New Treatments Have Changed the Game
Hepatitis C Treatment in Primary Care

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**KEYWORDS**
- Hepatitis C virus
- HCV
- Treatment
- Primary care
- Provider training
- Clinician training
- Primary care provider

**KEY POINTS**
- Although direct-acting antiviral regimens have driven up demand for hepatitis C virus (HCV) treatment, only a fraction of HCV-infected individuals are offered treatment within specialty settings.
- In 2016 to 2017, the San Francisco Health Network (SFHN) worked to improve treatment access and better understand barriers still inhibiting SFHN primary care providers from prescribing HCV treatment.

*Continued*
INTRODUCTION

San Francisco residents are profoundly impacted by the hepatitis C virus (HCV), with approximately 2.5% of the general population seropositive for HCV as of 2015 compared with a national seroprevalence estimate of 1.4% (95% CI, 0.9%–2.0%). HCV is a significant driver of morbidity, liver cancer, and death and disproportionately has an impact on marginalized populations, including people of color, homeless individuals, people with a history of incarceration, and people who inject drugs. The availability of highly effective oral HCV treatment with few side effects, known as direct-acting antivirals (DAAs), makes HCV cure possible in nearly all infected patients.

In the pre-DAA era, HCV treatments were complex and largely managed by hepatologists, gastroenterologists, and infectious disease physicians. As tolerable and highly effective DAA regimens have driven up demand for treatment, the relative scarcity of these specialists to the large number of infected individuals has created a bottleneck effect, resulting in only a fraction of HCV-infected individuals offered treatment in any given year. Even with reasonable capacity in the specialty setting, travel to specialty clinics or even the idea of attending appointments in unfamiliar settings with unfamiliar providers can be a barrier for marginalized populations disproportionately impacted by HCV. As treatment courses in the DAA era have become shorter, simplified, and remarkably well tolerated, recent studies have demonstrated the efficacy of treating HCV in high-prevalence primary care settings.

The San Francisco Health Network (SFHN) is San Francisco’s safety net system of care, and serves the majority of the low-income and homeless populations of San Francisco. The percentage of all active adult SFHN primary care patients who have been diagnosed with HCV is 5.5%. Part of the San Francisco Department of Public Health, the SFHN includes primary care in 10 community-based and 4 hospital-based clinics throughout the city. In 2016, in an effort to increase HCV treatment access for all patients, SFHN leadership committed to training its primary care providers to treat uncomplicated cases of HCV in the primary care setting using a team-based model of care.

METHODS

Through SFHN’s HCV treatment expansion intervention, primary care providers within the SFHN were invited to participate in a 4-hour overview training about
primary care–based HCV treatment and best practice models for team-based HCV care. A secure electronic referral system (eReferral) to support primary care–based HCV treatment was created to give providers individualized treatment consultations for their patients (Fig. 1). Finally, primary care clinics were supported by a team of HCV champions providing technical assistance to help design individualized treatment workflows within each clinic. The intervention was designed to be sustainable and scalable, requiring limited additional investment of resources. A grant from the California Department of Public Health supported 0.15 full-time equivalent of clinician and pharmacist time to staff the eReferral system and 0.4 full-time equivalent of an analyst to manage treatment data, and all other support for the initiative was provided in-kind from the SFHN (see Fig. 1).

