Effectiveness of a Decentralized Hub and Spoke Model for the Treatment of Hepatitis C Virus in a Federally Qualified Health Center

Sarah A. Rojas [1,2] Job G. Godino [1,3] Adam Northrup [1] Maureen Khasira,[1] Aaron Tam,[1] Lisa Asmus,[2] Catherine Frenette [4] and Christian B. Ramers [1,5]

Hepatitis C virus (HCV) is a major cause of cirrhosis, liver cancer, and mortality in the United States. We assessed the effectiveness of decentralized HCV treatment delivered by nurse practitioners (NPs), primary care physicians (PMDs), or an infectious disease physician (ID MD) using direct-acting antivirals in a Federally Qualified Health Center (FQHC) in urban San Diego, CA. We conducted a cross-sectional analysis of 1,261 patients who received treatment from six NPs, 10 PMDs, and one ID MD practicing in 10 clinics between January 2014 and January 2020. Care was delivered based on the Extension for Community Healthcare Outcomes (Project ECHO) model with one hub and nine spokes. HCV was deemed cured if a patient had a sustained virologic response (SVR) after 12 weeks of treatment (SVR12). We evaluated differences in the prevalence of cure between provider types and hub or spoke status using Poisson regression. Patients were 34% Latino, 16% black, 63% were aged >50 years, and 59% were homeless; 53% had advanced fibrosis, 69% had genotype 1, and 5% were coinfected with human immunodeficiency virus. A total of 943 patients achieved SVR12 (96% per protocol and 73% intention to treat). Even after adjustment for demographics, resources, and disease characteristics, the prevalence of cure did not differ between the ID MD and PMDs (prevalence ratio [PR], 1.00; 95% confidence interval [CI], 0.95-1.04) or NPs (PR, 1.01; 95% CI, 0.96-1.05). Similarly, there were no differences between the hub and spokes (PR, 1.01; 95% CI, 0.98-1.04). *Conclusion:* Among a low-income and majority homeless cohort of patients at urban FQHC clinics, HCV treatment administered by nonspecialist providers was not inferior to that provided by a specialist. (*Hepatology Communications* 2021;5:412-423).

With at least 2.4 million Americans infected, hepatitis C virus (HCV) is one of the most common blood-borne diseases in the United States.[1] New infections continue to increase, with 44,700 new HCV infections in 2017.[2] HCV is a leading cause of liver disease, liver cancer, and liver transplants and results in more deaths per year in the United States than human immunodeficiency virus (HIV), tuberculosis, and 58 other infections combined.[3] The morbidity and mortality associated with HCV costs billions of dollars annually, burdening patients, their families, caregivers, and the health care system.[4]

Abbreviations: CI, confidence interval; CRR, cure rate ratio; DAA, direct acting antiviral; ECHO, Extension for Community Healthcare Outcomes; EHR, electronic health record; FHC, Family Health Center; FHCSD, Family Health Center of San Diego; FQHC, Federally Qualified Health Center; GLE/PIB, glecaprevir/pibrentasvir; HCV, hepatitis C; HIV, human immunodeficiency virus; ID MD, infectious disease physician; NP, nurse practitioner; PCP, primary care provider; PMD, primary care physician; PR, prevalence ratio; PWID, people who inject drugs; SOF/LDV, sofosbuvir/ledipasvir; SVR, sustained virologic response; SVR12, sustained virologic response after 12 weeks of treatment.

Received July 6, 2020; accepted September 13, 2020.

Additional Supporting Information may be found at onlinelibrary.wiley.com/doi/10.1002/hep4.1617/suppinfo.

Supported in part by the Centers for Disease Control and Prevention Funding Opportunity Announcement FS12-1209FFHP12 (Award #U51PS003924 to David Wyles), California Department of Public Health Hepatitis C Virus Training (Award #15-10749 to Robert Lewis), Health Resources and Services Administration/Special Projects of National Significance Human Immunodeficiency Virus Workforce (Development Grant #H97HA27423 to Robert Lewis), Gilead FOCUS program (to Robert Lewis), and National Institute of Allergy and Infectious Diseases (Loan Repayment Program to S.A.R.).

The contents of this study are solely the responsibility of authors and do not necessarily represent the official views of the funding organizations.

Today, transmission of HCV is primarily through sharing needles, syringes, or other drug injection equipment; 70% of new infections are related to injection drug use.[2] In California, an estimated 400,700 individuals live with chronic HCV, but many do not know they are infected.[5] While almost half of HCV cases in California are among baby boomers (born from 1945 to 1965), the number of cases among young adults in their 20s has more than doubled from 2012 to 2016.[5] In San Diego, between 2011 and 2016, men and women aged 20-29 years experienced 47% and 62% respective increases in new HCV infections, spurred by injection drugs.[6] Expanded prevalence estimates indicate a population prevalence rate for HCV of 2.0% to 2.7% in San Diego County, suggesting that approximately 65,000 to 88,000 individuals in the region are likely HCV infected.[7]

In order to quell these alarming increases in new HCV infections, effective treatments need to be delivered to historically underserved populations, including those with ongoing substance use.[8] Advances in HCV treatment and care (e.g., the development of highly effective direct-acting antivirals [DAAs]) show promise for treating these populations and have led to worldwide HCV elimination goals.[9] Furthermore, emerging evidence indicates that people who inject drugs (PWID) achieve the same high cure rates as patients who are noninjection drug users when treated with DAAs.[10]

The American Association for the Study of Liver Diseases/Infectious Diseases Society of America frequently updates guidelines on their easily accessible website (hcvguidelines.org), simplifying treatment recommendations for nonhepatologists. It now boasts simplified algorithms for HCV evaluation and treatment for patients who are noncirrhotic and those with compensated cirrhosis.[11] This guidance and other publications calling for simplification[12,13] underscore that most patients, particularly younger PWID with a low risk of cirrhosis, may be lost to follow-up with overly complex, time-intensive, costly evaluations. These authors emphasize that a large number of patients infected with HCV can safely be treated by nonspecialists, e.g., nurse practitioners (NPs) and primary care physicians (PMDs), commonly referred to as task shifting in the patients' accessible medical homes.[14-16]

Supporting the decentralization of specialty care to underserved areas/populations, the University of New Mexico Health Sciences Center created the Extension for Community Healthcare Outcomes (ECHO) model in 2003. This was accomplished by using a new educational model of team-based interdisciplinary development to train and support

View this article online at wileyonlinelibrary.com.
DOI 10.1002/hep4.1617

Potential conflict of interest: Dr. Frenette advises, consults for, is on the speakers' bureau for, and received grants from Gilead; she is on the speakers' bureau for AbbVie. Dr. Ramers consults for, advises, is on the speakers' bureau for, and received grants from Gilead and AbbVie; he consults for and is on the speakers' bureau for Merck.

