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Direct-acting antiviral treatment for HIV/HCV patients in safety net settings: patient and provider preferences

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ABSTRACT
HIV/HCV coinfected patients are a priority for direct acting antiretroviral (DAA) treatment, yet barriers to treating vulnerable patients persist. This study surveyed safety net clinic patients and providers to quantify their preferences for DAA treatment and prioritize modifiable barriers. Preferences were assessed using best-worst scaling. General linear mixed models were used to determine whether attributes differed in importance and whether patients and providers valued attributes differently. 158 HIV/HCV coinfected patients and 49 providers participated. Patients and providers had strong preferences for treatment within the medical homes where patients receive HIV care. Support such as reminders and advice numbers were also important, but were more important to providers than patients. Providers identified lack of insurance coverage for DAA as the most significant barrier. Providers rated HIV primary care providers as best suited to deliver DAA to HIV+ patients. Addressing structural barriers is essential for increasing DAA treatment in safety net settings.

INTRODUCTION
Direct-acting antiviral therapies (DAAs) have transformed the treatment of hepatitis C (HCV). Compared to earlier interferon-based therapies, DAAs are better tolerated, easier to administer, and more efficacious across the range of HCV genotypes and fibrosis stages (Bidell, McLaughlin, Faragon, Morse, & Patel, 2016; Cuypers et al., 2016). Simulation studies suggest that providing DAAs to all HCV infected persons would yield long-term benefits for individuals, by improving long-term health outcomes, and for society, by lowering long-term health care costs and reducing transmission of HCV (Chahal et al., 2016; Duberg et al., 2015). Despite these benefits, the high cost of DAAs (Chahal et al., 2016) has led many public and private payers to restrict access to the new therapies based on extent of liver fibrosis and other patient characteristics (Attar & Van Thiel, 2016).

Access to DAAs is a particularly important concern for people coinfected with human immunodeficiency virus (HIV) and HCV because coinfection is associated with accelerated progression of fibrosis and increased liver-related morbidity and mortality (Rockstroh & Hardy, 2016; Shafran, 2015). People coinfected with HIV and HCV experienced lower response rates with interferon-based therapies than people infected only with HCV. However with current DAA therapies, coinfected and monoinfected persons experience similar sustained viral response rates of over 95% (Del Bello et al., 2015; Feeney, Chung, & Yazdanpanah, 2015; Rockstroh & Hardy, 2016; Wyles, Sulikowski, & Dieterich, 2016).

Despite the benefits of DAA therapy, delivering treatment to coinfected individuals can be challenging. At the patient level, coinfected persons often have histories of injection drug use and a substantial proportion have ongoing problems with substance use, mental illness, unstable housing, and other medical comorbidities that can compromise treatment adherence (Bova, Ogawa, & Sullivan-Bolyai, 2010; Cachay et al., 2015; Grebely et al., 2015). At the system level, there are structural barriers to delivering DAA therapy to coinfected persons. Hepatologists are experts in HCV treatment, yet they may not be familiar with best practices in HIV care and the management of antiretroviral-DAA drug interactions (McGovern, 2012). Similarly, HIV care providers...
may not have the HCV training or structural supports needed to deliver DAA therapy (Chastain et al., 2015). Patients may need specialized supports to initiate and adhere to DAA therapy (Fleming, Tumilty, Murray, & Nunes, 2005; Treloar, Gray, & Brener, 2014). Further, reliance on specialty care can limit access by restricting the number of HCV treatment providers. Given that as many as one third of persons with HIV are coinfected with HCV (Taylor, Swan, & Mayer, 2012) complex decisions must be made about how best to provide DAA therapy for this population and how capacity to provide therapy can be increased. This study was designed to inform these decisions by quantifying and comparing patients’ and providers’ preferences for DAA treatment and prioritizing modifiable barriers to care. Preferences and priorities were quantified using Best-Worst Scaling (BWS) (Louviere, Flynn, & Marley, 2015). BWS is one of several preference assessment methods that simulate the real-world trade-offs inherent to complex decisions and quantify the importance of the varied attributes upon which decisions are based (Sawtooth Software, Inc., 2013). Similar methods have been used successfully to understand patient and provider preferences for interferon-based and hypothetical treatments for HCV (Fraenkel, Chodkowski, Lim, & Garcia-Tsao, 2010; Fraenkel, Lim, Garcia-Tsao, Reyna, & Monto, 2016; Hauber, Mohamed, Beam, Medjedovic, & Mauskopf, 2011; Kauf, Mohamed, Hauber, Fetzer, & Ahmad, 2012; Mühlbacher et al., 2017; Mühlbacher & Bethge, 2016; Pacou et al., 2015). This study applied these proven methods to understand preferences for delivery of DAA treatment to people coinfected with HIV and HCV.