For the authors’ analysis, data from the SFHN’s electronic medical record (EMR) from October 1, 2014, through December 31, 2017, were reviewed. Data were collected on patients with at least 1 primary care visit in the previous 2 years (n = 53,039), including age, gender, and race/ethnicity; the number of patients tested for HCV (n = 22,447); the number with positive HCV RNA results (ie, confirmed to be chronically infected) (n = 2910); and the number initiating DAA treatment (n = 578). Patients receiving treatment during and after the primary care–based HCV treatment intervention were compared with those who had yet to receive treatment. These EMR data were supplemented with data from the primary care–based HCV treatment eReferral metrics to determine the number of primary care patients treated preintervention versus postintervention and the number and quantity of prescriptions written by each provider. Data were analyzed using SAS software SAS version 9.4 (SAS Institute, Cary, North Carolina) Version 9.4 (SAS Institute, Cary, North Carolina) and STATA version 15.0 (StataCorp, College Station, Texas) for summary statistics and Pearson chi-square tests.
These clinical data were supplemented by a brief survey of providers who had participated in 1 of the HCV treatment trainings held in 2016. Surveys were created via SurveyMonkey (www.surveymonkey.com) and a link was emailed to all providers who had attended an HCV treatment training. Of the 120 providers who participated in 1 of these trainings, 111 were still employed by the SFHN and were asked to participate. Two reminder emails were sent during the 4-week period that the survey was open; during that time 39.6% (n = 44) completed the survey, with representatives from every SFHN primary care clinic. Surveys included 16 questions, including 12 multiple-choice questions (“select all” or “choose one”), two 5-point Likert scales to measure satisfaction with the eReferral system, and 2 open-ended questions soliciting overall suggestions or comments about improving HCV treatment support. Questions included demographics (clinic of practice, clinical role, when and why they attended HCV treatment training, number of patients treated for HCV before and after the training[s], reasons for not yet treating patients for HCV [if applicable], use of eReferral and experience with the eReferral system, and barriers to treating patients for whom they had used eReferral) and other suggestions for learning modalities or technical assistance that they believed would increase HCV treatment rates in their practice or at their clinics overall. Survey responses were exported from SurveyMonkey into a Microsoft Excel file, then analyzed using Excel.

In addition to the surveys, 15 providers participated in 20-minute to 60-minute qualitative interviews to describe their experience with eReferral, the prescriber training, and HCV treatment in primary care overall. Interviews were conducted via phone, using a 10-question, semistructured interview guide. Interviews were thematically analyzed with open coding to allow themes to emerge from the data. Findings were merged into a final summary that was shared with HCV clinical champions for verification prior to dissemination.

RESULTS

Treatment and Prescribing Data

Analysis of SFHN data demonstrates that of the total 22,447 adults tested for HCV between October 1, 2014, and December 31, 2017, 2910 were found chronically HCV infected (13.0%). During the period of the analysis, 578 patients were treated (19.9%). Importantly, there were no statistically significant differences overall between the age, gender, or racial/ethnic demographics of those who had been treated by the SFHN (n = 578) and those who were chronically HCV infected but not yet been treated (n = 2332) (Table 1).

The number of patients treated in primary care tripled from the period during which DAAs were available but HCV primary care treatment trainings had not been conducted (10/1/2014–1/31/2016), referred to as the “pre-intervention period,” compared with the 23 month “post-intervention period” (2/1/2016–12/31/2017), with 143 patients treated preintervention (8.9 patients per month) compared with 435 treated postintervention (18.9 patients per month). The number of SFHN clinics providing primary care–based treatment also increased from 5 preintervention to 12 postintervention. These data indicate substantial increases in HCV treatment access in the SFHN primary care setting (Table 2).

Use of Capacity-Building Services in Relation to Prescribing Practices

From March 1, 2016, through November 30, 2017, 280 prescriptions for HCV treatment were written by 68 providers trained during 1 of the HCV treatment trainings. This was an average of 4.1 prescriptions per trained provider; however, when
### Demographics of all active San Francisco Health Network patients tested for HCV from October 1, 2014, to December 31, 2017, by HCV status and treatment status as of December 31, 2017

