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Comparison of hepatitis C treatment outcomes between telehepatology and specialty care clinics in the era of direct-acting antivirals

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Abstract

Introduction: Telehealth technologies for rural patients are increasingly being used to deliver care within the Department of Veterans Affairs (VA), and treatment of hepatitis C virus (HCV) is no exception. However, data evaluating outcomes with telehealth compared with specialty clinics in the era of direct-acting antiviral (DAA) agents is sparse.

Methods: In a retrospective analysis, we compared treatment outcomes for patients receiving DAAs followed solely in a telehepatology clinic (telehealth) versus an in-person specialty care clinic (standard of care) at the VA Eastern Colorado Health Care System. Patients with decompensated cirrhosis (CTP-B or CTP-C) were excluded from the study as they were exclusively followed via standard of care. Provider overlap occurred between clinics and consisted of physician specialists (hepatology and infectious diseases), physician assistants and clinical pharmacists.

Results: From 1 January 2014 to 31 December 2017, we treated 764 veterans for HCV infection. Standard of care was provided to 629 patients representing 654 treatment courses, and telehealth was provided to 135 patients representing 138 treatment courses. Sustained virologic response rates were not significantly different between the two clinics when looking at total treatment courses (93% telehepatology vs 89% specialty care, $p = 0.203$) and individual patients treated (95% telehepatology vs 93% specialty care, $p = 0.377$).

Discussion: Hepatitis C treatment utilizing telehealth technologies to improve access to care does not negatively impact treatment outcomes when compared with specialty care clinics in the era of DAAs.

Keywords

Telehealth, rural, Hepatology, infectious diseases, Hepatitis C, standard of care, Veterans Affairs

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Introduction

Individuals living in rural areas have more health disadvantages compared with their urban counterparts.[1] According to *Rural Healthy People 2020*, there are 59 million people living in rural or remote communities in the United States and the most important priority for rural health is access to quality health services.[1] Disparities in health care utilization exist for veteran populations living in rural areas, living further from a Veterans Affairs (VA) medical centre, or who are homeless.[2] As of 2019, 4.7 million veterans are considered rural or highly rural with only 58% enrolled in VA benefits.[3] The VA defines rural using the Rural–Urban Commuting Areas codes, which take into account both population density and socioeconomic links to larger urban areas.[3] At the VA, a score of 1.0 or 1.1 is considered urban, a score of 10.0 is considered highly rural, and rural is defined as anything between these two scores.[3] Telehealth technologies have been used to provide services to patients in rural areas in a cost-effective and well-received manner.[4] One such disease state with increased utilization of telehealth technologies is hepatitis C virus (HCV).

Chronic HCV infection is a substantial public health problem associated with significant morbidity and mortality.[5] HCV infects 3.5 million individuals in the United States and veterans are twice as likely to be infected as the general population.[5,6] The goal of treatment for HCV is sustained virologic response (SVR)

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defined as undetectable HCV ribonucleic acid (RNA) at 12 weeks post-treatment.[5] Since 2014, direct-acting antivirals (DAAs) have become the standard of care, with most SVR rates >90% and fewer side effects than previous treatments with pegylated interferon (PEG-IFN) and ribavirin (RBV).[7]

Prior research has focused on outcomes of telehealth versus standard of care or specialty care clinics in the setting of PEG-IFN and RBV treatment.[8–11] A study conducted by Beste et al. evaluated the impact of a VA program developed to promote primary care-based hepatitis C treatment using videoconferencing-based specialist support, Extension for Community Health Outcomes (ECHO), on hepatitis C treatment rates and sustained virologic response.[8] The study found that patients who saw providers who participated in the program, versus providers who did not, were more likely to receive antiviral treatment.[8] However, no difference in SVR was found.[8] Two studies from 2013 focused on telehealth interventions with PEG-IFN and RBV treatments.[9,10] A study in Northern California found similar rates of SVR between the telehealth and health centre patients and a higher proportion of patients completing treatment with telehealth.[9] A study conducted in Australia found that telehealth was non-inferior to face-to-face clinic visits in terms of SVR.[10] A satisfaction questionnaire was completed by patients in this study, with patients either agreeing or strongly agreeing that the service saved them time and money and stating they were confident and satisfied with the care they received.[10] An additional study looking at patient satisfaction for telehealth services in HCV found that patients were generally more satisfied with the telehealth clinic in comparison to in-person visits based on pharmacist–patient interaction, the level of security and privacy, and the level of healthcare received.[11]

