

# Virtual Consultations through the Veterans Administration SCAN-ECHO Project Improves Survival for Veterans with Liver Disease

Grace L Su, M.D. (1,2)

Lisa Glass, M.D. (1,2)

Elliot B. Tapper, M.D. (1,2)

Tony Van, M.A. (3)

Akbar K Waljee, M.D., MS (1,2,3,4)

Anne E Sales, PhD (3,5)

(1) Medicine Service, VA Ann Arbor Healthcare System

(2) University of Michigan Medical School

(3) VA Center for Clinical Management Research, VA Ann Arbor Healthcare System

(4) Department of Statistics, University of Michigan

(5) Department of Learning Health Science, University of Michigan

Corresponding Author

Grace L. Su, M.D.

VA Ann Arbor Healthcare System

2215 Fuller Road

Ann Arbor, MI 48105

734-845-5865

[gsu@umich.edu](mailto:gsu@umich.edu)

## Abstract:

Access to specialty care has been associated with improved survival in patients with liver disease but universal access is not always feasible. Novel methods of care delivery using virtual modalities including the SCAN-ECHO (Specialty Access Network- Extension of Community

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1002/HEP.30074](https://doi.org/10.1002/HEP.30074)

This article is protected by copyright. All rights reserved

Healthcare Outcome) program were implemented by the Veterans Health Administration (VHA) to address this need but limited data are available on patient outcomes. We sought to evaluate the efficacy of a SCAN-ECHO visit within the context of a regional cohort of patients with liver disease in the VHA (n= 62,237) following implementation of the Ann Arbor SCAN-ECHO Liver Clinic on 06/01/2011 to 03/31/2015. The effect of a SCAN-ECHO visit on all-cause mortality was compared to patients with no liver clinic visit. To adjust for the differences among patients who had a SCAN-ECHO visit versus those who had no visit, propensity score matching was performed conditioned on factors which affect the likelihood of a SCAN-ECHO visit: demographics, geographic location, liver disease diagnosis, severity and comorbidities.

During the study period, 513 patients who had a liver SCAN-ECHO visit were found within the cohort. Patients who had completed a virtual SCAN-ECHO visit were more likely younger, rural, with more significant liver disease, and evidence for cirrhosis. Propensity adjusted mortality rates using Cox Proportional Hazard Model showed that a SCAN-ECHO visit was associated with a hazard ratio of 0.54 (95% CI 0.36-0.81, p = 0.003) compared to no visit.

**Conclusion:** Improved survival in patients seen via SCAN-ECHO suggests that this novel approach may be an effective method to improve access for selected patients with liver disease, particularly in rural and underserved populations where access to specialty care is limited.

### Introduction

The conventional approach to specialty consultation begins with a question from a primary care provider and results in an in-person visit between the specialist and the patient. While this method has many advantages, there are also significant challenges. Most specialists cluster in urban tertiary centers, limiting access to these providers, particularly for rural patients with limited ability or means to travel. Furthermore, knowledge gaps among frontline providers, as well as other factors such as time pressures, can result in suboptimal patient care(1). In response to these issues, Arora and colleagues described in 2011 a novel approach to specialty care using the ECHO (Extension of Community Healthcare Outcome) program(2). The ECHO program formed collaborative networks between academic specialists at the University of New Mexico and primary care providers in community-based clinics throughout the state to address inadequate access to hepatitis C therapy in rural communities. Akin to a virtual medicine morning report, patient cases were discussed via videoconferencing between the specialist team

and primary care providers from multiple sites. Recommendations for patient care were made in real time and a didactic session was included during the conference/clinic. Continuing medical education credits (CME) were provided for all attendees for each conference, emphasizing the distance learning component of this model(3). In 2011, the Veterans Health Administration (VHA) adopted this program to innovate specialty care delivery and renamed the program SCAN-ECHO (Specialty Care Access Network-Extension of Community Healthcare Outcome). The VA Ann Arbor Healthcare System was one of the first to implement a SCAN-ECHO program for chronic liver disease. All providers within our referral base were invited to participate in the program. We specifically queried providers to accept a SCAN-ECHO consult in place of an in-person consult in patients who did not appear to have complex medical care requiring ongoing care such as decompensated cirrhosis. However, the decision to participate was determined by the provider.

