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Utilizing Telemedicine and Modified Fibrosis Staging Protocols to Maintain Treatment Initiation and Adherence Among Hepatitis C Patients During the COVID-19 Pandemic

Matthew O'Brien[1], Rachel Daws[2], Pooja Amin[2], and Kristen Lee[2]

Abstract

The COVID-19 pandemic exacerbated the decline in Hepatitis C Virus (HCV) screening and treatment globally in part due to lockdowns and restrictions at healthcare centers. The goal of this retrospective cohort study was to assess the effectiveness of an updated workflow implemented at Boston Medical Center (BMC) HCV clinics. Revised workflow incorporated appointments via telemedicine, transitioning to blood test-based fibrosis scoring, and delivering medication by mail to mitigate the lack of in-person services. We compared 2 cohorts of patients who attended at least the initial intake appointment at BMCHCV clinics: 170 before the pandemic and 133 after the pandemic. Outcome variables included treatment starts, fibrosis lab tests completed, appointment attendance, and SVR achievement. Proportions for outcome variables were compared between groups by use of χ^2 and 2-sample *t*-tests where appropriate. Our results showed a 14.43% decrease in completing fibrosis scoring tests (*P*-value: $<$.001) and a 15.21% decrease in medication initiation (*P*-value: $<$.001) among the patients who initiated care during the pandemic (modified workflow group). Furthermore, we found a 18.56% decrease in sustained virologic response (SVR) among the modified workflow group when compared to the controls. Overall, these results align with current trends of patients' decreasing engagement in HCV care but show higher retention than other published data. Furthermore, these figures support how appointments via telemedicine, transitioning to blood test-based fibrosis scoring, and medication delivery by mail can serve as tools to increase access to HCV care and successful HCV treatment completion even after COVID restrictions are lifted.

Keywords

COVID, primary care, prevention, underserved communities, community health, access to care

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Introduction

The COVID-19 pandemic has had deleterious effects the detection and treatment of Hepatitis C Virus (HCV). HCV remains a major public health concern with an estimated 2.1 million persons living with the virus in the United States.[1] Throughout the pandemic, health centers across the globe were ill equipped to continue HCV screening and treatment. Globally, 88% of HCV prevention, care and treatment centers experienced disrupted HCV treatment in 2020, with 80% indicating lower patient volumes than pre-COVID numbers.[2] HCV testing at 1 urban medical center decreased by 49.6% after March 2020 and new patient identification decreased by 42.1% hospital wide.[3] Some clinics saw treatment initiation decline between 25% and 40% since the onset of the COVID 19 pandemic.[4] Additionally, interventions and surveillance of cirrhosis and hepatocellular carcinoma were disrupted as elective procedures like Fibroscan and abdominal ultrasounds were delayed or suspended. In-person outpatient clinic visits rapidly decreased due to both patient and clinic cancelations.[1,5,6] Global models

[1]Boston University, Boston Medical Center, Boston, MA, USA
[2]Boston Medical Center, Boston, MA, USA

Corresponding Author:
Matthew O'Brien, Boston University, Boston Medical Center, 801 Massachusetts Avenue, 325a, Boston, MA 02118, USA.
Email: Brobrien@bu.edu

predict a delay in HCV intervention and treatment by even 1 year during COVID-19 would result in 121 000 excess infections and 906 000 missed diagnoses by 2030.[7] This rapid disengagement demonstrates the great need for health care centers to reevaluate traditional treatment approaches during times when in-person appointments are limited.

Telemedicine has been identified a useful technology that is poised to handle the challenges of these problems. Prior to the pandemic telemedicine has been a successful tool in coordinating testing and treatment of HCV. A study at the Ottawa Hospital–General Campus, a Canadian hospital, showed that treatment uptake and achievement of sustained virologic response (SVR) was similar between outpatient and telemedicine groups.[8] Another study for the ECHO program, which implements tele-education at a New Mexico health sciences center, found similar success in SVR among rural and underserved populations when compared to those treated by specialists.[9] These findings indicate that telemedicine eliminates structural barriers to treatment for some populations and is a potentially effective tool for healthcare centers to use for HCV intervention and treatment during and beyond the COVID-19 pandemic. More recently, some studies have built on the existing evidence of using telemedicine to treat HCV patients during COVID-19.[4,10,11]