ARTICLE INFORMATION:

From the [1]Laura Rodriguez Research Institute, Family Health Centers of San Diego, San Diego, CA; [2]Institute of Public Health, San Diego State University Research Foundation, San Diego, CA; [3]Center for Wireless and Population Health Systems, University of California San Diego, La Jolla, CA; [4]Department of Organ Transplant, Scripps Clinic, La Jolla, CA; [5]Division of Infectious Diseases, Department of Medicine, University of California San Diego, La Jolla, CA.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO:

Christian Ramers, M.D., M.P.H.
Laura Rodriguez Research Institute
Family Health Centers of San Diego
823 Gateway Center Way
San Diego, CA 92102
E-mail: christianr@fhcsd.org
Tel.: +1-619-798-3649

primary care providers (PCPs) to develop knowledge on how to treat HCV remotely through Zoom meetings. It established a network of PCPs, psychiatrists, pharmacists, and infectious disease specialists so that they could collaborate and exchange information on how to serve patients with HCV.[17,18] Since the introduction of the ECHO model, multiple studies have shown its effectiveness in expanding access to best practice care for underserved populations.[19] One study comparing treatment of HCV at university versus community sites found a nonsignificant 0.7% difference in sustained viral response (SVR) rates.[17]

Although recent studies demonstrate the PCP's efficacy in treating single HCV genotypes or patients without cirrhosis, the majority of PCPs feel they have limited or none of the necessary skills to treat HCV.[20] The question remains whether or not PCPs can treat complex disease in diverse, vulnerable, and medically complicated patients. To add to our understanding, Family Health Centers (FHCs) of San Diego (FHCSD), a Federally Qualified Health Center (FQHC), trained and longitudinally supported selected PCPs to assist in upscaling the delivery of HCV treatment. In the present study, we assessed the effectiveness of this treatment model, which used collaboration, task shifting, and decentralization in urban San Diego, CA.

Patients and Methods

STUDY DESIGN

We conducted a cross-sectional analysis of 1,261 patients who received treatment from six NPs, 10 PCPs, and one infectious disease physician (ID MD) practicing in 10 clinics between January 2014 and January 2020. This study was approved by the Institutional Review Board of San Diego State University (IRB# IORG0000333).

TREATMENT MODEL

Overwhelming demand for more treating providers prompted incorporation of HCV care and management into formalized clinical training programs, namely into a Health Resources and Services Administration/Special Projects of National

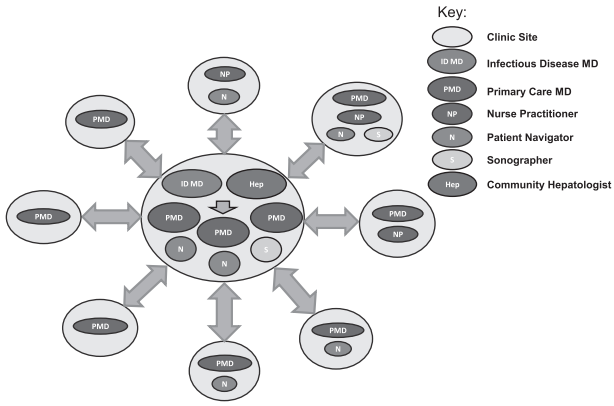

FIG. 1. Hub and spoke diagram composed of FQHC team members, 2019.

Significance-supported HIV treatment training track for residents and a state-funded HCV-specific 6-month training track for PCPs, including PMDs and NPs. The ID MD then expanded the treatment program, starting in 2015. He trained two to four providers and one to two clinics at a time, prioritizing high-quality didactic teaching during HCV treatment clinic blocks and self-guided learning, greatest need, and greatest reach. Currently, 10 PCPs now treat HCV spread among a hub and six surrounding clinics, or "spokes," supported by patient navigators and sonographers (Fig. 1) and most recently a champion community hepatologist. The ID MD and hepatologist provide ongoing learning opportunities and consultation through electronic health record (EHR) messaging and weekly telehealth ECHO didactics. The "HCV Huddle" ECHO video sessions include all team members: patient navigators, sonographers, PCPs, ID MD, hepatologist, and welcome guests, i.e., a community radiologist, a rural provider, or a county public health official. Importantly, the weekly calls also lend themselves to larger HCV elimination efforts, among them harm reduction, advocacy, and fundraising. Similarly, the hepatologist's support has also expanded into a corner stone of the HCV treatment program as she now attends a 4-hour clinic session within the FQHC monthly, has streamlined endoscopies for the uninsured, and counsels on all decompensated cirrhotic cases.

In addition to testing within the usual clinic care system, this larger FQHC performs community

outreach testing, prioritizing sober living environments, homeless populations, transitional housing, and a syringe services program. Community testers/counselors give rapid results, and those testing positive have phlebotomy offered on-site for a viral load confirmation. The HCV antibody-positive individual is immediately assigned a patient navigator to ensure they are linked to care, arrangement of transportation, insurance assistance, and an appointment with an HCV-treating provider. After the initial linkage occurs, patient navigators encourage retention in care and assist patients in overcoming individual and systemic barriers to HCV treatment, including completing and following up on prior authorizations. They are invaluable team members in a challenging FQHC population with varying insurance requirements for HCV treatment. In practice, a high-performing medical assistant would be identified and trained as an HCV patient navigator, then dedicate one-half day of administrative time for every clinic half day assigned to an HCV treating clinician(s).

