

Provider and Patient Correlates of Provider Decisions to Recommend HCV Treatment to HIV Co-Infected Patients

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Abstract

Despite low uptake of hepatitis C virus (HCV) treatment among HIV co-infected patients, few studies have examined the factors that contribute to provider decisions to recommend treatment. Surveys of 173 co-infected patients and their primary care providers, as well as patient chart data, were collected at 3 HIV clinics in Los Angeles; 73% of the patients had any history of being recommended HCV treatment. Multivariate predictors of being offered treatment included being Caucasian, greater HCV knowledge, receiving depression treatment if depressed, and one's provider having a lower weekly patient load and more years working at the study site. These findings suggest that provider decisions to recommend HCV treatment are influenced by patient factors including race and psychosocial treatment readiness, as well as characteristics of their own practice and treatment philosophy. With changes to HCV treatment soon to emerge, further evaluation of factors influencing treatment decisions is needed to improve HCV treatment uptake.

Keywords

hepatitis C, provider treatment decision making, treatment readiness

Introduction

Nearly 30% of HIV-positive Americans are co-infected with the hepatitis C virus (HCV). Hepatitis C virus is a leading cause of death among HIV co-infected patients,¹⁻³ with annual HCV-related mortality expected to peak at 13 000 in 2030 in this population.⁴ However, despite a majority of co-infected patients having signs of liver disease progression,^{5,6} only a minority (~30%) are deemed eligible for treatment and less than 10% actually receive treatment.⁷⁻¹⁰ Low treatment uptake is often attributed to the limited efficacy (20%-50% response rate among co-infected patients) and high toxicity of pegylated interferon (PEG-IFN) and ribavirin (RBV),¹¹⁻¹⁶ the current standard of care for HCV treatment, and yet treatment can essentially cure the disease.

Whether a patient starts treatment depends first on the provider's decision to recommend treatment. Despite the disparity between the need for aggressive HCV treatment and low treatment uptake, few studies have examined the factors that contribute to provider decisions to offer treatment. Nonetheless, we expect provider decisions to offer treatment are likely influenced by the following: severity and stage of liver disease; stability of the patient's HIV disease and presence of other medical comorbidities; perception of the patient's readiness

to tolerate and adhere to treatment; and the provider's beliefs and attitudes related to the urgency and expected outcomes of treatment.

CD4 counts temporarily decrease during the course of HCV treatment¹⁷; therefore, to limit the risk of developing opportunistic infections, the treatment is preferably started when the patient has a high CD4 count, low HIV viral load, and on a HIV antiretroviral therapy (ART).¹⁸ Treatment is typically recommended for patients with moderate liver disease,^{18,19} while patients with minimal disease progression are monitored and treatment are deferred.²⁰ However, some view the latter as optimal for treatment,¹⁹ given the more rapid disease progression among co-infected patients²¹ and the greater likelihood of

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treatment success with milder disease.^{22,23} These conditions hold for the predominant genotype 1 patients for whom treatment is considerably less successful, while patients with genotype 2 or 3 are generally considered good treatment candidates because they respond to treatment much more favorably.^{18,19}

Patients must also be ready to adhere to and tolerate treatment. Drug abuse and mental illness are among the most common reasons for patients being ineligible for HCV treatment,^{8-10,24-26} as clinicians are concerned that treatment side effects (eg, depression, fatigue, flu-like symptoms) may lead to psychiatric deterioration, relapse into substance abuse, and treatment nonadherence and discontinuation. However, there is some evidence that treatment can be equally effective when patients have active psychiatric illness and are using drugs.²⁷⁻³¹

Provider training and characteristics of their clinical practice may influence HCV treatment decisions, including experience and perceived skills and comfort in managing HCV care and treatment with HIV co-infected patients, and attitudes related to HCV treatment efficacy and patient readiness.^{32,33}

We surveyed primary care providers at 3 HIV clinics in Los Angeles, along with the HCV co-infected patients who attended these clinics over 4 months to examine patient and provider characteristics associated with provider decisions to offer or defer HCV treatment.