Methods

Participants

This study focused on low-income patients served by safety net clinics and the providers who care for them. Patients and providers were recruited from five university and public health clinics providing HIV and/or HCV care in San Francisco, CA. Between September 2014 and April 2015, patient participants were recruited using flyers posted in the clinics and were 18 years or older, English speaking, able to provide informed consent, co-infected with HIV and HCV, and eligible for DAA treatment (i.e., had never received HCV treatment or had received treatment but did not achieve a sustained virologic response). Between December 2014 and May 2015, providers were recruited via email using lists provided by clinic directors of all providers authorized to prescribe medication, including physicians, nurse practitioners, and physicians assistants, as well as pharmacists who monitor but do not prescribe medication. All research procedures were approved by the Institutional Review Board of the University of California, San Francisco.

Best-worst scaling (BWS) surveys

Web-based best-worst scaling (BWS) surveys were developed based on qualitative interviews conducted with patients and providers. Interviews identified relevant attributes in three domains of DAA treatment: (1) characteristics of DAA treatment delivery (10 attributes), (2) barriers to prescribing DAA (8 attributes), and (3) providers best suited to delivering DAA treatment (5 attributes).

The MaxDiff module of Sawtooth Software’s SSI Web software (version 8) (Sawtooth Software, Inc., 2014) was used to develop a separate survey for each of the three domains. With BWS, participants are presented with a series of lists presenting a subset of attributes. For each list, the participant chooses the “best” and “worst” attributes on the list. Efficient designs for each survey were generated to balance the number of times each attribute was presented, the order in which sets of attributes were presented, and the order in which attributes were presented within sets. Illogical combinations were prohibited. The individual attributes in each domain are shown in Figures 1–3 and are discussed in the Results section.

The number of attribute sets and the instructions for selecting the best and worst attributes varied across the three domains. In the treatment characteristics survey, participants evaluated 8 sets of 4 attributes and were asked,

When you think about what DAA treatment for hepatitis C should be like, what would be best? From this list, please pick the one thing that would be the best in a new treatment program and the one thing that would be the worst.

In the provider barriers survey, participants rated 8 sets of 3 attributes and were asked, “When you think about what keeps you from providing more DAA treatment to HIV/HCV coinfected patients, what are the biggest barriers? From this list, please pick the one thing that is the biggest barrier and the one thing that is the smallest barrier.” In the provider discipline survey, participants evaluated 5 sets of 3 attributes and were asked,

When you think about who should provide DAA treatment to HIV/HCV coinfected patients, which providers would be best? From this list please pick the one type of
provider that is best suited to providing DAA treatment and the one type of provider that is least suited to providing DAA treatment.

Patients completed one survey about treatment characteristics and providers completed all three surveys, about treatment characteristics, barriers to treatment, and provider discipline. Patients completed the web-based surveys in private offices with the assistance of specially trained research interviewers. Providers completed the web-based surveys independently. Completing the surveys took between 30 and 45 min. All patient and provider participants were offered a $25 grocery store gift card in compensation for their time.

**Data analyses**

The hierarchical Bayes estimation procedures included in the SSI Web MaxDiff module were used to estimate Relative Importance Scores (RIS) for each attribute for each participant. RIS are ratio-scaled such that an attribute with a score of 40 is twice as important as an attribute with a score of 20. Within each survey, a participant’s RIS sum to 100.

General linear mixed model (GLMM) methods (SAS PROC MIXED) were used to determine whether attributes differed in importance and whether patients and providers valued attributes differently. In all analyses, the RIS were the dependent variables. In analyses of the treatment characteristics survey that was completed

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**Figure 1.** Patient and provider preferences for DAA treatment.