MEASURES AND STATISTICAL ANALYSES

Patients were considered cured of HCV, the primary study endpoint, if they had an SVR after 12 weeks of treatment (SVR12). Patients were encouraged to undergo an additional course of treatment after any failed treatment. Thus, some patients had multiple treatments. Patients who did not follow up for at least 10 weeks posttreatment were considered lost to follow-up. Notably, medications were dispensed directly from clinic sites, usually in 2-week to 4-week quantities, depending on insurance dictates. All patients who completed lab testing and picked up their medications had likely completed treatment. Actual treatment adherence and completion were not recorded; patients who picked up their last 2-week to 4-week supply of medications but did not complete laboratory testing at that time were not reported. Patients who completed treatment fewer than 24 weeks before data pull and analysis who had not yet followed up were removed from the data set. Patients who failed to follow up 10 weeks posttreatment were considered treatment failures in the intention to treat analysis. These patients were excluded from the per protocol analysis.

Explanatory variables were chosen based on subject matter expertise and the potential of a variable to influence disease severity or cause bias related to location or provider type. Variables were grouped according to relationship to each other. Variables were either derived from the FHCSD EHRs or treatment-specific information, such as treatment dates, drug regimens, and providers, entered into a separate database by medical assistants on site. Missing start dates or test results indicated treatment was never started, which was confirmed by investigation of patient chart notes. In order to determine if treatment success was related to whether or not the patient was seen at a support clinic (a spoke clinic) or by a support PCP trained by the ID MD ("provider type"), provider types that were separately compared to the ID MD included NPs and PMDs. These variables of interest were considered separately. All variables besides age and year of treatment start were categorical by nature. Patient age at treatment start (transformed into categories of 17-29, 30-39, 40-49, 50-59, and at least 60 years), sex at birth (male/female), ethnicity (Latino/Hispanic or not), race (black or not), and homeless status were self-reported at initial patient registration. Insurance type (MediCal, Medicare, uninsured, or other) was confirmed through payment. Treatments began in 2014 and continued through the end of the data collection period at the end of 2019, with some test results through January 2020 being used to indicate treatment outcome.

For disease characteristics, we included advanced fibrosis, genotype, drug regimen, and HIV coinfection. Advanced fibrosis of F3 or greater fibrosis was defined by shear wave elastography ≥8.7, aspartate aminotransferase-to-platelet ratio index ≥1.5, FibroSure ≥0.72, or ultrasound-demonstrated scalloped liver margin, nodularity, or splenomegaly. Drug regimens that composed at least 1% of the prescriptions are included in Table 1; those prescribed less frequently were combined into the category "other." One patient was found to have both genotypes 1 and 2, and another patient had both genotypes 2 and 3. Each was considered as having the most virulent strain for the purposes of this analysis and were treated as genotypes 1 and 3, respectively.

We fit a series of nested Poisson regression models with sandwich variance estimation[21,22] in order to determine effects on treatment success of (1) being treated in a spoke clinic (compared to the hub) and (2) medical provider type (NP or PMD

TABLE 1. SAMPLE CHARACTERISTICS OF PATIENTS WHO RECEIVED HCV TREATMENT AT AN FQHC SYSTEM (n = 1,259)

Category	Unique Patients	Unique Treatments	Failed	Cured	Cure Rate	Lost
Total	1,259	1,288	44	920	95.4%	324
Demographics						
Age (years)						
17-29	100 (7.9%)	102 (7.9%)	5 (0.4%)	57 (4.4%)	91.9%	40 (3.1%)
30-39	155 (12.3%)	158 (12.3%)	2 (0.2%)	103 (8.0%)	98.1%	53 (4.1%)
40-49	210 (16.6%)	214 (16.6%)	5 (0.4%)	139 (10.8%)	96.5%	70 (5.4%)
50-59	441 (34.9%)	451 (35.0%)	21 (1.6%)	336 (26.1%)	94.1%	94 (7.3%)
60+	357 (28.3%)	363 (28.2%)	11 (0.9%)	285 (22.1%)	96.3%	67 (5.2%)
Sex at birth						
Male	892 (70.8%)	917 (71.2%)	36 (2.8%)	633 (49.1%)	94.6%	248 (19.3%)
Female	367 (29.2%)	371 (28.8%)	8 (0.6%)	287 (22.3%)	97.3%	76 (5.9%)
Ethnicity						
Latino	421 (33.4%)	432 (33.5%)	17 (1.3%)	308 (23.9%)	94.8%	107 (8.3%)
Not Latino	838 (66.6%)	856 (66.5%)	27 (2.1%)	612 (47.5%)	95.8%	217 (16.8%)
Race						
Black	199 (15.8%)	201 (15.6%)	6 (0.5%)	159 (12.3%)	96.4%	36 (2.8%)
Not black	1,060 (84.2%)	1,087 (84.4%)	38 (3.0%)	761 (59.1%)	95.2%	288 (22.4%)
Resources						
Housing status						
Homeless	738 (58.6%)	751 (58.3%)	24 (1.9%)	513 (39.8%)	95.5%	214 (16.6%)
Not homeless	521 (41.4%)	537 (41.7%)	20 (1.6%)	407 (31.6%)	95.3%	110 (8.5%)
Insurance						
MediCal	803 (63.8%)	824 (64.0%)	30 (2.3%)	568 (44.1%)	95.0%	226 (17.5%)
Medicare	228 (18.1%)	232 (18.0%)	5 (0.4%)	184 (14.3%)	97.4%	43 (3.3%)
Uninsured/self-pay	162 (12.9%)	166 (12.9%)	8 (0.6%)	117 (9.1%)	93.6%	41 (3.2%)
Other	66 (5.2%)	66 (5.1%)	1 (0.1%)	51 (4.0%)	98.1%	14 (1.1%)
Disease characteristics						
Fibrosis						
F3-F4	672 (53.4%)	695 (54.0%)	32 (2.5%)	508 (39.4%)	94.1%	155 (12.0%)
F0-F2	587 (46.6%)	593 (46.0%)	12 (0.9%)	412 (32.0%)	97.2%	169 (13.1%)
Genotype						
1	869 (69.0%)	887 (68.9%)	26 (2.0%)	648 (50.3%)	96.1%	213 (16.5%)
2	136 (10.8%)	140 (10.9%)	5 (0.4%)	100 (7.8%)	95.2%	35 (2.7%)
3	194 (15.4%)	200 (15.5%)	8 (0.6%)	127 (9.9%)	94.1%	65 (5.0%)
Other	60 (4.8%)	61 (4.7%)	5 (0.4%)	45 (3.5%)	90.0%	11 (0.9%)
Regimen						
GLE/PIB	359 (28.0%)	360 (28.0%)	4 (0.3%)	247 (19.2%)	98.4%	109 (8.5%)
SOF/LDV	334 (26.0%)	335 (26.0%)	14 (1.1%)	258 (20.0%)	94.9%	63 (4.9%)
SOF/VEL	233 (18.2%)	234 (18.2%)	10 (0.8%)	162 (12.6%)	94.2%	62 (4.8%)
ELB/GRZ	159 (12.4%)	159 (12.3%)	4 (0.3%)	113 (8.8%)	96.6%	42 (3.3%)
SOF/Riba	43 (3.4%)	43 (3.3%)	4 (0.3%)	29 (2.3%)	87.9%	10 (0.8%)
DCV/SOF	30 (2.3%)	30 (2.3%)	1 (0.1%)	19 (1.5%)	95.0%	10 (0.8%)
SOF/VEL + Riba	29 (2.3%)	30 (2.3%)	3 (0.2%)	19 (1.5%)	86.4%	8 (0.6%)
SOF/VEL/VOX	27 (2.1%)	27 (2.1%)	0 (0.0%)	19 (1.5%)	100.0%	8 (0.6%)
SOF/LDV + Riba	20 (1.6%)	20 (1.6%)	0 (0.0%)	17 (1.3%)	100.0%	3 (0.2%)
Other	27 (2.1%)	27 (2.1%)	0 (0.0%)	19 (1.5%)	100.0%	8 (0.6%)
HIV coinfection						
HIV positive	68 (1.6%)	69 (5.4%)	1 (0.1%)	60 (4.7%)	98.4%	8 (0.6%)
HIV negative	1191 (94.6%)	1219 (94.6%)	43 (3.3%)	860 (66.8%)	95.2%	316 (0.7%)

