbidities included the following: cirrhosis 44 (25.4%), kidney disease 30 (17.3%), mental health issues 105 (60.7%), alcohol abuse 53 (30.6%), and active drug use 94 (54.3%). The majority received Medicaid (90, 52%) and Medicare (63, 36.4%). We did not have any new acute HCV infections (based on Centers for Disease Control and Prevention surveillance case criteria) in our cohort.

Timeline of Treatment Initiation

The pace of treatment initiations starting in January 2014 is shown in Figure 1. There was a constant increment of treatment initiations between January 2014 and July 2016 (range of initiations 0 to 7 per month) with 122 initiations overall. By August 2016, there were fewer initiations (1–3 per month) because the pool of treatment-eligible patients decreased and included "hard-to-engage" patients (see below). As time elapsed, the team conducted enhanced outreach via phone calls to untreated patients. In January 2018, the team engaged in an innovative partnership with Proteus Discover, a company based in California that produces a technology using an ingestible sensor pill, connected to a mobile application, that tracks patients' adherence [24]. This technology was offered as an alternative means of undergoing DAA treatment to a subset of 10 patients who had not yet initiated treatment. This process was set up by our Specialty Pharmacy, which also conducted electronic

Table 1. Patient Demographics and Clinical Parameters Along Diagnosis-Based HCV Treatment Cascade

Characteristic		Total Coinfected N = 173	Coinfected N = 173		Referred N = 161		Linked N = 147	
			Referred N (%)	Not Referred	Linked	Not Linked	Treated	Not Treated
Total patients			161	12	147	14	122	25
Age (n, %)	<50 years old at time of study	31 (17.9)	25 (15.5)	6 (50.0)	20 (13.6)	5 (35.7)	18 (14.8)	2 (8.0)
	≥50 years old and ≤70 years old at time of study	140 (80.9)	134 (83.2)	6 (50.0)	125 (85.0)	9 (64.3)	102 (83.6)	23 (92.0)
	>70 years old at time of study	2 (1.2)	2 (1.2)	0	2 (1.4)	0 (0.00)	2 (1.6)	0 (0.00)
Age (mean, SD)		55.9 (7.0)	56.4 (6.8)	49.8 (8.2)	56.6 (6.6)	53.9 (8.3)	56.7 (6.8)	56.4 (5.5)
Gender (n, %)	Male	115 (66.5)	109 (67.7)	6 (50.0)	100 (68.0)	9 (64.3)	88 (72.1)	12 (48.0)
	Female	58 (33.5)	52 (32.3)	6 (50.0)	47 (32.0)	5 (35.7)	34 (27.9)	13 (52.0)
Race (n, %)	White or Caucasian	43 (24.9)	38 (23.6)	5 (41.7)	35 (23.8)	3 (21.4)	29 (23.8)	6 (24.0)
	Black or African American	99 (57.2)	94 (58.4)	5 (41.7)	86 (58.5)	8 (57.1)	70 (57.4)	16 (64.0)
	American Indian or Alaska Native	1 (0.6)	1 (0.6)	0	1 (0.7)	0	0	1 (4.0)
	Hispanic	23 (13.3)	21 (13.0)	2 (16.7)	19 (12.9)	2 (14.3)	18 (14.8)	1 (4.0)
	Patient Refused/Other/Unknown	7 (4.1)	7 (4.3)	0	6 (4.1)	1 (7.1)	5 (4.1)	1 (4.0)
Insurance (n, %)	Medicaid	90 (52.0)	84 (52.1)	6 (50.0)	75 (51.0)	9 (64.3)	60 (49.2)	15 (60.0)
	Medicare	63 (36.4)	58 (36.0)	5 (41.7)	54 (36.7)	4 (28.6)	46 (37.7)	8 (32.0)
	Private	17 (9.8)	16 (9.9)	1 (8.3)	15 (10.2)	1 (7.1)	13 (10.7)	2 (8.0)
	Ryan White	1 (0.6)	1 (0.6)	0	1 (0.7)	0	1 (0.8)	0
	Other	1 (0.6)	1 (0.6)	0	1 (0.7)	0	1 (0.8)	0
	Self-Pay	1 (0.6)	1 (0.6)	0	1 (0.7)	0	1 (0.8)	0
Liver cirrhosis (n, %)		44 (25.4)	41 (25.5)	3 (25.0)	38 (25.9)	3 (21.4)	33 (27.1)	5 (20.0)
Kidney disease (n, %)		30 (17.3)	27 (16.8)	3 (25.0)	26 (17.7)	1 (7.1)	20 (16.4)	6 (24.0)
Alcohol abuse (n, %)		53 (30.6)	50 (31.0)	3 (25.0)	46 (31.3)	4 (28.6)	38 (31.2)	8 (32.0)
Mental health (any issue) (n, %)		105 (60.7)	99 (61.5)	6 (50.0)	89 (60.5)	10 (71.4)	73 (59.8)	16 (64.0)
Active drug use (n, %)		94 (54.3)	90 (55.9)	4 (33.3)	78 (53.1)	12 (85.7)	64 (52.5)	14 (56.0)
HCV Genotype (n, %)	1, Unspecified	4 (2.3)	4 (2.5)	0	4 (2.7)	0	3 (2.5)	1 (4.00)
	1a	108 (62.4)	102 (63.4)	6 (50.0)	92 (62.6)	10 (71.4)	80 (65.6)	12 (48.0)
	1b	28 (16.2)	26 (16.2)	2 (16.7)	25 (17.0)	1 (7.1)	23 (18.9)	2 (8.0)
	2	8 (4.6)	7 (4.4)	1 (8.3)	6 (4.0)	1 (7.1)	3 (2.5)	3 (12.0)
	3	13 (7.5)	13 (8.0)	0	13 (8.8)	0	9 (7.4)	4 (16.0)
	4	7 (4.0)	7 (4.4)	0	6 (4.1)	1 (7.1)	3 (2.5)	3 (12.0)
	Not done, not classified	5 (2.9)	2 (1.2)	3 (25.0)	1 (0.7)	1 (7.1)	1 (0.8)	0