The VA has been expanding telehealth technologies since the 1990s and clinical video telemedicine (CVT), delivery of health care through interactive video, utilization within the VA continues to grow and exceed use within private health care.[12] Unlike the telementorship program, ECHO, which consists of primary care providers consulting specialists, CVT links patients directly to providers via clinic-to-clinic (CCVT) or clinic-to-home (CHVT).[12] Limited studies are available comparing SVR rates with DAAs in telehealth vs standard of care clinics. The aim of this study was to compare the rates of SVR between patients being treated in a CCVT telehepatology clinic versus a specialty care clinic (standard of care) in the era of DAAs.

Methods

This was a retrospective, cohort analysis comparing veterans treated at the VA Eastern Colorado Health Care System (ECHCS) in a specialty care clinic versus a telehepatology clinic. Telehepatology clinic consisted of clinic-to-clinic video telemedicine between the Denver VA Medical Centre specialty clinic providers and patients located at one of six rural community based outpatient clinics (CBOCs). Patients were eligible for telehepatology if their primary care provider was located at one of the six rural CBOCs, but could receive care at the Denver VA Medical Centre if desired. Specialty care clinic consisted of face-to-face clinic appointments. Frequency of follow-up in both specialty care clinic and telehepatology clinic were provider driven.

Veterans were identified using the VA ECHCS Pharmacy Services Hepatitis C Clinic Share Point website and data was obtained via chart review of the VA electronic medical record. All veterans who started HCV treatment on or after 1 January 2014 and had completed treatment by 31 December 2017 were evaluated for inclusion criteria. Inclusion criteria were veterans 18 years of age or older, who were infected with HCV, any genotype (1–6), non-cirrhotic or had compensated cirrhosis (Child Turcotte-Pugh (CTP)-A). Veterans were excluded if they had decompensated cirrhosis (CTP-B and CTP-C), were managed by a primary care pharmacist, had a transferal of care, or were monitored by outside facilities.

Demographic and baseline variables were determined upon treatment initiation and included age, sex, race/ethnicity, zip code, HCV genotype, comorbidities, number of medications, baseline values for height and weight (used to calculate body mass index), laboratory tests for alanine aminotransferase, aspartate aminotransferase, platelets (all used to calculate FIB-4 Score), and baseline HCV RNA (value immediately preceding treatment start). Rurality was measured based on documented residential ZIP codes, at the time of HCV treatment initiation, corresponding to a RUCA code.[14] Cirrhotic status was determined based on provider-reported CTP score or 'decompensated/compensated' status and included reviewing imaging (computed tomography, magnetic resonance imaging or ultrasound) and laboratory values.

SVR was defined as undetectable HCV RNA at least 10 weeks or more post-treatment. Patients were categorized as not achieving SVR if they had a detectable HCV RNA post-treatment, had not completed treatment for any reason and had a detectable HCV RNA or had not had viral load drawn for SVR determination, had no viral load testing 10 weeks or more post-treatment, or had passed away prior to 10 weeks after post-treatment.

The primary outcome was comparison of SVR rates between patients being treated in the telehepatology clinic versus the specialty care clinic. SVR rates were

calculated on a per episode basis (SVR rates by treatment course) and on a per patient basis which took into account the patients last course of treatment (SVR rates by patient). The secondary outcome was comparison of patient compliance with SVR laboratory testing between telehepatology and specialty care clinics.