Methods

Setting

Cross-sectional surveys were administered to primary care providers and HCV co-infected patients at 3 HIV clinics in Los Angeles: the Greater Los Angeles Veterans Administration (VA) Medical Center, Harbor-UCLA Medical Center, and AIDS Healthcare Foundation (AHF). The sites differ on a number of characteristics including the number of HIV patients (400-1700) and HCV co-infected patients (100-650), involvement of a liver specialist (at only 1 site), and HCV treatment rates (10%-40% of co-infected patients have received treatment). The clients at all 3 clinics are mostly racial/ethnic minorities and of lower socioeconomic status.

All 3 clinics provide comprehensive primary and subspecialty care, and thus patients receive their HCV care at the HIV clinic. At Harbor-UCLA, HIV and HCV primary care are provided predominantly by 4 nurse practitioners (NPs) who are supervised by 2 attending physicians, and treatment decisions are made jointly between the NPs and physicians. At the VA, HIV primary care is provided by 4 physicians, but HCV care and treatment for the co-infected patients are managed by one of the hospitals' gastroenterologists (with the assistance of a physician's assistant from the clinic) who comes to the clinic to conduct biweekly HCV care clinic sessions; the primary care physicians are consulted regarding HCV treatment decisions when warranted. The AHF clinic serves as the central HCV care site for the full system of AHF clinics in Los Angeles County; HCV care is provided mostly by 2 providers (1 physician and 1 NP), although the HCV care for some patients at the

clinic are managed by their primary care provider. Support staff at the sites includes pharmacists, nurses, case managers, and social workers; 1 clinic has a mental health professional on-site, the others refer out for psychiatric consultation and treatment.

Sample

All clinic patients who were HCV co-infected, aged 18 or older, and speak English were considered eligible for the study. During the 4-month study enrollment period, the study coordinator at each site performed a chart review of all patients attending the clinic for a routine visit to identify those who were eligible. Patients were informed of the study while they were waiting to be seen by their provider; those who were interested in participating provided signed informed consent for completing a self-report questionnaire prior to leaving the clinic and allowing the study to abstract data from their clinic chart. All primary care providers were asked to participate and complete a self-report survey. Patients (\$40) and providers (\$50) were compensated for their participation, except at the VA where providers were not compensated due to institutional policy. The study protocol was approved by the Institutional Review Boards at RAND Corporation and the individual clinics.

Measures

For patients who had been offered HCV treatment, data were abstracted from the clinic visit closest and prior to the date at which HCV treatment was offered to the patient; for patients who had not been offered treatment, the most recent data prior to the date of survey were abstracted as these represent the latest indicators upon which a decision had been made to not recommend treatment. However, some variables, including all provider measures, could only be assessed at study enrollment with the study survey as indicated below.

Patient Variables

The HCV treatment status was abstracted from the clinic charts by first determining whether the patient had ever been treated. Among those who had not been treated, it was determined whether the provider had ever offered or recommended treatment. Dates were abstracted for time HCV treatment was offered and started, if applicable.

Demographic and background characteristics that were assessed by the study survey included age, gender, race/ethnicity, and education. The date the patient was diagnosed with HIV and HCV and the date the patient started receiving care at the study site were abstracted.

Stability of HIV was assessed with CD4 count, HIV viral load, and whether or not the patient was on ART. With regard to the stability of HCV and liver disease, measures included HCV viral load, genotype, and other laboratory markers related to liver functioning (aspartate aminotransferase [AST]/alanine

aminotransferase [ALT], hemoglobin, absolute neutrophil count [ANC]). All of these variables were chart abstracted.

Psychosocial functioning was assessed with chart abstracted data related to whether the patient had a current diagnosis of depression or any other psychiatric disorder, and whether they were receiving any form of psychiatric treatment (eg, psychotropic medication, and counseling). We also abstracted data regarding alcohol and illicit drug use and history of injection drug use.