Abbreviations: HCV, hepatitis C virus; SD, standard deviation.

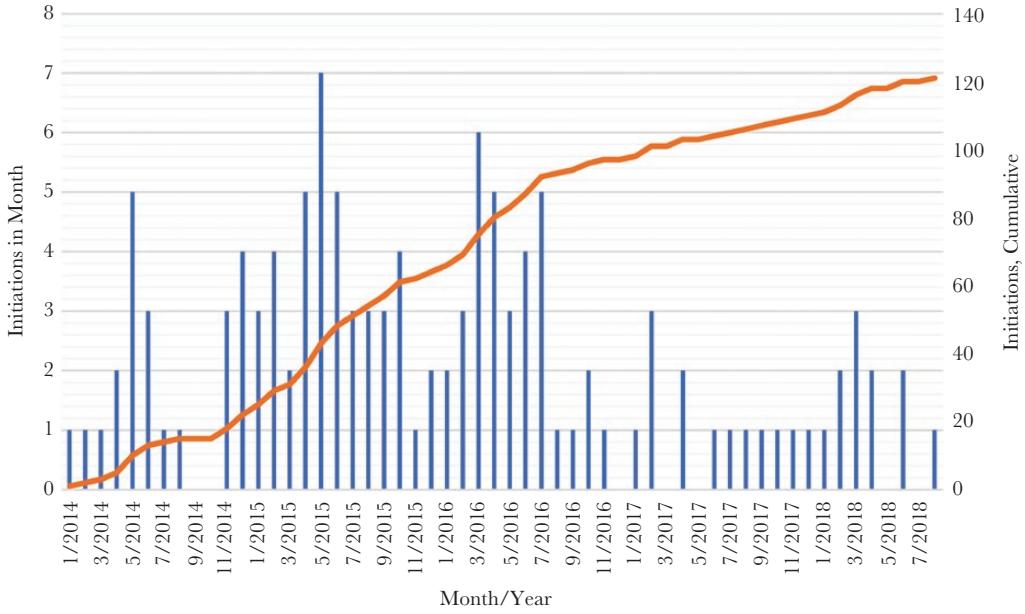

Figure 1. The figure depicts monthly direct antiviral agent treatment initiations (in blue) and cumulative treatment initiations (in red) between January 2014 and August 2018 for human immunodeficiency virus/hepatitis C virus-coinfected patients at the Nathan Smith Clinic in New Haven, Connecticut.