The chi-squared test was used to evaluate statistical significance for the primary and secondary outcomes. A p-value of <0.05 was considered statistically significant. Descriptive analysis was used on baseline characteristics.

The protocol was approved by the Colorado Multiple Institutional Review Board and the VA ECHCS Research and Development Committee.

Results

In total, 932 patients were treated for HCV infection in the study time frame for a total of 963 treatment courses (31 patients treated twice) at VA ECHCS. After applying exclusion criteria, 764 patients remained for 792 total treatment courses (28 patients treated twice). The specialty care clinic managed 654 treatment courses (629 patients) and the telehepatology clinic managed 138 treatment courses (135 patients) over the study time frame. Study enrollment is further described in Figure 1.

Overall, the median age of the cohort was 62 years old, 97% male, 69% white, 77% Genotype 1, 62% non-cirrhotic, 75% treatment naïve, and of those treated, 61% received ledipasvir/sofosbuvir. Compared to specialty care clinic, a larger proportion of telehepatology clinic patients lived in rural or highly rural areas (Table 1). Other baseline characteristics of the cohort are described in Table 1.

For the primary outcome, SVR rates were not statistically different between the two clinics. In terms of total treatment courses, in the specialty care clinic 583 of 654 treatment courses (89%) achieved SVR compared with 128 of 138 treatment courses (93%) in the telehepatology clinic ($p = 0.203$) (Figure 2). In total, 28 patients were treated twice, 25 in the specialty care clinic and 3 in the telehepatology clinic. There was no cross-over between clinics among the 28 patients that underwent retreatment. In terms of individual patient treatment outcomes, in the specialty care clinic 583 of 629 patients (93%) achieved SVR compared with 128 of 135 patients (95%) in telehepatology ($p = 0.377$) (Figure 3). Treatment failure rates were not statistically different (Table 2). In the specialty care clinic, 47