These existing studies, however, predominantly focused on treating patients in remote communities or in countries outside of the United States where the impact of COVID-19 on health care facilities may have looked different. Furthermore, while telemedicine can help bridge the gap in access to provider visits, typical pre-treatment evaluations for Hepatitis C still consist of lengthy, in-person processes including lab specimen collections, liver fibrosis staging, and medication administration and monitoring.[12,13] The purpose of this study is to evaluate solutions to these problems, while providing further evidence on the effectiveness of telemedicine on HCV treatment in a large urban safety net hospital in the Unites States. This was done by assessing the effectiveness of unique modifications to HCV treatment, including shifts in fibrosis screening and transition to telemedicine, over the months following the start of the COVID-19 pandemic. The secondary aim is to describe the implications of these modifications on patient linkage to care for similar health care centers in the years to come.

Methods

Study Setting and Intervention

Boston Medical Center is a large urban "safety-net" hospital that receives approximately 1 150 000 patient visits per year.[14] More than 70% of patients seen at the medical center identify as a racial minority while approximately 25% are homeless.[14] Historically, the prevalence of HCV RNA+ patients is 3.94%, which is greater than the national average.[14] BMC has a comprehensive HCV screening and linkage to care program and collocated HCV treatment programs embedded in multiple ambulatory care clinics across the hospital.[3,12] Each clinic has a multidisciplinary team including physicians and nurse practitioners clinically trained to treat HCV. Most clinics also work with specialty pharmacists, pharmacy liaisons, patient navigators, and social work case managers.

During the early days of the COVID-19 pandemic, in-person appointments at BMC were limited to urgent care and essential monitoring visits only. As a result, BMC saw a 71.9% decrease in testing across ambulatory clinics, and a 63.3% decrease in newly identified HCV+ cases after March 16 2020, even considering hospital-wide implementation of universal 1 time HCV testing in line with the April 2020 United States Preventative Services Taskforce guidelines.[3] Elective procedures were put on hold, meaning that access to HCV care would be delayed for many patients. In response to the challenges posed by the pandemic, HCV clinics at BMC recommended a modified workflow for treating HCV patients (Figure 1).

First, most appointments with HCV providers and all medication teaching visits with pharmacists were converted to telemedicine. Second, tests for liver fibrosis staging shifted from using in-person Fibroscan® tests to FibroSURE or FIB-4 laboratory tests that could be completed at the medical center or at another location based on patient preference. Both FibroSURE and Fib-4 have been demonstrated to be effective methods for evaluating severe fibrosis.[7,15] Fibrosis test results are defined on a scale between F0 and F4 in which F4 indicates the most severe fibrosis of the liver.[7] In keeping with national guidelines, patients with a fibrosis score of F3 or F4 were still recommended to complete an abdominal ultrasound to monitor for hepatocellular carcinoma.[7] Third, medication was dispensed by mail delivery, if possible, to further reduce the patients' need to come in-person. BMC changed the workflow beginning in March 2020 when an HCV clinic newsletter was circulated to all HCV providers with the above recommendations.

Population Data

Our study population included HCV positive patients who completed an HCV clinic intake appointment in the adult primary care, family medicine, or infectious diseases departments between March 1, 2019 and July 23, 2021. We assigned patients who had an HCV intake appointment between March 15th, 2019, and November 30th, 2019, as the control group, and those between March 15th, 2020, and November 30th, 2020, as the modified workflow group. We excluded patients who had an intake appointment between December 1st, 2019, and March 14th, 2020, in the control group since these patients' HCV care may extend beyond the first COVID pandemic lockdown period and become