Adherence was assessed in the study survey by asking respondents to report whether or not they had missed any scheduled clinic appointments over the past 6 months, and those on ART were asked how many doses they had missed over the past 7 days (from study entry). Both measured were then converted into dichotomous variables based on whether or not they had missed any clinic appointments or missed any ART doses.

Knowledge of HCV was assessed at study entry with a scale adapted from that used by Doab et al.³⁴ The 4-item scale evaluates the patient's understanding of HCV (eg, whether a cure is possible, HCV always leads to sickness, and HIV worsens HCV, and genotypes 2 and 3 respond best to treatment); a yes/no response option was used and a score was calculated summing the correct responses.

Provider Variables

Demographic characteristics included age, gender, and race/ethnicity. Medical practice and training characteristics that were assessed included training discipline (eg, physician, NP, physician's assistant), number of years at the clinic, number of HIV/HCV co-infected patients cared for, number of patients treated with PEG-IFN/RBV, and average patient load per week.

Perceived challenges regarding HCV care were assessed with a measure adapted from that used by Meredith et al³⁵; 11 items assess structural and patient factors that limit or challenge a provider's ability to provide optimal HCV care (eg, absence of a liver biopsy, mental health, or substance abuse counselors not readily available, patient reluctant to seek mental health or substance abuse treatment, patient's comorbid medical problems). Participants chose from 3 response options (ie, does not limit, limits somewhat, and limits a great deal). Mean item score was computed and higher scores indicate greater perceived challenges to providing optimal care. Internal reliability was high ($\alpha = .91$).

Provider philosophy regarding patient psychosocial treatment readiness was assessed by asking the provider about their approach to treatment if a patient reported (1) current drug use or (2) moderate depression, "but was otherwise a good HCV treatment candidate," in separate questions. Response options consisted of 5 scenarios that ranged from deferring treatment until the condition (drug use, depression) was treated and in remission, to counseling the patient about the risks of the condition for HCV treatment but letting the patient decide whether or not to start or defer treatment. Due to skewed response

distributions, the responses were dichotomized into providers who believed that HCV treatment should only be offered after the patient was in remission versus more lenient views of readiness.

Provider's general threshold for patient treatment readiness was measured with a scale developed for the study, which assessed the likelihood that a provider would prescribe HCV treatment to a patient with various conditions that could affect the patient's readiness or appropriateness for treatment (eg, decompensated liver disease, genotype 2 or 3, active depression, smokes marijuana regularly, etc). Providers responded on a 5-point Likert-type scale ranging from *very likely* to *very unlikely*, with regard to 14 specific conditions; internal reliability was high ($\alpha = .86$). The mean item score was calculated and higher scores represented a higher threshold for determining patient readiness for treatment.

Data Analysis

Descriptive statistics were used to examine the response distributions of variables and a number of variables were converted from continuous to dichotomous variables based on clinical significance (eg, CD4 count ≤ 200 cells/mm³; HIV viral load ≤ 400 copies/mL; genotype 1 or 4 versus 2 or 3) or the skewed distribution of responses (eg, none vs any missed ART doses). Bivariate statistics (independent 2-tailed *t* tests, chi-square tests) were used to examine the correlates of whether or not the patient was offered HCV treatment. Variables that were significant at $P < .05$ level in the bivariate analysis were then entered into a logistic regression model as independent variables, with the indicator of whether treatment was offered being the dependent variable. To account for potential correlations among outcomes of patients in the same clinic that share a provider, we computed robust standard errors for the regression models to account for intracluster correlations within provider.