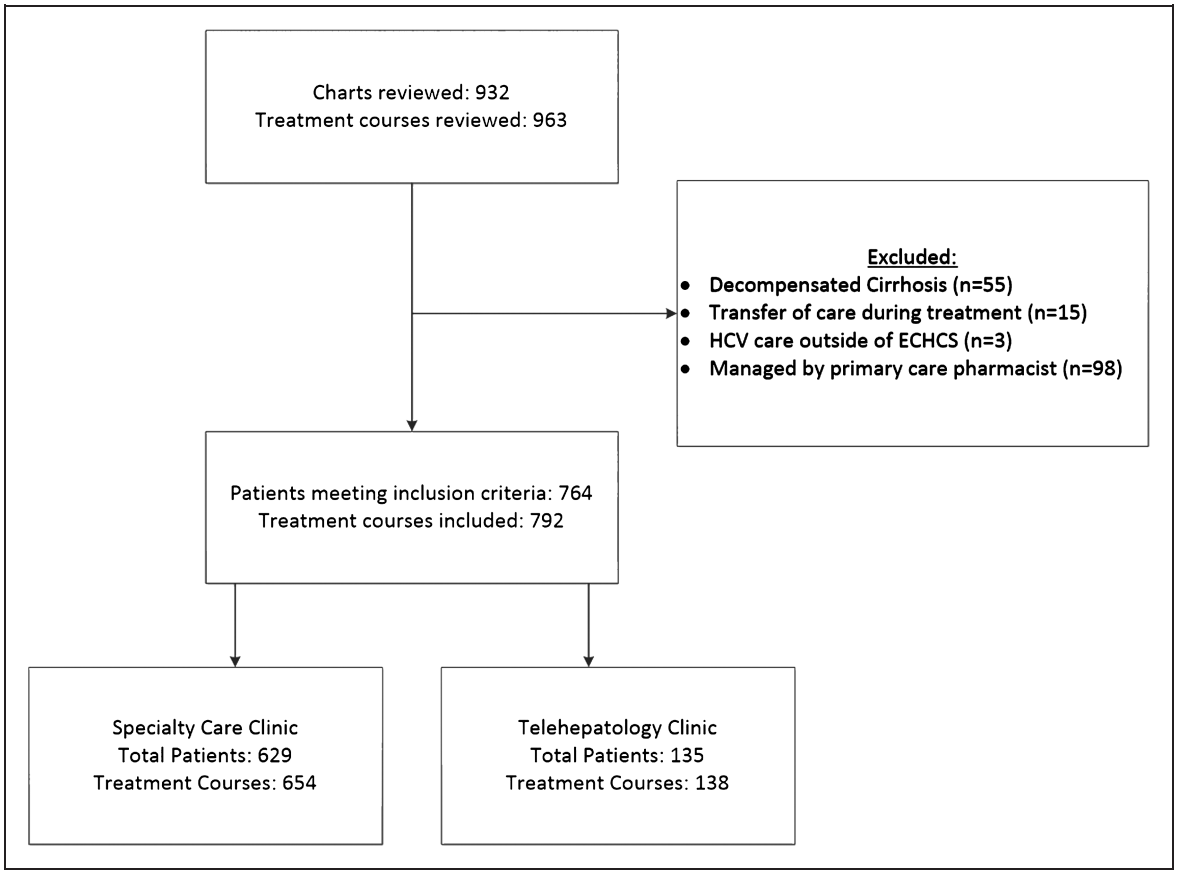

Figure 1. Enrolment.

Table 1. Baseline demographics.

Demographic	Specialty (n=654)	Telehepatology (n=138)	All (n=792)
Male, *n* (%)	636 (97)	131 (95)	767 (97)
White race, *n* (%)	428 (65)	117 (85)	545 (69)
Age, median years (IQR)	62 (59-66)	62 (59-66)	62 (59-66)
BMI, median kg/m^2 (IQR)	27 (24-30)	26 (24-31)	27 (24-30)
Rurality			
Urban, *n* (%)	585 (89)	81 (59)	666 (84)
Rural, *n* (%)	66 (10)	47 (34)	113 (14)
Highly Rural, *n* (%)	3 (1)	10 (7)	13 (2)
HCV genotype, *n* (%)			
1	513 (78)	99 (72)	612 (77)
2	70 (11)	21 (15)	91 (11)
3	55 (8)	15 (11)	70 (9)
4	14 (2)	1 (1)	15 (2)
5/6	–/–	–/–	–/–
Multiple	2 (1)	2 (1)	4 (1)
Cirrhosis, *n* (%)	244 (37)	54 (39)	298 (38)
Fib-4, median (IQR)	1.99 (1.3-3.3)	2.0 (1.0-4.0)	1.97 (1.3-3.4)
Treatment naïve, *n* (%)	489 (75)	115 (83)	604 (76)
Treatment experienced, *n* (%)	165 (25)	23 (17)	188 (24)
w/ DAA	44 (7)	5 (4)	49 (6)
w/ PEG-IFN/RBV	121 (19)	18 (13)	139 (18)
Treatment duration, *n* (%)			
8 weeks	96 (15)	29 (21)	125 (16)
12 weeks	476 (73)	96 (70)	572 (72)
16 weeks	14 (2)	2 (2)	16 (2)
24 weeks	68 (10)	11 (8)	79 (10)
Regimen, *n* (%)			
LDV/SOF +/– RBV	408 (62)	76 (55)	484 (61)
SOF/VEL +/– RBV	64 (10)	19 (14)	83 (10)
SOF + RBV	52 (8)	18 (13)	70 (9)
PrOD +/– RBV	47 (7)	5 (4)	52 (7)
EBR/GZR	34 (5)	12 (9)	46 (6)
SIM + SOF	21 (3)	6 (4)	27 (3)
SOF + PEG-IFN + RBV	10 (2)	1 (1)	11 (1)
DCV + SOF +/– RBV	10 (2)	0 (0)	10 (1)
SOF/VEL/VOX	6 (1)	1 (1)	7 (1)
EBR/GZR + SOF + RBV	2 (1)	0 (0)	2 (1)
RBV use, *n* (%)	188 (29)	27 (20)	215 (27)