<table>
<thead>
<tr>
<th></th>
<th>Tested(^a) for Hepatitis C Virus</th>
<th>Infected(^b) with Hepatitis C Virus</th>
<th>Untreated(^c) for Hepatitis C Virus</th>
<th>Treated for Hepatitis C Virus</th>
<th>Odds of Being Treated if Hepatitis C Virus Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22,447</td>
<td>2910</td>
<td>2332</td>
<td>578</td>
<td>19.9 —</td>
</tr>
<tr>
<td>Male(^d)</td>
<td>12,702</td>
<td>2065</td>
<td>1637</td>
<td>428</td>
<td>20.7 1.2 ((P = .07))</td>
</tr>
<tr>
<td>Female</td>
<td>9745</td>
<td>845</td>
<td>695</td>
<td>150</td>
<td>17.8 ref(^f)</td>
</tr>
<tr>
<td>Baby boomer (born 1945–1965)</td>
<td>10,188</td>
<td>2031</td>
<td>1615</td>
<td>416</td>
<td>20.5 1.1 ((P = .20))</td>
</tr>
<tr>
<td>Not baby boomer</td>
<td>12,259</td>
<td>879</td>
<td>717</td>
<td>162</td>
<td>18.4 ref(^f)</td>
</tr>
<tr>
<td>Asian</td>
<td>4977</td>
<td>153</td>
<td>131</td>
<td>22</td>
<td>14.4 .65 ((P = .07))</td>
</tr>
<tr>
<td>Black/African American</td>
<td>4040</td>
<td>1005</td>
<td>811</td>
<td>194</td>
<td>19.3 .92 ((P = .45))</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>200</td>
<td>58</td>
<td>43</td>
<td>15</td>
<td>25.9 1.3 ((P = .34))</td>
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<tr>
<td>Native Hawaiian/Pacific Islander</td>
<td>223</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>38.8 2.4 ((P = .12))</td>
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<tr>
<td>Hispanic</td>
<td>6116</td>
<td>379</td>
<td>299</td>
<td>80</td>
<td>21.1 1.02 ((P = .84))</td>
</tr>
<tr>
<td>White</td>
<td>5041</td>
<td>1081</td>
<td>858</td>
<td>223</td>
<td>20.6 ref(^f)</td>
</tr>
<tr>
<td>Unknown/missing</td>
<td>1850</td>
<td>221</td>
<td>182</td>
<td>39</td>
<td>17.6 .82 ((P = .31))</td>
</tr>
</tbody>
</table>

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\(^a\) “Tested” denotes having record of an HCV antibody, genotype, and/or viral load test between October 1, 2014, and December 31, 2017.

\(^b\) “Infected” specifies adult individuals with an active clinical record (i.e., seen in the last 2 years of pull date, 1/25/2018), an SFHN clinic as a primary care clinic, and evidence of HCV infection (a positive antibody test, detectable viral load, HCV genotype, and/or documented HCV treatment initiation) between October 1, 2014, and December 31, 2017.

\(^c\) “Untreated” is defined as having HCV infection, as defined previously, but with no HCV treatment initiation documented in the EMR.

\(^d\) Nonbinary gender (i.e., transgender) is not routinely captured in the SFHN EMR so is not reported here.

\(^e\) No statistically significant differences were found between the proportion of patients treated or untreated for their HCV by gender, age, or ethnicity.

\(^f\) ref, denotes to the reference in an odds ratio table.
excluding 3 “superprescribers” who fell more than 2 SDs from the mean, the total number of prescriptions dropped to 168, with an average of 2.6 per provider.

From February 1, 2016, through December 31, 2017, 63 providers used the eReferral system for a total of 261 individual patient cases (an average of 4.14 patient cases per provider). At the same time, 63 prescriptions were written by providers using eReferral, and another 330 prescriptions were written by providers who did not use eReferral (although 112, or 34%, of those were written by the 3 superprescribers [discussed previously]). See Table 3 for more details on the use of eReferral for HCV prescriptions in the SFHN.

**Provider Survey Data**

Survey and interview results provided additional insight into the effectiveness of the multimodal capacity-building intervention. Almost 2 of 3 survey respondents (28/44) were primary care providers licensed to prescribe HCV treatment directly. The remaining respondents were registered nurses (18%), pharmacists (4%), in an administrative roles (eg, program manager or nurse manager), 1 medical evaluation assistant, and 1 urgent care provider.