Results

Sample Description

A total of 173 patients were surveyed: 97 from AHF, 41 from the VA, and 35 from Harbor-UCLA. Most (87%) participants were male, mean age was 49.0 (SD = 9.1), 60% had at least some college education, 69% were racial/ethnic minorities (including 41% who were black and 21% who were Hispanic), 38% identified as heterosexual, and 58% had a history of injection drug use. Most had been diagnosed with HIV for several years (mean = 13.5 years) and had been receiving care from the study site for an average of 7.8 years. Mean time since HCV diagnosis was 7.1 years, and 78% had an HCV genotype of 1 or 4.

Fourteen primary HCV care providers completed the survey, accounting for the HCV care providers of 155 (90%) of the patient participants. Among the 14 providers surveyed, half were male, 57% were Caucasian, and 69% were physicians. The mean number of years of practice at the clinic site was

11.1 (SD = 6.1; range: 2-19); each provider sees an average of 34 HIV patients (HCV and non-HCV) per week (SD = 21; range: 5-90), and the mean number of co-infected patients that each provider had treated with interferon was 21 (SD = 19; range: 4-60).

Factors Associated with Recommending HCV Treatment

Of the 173 patients, 127 (73%) had been offered or recommended HCV treatment; 79 (62%) accepted the recommendation and started treatment, and the factors associated with this patient decision are presented elsewhere.³⁶ For those who had been offered treatment, this event took place an average of 6.2 years (SD = 5.8 years; range: 1 week to 23.0 years) after HCV diagnosis and 2.3 years (SD = 2.7 years; range: 1 week to 10.9 years) prior to the study survey. The proportion of surveyed patients at each site who had been offered treatment was 85% at Harbor-UCLA, 71% at AHF, and 66% at the VA; these site differences were not statistically significant ($p = .115$). Table 1 lists the characteristics of the subgroups that had been offered (N = 127) and not offered (N = 46) HCV treatment. Patients offered HCV treatment were more likely to have CD4 counts above 200 cells/mm³ and lower HIV viral loads; similarly, there were marginal trends ($p < .10$) for this group to have higher mean CD4 count and an undetectable HIV viral load. Other patient variables associated with being offered treatment included greater HCV knowledge, receiving depression treatment if depressed (compared to untreated depression), and not being black or Hispanic.

The providers of patients offered treatment were more likely to be female, to have worked longer at the clinic site, see fewer patients on a weekly basis, and to have a lower threshold for indicators of patient readiness for treatment (see Table 1). Provider-related correlates that had marginal significance included fewer perceived challenges to providing optimal HCV care and the treatment philosophy that HCV treatment did not require that a drug using patient had entered a drug treatment program and been in remission.

In logistic regression analysis, significant independent predictors of being offered treatment included the patient not being black or Hispanic, having greater HCV knowledge, and receiving depression treatment if depressed, as well as the patient's provider having a lower weekly patient load and more years in practice at the clinic; the patient having a CD4 count >200 cells/mm³ was marginally significant as a predictor (see Table 2).

Discussion

Findings from this study reveal that a majority of HIV/HCV co-infected patients are recommended PEG-IFN/RBV treatment by primary care providers over the course of receiving care, although like other studies,^{7-10,37} only a minority of patients had actually received treatment. The data reveal that factors influencing provider decisions to offer or defer treatment are multifaceted. Provider HCV treatment decision

Table 1. Patient and Provider Characteristics Associated with HCV Treatment Being Offered in Bivariate Analysis