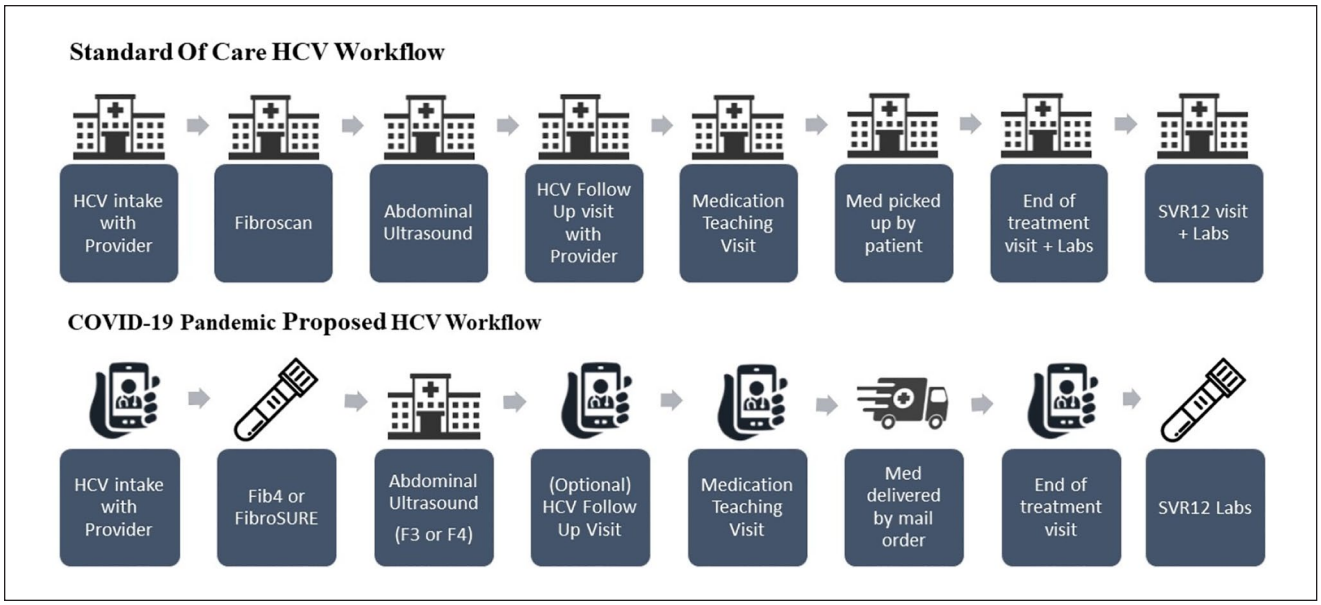

Figure 1. Workflow of Boston Medical Center HCV clinics both pre and during COVID-19 pandemic for patients with hepatitis C (March 2020).

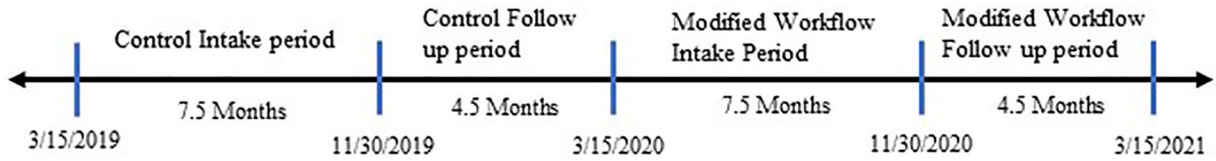

Figure 2. Timeline of observation periods for outcome variables in both the control and modified workflow group.

affected by modified workflow (Figure 2). Patients from this control group with follow-up appointments (follow-up with a provider, medication teaching with a pharmacist) after March 14th, 2020, were also excluded to ensure that the control group was not affected by the modified workflow. To ensure equal observation times, similar restrictions were applied to the modified workflow group 1 year later. All clinical data was retrieved from BMC's HealthCloud network.

Outcome Variables

The primary variables of interest include appointment type, fibrosis staging method used, abdominal ultrasound for hepatocellular carcinoma screening (yes; no), appointment attendance, treatment initiation (yes; no), and SVR status (confirmed, unconfirmed). Only patients eligible for SVR tests were included in SVR status; Patient's SVR eligibility was determined to be 12 weeks after treatment ended. Patients who cleared their original infection of HCV and were later re-infected with another genotype of HCV were designated confirmed SVR. We collected demographic information such as gender (male, female), ethnicity (Hispanic, Non-Hispanic), race (White, Black, Asian, Other, decided not to Answer), homelessness status, any recorded substance use, any recorded alcohol use, primary insurance type (Medicaid, Medicare, private, missing), and age. Other variables collected include medication type (sofosbuvir/velpatasvir 400/100 mg (Epclusa 400/100 mg), ledipasvir/sofosbuvir 90/400 mg (Harvoni 90/400 mg), glecaprevir/pibrentasvir 100/40 mg (Mayvret 100/40 mg), other), and reason for unconfirmed SVR.