adherence monitoring. Ten patients accepted treatment initiation with the Proteus digital technology and 6 achieved SVR12 (data not shown).

Hepatitis C Virus Care Cascade

Table 1 describes patient characteristics according to steps along the HCV care cascade. Of the 173 eligible patients, 161 (93.1%) were referred to DAA prescriber, 147 (85%) were linked to DAA prescriber, and 122 (70.5%) were prescribed DAA therapy. The majority were internal referrals (n = 148) as opposed to external referrals to Hepatology (n = 13). Among those referred, linked, and treated, the majority were between 50 and 70 years old (83.2%, 85%, 83.6%, respectively), male (67.7%, 68%, 72.1%), African American (58.4%, 58.5%, 57.4%), and received Medicaid or Medicare insurance (combined percentages of 88.1%, 87.7%, 86.9%, respectively). The majority had genotype 1a. Alcohol abuse occurred in approximately 31% of all groups, mental health issues occurred in approximately 60%, and active substance use issues occurred in over 52% of all groups.

Figure 2 shows the diagnosis-based HCV care cascade; overall, 97 (56.1%) had documented SVR12. Of patients prescribed treatment (n = 122), 79.5% had documented SVR12. Patients were treated with the following DAAs: sofosbuvir/ledipasvir (65.6%), sofosbuvir/ribavirin (8.2%), sofosbuvir/simeprevir (7.4%), elbasvir/grazoprevir (6.5%), sofosbuvir/velpatasvir (6.5%), sofosbuvir/daclatasvir (3.3%), and other (2.5%). Among the remaining treated patients without documented SVR12 (n = 25), 14 had completed treatment and were awaiting SVR12 documentation, 5 were on therapy, 4 stopped therapy early, 1 relapsed, ad 1 was lost to follow up. There were no reinfections based on available 1-year post-SVR follow-up HCV viral load testing.

Analysis of Untreated Patients

Overall, 51 (29.5%) patients who were not prescribed DAA treatment were defined as "not engaged in HCV care" (Figure 2). Of these, 12 (6.9%) had not been referred to a DAA prescriber, 14 (8.1%) were referred but failed to link, and 25 (14.5%) were linked but had not been prescribed treatment. The specific demographics of these subgroups are also shown in Table 1.

Further analysis of those not engaged in HCV care showed that 12 (6.9%) persons had either died, relocated, or were incarcerated, so they were no longer cared for by our clinic. Of the remaining untreated active patients (n = 39) (Table 2), 9 (23.1%) were not referred, 10 (25.6%) were referred but not linked, and 20 (51.3%) were linked but not treated; 36 (92.3%) had missed more than 1 clinic appointment, 25 (64.1%) had mental health issues, 24 (61.5%) had substance abuse issues, and 17 (43.6%) were not HIV virally suppressed; 33 (84.6%) were stably housed and 35 (89.7%) had public insurance. In the "not referred" group (n = 9), 77.8% of patients missed more than 1 appointment and 55.6% had mental health issues. In the "referred, not linked group" (n = 10), 70.0% were nonvirally suppressed for HIV, 100% missed more than 1 appointment, 70.0% had mental health issues, and 90.0% had substance abuse issues. In the "linked, but not treated group" (n = 20), 95.0% missed more than 1 appointment, 65.0% had mental health issues, and 60.0% had substance abuse issues.