| Variable | Treatment Offered (127) | Treatment Not Offered (N = 46) |
|---|-------------------------|--------------------------------|
| Patient demographics | | |
| Male gender | 87% | 94% |
| Black or Hispanic | 58% ^b | 74% ^b |
| Mean age (years) | 49.4 | 47.7 |
| At least some college education | 58% | 65% |
| Stability of HIV | | |
| Mean CD4 count (cells/mm ³) | 485 ^a | 403 ^a |
| CD4 ≤200 (cells/mm ³) | 9% ^b | 22% ^b |
| Mean log ₁₀ HIV RNA (copies/mL) | 2.21 ^b | 2.61 ^b |
| Undetectable HIV RNA | 81% ^a | 67% ^a |
| On ART | 93% | 94% |
| HCV disease stage | | |
| HCV genotype 1 or 4 | 76% | 86% |
| Mean log ₁₀ HCV RNA (copies/mL) | 6.15 | 5.90 |
| Mean AST/ALT (IU/L) | 0.97 | 0.97 |
| Mean ANC (cells/mm ³) | 1059 | 1765 |
| Mean hemoglobin (g/dL) | 14.1 | 13.9 |
| Psychosocial Functioning | | |
| On depression treatment, if depressed | 28% ^b | 7% ^b |
| Frequent alcohol use (past 6 months) | 10% | 17% |
| Any illicit drug use (past 6 months) | 17% | 24% |
| Any IVDU history | 60% | 52% |
| Any missed ART doses (past week) | 27% | 31% |
| Any missed clinic appointments (past 6 months) | 34% | 26% |
| HCV knowledge | 1.70 ^b | 1.26 ^b |
| Provider characteristics | | |
| Male gender | 32% ^c | 55% ^c |
| Caucasian | 42% | 45% |
| Number of co-infected patients | 244.8 | 214.9 |
| Number of patients treated with INF/RBV | 40.5 | 34.9 |
| Treat only if drug use treated and in remission | 48% ^a | 65% ^a |
| Treat only if depression treated and in remission | 54% | 63% |
| Years in practice at study clinic | 12.3 ^b | 9.9 ^b |
| Number of patient seen weekly | 36.9 ^b | 45.3 ^b |
| Perceived challenges to optimal HCV care | 1.78 ^a | 1.96 ^a |
| Threshold for patient treatment readiness | 2.60 ^b | 2.90 ^b |

Abbreviations: HCV, hepatitis C virus; IVDU, intravenous drug user; ART, antiretroviral therapy; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ANC, absolute neutrophil count.

^a $P < .10$.

^b $P < .05$.

^c $P < .01$.

making is influenced by patient factors including the patient's stability of HIV disease and psychosocial readiness for treatment. However, the provider's decision process is not only influenced by patient characteristics but also aspects of the provider's clinical practice, attitudes toward HCV treatment and philosophy about patient treatment readiness.

Table 2. Patient and Provider Characteristics Associated with HCV Treatment Being Offered in Multivariate Analysis^a

| | Predicting Treatment Offer OR (95% CI) |
|---|--|
| Patient variables | |
| CD4 count <200 cells/mm ³ | 0.30 (0.06, 1.49) ^b |
| Mean HIV RNA | 0.84 (0.51, 1.38) |
| On depression treatment if depressed | 4.87 (1.32, 17.95) ^c |
| HCV knowledge | 1.48 (1.05, 2.10) ^c |
| Black or Hispanic | 0.32 (0.15, 0.70) ^d |
| Provider variables | |
| Gender | 1.03 (0.17, 6.31) |
| Weekly patient load | 0.96 (0.95, 0.98) ^d |
| Threshold for assessing patient readiness | 0.46 (0.14, 1.52) |
| Years in practice at study clinic | 1.07 (1.00, 1.15) ^c |

Abbreviations: HCV, hepatitis C virus; OR, odds ratio; CI, confidence interval.

^a Continuous predictors included HIV RNA, HCV knowledge, weekly patient load, and years in practice at study clinic; dichotomous predictors included CD4 count, treated depression, race/ethnicity, gender, and threshold for assessing patient readiness.

^b $P < .10$.

^c $P < .05$.

^d $P < .01$.