BMI = body mass index; HCV = hepatitis C virus; FIB-4 = fibrosis-4 score; DAA = direct-acting antiviral; PEG-IFN/RBV = pegylated interferon/ribavirin; LDV = ledipasvir; SOF = sofosbuvir; DCV = daclatasvir; VEL = velpatasvir; PrOD = paritaprevir/ritonavir/ombitasvir/dasabuvir; EBR = elbasvir; GZR = grazoprevir; SIM = Simeprevir; VOX = voxilaprevir.

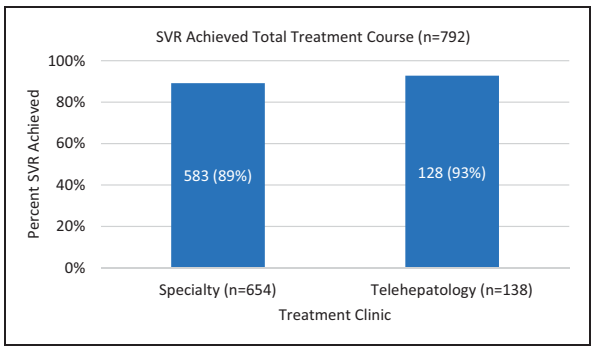

Figure 2. SVR rates by treatment course.

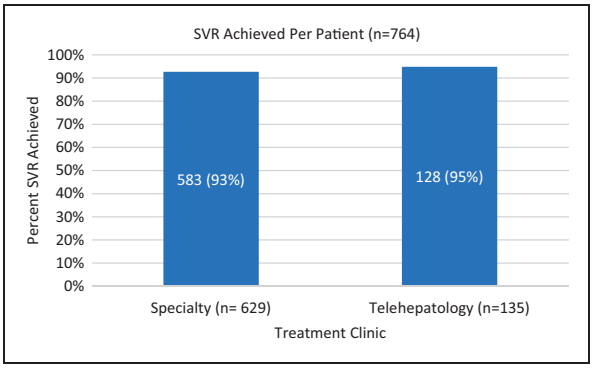

Figure 3. SVR rates by patient.

Table 2. Primary outcome – treatment failure.

	Specialty care ($n = 654$)	Telehepatology ($n = 138$)	*P*-value
Treatment failure, *n* (%)	47 (7)	6 (4)	0.187
SVR was detectable	33 (70)	3 (50)	
Discontinuation (side effects)	11 (24)	3 (50)	
Medication non-compliance	3 (6)	0 (0)	

Table 3. Secondary outcome – compliance with SVR laboratory testing.

	Specialty care ($n = 654$)	Telehepatology ($n = 138$)	*P*-value
Lost to follow-up, *n* (%)	24 (4)	4 (3)	0.487
Did not complete SVR (12) lab follow-up	17 (71)	2 (50)	
Patient passed away prior to SVR date	7 (29)	2 (50)	

SVR = sustained virologic response.

patients (7%) compared with 6 patients (4%) in the telehepatology clinic failed treatment ($p = 0.187$). Among treatment failures, 33 patients in specialty care (70%) and three patients in telehepatology (50%) had a detectable HCV RNA at SVR. Other reasons for classification as treatment failure included side effects leading to the patient discontinuing therapy (24% for specialty and 50% for telehepatology) and medication non-compliance leading to failure (6% for specialty and 0% for telehepatology).