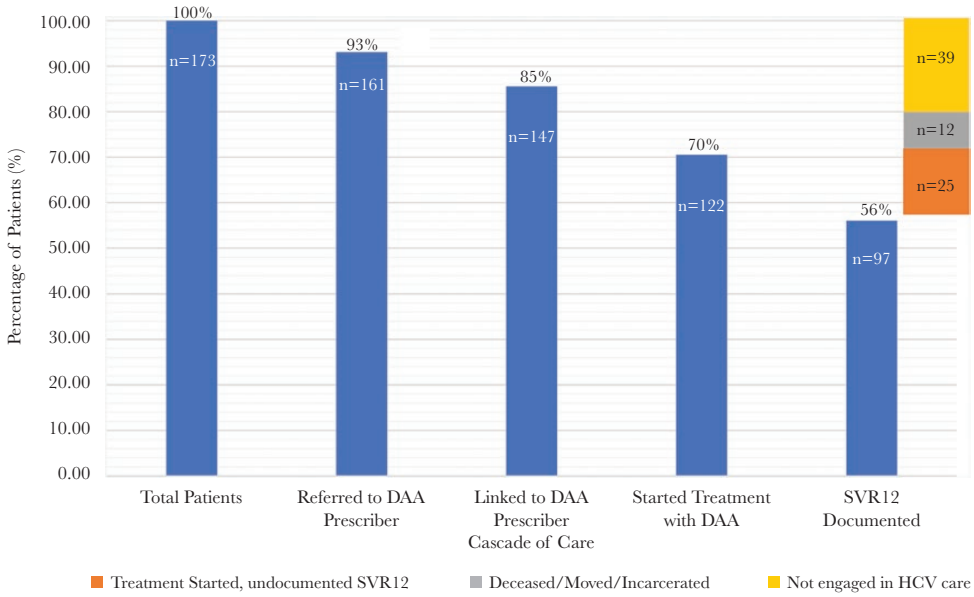

Figure 2. The figure depicts the diagnosis-based hepatitis C virus (HCV) cascade of care among human immunodeficiency virus/HCV-coinfected patients at the Nathan Smith Clinic in New Haven, Connecticut between January 2014 and August 2018. The starting point is for the total number patients with diagnosed coinfection. DAA, direct-acting antivirals; SVR12, SVR at 12 weeks posttreatment or cure.

Comparison of Patients With Documented SVR12 and Untreated

Table 3 shows a bivariate analysis comparing those who had not been treated (n = 51) with those who had successfully documented SVR12 (n = 97). Among patients who had not been treated, the mean age was slightly younger (mean age 54.2 years vs 57.0 years, P = .022) and there were more female patients (P = .001). There were no statistically significant differences in race, ethnicity, or presence of comorbidities such as cirrhosis, renal disease, mental health issues, alcohol and substance use issues, and insurance type.

DISCUSSION

In this study, we described the implementation of a colocated HCV clinic within an HIV clinic to systematically promote movement along the HCV care cascade. We found that after almost 5 years of implementing this model, 93.1% of coinfected persons were referred, 85% were linked, 70.5% were initiated on DAAs, and 56.1% had documented SVR12. This cascade compares favorably to published national cascades for monoinfected patients using the first-generation of DAAs [13, 25, 26]. A 56.1% SVR12 rate in an HIV/HCV-coinfected patient population is a significant success and shows the effectiveness of our model. We anticipate that the SVR12 rate will increase further as additional follow-up data are available. We have successfully overcome common barriers to care such as availability of trained providers, access to and approval for availability of DAAs, and facilitation of treatment adherence. More important, despite a significant presence of comorbid alcohol, substance use, and mental health issues in the study group, our dedicated service delivery model was able to overcome traditional barriers in achieving SVR12.

Others showed similar success rates with the availability of DAAs. In a cohort of both mono- and coinfected patients in an academic referral ID clinic in Tennessee in 2015–2016, Zuckerman et al [27] showed that 64% were linked to care for HCV treatment, 60% initiated treatment, and 53% achieved SVR12; these results were similar to ours. In some cases, the SVR12 rates described in coinfected patients were better than those reported in monoinfected patients [27–29], perhaps because PWH are more likely to have access to HIV-specific medical care than the monoinfected population and HIV providers are well equipped to engage and retain patients in care.