Despite wide uptake of the SCAN-ECHO program in the Veterans Health Administration (VHA), data are limited regarding the clinical impact of VA SCAN-ECHO, particularly on patient outcomes such as mortality(2, 4-10). We have previously shown that an in-person specialist consultation visit is associated with improved survival in liver disease patients(11). This study sought to extend those findings by examining whether a virtual specialty SCAN-ECHO consultation visit had a similar positive effect on survival of patients with liver disease.

#### Materials and Methods:

Population: The liver disease cohort was retrieved from the VA corporate data warehouse (CDW) and included any patients with a liver disease diagnosis (based on ICD-9 codes) in either an inpatient visit or outpatient encounter in the historical VISN (Veterans Integrated Service Network) 11, from the time of the inception of Ann Arbor VA SCAN-ECHO Liver program in 06/01/2011 to 03/31/2015. The historical VISN 11 was one of twenty-one regions encompassing a 90,100 square mile geographic area including Michigan, central Indiana, and northwest Ohio that was the VA Ann Arbor Healthcare System referral base during the study period. The liver disease cohort included any patient who had any one of the ICD-9 codes for liver diseases which might result in specialty care referral and have been previously validated within the VHA system(11) and provided in supplementary Table 1. To account for late referral bias (i.e. very

sick patients who may have died before being able to complete an outpatient visit), we excluded all patients who died within 6 months of their index liver disease diagnosis. This analysis, conducted as part of the operational evaluation of the Ann Arbor VA SCAN-ECHO Liver Program, was deemed non-research quality improvement under VHA Handbook 1058.05. It was conducted with the approval of clinical leadership at VA Ann Arbor Healthcare System.

#### Study Definitions:

##### Primary Outcome:

The primary outcome was all cause mortality as determined by linking the patient data files with the Vital Status Files in CDW. Deaths were recorded from the beginning of study period (6/1/2011) until 03/31/2015.

##### VA SCAN-ECHO Visit Group:

The intervention of primary interest was a VA Liver SCAN-ECHO consultation visit. Since the inception of the Ann Arbor VA SCAN-ECHO clinic in June 2011, the patients discussed at these clinics were tracked prospectively. 520 unique patients had a VA SCAN-ECHO visit during the study period. 513 were found within the cohort extracted from the CDW. 7 were excluded because the only ICD 9 code they had was for abnormal imaging of the gastrointestinal tract. This code was not included in our liver disease patient cohort as this code is not specific for liver disease. (Supplementary Figure 1)

##### No Visit Group:

Within the population of patients with liver disease, we defined patients as having no visit if they were not in the VA SCAN-ECHO cohort and did not receive a traditional in-person hepatology consultation visit during the study period as indicated by the presence of codes in the electronic record indicating a completed liver clinic visit

##### Predictors of a SCAN-ECHO visit:

Predictors of a visit were defined as follows: demographic predictors were age at diagnosis, gender, and race/ethnicity. Urban, rural, and highly rural patient residence was determined based upon VA Planning Systems Support Group geocoding(12). Liver disease diagnoses (hepatitis B and C), cirrhosis and cirrhosis comorbidities, including ascites,

spontaneous bacterial peritonitis, hepatorenal syndrome, variceal bleed, hepatocellular carcinoma, hepatic encephalopathy, and thrombocytopenia were identified by ICD 9 codes. Cirrhosis complications were defined by the presence of codes for variceal bleeding, ascites, and hepatic encephalopathy. The alanine aminotransferase (ALT) value used was the highest ALT level within 365 days but *prior to* diagnosis to account for triggers for consultation. The bilirubin level used was the value closest to diagnosis date and within 180 days prior to diagnosis to account for severity of liver disease. Modified Elixhauser comorbidity scores were calculated using diagnosis codes present 365 days prior to the first liver disease diagnosis and excluded liver disease and alcoholism(13). The presence of a procedure: abdominal computed tomography (CT), magnetic resonance imaging (MRI), abdominal ultrasound, esophagoduodenoscopy, liver biopsy and paracentesis was defined by the presence of a CPT code for the procedure within the 1 year prior to enrollment into the cohort.