For the secondary outcome, compliance with SVR laboratory testing was not statistically different between the two clinics (Table 3). In the specialty care clinic 24 patients (4%) compared with 4 patients (3%) in the telehepatology clinic were lost to follow-up ($p = 0.487$). Reasons included patients not presenting to complete SVR laboratory follow-up at 10 weeks or after post-treatment (71% specialty vs 50% telehepatology) and patients passing away prior to the SVR date (29% specialty vs 50% telehepatology).

Discussion

In this observational, cohort study, rates of cure between the specialty care clinic and the telehepatology clinic at VA ECHCS were not statistically different, with overall patient treatment success rates of 93% and 95% respectively. These rates are similar to other real-world comparisons using DAAs.[15] The 28 patients lost to follow-up were not included in the SVR

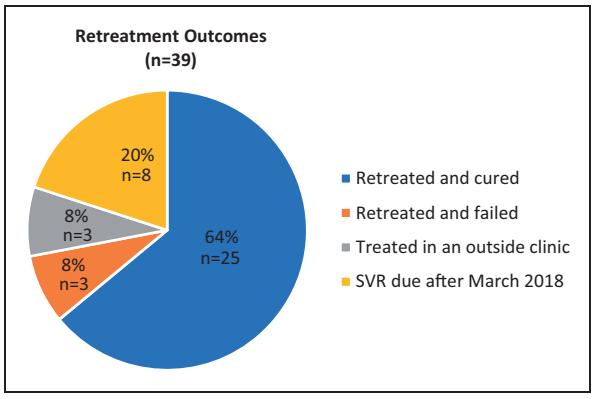

Figure 4. Re-treatment outcomes.

achieved groups because appropriate laboratory follow-up at or after 10 weeks was not completed by the patient. If these laboratory tests had been completed, SVR rates may have been affected. Of the 53 patients who failed treatment, 28 were re-treated during the study period and 11 additional patients were re-treated but not included in the study because they had either initiated treatment outside of the study period or no longer met the inclusion criteria (Figure 4). Future research could continue to look at patients who are re-treated to observe the increasing overall SVR rates.

This study has some limitations. The majority of the patients (77%) were Genotype 1. This is not surprising as it is the most common genotype in the United States.[16] However, this does make the results less generalizable to patients with other genotypes. The majority of the patients (61%) were treated with ledipasvir/sofosbuvir. Although there was representation for the other treatment regimens recommended by the guidelines during the time period, it is less generalizable to these treatment courses because of the lower numbers. When determining whether a patient should be excluded based on compensated or decompensated cirrhotic status, it was difficult to determine objectively if the provider had not included the CTP score in the medical record. There are objective data points such as encephalopathic status and moderate versus slight ascites that could possibly have not been reported. To determine whether a patient could be included, in situations where the CTP score was not calculated, a provider report of 'compensated or decompensated' in the medical record was used. However, this might not accurately reflect excluding every patient with decompensated cirrhosis. Additionally, this was a retrospective chart review of all patients at this institution treated in the study time frame and power was not calculated a priori. As a difference was not found, there is a possibility of a type II error.

As of August 2019, the VA has cured more than 100,000 veterans of HCV, which leaves less than 25,000 veterans remaining to be treated.[17] It is unclear how many veterans have been treated, but have yet to complete SVR12 or were lost to follow up upon completion of HCV treatment. During the timeframe of this single centre study, 128 veterans were cured of hepatitis C utilizing telehealth technology and there was no statistically significant difference between the specialty care clinic and the telehepatology clinic in terms of SVR or patient compliance with SVR laboratory testing. Based on the higher proportion of telehepatology clinic patients living in rural or highly rural areas it is unclear if these veterans would have otherwise received care. In conclusion, treating rural veterans using telehealth technology to improve access to care provides similar outcomes as having veterans travel to a specialty care clinic and will continue to serve as a valid option for treatment in the campaign to eliminate hepatitis C.

Declaration of conflicting interests

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