**Figure 2.** Provider perceptions of the importance of barriers to DAA treatment.
by both patients and providers, Group (patient vs provider) was included as a between-subjects factor and Attribute was included as a within-subjects factor. The Group × Attribute interaction was examined. In analyses of the barriers and provider discipline surveys that were completed only by providers, only the within-subjects factor, Attribute, was examined. GLMM were also used to evaluate whether provider respondents’ clinical role was associated with their preferences for disciplines best suited to providing DAA treatment.

Results

Sample characteristics

A total of 165 eligible patients gave informed consent and began the BWS surveys. Two patients were too tired to complete the surveys, two were called away to medical appointments, and 3 skipped individual survey items and their data could not be used because the Sawtooth Software MaxDiff module does not permit missing data. As a result, 158 patient participants were included in the analysis sample. As summarized in Table 1, patient participants were middle-aged (mean age of 50.7 years), 69% male, and racially and ethnically diverse. Patient participants were low-income; 84.2% had a monthly income of $1000 or less which was less than 25% of the per capita income in San Francisco at the time of the study (U.S. Census Bureau, 2016). Eighty-seven percent of patient participants had been homeless at some time and 10% were currently homeless. Seventy-seven percent of patient participants had a history of injection drug use and 33% had injected drugs in the previous six months. Ninety-one percent of patient participants were currently receiving antiretroviral therapy (ART) for HIV and 81% reported good, very good, or excellent adherence to their ART regimen in the past 30 days.

Recruitment emails were sent to 109 providers who care for patients with HIV and/or HCV in safety net settings. Nine actively declined to participate, 51 did not respond, and 49 consented to participate and completed surveys. As summarized in Table 2, the mean age of provider participants was 44. Forty percent were male. Most providers were white (71.4%) or Asian (18.4%). Provider participants were primarily physicians (67.4%) and nurse practitioners or physicians assistants (20.4%). Providers characterized the primary focus of their clinical work as infectious disease/HIV care (42.9%), primary care (22.5%), hepatology (22.5%), addiction health services (8%), and other (4%). Overall, provider participants were highly experienced in treating HIV and in assessing and monitoring progression of HCV; however, only 53% had direct experience with HCV treatment.

Preferences for DAA treatment characteristics

As shown in Figure 1, patients and providers shared similar overall rankings of treatment characteristics.
Table 2. Characteristics of provider participants.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (sd)/count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>44.4 (9.2)</td>
</tr>
<tr>
<td>Male gender</td>
<td>20 (40.8%)</td>
</tr>
<tr>
<td>Hispanic ethnicity</td>
<td>4 (8.2%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>African American/Black</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Native American</td>
<td>–</td>
</tr>
<tr>
<td>Asian American/Pacific Islander</td>
<td>9 (18.4%)</td>
</tr>
<tr>
<td>White</td>
<td>35 (71.4%)</td>
</tr>
<tr>
<td>More than one race</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>–</td>
</tr>
<tr>
<td>Provider type</td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>33 (67.4%)</td>
</tr>
<tr>
<td>Nurse Practitioner/Physicians Assistant</td>
<td>10 (20.4%)</td>
</tr>
<tr>
<td>Nurse</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Pharmacist</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Primary clinical focus</td>
<td></td>
</tr>
<tr>
<td>Infectious disease/HIV care</td>
<td>21 (42.9%)</td>
</tr>
<tr>
<td>Primary care</td>
<td>11 (22.5%)</td>
</tr>
<tr>
<td>Hepatology</td>
<td>11 (22.5%)</td>
</tr>
<tr>
<td>Addiction medicine</td>
<td>4 (8.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (4.0%)</td>
</tr>
<tr>
<td># Patients treated for HIV</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>11 (22.5%)</td>
</tr>
<tr>
<td>1–99</td>
<td>11 (22.5%)</td>
</tr>
<tr>
<td>100+</td>
<td>27 (55.1%)</td>
</tr>
<tr>
<td># Patients treated for HCV</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>22 (46.9%)</td>
</tr>
<tr>
<td>1–99</td>
<td>18 (36.7%)</td>
</tr>
<tr>
<td>100+</td>
<td>6 (12.4%)</td>
</tr>
<tr>
<td># HCV+ patients assessed and monitored</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2 (4.0%)</td>
</tr>
<tr>
<td>1–99</td>
<td>19 (38.8%)</td>
</tr>
<tr>
<td>100+</td>
<td>28 (57.1%)</td>
</tr>
<tr>
<td>Familiarity with DAA</td>
<td></td>
</tr>
<tr>
<td>Very familiar</td>
<td>17 (34.7%)</td>
</tr>
<tr>
<td>Somewhat familiar</td>
<td>25 (51.0%)</td>
</tr>
<tr>
<td>Somewhat familiar</td>
<td>7 (14.3%)</td>
</tr>
</tbody>
</table>