#### Statistical Analysis:

Baseline covariates were defined within 1 year of the index date, defined as the first appearance of any of the liver disease diagnosis codes. We conducted two separate analyses: (1) A descriptive analysis of veterans in an unmatched cohort with a VA SCAN-ECHO visit compared to those with no visit, and (2) A survival analysis using a propensity score matched cohort to evaluate mortality among veterans with a VA SCAN-ECHO visit compared to those with no visit. ANOVA with Tukey's adjustment for multiple group comparisons was used for bivariate analyses of categorical and continuous predictors of access. Multivariable logistic regression was performed to determine independent predictors of a SCAN-ECHO visit. Survival analysis was performed to analyze the time from index date to death or end of follow-up (April 1, 2015). All relevant variables were included in the final model regardless of their statistical significance in bivariate testing.

In order to determine whether a SCAN-ECHO visit was independently associated with mortality, the propensity score model was developed adjusting for the likelihood of a SCAN-ECHO visit using a binary logistic regression on the baseline covariates. SCAN-ECHO patients were matched 1:1 to patients with no visit, taking the closest or best available match without replacement. The quality of the matching was assessed using the absolute standardized mean difference as a balance measure. Survival differences were computed using the Cox Proportional

Hazard models and Kaplan-Meier survival curves. Additional sensitivity analyses were performed after dividing the cohorts into two groups based on a Fibrosis-4 (FIB-4 score) as a surrogate for presence of advanced liver disease/cirrhosis(14). A cutoff of greater 3.25 was used to identify patients with a high probability of advanced liver disease(15). All statistical analyses were performed using the statistical language R, using the packages *MatchIt* (for propensity matching) and *Survival* (for Cox proportional hazard modeling).

## Results:

### *Demographics and Clinical Characteristics*

During the study period, 513 eligible patients had a VA SCAN-ECHO visit and 62,237 had no visit within a cohort of 67,314 patients with a liver disease diagnosis (Table 1, Supplementary Figure 1). 4,564 patients had a traditional in-person liver clinic visit and were excluded from the no visit group. In comparing the characteristics of patients who received a SCAN-ECHO consultation vs. no visit, the patients in SCAN-ECHO were more likely rural or highly rural. This likely reflects the particular affinity for providers and patients to use a virtual modality when patients live far from a specialty site. Patients with a well-characterized liver diagnosis such as hepatitis B, hepatitis C, cirrhosis and cirrhosis complications were more likely to have had a SCAN-ECHO visit. This is consistent with prior patterns seen, where patients who had these diagnosis were more likely to have a specialty consultation leading to a visit(11). Similarly, patients with indicators suggestive of more severe liver disease such as elevated ALT and bilirubin were more likely to have had a SCAN-ECHO visit than the no-visit. The SCAN-ECHO visit group also had more imaging or endoscopic procedures consistent with our prior reports that patients who had specialty consultation were more likely to have more imaging studies and procedures(11). On multivariable analysis, the likelihood of having a SCAN-ECHO visit was increased in patients who were younger, lived in rural location, had ultrasound performed, a diagnosis of cirrhosis complication, hepatitis C or thrombocytopenia.

*Among patients with liver disease diagnosis, having had a SCAN-ECHO visit was associated with improved survival*

The effect of a SCAN-ECHO visit on all-cause mortality was compared to patients with no visit. To adjust for the differences among patients who had a SCAN-ECHO visit versus no visit, propensity score matching was performed. Propensity scores were developed on factors which affect the likelihood of a SCAN-ECHO visit (Table 1). The balance of matching is illustrated in Figure 1 (SCAN-ECHO vs No Visit). In the matched cohorts, patients who had a SCAN-ECHO visit had significantly improved survival as compared to those who had no visit (Figure 2). Compared to having no visit, matched patients who had consultation through the SCAN-ECHO program were associated with decreased risk of death (Hazard Ratio 0.54, 95% CI 0.36-0.81,  $p = 0.003$ ), with a 46% decreased likelihood of dying compared to the matched patients with no visit during the follow up period. Although our primary comparison was between those patients who had a SCAN-ECHO visit vs no visit, we also examined whether specialty care delivery via SCAN-ECHO might result in different survival benefit than those with in person visit. We found using the same propensity score matching methods that matched cohorts of patients with SCAN-ECHO visits and traditional in person liver visits had similar survival (Supplementary Figure 2).