Having a CD4 count above 200 and low HIV viral load were bivariate correlates of having been offered treatment, as treatment response is positively correlated with CD4 count,³⁸ and PEG-IFN/RBV can temporarily deplete CD4 counts,¹⁷ rendering clients vulnerable to opportunistic infections if they have severe immunosuppression. However, some patients with CD4 counts below even 100 had been offered treatment, which is consistent with some Hepatitis Research Network clinical trials, and this highlights how even patients whose immune systems are severely compromised can still be considered appropriate for treatment. Also, the vast majority of all participants were on ART when the treatment was offered, which can help limit the risks associated with treatment of patients with low CD4 counts. Provider decisions to offer treatment were not related to our measures of HCV disease, including HCV genotype and HCV RNA, which are correlates of treatment response¹¹⁻¹³; however, we did not have measures of liver fibrosis.

Psychosocial indicators of patient treatment readiness, such as mental health, substance use, and adherence to clinical appointments and ART have been shown to be associated with HCV treatment eligibility in several other studies.^{9,10} However, in this study, depression treatment status for current depression and patient knowledge of the goals and potential costs and benefits of treatment were the only psychosocial variables associated with whether the treatment was recommended. Past history of depression, or current depression that was being managed with treatment, was not the limiting factor to being recommended treatment, which is consistent with data suggesting that such factors are not necessarily impediments to HCV treatment response.²⁷⁻²⁹ Greater HCV knowledge may be an indicator of patient self-advocacy or motivation for treatment,³² at least in the perception of providers, and may explain

in part its relationship to the offering of treatment; however, this relationship could also be bidirectional, with patients who are offered treatment consequently developing greater knowledge about the disease and treatment from their provider or through actively seeking out information.

The other patient characteristic associated with treatment being offered was race or ethnicity. African American and Hispanic patients, who together comprise the majority of the study sample, were less likely to be offered HCV treatment compared to the Caucasian patients, even after controlling for other significant correlates. This finding may reflect health disparities that are commonly seen among minority ethnic groups in the United States.³⁹ However, data show lower response rates to PEG-IFN/RBV among African American and Hispanic patients,⁴⁰⁻⁴² and this could tip the cost-benefit ratio in the favor of the potential burden on patients in the minds of providers.

Provider decisions of whether to recommend HCV treatment to an individual patient are not only predicted by characteristics of the patient but also by provider-related variables. Having a smaller weekly patient load was associated with a greater likelihood of recommending treatment, which may be a proxy for how availability of time for the provider to manage what is often complex treatment can influence provider treatment decisions. Years in practice at the study site was also associated with provider decisions to offer treatment, suggesting that greater experience in providing care may translate into greater comfort offering and managing HCV treatment. In bivariate analysis, treatment offers were more likely when the provider had a lower threshold for gauging patient readiness, which may also be an indicator of how urgent the provider considers the HCV treatment in general.³³

The primary limitation of the study findings is the largely retrospective nature of the study design, and associated reliance on available chart abstracted data or current assessments that may not be reflective of the conditions present when the treatment was offered. While a prospective design that measured variables at the time the treatment decision was actually made would be optimal, such a design was not feasible in terms of time and resources. The findings cannot be considered generalizable to all co-infected patients, although nearly all co-infected patients who attended the clinic during the study enrollment period did participate. Also, we were unable to reliably abstract data regarding medical comorbidities from patient's charts and therefore cannot account for the role of this important factor in provider decision making. Furthermore, with newer, more efficacious (but perhaps even more burdensome) treatments soon to be available,⁴³ it is unknown how this will affect provider decisions about the balance of the costs and benefits of treatment.

With HCV treatment rates continuing to be steadily low among HIV co-infected patients, the results of this study highlight both patient and provider variables that influence provider decisions to recommend treatment. Program administrators and intervention developers with an intent to increase treatment uptake should focus not only on factors that improve patient

readiness for treatment but also on provider attitudes and comfort level regarding treatment, as well as patient load and time availability. With changes to HCV treatment soon to emerge, and its uncertain effects on both the benefits and burden associated with treatment, further evaluation of factors influencing treatment decision making and treatment uptake will be needed to promote optimal HCV care management among HIV co-infected patients.

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