Abbreviations: DCV, daclatasvir; ELB, elbasvir; GRZ, grazoprevir; Riba, ribavirin; VEL, velpatasvir; VOX, voxilaprevir.

compared to ID MD). We started with an unadjusted (crude) model fit with only the variable of interest against the treatment outcome. Nested models contained progressively more information, with each model fitting an additional set of related explanatory variables. After the crude model, model 2 added demographic variables, including start year; model 3 added patient resources, such as insurance and housing status; and model 4 added variables related to disease characteristics. The result was four models for each of two variables of interest on two outcomes (sensitivity analysis for per protocol vs. intention to treat).

Factors shown to influence treatment success in the analysis of intention to treat but not in per protocol may indicate factors that influence loss to follow-up. Thus, a second supplemental analysis was performed to investigate the effect of each of the above variables on loss to follow-up by using Poisson regression. The observational unit for both analyses was treatment rather than patient.

We considered models other than Poisson but ultimately disregarded them due to similar results and preference in favor of prevalence ratio for results. A mixed-effect model fit with patient as a random effect (due to there being some patients with multiple treatments) was also rejected in favor of more parsimonious models. Data cleaning and models were built using R 3.6.2.[23] Plots were created using ggplot2.[24]

Results

The FQHC multidisciplinary group initiated 1,288 treatment regimens in 1,259 unique patients from January 2014 to December 2019. Patient demographics and clinical information are shown in Table 1. Among the 1,259 patients who initiated treatment, the majority were ≥50 years old, men, and/or white. Notably, a sizable minority of 33% identified as Latino and 16% as black. While 59% reported homelessness, 82% had Medicaid or Medicare for insurance, and 12% were uninsured. The disease characteristics varied: 53% had advanced fibrosis of F3 or greater, including 125 individuals with decompensated cirrhosis; 69% had genotype 1, 11% genotype 2, and 15% genotype 3; 5% (n = 68) were coinfected with HIV. Most treatment regimens were composed of either glecaprevir/pibrentasvir (GLE/PIB) or sofosbuvir/ledipasvir (SOF/LDV) (28% and 26%, respectively).

The FQHC HCV team members are shown in the Hub and Spoke Model of specialty support with bidirectional learning in Fig. 1. As a cross-section of staffing in 2019, this model exemplified the staff infrastructure of having a designated patient navigator for every one to two sites. While the absolute number of treatments prescribed by the ID MD decreased, the capacity to treat HCV continued to grow, particularly in the spoke clinics and with nonspecialist clinicians (Fig. 2A,B). Of the 1,503 unique initiated treatments (1,470 unique patients), 1,259 treatments were at least 12 weeks posttherapy; 964 completed laboratory tests at least 12 weeks posttreatment, while 324 treatments did not ("Lost"). We estimated that 172 of those lost to follow-up had completed treatment based on completing laboratory tests 2 weeks before 11 weeks after their end of treatment date (Table 2).

Overall SVR12 cure rates were 95% per protocol (920/964) and 71% per intention to treat (920/1,288). While the infectious disease specialist saw a higher percentage of patients with advanced fibrosis, the ID MD cure rates (93.9% per protocol, 73.3% intention to treat) were similar to those of NPs (96.5% per protocol, 73.5% intention to treat) and PMDs (96.1% per protocol, 68.8% intention to treat) in patients with and without cirrhosis (Fig. 3). Notably, there were 125 treatments with ribavirin for decompensated cirrhosis. Forty-three patients experienced treatment failure, and 31 of those patients had advanced fibrosis; 15 have now been cured, 2 are still on treatment, and 6 have been lost to follow-up thus far. Two patients failed twice; 1 was eventually cured and 1 lost to follow-up. There were also nine reinfections.