To examine whether the reduction in mortality was only seen in patients with advanced liver disease or all patients, we divided the matched cohorts by FIB-4 score. In the propensity matched cohorts, a SCAN-ECHO visit was associated with reduced risk of death in patients with and without advanced fibrosis. A SCAN-ECHO visit was associated a decreased risk of death compared to those with no visit, with a hazard ratio of 0.40 in the cohorts of patients where FIB-4 was greater than 3.25 ( $n= 260$ ,  $p = 0.0004$ ) and 0.42 in patients with FIB-4 score of less than 3.25 ( $n=676$ ,  $p = 0.03$ ). The analysis was only performed on the patients who had complete data for FIB-4.

To examine whether the matched cohorts had differences in alcohol intake, we examined the Alcohol Use Disorder Identification Test-C (AUDIT-C) scores in the propensity matched cohorts. AUDIT-C is widely implemented within the VHA and is mandated as a performance measure(16). This simple 3 question scored questionnaire has been validated within and outside

the VHA for identifying patients with alcohol use disorder(17, 18). We found in our matched cohorts that the AUDIT-C scores were similar between those with a SCAN-ECHO visit and those with no visit ( $1.96 \pm 2.93$  vs  $1.93 \pm 2.73$ ,  $p > 0.05$ ).

Seeking potential mechanisms for improved survival, we examined the relative frequency of HCC surveillance (defined as an abdominal imaging study at least once a year) and variceal surveillance (defined as an EGD at least every 3 years) in the unmatched cohort of patients with FIB-4 scores  $> 3.25$ . We found that those with a SCAN-ECHO visit had higher rate of HCC (42% vs 25%) and variceal surveillance (25% vs 15%) compared to those with no visit.

### Discussion:

Novel strategies are needed to provide specialty care to patients with complex liver disease whose access is limited by geographic distance from referral centers. We evaluated the SCAN-ECHO program, a virtual form of electronic consultation, which combines real time consultation with didactic learning for front-line providers. In this large regional cohort of patients with liver disease, we found that patients who received consultation via the SCAN-ECHO program had improvements in several measures of care quality and higher survival rates than patients who had no specialty care visit. These data extend the findings of prior studies where we and others have found a benefit of access to traditional, in-person specialty care consultations in patients with liver disease(11, 19-21). Previously, the ECHO (2, 22-24) and other more traditional (involving direct patient to provider contact)(25, 26) telemedicine programs have been reported, with some showing effectiveness for treating hepatitis C both within and outside of the VHA with equal outcomes. In this study, we extend the impact of SCAN-ECHO beyond hepatitis C therapy to show that this intervention is associated with improved survival for patients with all liver diseases.

Beyond the novelty of the intervention, we feel that there were several strengths in these analyses. First, we found benefit even after applying propensity matching using broad demographic and clinical characteristics to adjust effect estimates. Second, we demonstrate clinically significant improvements in screening procedures and enhanced survival benefit for patients with elevated FIB-4 scores (indicating cirrhosis), establishing a mechanism for the observations. Third, based on Kaplan-Meier analysis, the improved outcomes specific to the



SCAN-ECHO program emerge after 1 year suggesting both equal matching at baseline and plausible effects based on the types of intervention differences which may have resulted from specialist consultation (i.e. varices or HCC screening).

These data must be interpreted in the context of the study design. First, the consultations addressed many issues for patients with diverse liver diseases. Accordingly, the underlying mechanism for generalized improvement in mortality is not clear from these data. We present analyses, however, that demonstrate beneficial effects for patients at the highest risk of death, namely those with possible cirrhosis (FIB-4 > 3.25). Specifically, we show that SCAN-ECHO is associated with improved process measures such as screening for liver cancer and varices that could be linked with improved survival. Further, though patients were not randomized to receive either form of consultation, we adjusted for confounders using propensity score matching. While every attempt was made to match patient characteristics between control and cases, certain features such as patient socioeconomic status were not completely available. There is always concern that we did not account for all patient differences or eliminate confounding by indication. Second, our propensity matching only accounts for patient factors. It is also possible that the difference may be due to provider-level factors which are not accounted for here. All providers within our referral base were offered the option to participate in the program. However, as all consultations were voluntary, the choice to accept the use of the SCAN-ECHO visit on the part of the front-line provider may reflect providers with baseline elevated knowledge or interest in practice improvement. We plan to study this as a possible mechanism for improved survival. In addition to intrinsic provider differences, the ECHO program may allow for more effective dissemination of patient specific information or improved knowledge base. A prior study on the improvement of knowledge base using provider surveys has shown surprising dissemination of liver knowledge(27). Third, these data reflect the VA experience which is a fully integrated healthcare system with a unique population. Both factors may constrain the generalizability of these findings to other settings. Regulatory issues such state specific licensing and legal issues such as malpractice may be limitations in non-VA settings.