Of the respondents who were prescribing providers and participated in 1 of the 2 HCV treatment trainings (n = 31), more than 85% had never treated a patient for HCV prior to the training session. At the time of the survey (6–16 months post-training, depending on which training they had attended), that number dropped below 50%, with 15 of the 27 people who said they had treated no patients before the training reporting treating at least 1 patient post-training. The distribution of the number of patients treated pretraining and post-training is seen in Fig. 2.

For those clinicians who said they still had not treated any patients for HCV post-training (n = 20), 8 reported having no patients in need of HCV treatment (eg, patients

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**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Preintervention (16 mo)</th>
<th>Postintervention (23 mo)</th>
<th>Increase (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients treated</td>
<td>143</td>
<td>435</td>
<td>112</td>
</tr>
<tr>
<td>Total No./mo</td>
<td>8.9</td>
<td>18.9</td>
<td></td>
</tr>
<tr>
<td>Total clinics represented</td>
<td>5</td>
<td>12</td>
<td>140</td>
</tr>
</tbody>
</table>

* Five treated cases had no listed primary care provider.

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**Table 3**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
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<tbody>
<tr>
<td>Number of eReferrals made</td>
<td>261</td>
</tr>
<tr>
<td>Number of eReferrals that started treatment</td>
<td>105</td>
</tr>
<tr>
<td>Number of treatment starts with no eReferral on record</td>
<td>330</td>
</tr>
<tr>
<td>Number of providers using eReferral system</td>
<td>63</td>
</tr>
<tr>
<td>Number of unique providers with at least 1 treatment start</td>
<td>37</td>
</tr>
</tbody>
</table>

* Four patients were referred twice during the period.
with HCV were already being treated in another setting) or being unable to prescribe (eg, none of their patients had HCV or their patients’ HCV was being treated in another setting). Of the remaining 12, 8 said they did not have any patients they thought could adhere to treatment, and/or their patients had too many competing priorities to allow for HCV treatment at the current time. The other 4 said they did not know how to navigate the prior authorization process to obtain medications (2 people), did not feel comfortable prescribing treatments to their patients yet (3 people), or they knew how to do it but there was no one at the clinic to assist and they believed they could not do it themselves (2 people).

Interview feedback regarding the technical assistance component for clinics was generally positive, although some respondents acknowledged it was not sufficient in and of itself, thereby validating the importance of the multimodal intervention design. Although technical assistance was beneficial for clinic workflow and reminders to use the eReferral system, the most successful clinics were those with at least 1 clinician HCV champion in-house. “Having dedicated people who are helping with this topic makes it easier,” a provider explained. “They can be the expert...we have providers who are experts on HIV medicine, or experts on trans medicine, and that makes it easier for me to help with prescribing those things.” Numerous providers noted that sometimes inexperienced providers needed more than education to begin treating; consistent support was needed until they could “build muscle memory.” More information about the types of additional clinic-specific support providers requested is in Fig. 3.

DISCUSSION

The tolerability and efficacy of HCV DAAs present an opportunity for care systems to provide curative treatment of patients living with HCV in new and innovative ways. This

![Fig. 2. Provider self-report of the number of patients treated for HCV before the treatment trainings versus at the time the provider survey was sent out. Depending on the date of the treatment training the provider completed, the post-training time interval ranged from 6 months to 16 months.](image)

![Fig. 3. Provider survey responses (n = 44) to a multiple choice (“select all”) question about what more could be offered at their clinic to increase the number of patients treated for HCV.](image)
article is one of the first to comment on the process and outcomes of an intervention that aimed to shift HCV care for uncomplicated patients from the subspecialty to primary care setting.

The SFHN primary care–based HCV treatment initiative has demonstrated the feasibility and impact of providing capacity-building support to primary care providers in high-prevalence settings. With minimal financial and time commitments for training providers, primary care–based HCV treatment access increased 3-fold in a period of just over 3 years as a result of this initiative. Providers within the authors’ system showed rapid learning and deployment of the skills of HCV treatment.