The models demonstrated no statistically significant difference in cure rates among our primary variables of interest of provider type or treatment site. Per protocol analyses revealed that spoke clinics had a 1.03 (95% confidence interval [CI], 1.00-1.06) cure rate ratio (CRR), indicating no difference in cure rates from the hub in the crude model (Table 3). Similarly, the CRRs were nearly identical in each progressive model with demographics (CRR, 1.01; 95% CI, 0.98-1.03), demographics and resources (CRR, 1.00; 95% CI, 0.98-1.03), and demographics, resources, and disease characteristics (CRR, 1.01; 95% CI, 0.98-1.04). Intention to treat analyses also showed no evidence

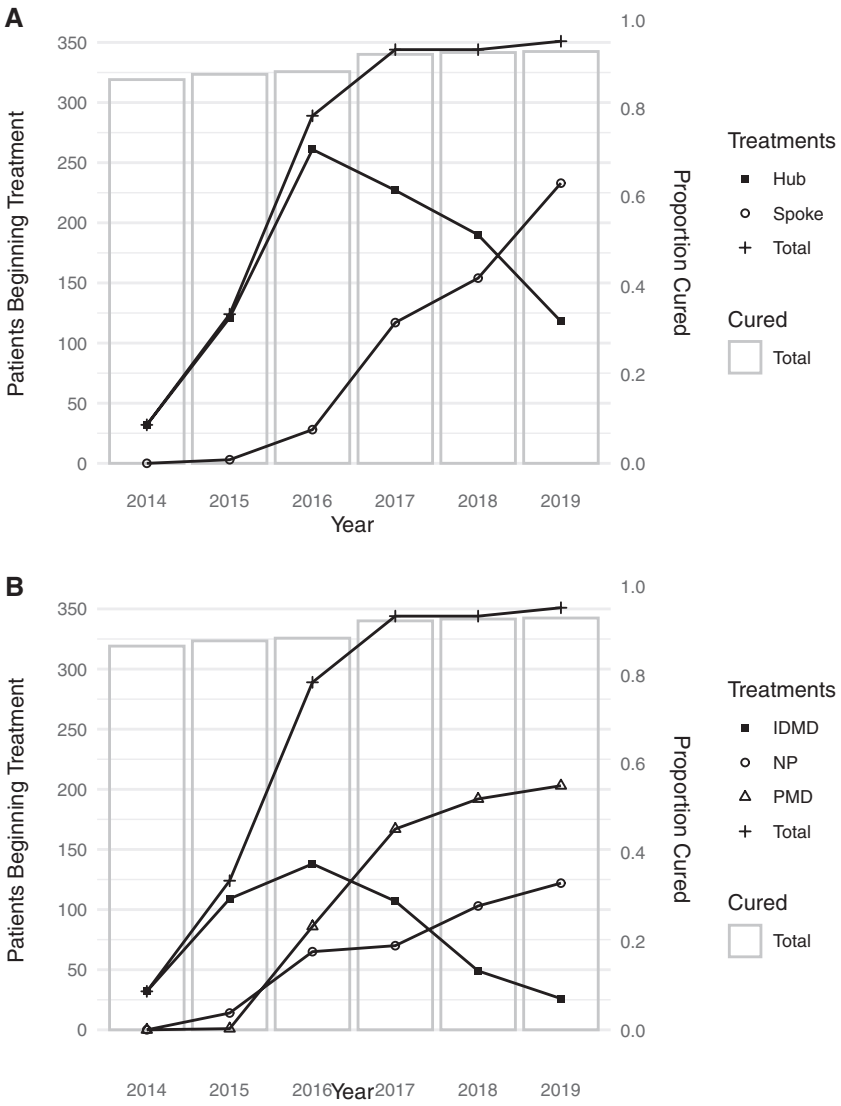

FIG. 2. Starts of treatment over time by target variable (n = 1,503). (A) Treatments per year by location. (B) Treatments per year by provider type. Data points represent total number of patients.

of an effect in cure rates for spoke clinics relative to the hub, despite differences in cure rates from the per protocol analysis (71% intention to treat vs. 95% per protocol). The crude model with cure regressed on spoke only had a CRR of 0.99 (95% CI, 0.92-1.07). The CRR for spoke clinics relative to the hub in the more complex models are as follows: 1.01 (95% CI, 0.93-1.10) for both the demographics and the demographics plus resources models and 1.03 (95% CI, 0.94-1.12) for the demographics, resources, and disease characteristics model.

We also assessed differences in cure rates between provider types (Table 4) and found no effect compared to the ID MD, with CRRs for PMDs and NPs of 1.02 (95% CI, 0.99-1.06) and 1.03 (95% CI, 0.99-1.07), respectively, in the crude per protocol analysis. When we accounted for other variables, the result was the same in that there was no apparent difference between PMD or NP and ID MD, with identical CRRs of 1.00 for both provider types and for all three more complex models (95% CI, 0.96-1.04 for PMDs and 0.97-1.014 for NPs for all three models). The intention to treat analysis showed CRRs of 0.94 (95% CI, 0.87-1.02) and 1.00 (95% CI, 0.91-1.10) for PMDs for the crude and most complex model with all variables, respectively. CRRs were 1.00 (95% CI,

TABLE 2. CLINICAL THROUGHPUT

Clinic	Enrolled	Began Tx	Enrolled On Time	Complete Data (ITT)	Completed Tx	PP
Hub						
Hillcrest FHC	1,008	934	869	857	756	649
Elm Street FHC	28	26	26	26	22	19
Total	1,036	960	895	883	778	668
Spoke						
City Heights FHC	218	203	174	170	145	120
Chase Avenue FHC	83	60	66	66	60	54
Chula Vista FHC	89			59	55	41
Downtown FHC at connections	70	61	33	33	31	25
Logan Heights FHC	69	61	46	46	39	29
FHC on commercial	35	32	22	22	20	19
Grossmont Spring Valley FHC	11	8	1	1	1	1
Sherman Heights FHC	9	8	8	8	7	7
Total	598	543	410	405	358	296
All clinics						
Total	1,635	1,503	1,305	1,288	1,136	964

Abbreviations: ITT, intention to treat; PP, per protocol; Tx, treatment.

0.92-1.10) and 1.04 (95% CI, 0.95-1.15) for the NPs for the crude and most complex models, respectively.