Our model resembled similar published approaches for treatment of HIV/HCV-coinfected populations. Other authors described colocated clinics that have coordinated approaches to manage referrals [16, 27, 28]. In all of these approaches, coinfected patients were voluntarily referred by other providers for specific HCV management. Our approach differed in that we requested our HIV providers to refer patients for HCV co-management, at times with prompting from the HCV nurse. This approach required initial buy-in from providers, but with time it was welcomed as the standard of care with high provider satisfaction. Despite these efforts, not all patients (7%) were successfully referred, and we are currently requiring that all coinfected patients have automatic HCV clinic appointments without an HIV provider referral. Our model also built on a multidisciplinary team effort that monitored the registry and brainstormed regularly to promote engagement in care. For example, when lists of patients who were not linked to care were

Table 2. Qualitative Analysis of HIV/HCV-Coinfected Patients Who Did Not Start DAA Treatment

Characteristic N (% of total)	Not Referred N = 9[a] (23.1%)	Referred, Not linked N = 10[b] (25.6%)	Linked, Not Treated N = 20[c] (51.3%)	Total N = 39
Nonvirally suppressed (HIV viral load >20 copies/mL)	3 (33.3%)	7 (70.0%)	7 (35.0%)	17 (43.6%)
CD4 count >200 cells/μL	5 (55.6%)	8 (80.0%)	17 (85.0%)	30 (76.9%)
Missed clinic appointments (>1 no show)	7 (77.8%)	10 (100.0%)	19 (95.0%)	36 (92.3%)
Private insurance	1 (11.1%)	0 (0%)	2 (10.0%)	9 (23.1%)
Public insurance	8 (88.9%)	9 (90.0%)	18 (90.0%)	35 (89.7%)
No insurance	0 (0%)	1 (10.0%)	0 (0%)	1 (2.6%)
Stable home	6 (66.7%)	10 (100.0%)	17 (85.0%)	33 (84.6%)
Department of correction (in time frame)	2 (22.2%)	0 (0%)	1 (5.0%)	3 (7.7%)
Mental health issues	5 (55.6%)	7 (70.0%)	13 (65.0%)	25 (64.1%)
Substance use	3 (33.3%)	9 (90.0%)	12 (60.0%)	24 (61.5%)

Abbreviations: DAA, direct-acting antivirals; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

[a]Not referred total equals 12; however, 1 incarcerated and 2 deceased.

[b]Not linked total equals 14; however, 1 moved and 3 deceased.

[c]Not treated total equals 25; however, 1 moved and 4 deceased.

generated, clinic staff made intensive efforts to call and make necessary appointments. Patients who were residents of extended care facilities or admitted to the hospital were ensured continuity of HCV treatment. The adoption of innovative digital technology for intensive monitoring was an attempt to promote engagement for some patients. Pharmacy staff were

Table 3. Comparison of Patients With Documented SVR12 and Patients Who Were Not Engaged in HCV Care

Characteristic		SVR12	Not Engaged in HCV Care[a]	*P* Value
Total Patients		97[b]	51	
Age (n, %)	<50 years old	13 (13.4)	13 (25.5)	.11
	≥50 and ≤70 years old	82 (85.4)	38 (74.5)	
	>70 years old	2 (2.1)	0	
Age (mean, SD)		57.0 (6.8)	54.2 (7.4)	.022
Gender (n, %)	Male	76 (78.4)	27 (52.9)	.001
	Female	21 (21.7)	24 (47.1)	
Race (n, %)	White or Caucasian	27 (27.8)	14 (27.5)	.64
	Black or African American	52 (53.6)	29 (56.9)	
	American Indian or Alaska Native	0	1 (2.0)	
	Hispanic	14 (14.4)	5 (9.8)	
	Other/Unknown/Patient Refused	4 (4.1)	2 (3.9)	
Insurance n (%)	Medicaid	42 (43.3)	30 (58.8)	.42
	Medicare	41 (42.3)	17 (33.3)	
	Private	12 (12.4)	4 (7.8)	
	Ryan White	1 (1.0)	0	
	Other	0	0	
	Self-Pay	1 (1.0)	0	
Liver cirrhosis (n, %)		25 (25.8)	11 (21.6)	.57
Kidney disease (n, %)		18 (18.6)	10 (19.6)	.88
Alcohol abuse (n, %)		31 (21.0)	15 (10.1)	.75
Mental health (any issue) (n, %)		55 (56.7)	32 (62.8)	.48
Active drug use (n, %)		50 (51.6)	30 (58.8)	.4
HCV genotype (n, %)	1, Unspecified	3 (3.1)	1 (2.0)	.008
	1a	64 (66.0)	28 (54.9)	
	1b	18 (18.6)	5 (9.8)	
	2	2 (2.1)	5 (9.8)	
	3	8 (8.3)	4 (7.8)	
	4	2 (2.1)	4 (7.8)	
	Not done, not classified	0	4 (7.8)	