A strength of the authors’ eReferral model is that the primary skill required of providers to treat HCV is the ability to assess treatment readiness. The central eReferral team provides case consultation, including treatment recommendations. As a result, trainings do not require providers to become individually competent to understand the nuances of regimen selection or follow ongoing changes in DAA options. By shifting the responsibility of regimen selection to the eReferral consultation team, providers more readily become able to treat HCV in the primary care setting. The authors suspect that the providers who began treating HCV during this period were a group already interested in and motivated to offer HCV treatment within their practices; the additional supports offered through the treatment initiative merely provided a catalyst for action. The results of the provider survey reveal that even after the trainings, providers felt supported by both the eReferral system and other colleagues in their own clinics with a breadth of experience in treating HCV.

One of the treatment initiative’s major goals was to ensure that treatment access was equitable across population groups. The authors’ data show that primary care providers are treating a representative population of those infected with HCV within the SFHN; the demographics of patients treated for HCV in primary care were statistically similar to those HCV-infected patients who had not yet been treated. The authors are currently undertaking a formal analysis of patients who have been treated for HCV in primary care to ensure effective and high-quality treatment through this initiative and to ensure that patients marginalized by social factors not explored in this article are able to obtain HCV treatment in primary care.

The authors’ analysis is limited by a fairly small sample size from the provider survey; it is also true that providers may have been more likely to respond to the survey invitation if they were enthusiastic about HCV treatment or about the training intervention. Primary care providers, however, indicated a willingness to take on the task of HCV treatment with the support of experienced providers and clinic teams. Taken together, introductory trainings, eReferral, and clinic technical assistance provided a variety of options to support prescriber knowledge and confidence. Providers reported appreciation of the support provided.

Despite the increases in access to care for patients living with HCV in San Francisco’s safety net primary care settings as a result of these capacity-building interventions, many barriers to treatment persist for patients. Providers who received training but had not yet prescribed HCV treatment highlighted concerns about patient adherence, lack of team support, and burdensome treatment authorization processes as reasons why they were still unable to initiate HCV treatment.

The authors have several plans to continue to scale up numbers of providers treating HCV in primary care. One of the largest ongoing barriers identified by providers was the lack of logistical clinic level support; the authors plan to provide ongoing training to nursing and clinical pharmacy staff to assist with the necessary tasks associated with HCV treatment (ie, procuring medication, supporting adherence, and monitoring laboratory test results). The impact of having a trained nursing or pharmacy
staff member is that that 1 of these team members can support multiple clinical providers, thereby increasing the number of providers treating and total number of patients treated. The authors also aim to organize more provider trainings for providers who missed the first trainings or have subsequently joined the network. These trainings will highlight community-based patient navigation programs that can support more challenging patients through treatment. The authors will continue to offer individualized support through eReferral. Resident teaching is a final piece of the efforts to scale up overall numbers of providers treating in primary care.

PUBLIC HEALTH IMPLICATIONS

Many of the patients treated in SFHN primary care settings were unlikely to have been successfully treated in specialty clinics. As an example, in 1 study in Zuckerberg San Francisco General Hospital’s liver specialty clinic, 42% of patients living with HCV were determined by providers to be treatment ineligible, with substance use and housing instability a major reason for provider-determined treatment ineligibility among African American patients. For those determined appropriate for treatment, approximately 1 of every 3 patients were lost to follow-up before treatment was completed.¹⁴

Although the data related to primary care–based treatment are encouraging, an even broader spectrum of patients likely could be treated with the offer of additional support within the primary care setting, such as patient navigators, social workers, and nurses or pharmacists onsite to support directly observed therapy for HCV medications. Large-scale improvements in HCV treatment rates for patients in primary care settings could substantially contribute to local,⁷ regional,¹⁵ and national efforts¹⁶ to eliminate HCV as a public health threat.

REFERENCES