The spoke clinics evaluated and started treatment on 543 individuals at six distinct clinics throughout San Diego. All spoke clinics except the newest site, established in 2019, started at least 50 patients on treatment (range 8-203 patients). The throughput appeared similar for each of the satellite clinics or spokes; of the 410 patients enrolled early enough to have a SVR12 result drawn, 358 completed treatment (range of patients completing treatment, excluding the newest test site, 31-145).

Although we initially sought to determine efficacy of the decentralized treatment model through hub/spoke and provider-type variables of interest, we have also included adjusted and unadjusted prevalence ratios for additional variables in the full models (model 4) in Supporting Table S1. There is minimal evidence of any effects from the explanatory variables on treatment outcome in the per protocol analysis. Female sex at birth had slightly higher probability of treatment success over male sex at birth (prevalence ratio [PR], 1.03; 95% CI, 1.01-1.06). Treatment with SOF/LDV + ribavirin had a slight advantage over treatments with GLE/PIB (PR, 1.07; 95% CI, 1.01-1.13). Other medications appeared to perform similarly to GLE/PIB and thus to each other. A few variables appeared to improve chances of treatment success in the intention to treat analysis: age at treatment start for those 50-59 years (PR, 1.31; 95% CI, 1.09-1.57), and those 60+ (PR, 1.37; 95% CI, 1.13-1.67); female sex at birth (PR, 1.14; 95% CI, 1.06-1.23); and patients who were HIV positive (PR, 1.27; 95% CI, 1.13-1.42).

Similarly, in order to describe those who were lost to follow-up (Supporting Table S2), we repeated regression analyses using an indicator of loss to follow-up as the outcome variable. The following variables were shown to reduce the probability of a patient being lost to follow-up for any single treatment: patients aged 50-59 years (PR, 0.59; 95% CI, 0.43-0.81); patients aged 60+ years (PR, 0.53; 95% CI, 0.36-0.78); female sex at birth (PR, 0.73; 95% CI, 0.58-0.92); and patients who were HIV positive (PR, 0.45; 95% CI, 0.23-0.86).

Discussion

In the present study, we observed that among a low-income and majority homeless cohort of patients at urban FQHC clinics, HCV treatment administered by nonspecialist providers was not inferior to that provided by a specialist and resulted in a cure rate of 95%. This finding was not influenced by demographics, resources, or disease characteristics of patients. Importantly, our findings are aligned with similar research that indicates that nonspecialists can safely and effectively treat HCV.

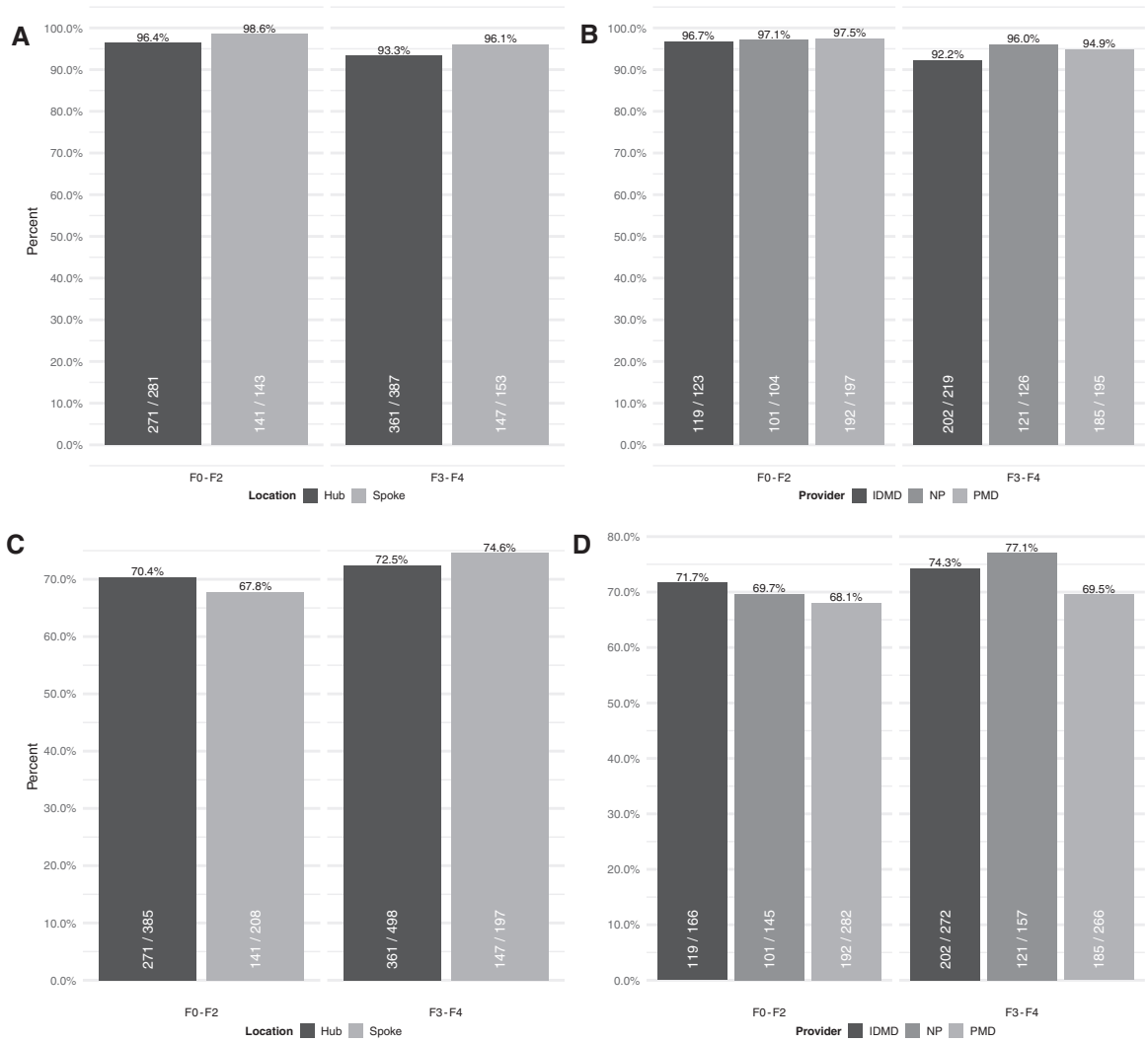

FIG. 3. Cure rates by cirrhosis level and target variable (n = 964). (A) Hub and spoke per protocol cure rates. (B) Provider type per protocol cure rates. (C) Hub and spoke intention to treat cure rates. (D) Provider type intention to treat cure rates. Numbers at the bottom of each bar show total number of patients cured of the total for that cirrhosis level and target variable.