Abbreviations: DAA, direct-acting antivirals; HCV, hepatitis C virus; SD, standard deviation; SVR, sustained viral response; SVR12, SVR at 12 weeks posttreatment or cure.

[a]Includes the following patients: not referred, not linked, not prescribed DAA treatment.

[b]Excludes 25 patients who started treatment but are awaiting treatment completion or SVR documentation.

actively involved including calling patients to ensure adherence to medications and laboratory monitoring. This concerted effort required considerable time and resources, and it remains to be seen whether the model is scalable within other clinics in the United States and internationally.

Despite this approach, 22.5% of patients were not engaged in HCV care. We did not collect data on HIV risk factors for this project, so risk-related behavioral reasons for poor engagement in HCV care cannot be specifically addressed. Previous studies have found that there are higher rates of linkage to care for men who have sex with men compared with people who inject drugs [30]. In our study, the group not engaged in HCV care was also characterized by multiple missed HIV clinic appointments and nonsuppressed HIV viral load suggestive of generalized lack of engagement in HIV care. The "no-show" phenomenon, which could reflect inherent barriers such as lack of transportation or active coexisting mental health and substance use issues, likely contributed to the barrier in prescribing DAAs. In our study, this group had high co-occurrence of mental health (64.1%) and substance use disorder ([SUD] 61.5%).

These findings in a "hard-to-treat" group are similar to those found by other investigators. In an earlier study in coinfected populations by Cachay et al [14], lack of engagement in HIV care (odds ratio [OR] = 5.08) was the most important predictor of nonreferral for HCV therapy, followed by unstable housing (OR = 2.26), acquired immune deficiency syndrome (OR = 1.83), having a detectable HIV viral load (OR = 1.98), and being nonwhite (OR = 1.67). In a later analysis, predictors for not establishing HCV care among coinfected patients were mental health disease, ongoing drug use, being non-white, CD4 <200, and detectable HIV viral load [31]. Nonetheless, Falade-Nwulia et al [32] showed that persons who were traditionally underserved (black and Hispanic) were able to successfully achieve SVR12, showing that persistent and innovative clinic strategies can overcome certain social determinants of health. Underinsurance (eg, Medicaid) may still be a barrier as shown by Zuckerman et al [27]. In our bivariate analysis, we did not find statistically significant racial/ethnic differences or presence of active mental health or substance use issues between those who had documented SVR12 and those who showed lack of engagement in HCV care. This is in keeping with various studies that show that substance abuse is not a contraindication to DAA treatment [9, 11, 33]. Therefore, although HCV is a curable disease with excellent drugs available, implementing treatment has some real-life barriers to achieving microelimination. Additional interventions are still needed to target the hard-to-treat patients.