However, GLMM analysis revealed a statistically significant Group × Attribute interaction indicating that patients and providers valued some specific DAA treatment characteristics differently ($F_{8,198} = 13.24, p < .0001$). Both patients and providers rated receiving DAA treatment from the patient’s current clinic and current provider, ie. their “medical home”, as the most important characteristics. However, patients (mean RIS = 20.93, sd = 7.59) rated receiving treatment from their current provider as more important than did providers (mean = 16.95, sd = 8.38, t = 3.13, p = .002).

Strategies to support patients during treatment (check-ins by providers, reminders about medications and appointments, support groups, and an advice number) were rated as moderately important by both patients and providers, with mean RIS between 6.76 and 16.28. However, providers’ mean RIS were higher than patients’ for checking in between visits ($16.55 \text{ vs. } 14.37, t = 1.97, p = .05$), reminders about medications and appointments ($16.28 \text{ vs. } 12.28, t = 4.19, p < .0001$), and having an advice number ($10.47 \text{ vs. } 6.31, t = 4.86, p < .0001$). Neither patients (mean RIS = 3.16, sd = 3.37) nor providers (mean RIS = 1.21, sd = 2.05) viewed a website with information about DAA treatment as an important aspect of care.

Patients and providers both viewed needing to switch to different HIV medications as the least preferred characteristic of DAA treatment. However, patients’ RIS for switching HIV medications (mean = 1.16, sd = 1.97) were statistically significantly more favorable than providers’ RIS (mean = 0.35, sd = 0.87).

Provider perceptions of barriers to providing DAA treatment

GLMM analyses indicated that providers perceive differences in the impact of barriers to providing DAA treatment ($F_{6,43} = 28.24, p < .0001$). As shown in Figure 2, lack of insurance coverage for DAA treatment was by far the greatest barrier, followed by paperwork required to obtain treatment, patients’ other health concerns, lack of staffing and other resources to provide treatment, and delays obtaining medication. Staffing and other resources needed to evaluate patients for DAA treatment and training in identifying patients and selecting DAA medications for patients were seen as less significant barriers. Lack of insurance coverage for DAAs was more important than all other barriers (all $ts > 3.8$, all $ps < .0004$). Lack of staffing and other resources for providing DAA treatment (mean RIS = 13.39, sd = 10.02) was a more important barrier than staffing and resources for evaluating patients (mean = 8.25, sd = 6.97, $t = 5.97, p < .0001$), training in selecting drugs (mean = 8.24, sd = 9.58, $t = 2.68, p = .01$) and training on identifying eligible patients (mean = 4.65, sd = 7.57, $t = 4.63, p = .001$).

Provider preferences for disciplines delivering DAA treatment

GLMM analysis, summarized in Figure 3, showed that providers had strong preferences for which provider disciplines should provide DAA treatment to HIV/HCV coinfected patients ($F_{3,46} = 409.5, p < .0001$). HIV primary care providers who have completed an infectious disease fellowship were seen as best suited to provide DAA treatment (mean RIS = 39.80, sd = 2.81). Hepatologists (mean RIS 27.92, sd = 15.86) and HIV primary care providers without specific infectious disease training (mean RIS 21.28, sd = 12.82) were seen as somewhat less suited to providing DAA treatment to this patient population. Infectious disease specialists who do not provide HIV primary care (mean RIS 9.43, sd = 10.23) and addiction medicine specialists (mean RIS 1.57, sd = 5.63) were seen as least suited to providing DAA treatment.
In some instances, provider respondents’ primary clinical role was associated with their preferences for which disciplines should provide DAA treatment. Hepatologist respondents rated hepatologists as being highly suited to providing DAA treatment (42.91, sd = 3.18). In contrast, provider respondents from other disciplines rated hepatologists as being significantly less suitable; mean RIS for hepatologists providing treatment were 25.08 (sd = 19.03) from addiction medicine specialists, 21.11 (sd = 16.22) from infectious disease/HIV care providers, and 25.38 (sd = 13.80) from primary care (all ts > 2.18, all ps < .04). HIV primary care providers who have not completed an infectious disease fellowship were seen as more suitable providers of DAA treatment to coinfected patients by primary care providers (mean RIS 29.94, sd = 12.54) and infectious disease/HIV care providers (mean RIS 25.09, sd = 11.14) than by addiction medicine specialists (mean RIS 15.05, sd = 8.49) and hepatologists (mean RIS 7.96, sd = 5.16, all ts > 2.48, all ps < .02). Respondent discipline was not associated with RIS for provision of DAA treatment by addiction medicine specialists or HIV primary care providers with infectious disease training.