In a study in which nonspecialist providers received a 3-hour training and no ongoing specialist support,[14] the researchers found a sustained virologic rate of 86% without differences between type of treatment provider in a nonrandomized underserved sample of PWID in Washington D.C.

There are a number of factors that may have influenced the observed success. First, task shifting is key to providing quality care to the public, especially with physician shortages. We see this in shifting what was once specialty care to primary care and what was once physicians' responsibility to complete prior authorizations to patient navigators. However, we carefully constructed this model while rigorously evaluating it to ensure that treatment and cure rates did not suffer as a result. While the growing capacity to treat HCV, particularly in the spoke clinics, is demonstrated in Fig. 2A,B, the decreased number of treatments at the hub does not reflect a decrease in capacity. Instead, this is thought to be related to two factors: 1) patient preference of being treated in their medical home when that is an option and 2) a decline in the prevalence of easier-to-treat patients. To the second reason, those who were treated initially were probably aware of their disease for a longer period of time and perhaps more highly

motivated to receive treatment. They were also more likely to have sufficient individual and familial facilitators to overcome the social barriers common to an FQHC population. It also reflects effective task shifting. As PMDs and NPs became more proficient in treatment, the ID MD focused on optimizing testing and linkage activities, participating in local advocacy efforts, and applying for research funding, in addition to providing specialty consultations outside of HCV.

Care was first decentralized by the ID MD by offering treatment outside of the local academic institution where few specialists were willing to accept Medicaid patients. Treatment was further decentralized by training the furthest reaching clinics (the spokes). This was successful and sustainable because each clinic has a well-trained physician–patient navigator team and ongoing support. Patient navigation starts from the moment individuals are tested in the community and lasts until that person no longer requires HCV treatment or surveillance. The ID MD and hepatologist employ an ECHO model for weekly didactic learning sessions, which include case presentations and advisement. Additionally, there is accessibility in real time, i.e., through EHR messaging or cell phone exchange. While the similar cure rates between treatment locations and provider types indicate a successful learning and supportive model for PCPs, the extent to which this is efficacious lies in the nearly one third of patients seen at the spokes. We are unable to confidently report higher intention to treat cure rates given the proportion of patients lost to follow-up, especially for individuals who were homeless or insured by Medicaid. However, over 50% of those who were lost to follow-up likely completed treatment (based on the fact that they received their last 2-week to 4-week supply of medications) and thus would also be likely to have successful treatment outcomes. While expected, further research might consider designs to encourage completion of laboratory testing, specifically among those most vulnerable to infecting others or reacquiring infection, i.e., the homeless and PWID. Because housing and insurance can be temporary, paying for the final visit and laboratory tests should be considered for future studies. Completion of SVR laboratory tests could also reassure that their vulnerabilities do not affect treatment efficacy, i.e., food insecurity and GLE/PIB.

The value of patient navigation and task shifting in a busy underserved clinic cannot be overstressed. Active patient navigation occurs when obtaining prior authorization to the end of treatment. When individuals complete treatment, patient navigators shift their focus to new treatment-pending patients. The loss of navigational support at the end of treatment may have contributed to the large number lost to follow-up. Knowing those who were more likely to be lost to follow-up, particularly men younger than 50 years of age who are HIV negative, might help FQHCs direct limited resources where it stands to make the greatest impact.

In this setting, a PMD or NP is permitted to treat patients with compensated cirrhosis (Fig. 3B). While we prefer those with decompensated cirrhosis attend an academic or liver transplant center for treatment,

TABLE 3. CURE RATE RATIOS, SPOKE CLINICS RELATIVE TO HUB

	Per Protocol (n = 964)		Intention to Treat (n = 1,288)	
Model	PR	95% CI	PR	95% CI
Crude	1.03	1.00-1.06	0.99	0.92-1.07
Model 2: crude + demographics	1.01	0.98-1.03	1.01	0.93-1.10
Model 3: model 2 + resources	1.00	0.98-1.03	1.01	0.93-1.10
Model 4: model 3 + disease characteristics	1.01	0.98-1.04	1.03	0.94-1.12

TABLE 4. CURE RATE RATIOS, DIFFERENT PROVIDER TYPES RELATIVE TO ID MD

	Per Protocol (n = 964)				Intention to Treat (n = 1,288)			
	PMD		NP		PMD		NP	
Model	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
Crude	1.02	0.99-1.06	1.03	0.99-1.07	0.94	0.87-1.02	1.00	0.92-1.10
Model 2: crude + demographics	1.00	0.96-1.04	1.00	0.97-1.04	0.98	0.90-1.08	1.03	0.93-1.13
Model 3: model 2 + resources	1.00	0.96-1.04	1.00	0.97-1.04	0.99	0.90-1.08	1.03	0.93-1.13
Model 4: model 3 + disease characteristics	1.00	0.96-1.04	1.00	0.97-1.04	1.00	0.91-1.10	1.04	0.95-1.15

there are occasionally insurmountable obstacles, i.e., patients who are uninsured and nontransplant candidates. They might be safely treated in conjunction with the community hepatologist, decreasing the individual's morbidity and mortality while also reducing incident infections.

Taken together, our results lend strong support to the growing body of evidence that PCPs can treat HCV as well as their specialist counterparts even in more challenging patient cases when well trained and provided ongoing support. PCPs are uniquely equipped to improve care and treatment access to the most vulnerable populations. For example, they are better positioned to deliver guideline-driven harm-reduction services, including substance abuse counseling and treatment.[25] PCPs often cite the lack of time and experience as barriers for providing specialty services, such as HCV treatment. Thus, by adopting a model in which there is ongoing specialty support coupled with patient navigation support, the impact on PCPs day-to-day is limited.