Another relevant finding was a difference in proportions for slightly younger and female patients not being treated for HCV compared with those who achieved SVR12. Some studies have shown gender differences in the quality of HIV care in Ryan White CARE Act-funded clinics, with women less likely to obtain *antiretroviral therapy* and HCV screening despite having more clinic visits compared with men [34]. The authors also noted that those differences were not due to lower quality care towards women, but possibly due to different priorities expressed by women. Zuckerman et al [27] found that women were also less likely to be treated for HCV. In our study, coinfected females were likely to also have IDU as an HIV risk factor, potentially contributing to an increased likelihood of lower linkage to care. It has been speculated that women tend to prioritize their families or are preoccupied with other responsibilities and delay their HCV treatment. Additional help can be provided by the clinic to female patients through support services such as medical case management and counseling [35]. In general, the younger patient population (<30 years old) has been a challenging group to retain in HIV care as noted by Griffith et al [36]. This gap in retention is due to many barriers such as unemployment, unstable housing, mental health issues, and substance use. In our study, however, the proportion of patients <50 years old was not statistically different between those who achieved SVR12 and those not engaged in care, although numbers were small.

From a patient standpoint, given the short course and excellent tolerability of most DAAs, it would be predicted that treatment engagement would be high. In this study, we evaluated treatment outcomes before the wider availability of pan-genotypic regimens with shorter treatment courses (eg, glecaprevir/pibrentasvir), which could be predicted to improve treatment acceptability. Nonetheless, there are still obstacles familiar to providers of HIV care, and innovative approaches to encourage engagement in care are needed. Various interventions have been proposed as best practices including (1) access to substance use providers and (2) peer navigators [28, 37, 38]. For example, active substance use and mental health issues can prevent successful linkage to HCV care; onsite HCV treatment in SUD clinics or convenient referral systems to SUD clinics and Syringe Services Programs may help [39]. Patient barriers to adherence to clinic visits and medications need to be addressed; other approaches should be considered such as telemedicine visits. We piloted a digital technology approach that off-loaded follow-up monitoring to specialty pharmacies and required patient self-management through digital monitoring; this approach may be successful in some patients [40]. Treatment in mobile units has shown success in other settings [24]. Use of long-term care facilities where patients may be undergoing rehabilitation and prison settings may represent useful venues for completing treatment. Finally, in situations in which patients are not amenable to pursuing treatment (eg, not concordant with other goals of care), it would be important to intensify prevention strategies so that the epidemic is not perpetuated.

Strengths and Limitations of Project

A strength of the project is that granular data characterizing details of engagement in care and patient comorbidities were

abstracted using various sources in the EMR, and that the team sustained continuous cycles of engagement. Limitations of the project are our smaller sample size, which prevented us from analyzing the different groups lost at each stage of the care cascade separately and from performing multivariable analyses. In addition, inclusion of comorbidities was reliant on ICD-coded problem lists, which may not be fully accurate. We propose this model as a possible approach to achieving HCV microelimination. The WHO HCV elimination targets for 2030 propose that 90% are diagnosed and 80% of eligible persons are treated. One limitation is that we have insufficient data in this study period to fully quantify if our clinic has achieved these particular targets. Given that our Ryan White-funded clinic has approximately 100% baseline HCV antibody testing and that the current standard of care is reflex PCR testing, we have the capacity to achieve the 90% diagnosis target; nonetheless, quantifying these efforts will be an area of future research. Our achievement of 70% DAA treatment in this small population is approaching the 80% treatment target rate, and additional efforts as discussed above could enable reaching the additional 10%. We have not calculated incremental cost of this model because we acknowledge that additional personnel time was necessary to accomplish the clinical and data monitoring efforts. Such calculations would be important to assess whether these efforts are scalable and constitute a sustainable approach for achieving WHO microelimination targets.

CONCLUSIONS

Establishing a colocated HCV clinic within an HIV clinic model has been successful in facilitating pretreatment evaluation in 93.1% of coinfected patients with overall SVR12 documented in 56.1% of patients (79.5% of treated patients). This compares favorably with published national HCV treatment cascades in monoinfected patients. Of the 22.5% of patients who were not successfully started on treatment, ongoing issues included lack of engagement in healthcare. Targeted assessment of patient and provider barriers to completing clinic-wide HCV microelimination and novel approaches for promoting engagement in care are needed.

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