Statistical Analysis

All data were analyzed using SAS software (Version 9.4; SAS Institute Inc. Cary, NC). Statistical comparisons of variables between modified workflow and control groups were made by χ^2 for categorical variables and 2-sample *t*-tests for continuous variables. Statistical significance was performed at the 5% level.

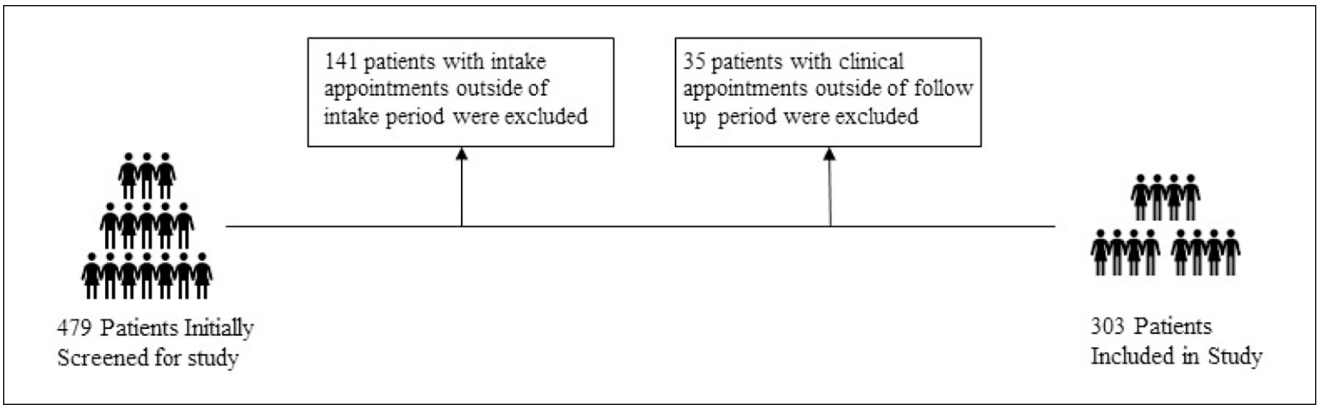

Figure 3. Exclusion criteria for study population based on initially screened patients from Boston Medical Center HCV clinics, March 1, 2019 to July 23, 2021.

Results

A total of 479 patients were screened who attended their intake appointments at BMCHCV clinics between March 15th, 2019 and July 17th, 2021. These patients were then separated into control group or modified exposure group based on intake date. A final study population of 303 patients was reached: 170 were the controls and 133 were under the modified workflow group (Figure 3).

Patients were middle-aged, with a mean age of 47 years in the control group and 42.5 years in the modified workflow group. Patients in the modified workflow group were 4.88 years younger on average than the control group (*P*-value: $<.001$). In addition, 70.8% of patients from the control group had Medicaid as their primary insurance compared to 84.1% in the modified workflow group (*P* value = .025). Patients in each group did not differ by gender, race, housing status, and substance use (Table 1).

Between the 2 groups, fibrosis staging, appointment attendance, and medication initiation differed across most variables (Table 2). For fibrosis staging, we see that number of Fibroscan performed decreased from control group to modified workflow group by 41.95%, FibroSURE tests increased by 25.83%, and any fibrosis test decreased by 14.43%. Appointment attendance decreased across the board between groups as follow up appointment attendance decreased by 18.24% and medication teaching appointments decreased by 11.00%. Medication initiation decreased as 39 less patients started medication and percent of patients who did decreased by 13.29.

Patients who had received treatment were analyzed for treatment result variables (Table 3). Medication prescription was generally the same between groups (*P*-value = .82). SVR confirmation was higher in the control group with a SVR confirmation proportion of 85% compared to 66.04% (18.56% different) in the modified workflow group. The primary reason for unconfirmed SVR data was loss to follow up.