This study has important strengths, including a low-income and majority homeless patient population in an urban setting. Additionally, the primary study endpoint was assessed through laboratory findings over the course of 6 years, and the inclusion of EHR data allowed us to robustly evaluate the potential impact of a variety of explanatory variables. The findings of this study should be considered within its limitations. First, there was no comparison group of patients being treated in an urban setting without a decentralized approach. Second, we were not able to randomly allocate patients to providers due to logistical constraints of clinical practice at FHCSD. Third, there may be factors that influence the observed cure rate that were not measured and included in multivariable models.

In the era of pangenotypic DAA regimens, streamlined HCV guidelines, and accessible ECHO technologies, PMDs and NPs can and should be encouraged and supported to effectively treat HCV in the patient's medical home. Our findings are likely generalizable to the other low-income and majority homeless cohort of patients at urban FQHC clinics in the United States, highlighting the potential for a decentralized approach to HCV elimination efforts.

Acknowledgment: We thank all of the FHCSD clinicians, staff, and patients who have made this study possible.

REFERENCES

1) Hofmeister MG, Rosenthal EM, Barker LK, Rosenberg ES, Barranco MA, Hall EW, et al. Estimating prevalence of hepatitis C virus infection in the United States, 2013-2016. Hepatology 2019;69:1020-1031.
2) Centers for Disease Control and Prevention. Viral hepatitis surveillance-United States, 2017. https://www.cdc.gov/hepatitis/statistics/2017surveillance/index.htm. Updated November 14, 2019. Accessed July 2020.
3) Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising mortality associated with hepatitis C virus in the United States, 2003-2013. Clin Infect Dis 2016;62:1287-1288.
4) Razavi H, Elkhoury AC, Elbasha E, Estes C, Pasini K, Poynard T, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. Hepatology 2013;57:2164-2170.
5) California Viral Hepatitis Coordinating Committee and California Department of Public Health. California Viral Hepatitis Prevention Strategic Plan, 2016-2020. Published May 2018. Accessed July 2020.
6) California Department of Public Health, Office of Viral Hepatitis Prevention. Local health jurisdiction specific data tables, chronic hepatitis C, 2017.
7) Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an estimate of true prevalence. Liver Int 2011;31:1090-1101.
8) Martin NK, Vickerman P, Dore GJ, Grebely J, Miners A, Cairns J, et al.; STOP-HCV Consortium. Prioritization of HCV treatment in the direct-acting antiviral era: an economic evaluation. J Hepatol 2016;65:17-25.
9) Brady J, Vellozzi C, Hariri S, Kruger D, Nerenz D, Ann Brown K, et al. Hepatitis C care cascade among persons born 1945-1965: 3 medical centers. Am J Manag Care 2018;24:421-427.
10) Norton BL, Fleming J, Bachhuber MA, Steinman M, DeLuca J, Cunningham CO, et al. High HCV cure rates for people who use drugs treated with direct acting antiviral therapy at an urban primary care clinic. Int J Drug Policy 2017;47:196-201.
11) American Association for the Study of Liver Diseases and Infectious Diseases Society of America. HCV guidance: recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org/. Updated 2020. Accessed July 2020.
12) Dieterich DT. A simplified algorithm for the management of hepatitis C infection. Gastroenterol Hepatol (N Y) 2019;15(Suppl. 3):1-12.
13) Pawlotsky J-M, Ramers CB, Dillon JF, Feld JJ, Lazarus JV. Simplification of care for chronic hepatitis C virus infection. Sem Liv Dis 2020. https://doi.org/10.1055/s-0040-1713657.
14) Kattakuzhy S, Gross C, Emmanuel B, Teferi G, Jenkins V, Silk R, et al.; ASCEND Providers. Expansion of treatment for hepatitis C virus infection by task shifting to community-based nonspecialist providers: a nonrandomized clinical trial. Ann Intern Med 2017;167:311-318.
15) Castro R, Perazzo H, de Araujo LAMM, Gutierres IG, Grinsztejn B, Veloso VG. Effectiveness of implementing a decentralized delivery of hepatitis C virus treatment with direct-acting antivirals: a systematic review with meta-analysis. PLoS One 2020;15:e0229143.
16) Jayasekera CR, Perumpail RB, Chao DT, Pham EA, Aggarwal A, Wong RJ, et al. Task-shifting: an approach to decentralized hepatitis C treatment in medically underserved areas. Dig Dis Sci 2015;60:3552-3557.
17) Arora S, Thornton K, Murata G, Deming P, Kalishman S, Dion D, et al. Outcomes of treatment for hepatitis C virus infection by primary care providers. N Engl J Med 2011;364:2199-2207.
18) Tahan V, Almashhrawi A, Kahveci AM, Mutrux R, Ibdah JA. Extension for community health outcomes-hepatitis C: small steps carve big footprints in the allocation of scarce resources for

hepatitis C virus treatment to remote developing areas. World J Hepatol 2016;8:509-512.
19) Marciano S, Haddad L, Plazzotta F, Mauro E, Terraza S, Arora S, et al. Implementation of the ECHO® telementoring model for the treatment of patients with hepatitis C. J Med Virol 2017;89:660-664.
20) Falade-Nwulia O, McAdams-Mahmoud A, Irvin R, Niculescu A, Page K, Mix M, et al. Primary care providers knowledge, attitude and practices related to hepatitis C screening and treatment in the oral direct acting antiviral agents era. J Community Med Health Educ 2016;6:481.
21) Zeileis A. Econometric computing with HC and HAC covariance matrix estimators. J Stat Softw 2004;11:1-17.
22) Zeileis A. Object-oriented computation of sandwich estimators. J Stat Softw 2006;16:1-16.
23) The R Foundation. The R project for statistical computing. https://www.R-project.org/. Accessed July 2020.
24) Wickham H. ggplot2: elegant graphics for data analysis. New York, NY: Springer-Verlag; 2016.
25) American Association for the Study of Liver Diseases and Infectious Diseases Society of America. Key populations: identification and management of HCV in people who inject drugs. https://www.hcvguidelines.org/unique-populations/pwid. Updated 2020. Accessed July 2020.

Supporting Information

Additional Supporting Information may be found at onlinelibrary.wiley.com/doi/10.1002/hep4.1617/suppinfo.