Discussion

This exploration of patient and provider preferences can inform the design of services to optimize provision of DAA treatment to HIV/HCV coinfected patients. Patients and providers had generally similar views about the form and content of services. Both groups indicated that providing DAA treatment in the patient’s HIV primary care medical home and by the patient’s current regular provider were the most important aspects of optimal DAA treatment. Empirical findings suggest that providing DAA treatment in primary care settings is both feasible and effective (Kattakuzhy et al., 2016) and it is important to recognize that both patients and providers have a strong preference for this model of care. While patients and providers gave similar ratings to receiving treatment in the patient’s current clinic, patients rated receiving treatment from their current provider as being more important than did clinicians. Patients and providers also valued support during DAA treatment, such as check-ins between visits, reminders about medications and appointments, support groups, and an advice number. However, providers rated this support as being more important than did patients. Taken together, these findings suggest that adding support such as patient navigators to the treatment team could be beneficial in expanding treatment capacity and enhancing patient outcomes (Kwong & Epstein, 2015). Paraprofessional patient navigators have proven effective in other HCV care contexts (Falade-Nwulia et al., 2016; Ramirez et al., 2016; Trooskin et al., 2015) and could provide HIV/HCV coinfected patients with support and personal contact while leaving prescribing providers available to engage other patients in DAA treatment.

When providers were asked about barriers to providing DAA treatment to HIV/HCV coinfected patients, the most significant barriers – lack of insurance coverage and paperwork – were structural barriers that are largely independent from the clinical setting. The primary barrier within the clinic setting was lack of staffing and other resources to provide treatment. Lack of training and staffing for evaluating and identifying patients and selecting DAA medications were not seen as significant barriers.

Providers’ preferences suggest that the most promising way to expand capacity for DAA treatment for coinfected patients is to involve HIV primary care providers. Overall, provider respondents viewed HIV primary care providers with infectious disease training as best suited to provide DAA treatment to coinfected patients. HIV primary care providers without specialized infectious disease training were also seen as suitable, particularly by respondents who provide HIV primary care. These preferences for which providers should deliver treatment fit well with patients and provider preferences for DAA treatment in the patient’s medical home. This finding stands in contrast to evidence documenting low interest in providing HCV treatment in a broad sample of primary care providers (Falade-Nwulia et al., 2016). It may be that HIV primary care providers’ expertise translates more readily to treating HCV. Additionally, it may be that, with time, providers have become more aware that DAAs are generally well tolerated and do not typically require subspeciality referral and management.

The results of this study may not generalize to DAA treatment for HIV/HCV coinfected patients in all settings. The study was conducted in a single setting, San Francisco, which has a well-developed system of care for HIV in which efforts are underway to expand access to HCV treatment. At the time of the study, some HCV care was provided by HIV primary care providers, some by specialists embedded in primary care clinics, and some by referral to specialists at a different site. In any case, the low income patient population included in this study faces significant barriers to care with a substantial proportion having ongoing problems with substance use and unstable housing, although the majority reported being able to adhere to medication. Patient and provider experiences may be different elsewhere and it would be important to examine preferences in other contexts.
This initial exploration of patient and provider preferences for DAA treatment for HIV/HCV coinfected patients highlights the importance of delivering DAA in the HIV primary care settings that constitute the patients’ medical home, which necessitates that HIV primary care providers have the training and structural support needed to manage DAA therapy. Given the clinical complexities and competing demands that coinfected patients experience, additional support in the medical home is needed to promote engagement and adherence. A range of treatment team members, including nurses, pharmacists, and others, could provide support and increase the efficiency and effectiveness of care. Attention is needed to structural barriers related to insurance coverage and administrative issues that limit providers’ ability to provide DAA treatment.

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Disclosure statement

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