Discussion

Across clinic interface and treatment initiation, we observe a net decrease across most variables and a general decrease in engagement with HCV prevention and treatment. As expected, less patients received a Fibroscan test and more received a FibroSURE or FIB-4 test which aligns with updated clinic guidelines. Even with telemedicine and updated protocols, however, overall patient engagement decreased in terms of fibrosis screening, appointment attendance, and treatment uptake. These are similar results as other healthcare settings during the pandemic. One study that used national estimates of dispensed prescriptions for HCV treatment saw that prescriptions decreased 43% in May, 37% in June, and 38% in July when compared to the same months in 2018 and 2019.[16] A recently published article showed that in rural communities in Canada, telemedicine for HCV treatment was associated with lower no-show rates compared to in-person appointments and still saw a 30% decline in pre-pandemic treatment starts.[4] Furthermore, a study in the republic of Georgia found 59% fewer people with HCV infection were treated and 46% fewer achieved SVR when comparing data from 2020 to that of 2019.[17] Our results only show a 15% decline in treatment starts which is nearly half the percentage decrease that these other 2 studies estimated. Although these studies were not assessing the same populations, this comparison indicates that the clinic protocols implemented at BMC were effective in mitigating the effects of the pandemic.

These findings become even more relevant when considering World Health Organization's goal to eliminate HCV by 2030. National estimates prior to the pandemic proposed that the USA would not reach HCV elimination until 2037, with some states not reaching HCV elimination until 2050.[18] Nationwide, there is no single, standardized protocol for hepatitis C treatment and AASLD guidelines leave room for healthcare organizations to implement the methods and

Table 1. Demographic Statistics Comparing BMC HCV Clinic Patients Between Modified Workflow Group and Control Group.

	Control group (n = 170)		Modified workflow group (n = 133)		
Demographic variables	N	%	N	%	*P*-value
Gender	—	—	—	—	.41
Male	115	67.65%	84	63.16%%	—
Female	55	32.35%	49	36.84%	—
Ethnicity					.18
Not Hispanic/Latino	139	84.76%	104	78.79%	—
Hispanic/Latino	25	15.24%	28	21.21%	—
Missing	(6)	—	(1)	—	—
Race	—	—	—	—	.54
White	91	53.84%	70	52.33%	—
Black	53	31.36%	33	25.19%	—
Asian	21	12.43%	22	16.79%	—
Decided not to Answer	4	2.37%	6	4.58%	—
Missing	(1)	—	(2)	—	—
Homeless	—	—	—	—	.70
Yes	49	28.82%	41	30.93%	—
No	121	71.18%	92	69.17%	—
Substance use**	—	—	—	—	.98
Yes	85	50.30%	65	48.87%	—
No	84	49.70%	64	48.12%	—
Missing	(1)	—	(4)	—	—
Alcohol use**	—	—	—	—	.22
Yes	30	17.65%	16	12.50%	—
No	140	82.35%	112	87.50%	—
Primary insurance*	—	—	—	—	.025
Medicaid	114	70.81%	111	84.09%	—
Medicare	34	21.12%	14	10.61%	—
Private	13	8.07%	7	5.30%	—
Missing	(9)	—	(1)	—	—
	Mean	Std	Mean	Std	
Age*	47.33	13.28	42.45	12.53	.001

*Indicates significant statistical difference at the 5% level between modified workflow and control groups.
**Patient has ever indicated use since intake appointment.

approaches that are available to them. Increasing access to treatment by streamlining the fibrosis staging process and utilizing telemedicine may be an effective and accessible way to help increase treatment engagement across the board and work toward that goal, even as health care operations begin to return to pre-pandemic functioning.[19]

Looking at treatment result data, we see that SVR confirmation was statistically higher among the control group when compared to the modified workflow group (85.42% and 66.02% respectfully). These data are acceptable results given the length of time patients were observed and shows both protocols are effective in achieving SVR. Loss to follow up was the largest factor for patients with unconfirmed SVR. The high substance usage and homeless status of our hospital population may contribute to why SVR has been historically difficult to track at BMC. This is not unusual given our patient demographics. A study of HCV treatment in an internal medicine clinic in Seattle, Washington with very similar patient demographics also reported as high as 46% of patients did not return for treatment labs and patients who completed SVR labs took anywhere from 12 weeks to 1 year after completing treatment.[20]