In a highly integrated healthcare system, a novel approach such as the SCAN-ECHO program may be an effective, scalable method to improve access for selected patients with liver disease, particularly in rural and underserved populations where access to specialty care is limited.

## Legends:

Table 1: Descriptive characteristics of unmatched cohort of patients with SCAN-ECHO visit vs no visit

Figure 1: Absolute standardized mean difference of the baseline covariates between patients with a SCAN-ECHO visit vs no visit

Figure 2: Kaplan-Meier Survival. Survival curve between those with a SCAN-ECHO vs propensity matched cohort of patients with no visit

Supplementary Table 1: ICD 9 codes used to define Liver Disease Cohort

Supplementary Figure 1: Enrollment and exclusions

Supplementary Figure 2a: Absolute standardized mean difference of the baseline covariates between patients with a SCAN-ECHO visit vs in person visit

Supplementary Figure 2b: Kaplan-Meier Survival. Survival curve between those with a SCAN-ECHO vs propensity matched cohort of patients with in person visit

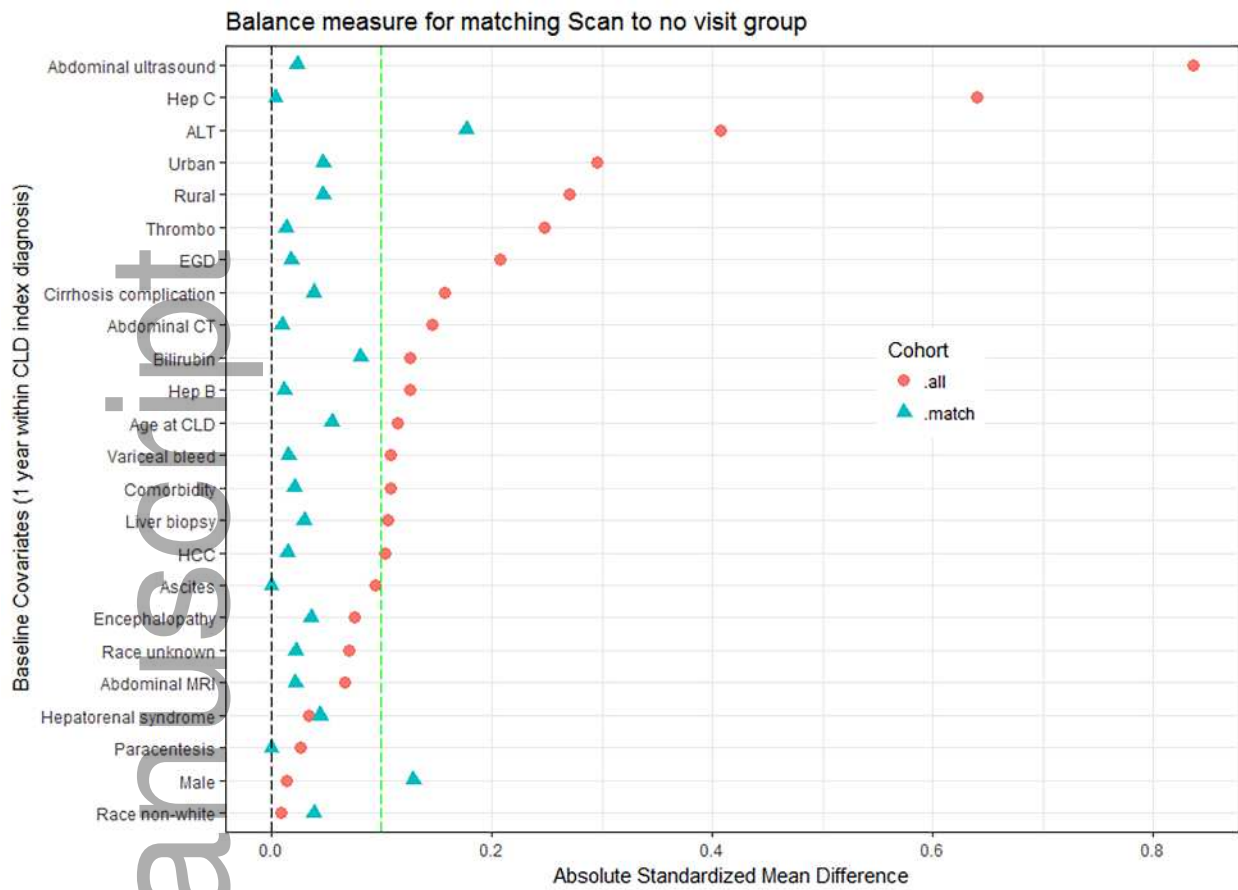
## References

1. Beste LA, Harp BK, Blais RK, Evans GA, Zickmund SL. Primary Care Providers Report Challenges to Cirrhosis Management and Specialty Care Coordination. *Dig Dis Sci* 2015;60:2628-2635.
2. Arora S, Thornton K, Murata G, Deming P, Kalishman S, Dion D, Parish B, et al. Outcomes of treatment for hepatitis C virus infection by primary care providers. *N Engl J Med* 2011;364:2199-2207.
3. Arora S, Kalishman S, Thornton K, Dion D, Murata G, Deming P, Parish B, et al. Expanding access to hepatitis C virus treatment--Extension for Community Healthcare Outcomes (ECHO) project: disruptive innovation in specialty care. *Hepatology* 2010;52:1124-1133.
4. Kirsh S, Su GL, Sales A, Jain R. Access to outpatient specialty care: solutions from an integrated health care system. *Am J Med Qual* 2015;30:88-90.
5. Stevenson L, Ball S, Haverhals LM, Aron DC, Lowery J. Evaluation of a national telemedicine initiative in the Veterans Health Administration: Factors associated with successful implementation. *J Telemed Telecare* 2016.

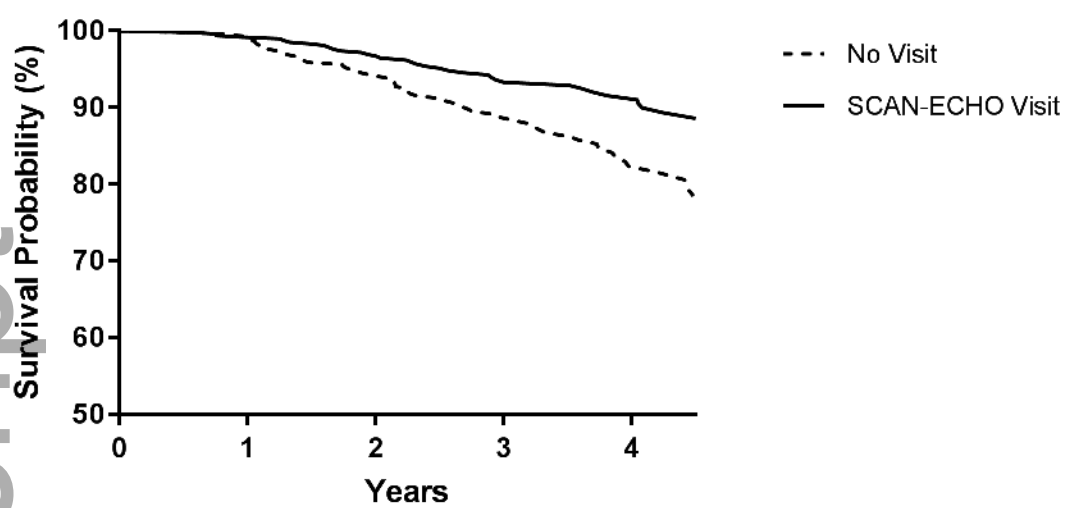
6. Watts SA, Roush L, Julius M, Sood A. Improved glycemic control in veterans with poorly controlled diabetes mellitus using a Specialty Care Access Network-Extension for Community Healthcare Outcomes model at primary care clinics. *J Telemed Telecare* 2016;22:221-224.
7. Glass LM, Waljee AK, McCurdy H, Su GL, Sales A. Specialty Care Access Network-Extension of Community Healthcare Outcomes Model Program for Liver Disease Improves Specialty Care Access. *Dig Dis Sci* 2017;62:3344-3349.
8. Zhou C, Crawford A, Serhal E, Kurdyak P, Sockalingam S. The Impact of Project ECHO on Participant and Patient Outcomes: A Systematic Review. *Acad Med* 2016;91:1439-1461.
9. Carey EP, Frank JW, Kerns RD, Ho PM, Kirsh SR. Implementation of telementoring for pain management in Veterans Health Administration: Spatial analysis. *J Rehabil Res Dev* 2016;53:147-156.
10. Sayre GG, Haverhals LM, Ball S, Stevenson L, Battaglia C, Aron DC, Kirsh S, et al. Adopting SCAN-ECHO: The providers' experiences. *Healthc (Amst)* 2017;5:29-33.
11. Mellinger JL, Moser S, Welsh DE, Yosef MT, Van T, McCurdy H, Rakoski MO, et al. Access to Subspecialty Care And Survival Among Patients With Liver Disease. *Am J Gastroenterol* 2016;111:838-844.
12. West AN, Lee RE, Shambaugh-Miller MD, Bair BD, Mueller KJ, Lilly RS, Kaboli PJ, et al. Defining "rural" for veterans' health care planning. *J Rural Health* 2010;26:301-309.
13. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8-27.
14. Tapper EB, Lok AS. Use of Liver Imaging and Biopsy in Clinical Practice. *N Engl J Med* 2017;377:2296-2297.
15. Vallet-Pichard A, Mallet V, Nalpas B, Verkarre V, Nalpas A, Dhalluin-Venier V, Fontaine H, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. comparison with liver biopsy and fibrotest. *Hepatology* 2007;46:32-36.
16. Bradley KA, Williams EC, Achtmeyer CE, Volpp B, Collins BJ, Kivlahan DR. Implementation of evidence-based alcohol screening in the Veterans Health Administration. *Am J Manag Care* 2006;12:597-606.
17. Bush K, Kivlahan DR, McDonnell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking.

Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med* 1998;158:1789-1795.

18. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. *Alcohol Clin Exp Res* 2007;31:1208-1217.
19. Davila JA, Kramer JR, Duan Z, Richardson PA, Tyson GL, Sada YH, Kanwal F, et al. Referral and receipt of treatment for hepatocellular carcinoma in United States veterans: effect of patient and nonpatient factors. *Hepatology* 2013;57:1858-1868.
20. Kanwal F, Kramer JR, Buchanan P, Asch SM, Assioun Y, Bacon BR, Li J, et al. The quality of care provided to patients with cirrhosis and ascites in the Department of Veterans Affairs. *Gastroenterology* 2012;143:70-77.
21. Ko CW, Kelley K, Meyer KE. Physician specialty and the outcomes and cost of admissions for end-stage liver disease. *Am J Gastroenterol* 2001;96:3411-3418.
22. Beste LA, Glorioso TJ, Ho PM, Au DH, Kirsh SR, Todd-Stenberg J, Chang MF, et al. Telemedicine Specialty Support Promotes Hepatitis C Treatment by Primary Care Providers in the Department of Veterans Affairs. *Am J Med* 2017;130:432-438 e433.
23. Serper M, Volk ML. Current and Future Applications of Telemedicine to Optimize the Delivery of Care in Chronic Liver Disease. *Clin Gastroenterol Hepatol* 2018;16:157-161 e158.
24. Rossaro L, Torruellas C, Dhaliwal S, Botros J, Clark G, Li CS, Minoletti MM. Clinical outcomes of hepatitis C treated with pegylated interferon and ribavirin via telemedicine consultation in Northern California. *Dig Dis Sci* 2013;58:3620-3625.
25. Cooper CL, Hatashita H, Corsi DJ, Parmar P, Corrin R, Garber G. Direct-Acting Antiviral Therapy Outcomes in Canadian Chronic Hepatitis C Telemedicine Patients. *Ann Hepatol* 2017;16:874-880.
26. You A, Kawamoto J, Smith JP. A pharmacist-managed telemedicine clinic for hepatitis C care: a descriptive analysis. *J Telemed Telecare* 2014;20:99-101.
27. Salgia RJ, Mullan PB, McCurdy H, Sales A, Moseley RH, Su GL. The educational impact of the Specialty Care Access Network-Extension of Community Healthcare Outcomes program. *Telemed J E Health* 2014;20:1004-1008.



hep\_30074\_f1.tif



Number at risk					
	0	1	2	3	4
No Visit	511	420	326	232	129
SCAN-ECHO	511	474	407	294	182
Year	0	1	2	3	4

hep\_30074\_f2.tif