The modified workflow group showed lower confirmation of SVR, this could be attributed to the study design and limitations in observation period for this variable. Patients in the control group were given a larger observation period for SVR confirmation than the modified workflow and may indicate that those treated and eligible for SVR is higher than the data suggests. The difference in SVR rates may also be indicative of patients' ongoing hesitancy in leaving their homes during the COVID-19 pandemic, even if offered to complete labs at a more convenient location, suggesting areas for improvement in outreach and education to increase rates of SVR testing after treatment.

Table 2. Appointment Attendance and HCV Interventions Among Modified Workflow Group and Control Group in BMC HCV Clinics.

	Control group (n = 170)		Modified workflow group (n = 133)		Percent difference**	
	N	%	N	%	%	*P* value
Intake appointment type*						<.0001
In-person	170	100	16	12.03	−87.97	
Telemedicine	0	0	116	87.21	87.21	
Fibrosis staging method*						<.0001
Fibroscan	125	73.53	42	31.58	−41.95	
FibroSURE or FIB-4	20	11.76	50	37.59	25.83	
Severe fibrosis (F3-F4)*	31	18.24	7	5.3	−12.94	<.0001
Received any fibrosis test*	137	80.59	88	66.16	−14.43	<.0001
Abdominal ultrasound done						<.0001
All	132	77.65	48	36.09	−41.56	
Patients with severe fibrosis*	30	96.77	7	100		.63
Attended follow-up*	109	64.1	61	45.86	−18.24	.0019
Attended medication teaching appointment	89	52.35	55	41.35	−11.00	.065
Started medication	98	57.65	59	44.36	−13.29	.013

*Indicates significant statistical difference at the 5% level between modified workflow group and control group.
**Calculated by modified workflow group minus control group.

Table 3. Treatment Results Among Modified Workflow Group and Control Group in BMC HCV Clinics Who Started Treatment.

	Control (n = 98)		Modified workflow group (n = 59)		
Treatment variables	N	%	N	%	*P* value
Medication prescribed					.82
Sofosbuvir/velpatasvir	61	62.24	33	56.90	
Ledipasvir/sofosbuvir	13	13.27	11	17.24	
Glecaprevir/pibrentasvir	21	21.43	14	24.14	
Other	4	3.06	1	1.72	
SVR eligible*					
Eligible	96	97.96	53	89.83	.025
Non-eligible	2	2.04	6	10.17	
SVR result of eligible*					.0069
Unconfirmed	13	13.54	17	32.08	
Confirmed	83	86.46	36	67.92	
Reason for unconfirmed					.59
Loss to follow up	8	57.14	14	80.00	
Detected	5	35.71	3	15.00	

*Indicates significant statistical difference at the 5% level between modified workflow group and control group.

Conclusion

The pandemic impacted the effectiveness of health care centers worldwide to screen and treat HCV and forced many facilities to put non-urgent treatment on hold or adapt approaches to care. Even with streamlined treatment protocol to mitigate the impact of the pandemic on access to HCV care, BMC HCV clinics still saw a reduction in patient retention, treatment initiation and SVR in 2020 compared to 2019. Rates for liver fibrosis screening, treatment initiation, and SVR confirmation decreased after the pandemic began and will have negative health consequences on those living with chronic HCV. This is not to say that telemedicine and offering remote services is not effective in the HCV clinic, however, it appears that a lack of in-person services has had a negative impact on the clinic's ability to address this public health issue. We do see promising results in updated clinic workflow as increased services in telemedicine and medication delivery by mail appear to have mitigated the effect of the

pandemic on clinic engagement when compared to other health centers. The added flexibility for treatment and screening options are important tools that would be best included in other similar healthcare settings. Our research indicates that in-person patient engagement is still important, however, and a combination of both in-person and telemedicine options will quite possibly lead to the more optimal health outcomes for those with HCV.

Declaration of Conflicting Interests

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ORCID iD

Matthew O'Brien https://orcid.org/0000-0002-5630-1369

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